METHODS AND COMPOSITIONS FOR DIAGNOSING AND MONITORING TRANSPLANT REJECTION

Related Applications

This application claims priority to U.S. Application No. 10/131,831, filed April 24, 2002, and U.S. Application No. 10/325,899, filed December 20, 2002.

Field of the Invention

This invention is in the field of expression profiling following organ transplantation.

Background of the Invention

Many of the current shortcomings in diagnosis, prognosis, risk stratification and treatment of disease can be approached through the identification of the molecular mechanisms underlying a disease and through the discovery of nucleotide sequences (or sets of nucleotide sequences) whose expression patterns predict the occurrence or progression of disease states, or predict a patient's response to a particular therapeutic intervention. In particular, identification of nucleotide sequences and sets of nucleotide sequences with such predictive value from cells and tissues that are readily accessible would be extremely valuable. For example, peripheral blood is attainable from all patients and can easily be obtained at multiple time points at low cost. This is a desirable contrast to most other cell and tissue types, which are less readily accessible, or accessible only through invasive and aversive procedures. In addition, the various cell types present in circulating blood are ideal for expression profiling experiments as the many cell types in the blood specimen can be easily separated if desired prior to analysis of gene expression. While blood provides a very attractive substrate for the study of diseases using expression profiling techniques, and for the development of diagnostic technologies and the identification of therapeutic targets, the value of expression profiling in blood samples rests on the degree to which changes in gene expression in these cell types are associated with a predisposition to, and pathogenesis and progression of a disease.

Hematopoiesis is the development and maturation of all cell types of the blood. These include erythrocytes, platelets and leukocytes. Leukocytes are further subdivided into granulocytes (neutrophils, eosinophils, basophils) and mononuclear cells (monocytes, lymphocytes). These cells develop and mature from precursor cells to replenish the circulating pool and to respond to insults and challenges to the system. This occurs in the bone marrow, spleen, thymus, liver, lymph nodes, mucosal associated lymphoid tissue (MALT) and peripheral blood.

Precursor cells differentiate into immature forms of each lineage and these immature cells develop further into mature cells. This process occurs under the influence and direction of hematopoietic growth factors. When hematopoiesis is stimulated, there is an increase in the number of immature cells in the peripheral blood and in some cases, precursor cells are found at increased frequency. For example, CD34+ cells (hematopoietic stem cells) may increase in frequency in the peripheral blood with an insult to the immune system. For neutrophils, "band" forms are increased, for erythrocytes, reticulocytes or nucleated red cells are seen. Lymphocytes are preceeded by lymphoblasts (immature lymphocytes).

It may be an important clinical goal to measure the rate of production of blood cells of a variety of lineages. Hematological disorders involving over or under production of various blood cells

may be treated pharmacologically. For example, anemia (low red blood cells) may be treated with erythropoietin (a hematopoietic growth factor) and response to this therapy can be assessed by measuring RBC production rates. Low neutrophils counts can be treated by administration of G-CSF and this therapy may be monitored by measuring neutrophil production rates. Alternatively, the diagnosis of blood cell disorders is greatly facilitated by determination of lineage specific production rates. For example, anemia (low RBCs) may be caused by decreased cellular production or increased destruction of cells. In the latter case, the rate of cellular production will be increased rather than decreased and the therapeutic implications are very different. Further discussion of the clinical uses of measures of blood cell production rates is given in below.

Assessment of blood cell production rates may be useful for diagnosis and management of non-hematological disorders. In particular, acute allograft rejection diagnosis and monitoring may benefit from such an approach. Current diagnosis and monitoring of acute allograft rejection is achieved through invasive allograft biopsy and assessment of the biopsy histology. This approach is sub-optimal because of expense of the procedure, cost, pain and discomfort of the patient, the need for trained physician operators, the risk of complications of the procedure, the lack of insight into the functioning of the immune system and variability of pathological assessment. In addition, biopsy can diagnose acute allograft rejection only after significant cellular infiltration into the allograft has occurred. At this point, the process has already caused damage to the allograft. For all these reasons, a simple blood test that can diagnose and monitor acute rejection at an earlier stage in the process is needed. Allograft rejection depends on the presence of functioning cells of the immune system. In addition, the process of rejection may cause activation of hematopoiesis. Finally, effective immunosuppressive therapy to treat or prevent acute rejection may suppress hematopoiesis. For these reasons, assessment of hematopoietic cellular production rates may be useful in the diagnosis and monitoring of acute rejection.

Current techniques for measuring cellular development and production rates are inadequate. The most common approach is to measure the number of mature cells of a lineage of interest over time. For example, if a patient is being treated for anemia (low red blood cell counts), then the physician will order a blood cell count to assess the number of red blood cells (RBCs) in circulation. For this to be effective, the physician must measure the cell count over time and may have to wait 2-4 weeks before being able to assess response to therapy. The same limitation is true for assessment of any cell lineage in the blood.

An alternative approach is to count the number of immature cells in the peripheral blood by counting them under the microscope. This may allow a more rapid assessment of cellular production rates, but is limited by the need for assessment by a skilled hematologist, observer variability and the inability to distinguish all precursor cells on the basis of morphology alone.

Bone marrow biopsy is the gold standard for assessment of cellular production rates. In addition to the limitations of the need for skilled physicians, reader variability and the lack of sensitivity of morphology alone, the technique is also limited by the expense, discomfort to the patient and need for a prolonged visit to a medical center. Thus there is a need for a reliable, rapid means for measuring the rate of hematopoeisis in a patient.

In addition to the relationship between hematopoiesis and variety of disease processes, there is an extensive literature supporting the role of leukocytes, e.g., T-and B-lymphocytes, monocytes and granulocytes, including neutrophils, in a wide range of disease processes, including such broad classes as cardiovascular diseases, inflammatory, autoimmune and rheumatic diseases, infectious diseases, transplant rejection, cancer and malignancy, and endocrine diseases. For example, among cardiovascular diseases, such commonly occurring diseases as atherosclerosis, restenosis, transplant vasculopathy and acute coronary syndromes all demonstrate significant T cell involvement (Smith-Norowitz et al. (1999) Clin Immunol 93:168-175; Jude et al. (1994) Circulation 90:1662-8; Belch et al. (1997) Circulation 95:2027-31). These diseases are now recognized as manifestations of chronic inflammatory disorders resulting from an ongoing response to an injury process in the arterial tree (Ross et al. (1999) Ann Thorac Surg 67:1428-33). Differential expression of lymphocyte, monocyte and neutrophil genes and their products has been demonstrated clearly in the literature. Particularly interesting are examples of differential expression in circulating cells of the immune system that demonstrate specificity for a particular disease, such as arteriosclerosis, as opposed to a generalized association with other inflammatory diseases, or for example, with unstable angina rather than quiescent coronary disease.

A number of individual genes, e.g., CD11b/CD18 (Kassirer et al. (1999) Am Heart J 138:555-9); leukocyte elastase (Amaro et al. (1995) Eur Heart J 16:615-22; and CD40L (Aukrust et al. (1999) Circulation 100:614-20) demonstrate some degree of sensitivity and specificity as markers of various vascular diseases. In addition, the identification of differentially expressed target and fingerprint genes isolated from purified populations of monocytes manipulated in various in vitro paradigms has been proposed for the diagnosis and monitoring of a range of cardiovascular diseases, see, e.g., US Patents Numbers 6,048,709; 6,087,477; 6,099,823; and 6,124,433 "COMPOSITIONS AND METHODS FOR THE TREATMENT AND DIAGNOSIS OF CARDIOVASCULAR DISEASE" to Falb (*see also*, WO 97/30065). Lockhart, in US Patent Number 6,033,860 "EXPRESSION PROFILES IN ADULT AND FETAL ORGANS" proposes the use of expression profiles for a subset of identified genes in the identification of tissue samples, and the monitoring of drug effects.

The accuracy of technologies based on expression profiling for the diagnosis, prognosis, and monitoring of disease would be dramatically increased if numerous differentially expressed nucleotide sequences, each with a measure of specificity for a disease in question, could be identified and assayed in a concerted manner. PCT application WO 02/057414 "LEUKOCYTE EXPRESSION PROFILING" to Wohlgemuth identifies one such set of differentially expressed nucleotides.

In order to achieve this improved accuracy, the sets of nucleotide sequences once identified need to be validated to identify those differentially expressed nucleotides within a given set that are most useful for diagnosis, prognosis, and monitoring of disease. The present invention addresses these and other needs, and applies to transplant rejection and detection of the rate of hematopoeisis for which differential regulation of genes, or other nucleotide sequences, of peripheral blood can be demonstrated.

Summary of the Invention

In one aspect, there is provided an *in-vitro* method for assessing the immune status of an individual comprising (a) selecting one or more nucleic acids having an expression level that correlates with the rate of hematopoiesis or the distribution of hematopoietic cells along their maturation pathway in said individual and also correlates with the immune status of said individual; and (b) detecting the expression level of said nucleic acid to assess the immune status of said individual.

Embodiments of the present invention are directed to a system for detecting differential gene expression. In one format, methods are provided for assessing the immune status of an individual by detecting the expression level of one or more genes expressed at different levels depending upon the rate of hematopoiesis or the distribution of hematopoietic cells along their maturation pathway in the individual. The one or more genes may include a nucleotide selected from a nucleotide sequence selected from SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:78, SEQ ID NO:79, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:92, SEQ ID NO:93, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:97, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:100, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108, SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:114, SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:117, SEQ ID NO:118, SEQ ID NO:119, SEQ ID NO:120, SEQ ID NO:121, SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID

NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:192, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198,

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NO:2640, SEQ ID NO:2723, SEQ ID NO:2658, SEQ ID NO:2688, SEQ ID NO:2735, SEQ ID NO:2702, SEQ ID NO:2681, SEQ ID NO:2755, SEQ ID NO:2715, SEQ ID NO:2732, SEQ ID NO:2652, SEQ ID NO:2651, SEQ ID NO:2718, SEQ ID NO:2673, SEQ ID NO:2733, SEQ ID NO:2712, SEQ ID NO:2659, SEQ ID NO:2654, SEQ ID NO:2636, SEQ ID NO:2639, SEQ ID NO:2690, SEQ ID NO:2705, SEQ ID NO:2685, SEQ ID NO:2692, SEQ ID NO:2693, SEQ ID NO:2648, SEQ ID NO:2650, SEQ ID NO:2720, SEQ ID NO:2660, SEQ ID NO:2666, SEQ ID NO:2699, SEQ ID NO:2633, SEQ ID NO:2672, SEQ ID NO:2642, SEQ ID NO:2682, SEQ ID NO:2655, SEQ ID NO:2630, SEQ ID NO:2745, SEQ ID NO:2643, SEQ ID NO:2694, SEQ ID NO:2749, SEQ ID NO:2665, SEQ ID NO:2649, SEQ ID NO:2637, SEQ ID NO:2634, SEQ ID NO:2709, SEQ ID NO:2653, SEQ ID NO:2729. The expression level may be detected by measuring the RNA level expressed by the one or more genes. In one variation, the RNA level is detected by PCR. In another variation, the RNA level is detected by hybridization. The expression level may also be detected by measuring one or more proteins expressed by the one or more genes.

Embodiments of the present invention are further directed to methods of diagnosing or monitoring transplant rejection in an individual by detecting a rate of hematopoiesis. The detection may be applied directly to the individual, or to a sample isolated from the individual. Detection may be accomplished by RNA profiling assay, immunoassay, fluorescent activated cell sorting, protein assay, peripheral blood cytology assay, MRI imaging, bone marrow aspiration, and/or nuclear imaging. In one variation, the RNA profile assay is a PCR based assay. In another variation, the RNA profile assay is a hybridization based assay. The RNA profile assay may further include detecting the expression level of one or more genes in the individual where the one or more genes include a nucleotide sequence selected from SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:78, SEQ ID NO:79, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:92, SEQ ID NO:93, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:97, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:100, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108, SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:114, SEQ ID NO:115, SEQ ID

NO:116, SEQ ID NO:117, SEQ ID NO:118, SEQ ID NO:119, SEQ ID NO:120, SEQ ID NO:121, SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:192, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, SEQ ID NO:242, SEQ ID NO:243, SEQ ID NO:244, SEQ ID NO:245, SEQ ID NO:246, SEQ ID NO:247, SEQ ID NO:248, SEQ ID NO:249, SEQ ID NO:250, SEQ ID NO:251, SEQ ID NO:252, SEQ ID NO:253, SEQ ID NO:254, SEQ ID NO:255, SEQ ID NO:256, SEQ ID NO:257, SEQ ID NO:258, SEQ ID NO:259, SEQ ID NO:260, SEQ ID NO:261, SEQ ID NO:262, SEQ ID NO:263, SEQ ID NO:264, SEQ ID NO:265, SEQ ID NO:266, SEQ ID NO:267, SEQ ID NO:268, SEQ ID NO:269, SEQ ID NO:270, SEQ ID NO:271, SEQ ID NO:272, SEQ ID NO:273, SEQ ID NO:274, SEQ ID NO:275, SEQ ID NO:276, SEQ ID NO:277, SEQ ID NO:278, SEQ ID NO:279, SEQ ID NO:280, SEQ ID NO:281, SEQ ID NO:282, SEQ ID NO:283, SEQ ID NO:284, SEQ ID NO:285, SEQ ID NO:286, SEQ ID NO:287, SEQ ID NO:288, SEQ ID NO:289, SEQ ID NO:290, SEQ ID NO:291, SEQ ID NO:292, SEQ ID NO:293, SEQ ID NO:294, SEQ ID NO:295, SEQ ID NO:296, SEQ ID NO:297, SEQ ID NO:298, SEQ ID NO:299, SEQ ID NO:300, SEQ ID NO:301, SEQ ID NO:302, SEQ ID NO:303, SEQ ID NO:304, SEQ ID NO:305, SEQ ID NO:306, SEQ ID NO:307, SEQ ID NO:308, SEQ ID NO:309, SEQ ID NO:310, SEQ ID NO:311, SEQ ID NO:312, SEQ ID NO:313, SEQ ID NO:314, SEQ ID NO:315, SEQ ID NO:316, SEQ ID NO:317, SEQ ID NO:318, SEQ ID NO:319, SEQ ID NO:320, SEQ ID NO:321, SEQ ID NO:322, SEQ ID NO:323, SEQ ID NO:324, SEQ ID NO:325, SEQ ID NO:326, SEQ ID NO:327, SEQ ID NO:328, SEQ ID NO:329, SEQ ID NO:330, SEQ ID NO:331, SEQ ID NO:332, SEQ ID NO:2697, SEQ ID NO:2645, SEQ ID NO:2707, SEQ ID NO:2679, SEQ ID NO:2717, SEQ ID NO:2646, SEQ ID NO:2667, SEQ ID NO:2706, SEQ ID NO:2740, SEQ ID

NO:2669, SEQ ID NO:2674, SEQ ID NO:2743, SEQ ID NO:2716, SEQ ID NO:2727, SEQ ID NO:2721, SEQ ID NO:2641, SEQ ID NO:2671, SEQ ID NO:2752, SEQ ID NO:2737, SEQ ID NO:2719, SEQ ID NO:2684, SEQ ID NO:2677, SEQ ID NO:2748, SEQ ID NO:2703, SEQ ID NO:2711, SEQ ID NO:2663, SEQ ID NO:2657, SEQ ID NO:2683, SEQ ID NO:2686, SEQ ID NO:2687, SEQ ID NO:2644, SEQ ID NO:2664, SEQ ID NO:2747, SEQ ID NO:2744, SEQ ID NO:2678, SEQ ID NO:2731, SEQ ID NO:2713, SEQ ID NO:2736, SEQ ID NO:2708, SEQ ID NO:2670, SEQ ID NO:2661, SEQ ID NO:2680, SEQ ID NO:2754, SEQ ID NO:2728, SEQ ID NO:2742, SEQ ID NO:2668, SEQ ID NO:2750, SEQ ID NO:2746, SEQ ID NO:2738, SEQ ID NO:2627, SEQ ID NO:2739, SEQ ID NO:2647, SEQ ID NO:2628, SEQ ID NO:2638, SEQ ID NO:2725, SEQ ID NO:2714, SEQ ID NO:2635, SEQ ID NO:2751, SEQ ID NO:2629, SEQ ID NO:2695, SEQ ID NO:2741, SEQ ID NO:2691, SEQ ID NO:2726, SEQ ID NO:2722, SEQ ID NO:2689, SEQ ID NO:2734, SEQ ID NO:2631, SEQ ID NO:2656, SEQ ID NO:2696, SEQ ID NO:2676, SEQ ID NO:2701, SEQ ID NO:2730, SEQ ID NO:2710, SEQ ID NO:2632, SEQ ID NO:2724, SEQ ID NO:2698, SEQ ID NO:2662, SEQ ID NO:2753, SEQ ID NO:2704, SEQ ID NO:2675, SEQ ID NO:2700, SEQ ID NO:2640, SEQ ID NO:2723, SEQ ID NO:2658, SEQ ID NO:2688, SEQ ID NO:2735, SEQ ID NO:2702, SEQ ID NO:2681, SEQ ID NO:2755, SEQ ID NO:2715, SEQ ID NO:2732, SEQ ID NO:2652, SEQ ID NO:2651, SEQ ID NO:2718, SEQ ID NO:2673, SEQ ID NO:2733, SEQ ID NO:2712, SEQ ID NO:2659, SEQ ID NO:2654, SEQ ID NO:2636, SEQ ID NO:2639, SEQ ID NO:2690, SEQ ID NO:2705, SEQ ID NO:2685, SEQ ID NO:2692, SEQ ID NO:2693, SEQ ID NO:2648, SEQ ID NO:2650, SEQ ID NO:2720, SEQ ID NO:2660, SEQ ID NO:2666, SEQ ID NO:2699, SEQ ID NO:2633, SEQ ID NO:2672, SEQ ID NO:2642, SEQ ID NO:2682, SEQ ID NO:2655, SEQ ID NO:2630, SEQ ID NO:2745, SEQ ID NO:2643, SEQ ID NO:2694, SEQ ID NO:2749, SEQ ID NO:2665, SEQ ID NO:2649, SEQ ID NO:2637, SEQ ID NO:2634, SEQ ID NO:2709, SEQ ID NO:2653, SEQ ID NO:2729. Transplant rejection may include one or more of heart transplant rejection, kidney transplant rejection, liver transplant rejection, pancreas transplant rejection, pancreatic islet transplant rejection, lung transplant rejection, bone marrow transplant rejection, stem cell transplant rejection, xenotransplant rejection, and mechanical organ replacement rejection.

In another embodiment, there is provided a method of diagnosing or monitoring transplant rejection in a patient by detecting the expression level of one or more genes in the patient to diagnose or monitor transplant rejection in the patient, wherein the one or more genes include a nucleotide sequence selected from SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6,
SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID

NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:92, SEQ ID NO:93, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:98, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108, SEQ ID NO:109, SEQ ID NO:114, SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:117, SEQ ID NO:118, SEQ ID NO:119, SEQ ID NO:120, SEQ ID NO:121, SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:192, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, SEQ ID NO:242, SEQ ID NO:243, SEQ ID NO:244, SEQ ID NO:245, SEQ ID NO:246, SEQ ID NO:247, SEQ ID NO:248, SEQ ID NO:249, SEQ ID NO:250, SEQ ID NO:251, SEQ ID NO:252, SEQ ID NO:253, SEQ ID NO:254, SEQ ID NO:255, SEQ ID NO:256, SEQ ID NO:257, SEQ ID NO:258, SEQ ID NO:259, SEQ ID NO:260, SEQ ID NO:261, SEQ ID NO:262, SEQ ID NO:263, SEQ ID NO:264, SEQ ID NO:265, SEQ ID NO:266, SEQ ID NO:267, SEQ ID NO:268, SEQ ID NO:269, SEQ ID NO:270, SEQ ID NO:271, SEQ ID NO:272, SEQ ID NO:273, SEQ ID NO:274, SEQ ID NO:275, SEQ ID NO:276, SEQ ID NO:277, SEQ ID NO:278, SEQ ID NO:279, SEQ ID NO:280, SEQ ID NO:281, SEQ ID NO:282, SEQ ID NO:283, SEQ ID NO:284, SEQ ID NO:285, SEQ ID NO:286, SEQ ID NO:287, SEQ ID NO:288, SEQ ID NO:289, SEQ ID NO:290, SEQ ID NO:291, SEQ ID NO:292, SEQ ID NO:293, SEQ ID NO:294, SEQ ID NO:295, SEQ ID NO:296, SEQ ID NO:297, SEQ ID NO:298, SEQ ID NO:299, SEQ ID NO:300, SEQ ID NO:301, SEQ ID NO:302, SEQ ID NO:303, SEQ ID NO:304, SEQ ID NO:305, SEQ ID NO:306, SEQ ID NO:307, SEQ ID NO:308, SEQ ID NO:309, SEQ ID NO:310, SEQ ID NO:311, SEQ

ID NO:312, SEQ ID NO:313, SEQ ID NO:314, SEQ ID NO:315, SEQ ID NO:316, SEQ ID NO:317, SEQ ID NO:318, SEQ ID NO:319, SEQ ID NO:320, SEQ ID NO:321, SEQ ID NO:322, SEQ ID NO:323, SEQ ID NO:324, SEQ ID NO:325, SEQ ID NO:326, SEQ ID NO:327, SEQ ID NO:328, SEQ ID NO:329, SEQ ID NO:330, SEQ ID NO:331, SEQ ID NO:332, SEQ ID NO:2697, SEQ ID NO:2645, SEQ ID NO:2707, SEQ ID NO:2679, SEQ ID NO:2717, SEQ ID NO:2646, SEQ ID NO:2667, SEQ ID NO:2706, SEQ ID NO:2740, SEQ ID NO:2669, SEQ ID NO:2674, SEQ ID NO:2743, SEQ ID NO:2716, SEQ ID NO:2727, SEQ ID NO:2721, SEQ ID NO:2641, SEQ ID NO:2671, SEQ ID NO:2752, SEQ ID NO:2737, SEQ ID NO:2719, SEQ ID NO:2684, SEQ ID NO:2677, SEQ ID NO:2748, SEQ ID NO:2703, SEQ ID NO:2711, SEQ ID NO:2663, SEQ ID NO:2657, SEQ ID NO:2683, SEQ ID NO:2686, SEQ ID NO:2687, SEQ ID NO:2644, SEQ ID NO:2664, SEQ ID NO:2747, SEQ ID NO:2744, SEQ ID NO:2678, SEQ ID NO:2731, SEQ ID NO:2713, SEQ ID NO:2736, SEQ ID NO:2708, SEQ ID NO:2670, SEQ ID NO:2661, SEQ ID NO:2680, SEQ ID NO:2754, SEQ ID NO:2728, SEQ ID NO:2742, SEQ ID NO:2668, SEQ ID NO:2750, SEQ ID NO:2746, SEQ ID NO:2738, SEQ ID NO:2627, SEQ ID NO:2739, SEQ ID NO:2647, SEQ ID NO:2628, SEQ ID NO:2638, SEQ ID NO:2725, SEQ ID NO:2714, SEQ ID NO:2635, SEQ ID NO:2751, SEQ ID NO:2629, SEQ ID NO:2695, SEQ ID NO:2741, SEQ ID NO:2691, SEQ ID NO:2726, SEQ ID NO:2722, SEQ ID NO:2689, SEQ ID NO:2734, SEQ ID NO:2631, SEQ ID NO:2656, SEQ ID NO:2696, SEQ ID NO:2676, SEQ ID NO:2701, SEQ ID NO:2730, SEQ ID NO:2710, SEQ ID NO:2632, SEQ ID NO:2724, SEQ ID NO:2698, SEQ ID NO:2662, SEQ ID NO:2753, SEQ ID NO:2704, SEQ ID NO:2675, SEQ ID NO:2700, SEQ ID NO:2640, SEQ ID NO:2723, SEQ ID NO:2658, SEQ ID NO:2688, SEQ ID NO:2735, SEQ ID NO:2702, SEQ ID NO:2681, SEQ ID NO:2755, SEQ ID NO:2715, SEQ ID NO:2732, SEQ ID NO:2652, SEQ ID NO:2651, SEQ ID NO:2718, SEQ ID NO:2673, SEQ ID NO:2733, SEQ ID NO:2712, SEQ ID NO:2659, SEQ ID NO:2654, SEQ ID NO:2636, SEQ ID NO:2639, SEQ ID NO:2690, SEQ ID NO:2705, SEQ ID NO:2685, SEQ ID NO:2692, SEQ ID NO:2693, SEQ ID NO:2648, SEQ ID NO:2650, SEQ ID NO:2720, SEQ ID NO:2660, SEQ ID NO:2666, SEQ ID NO:2699, SEQ ID NO:2633, SEQ ID NO:2672, SEQ ID NO:2642, SEQ ID NO:2682, SEQ ID NO:2655, SEQ ID NO:2630, SEQ ID NO:2745, SEQ ID NO:2643, SEQ ID NO:2694, SEQ ID NO:2749, SEQ ID NO:2665, SEQ ID NO:2649, SEQ ID NO:2637, SEQ ID NO:2634, SEQ ID NO: 2709, SEQ ID NO:2653, SEQ ID NO:2729. In one variation, embodiments of the invention are further directed to detecting the expression level of one or more additional genes in the patient to diagnose or monitor transplant rejection in the patient, wherein the one or more additional genes include a nucleotide sequence selected from SEQ ID NO:8, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:78, SEQ ID NO:79, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:89, SEQ ID NO:97, SEQ ID NO:99, SEQ ID NO:100, SEQ ID NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:15.

In a further variation, there is provided a method of diagnosing or monitoring cardiac transplant rejection in a patient by detecting the expression level of one or more genes in the

patient to diagnose or monitor cardiac transplant rejection in the patient wherein the one or more genes include a nucleotide sequence selected from SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:92, SEQ ID NO:93, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:100, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108, SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:114, SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:117, SEQ ID NO:118, SEQ ID NO:119, SEQ ID NO:120, SEQ ID NO:121, SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:192, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, SEQ ID NO:242, SEQ ID NO:243, SEQ

ID NO:244, SEQ ID NO:245, SEQ ID NO:246, SEQ ID NO:247, SEQ ID NO:248, SEQ ID NO:249, SEQ ID NO:250, SEQ ID NO:251, SEQ ID NO:252, SEQ ID NO:253, SEQ ID NO:254, SEQ ID NO:255, SEQ ID NO:256, SEQ ID NO:257, SEQ ID NO:258, SEQ ID NO:259, SEQ ID NO:260, SEQ ID NO:261, SEQ ID NO:262, SEQ ID NO:263, SEQ ID NO:264, SEQ ID NO:265, SEQ ID NO:266, SEQ ID NO:267, SEQ ID NO:268, SEQ ID NO:269, SEQ ID NO:270, SEQ ID NO:271, SEQ ID NO:272, SEQ ID NO:273, SEQ ID NO:274, SEQ ID NO:275, SEQ ID NO:276, SEQ ID NO:277, SEQ ID NO:278, SEQ ID NO:279, SEQ ID NO:280, SEQ ID NO:281, SEQ ID NO:282, SEQ ID NO:283, SEQ ID NO:284, SEQ ID NO:285, SEQ ID NO:286, SEQ ID NO:287, SEQ ID NO:288, SEQ ID NO:289, SEQ ID NO:290, SEQ ID NO:291, SEQ ID NO:292, SEQ ID NO:293, SEQ ID NO:294, SEQ ID NO:295, SEQ ID NO:296, SEQ ID NO:297, SEQ ID NO:298, SEQ ID NO:299, SEQ ID NO:300, SEQ ID NO:301, SEQ ID NO:302, SEQ ID NO:303, SEQ ID NO:304, SEQ ID NO:305, SEQ ID NO:306, SEQ ID NO:307, SEQ ID NO:308, SEQ ID NO:309, SEQ ID NO:310, SEQ ID NO:311, SEQ ID NO:312, SEQ ID NO:313, SEQ ID NO:314, SEQ ID NO:315, SEQ ID NO:316, SEQ ID NO:317, SEQ ID NO:318, SEQ ID NO:319, SEQ ID NO:320, SEQ ID NO:321, SEQ ID NO:322, SEQ ID NO:323, SEQ ID NO:324, SEQ ID NO:325, SEQ ID NO:326, SEQ ID NO:327, SEQ ID NO:328, SEQ ID NO:329, SEQ ID NO:330, SEQ ID NO:331, SEQ ID NO:332. In one variation, the method includes detecting the expression level of one or more additional genes in the patient to diagnose or monitor cardiac transplant rejection in the patient, wherein the one or more additional genes include a nucleotide sequence selected from SEQ ID NO:8, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:78, SEQ ID NO:79, SEQ ID NO:97, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151.

Embodiments of the invention are also directed to a method of diagnosing or monitoring kidney transplant rejection in a patient by detecting the expression level of one or more genes in the patient to diagnose or monitor kidney transplant rejection in the patient wherein the one or more genes include a nucleotide sequence selected from SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:78, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:92, SEQ ID NO:93, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:97, SEQ ID

NO:98, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108, SEQ ID NO:109, SEQ ID NO:114, SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:117, SEQ ID NO:118, SEQ ID NO:119, SEQ ID NO:120, SEQ ID NO:121, SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:192, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, SEQ ID NO:242, SEQ ID NO:243, SEQ ID NO:244, SEQ ID NO:245, SEQ ID NO:246, SEQ ID NO:247, SEQ ID NO:248, SEQ ID NO:249, SEQ ID NO:250, SEQ ID NO:251, SEQ ID NO:252, SEQ ID NO:253, SEQ ID NO:254, SEQ ID NO:255, SEQ ID NO:256, SEQ ID NO:257, SEQ ID NO:258, SEQ ID NO:259, SEQ ID NO:260, SEQ ID NO:261, SEQ ID NO:262, SEQ ID NO:263, SEQ ID NO:264, SEQ ID NO:265, SEQ ID NO:266, SEQ ID NO:267, SEQ ID NO:268, SEQ ID NO:269, SEQ ID NO:270, SEQ ID NO:271, SEQ ID NO:272, SEQ ID NO:273, SEQ ID NO:274, SEQ ID NO:275, SEQ ID NO:276, SEQ ID NO:277, SEQ ID NO:278, SEQ ID NO:279, SEQ ID NO:280, SEQ ID NO:281, SEQ ID NO:282, SEQ ID NO:283, SEQ ID NO:284, SEQ ID NO:285, SEQ ID NO:286, SEQ ID NO:287, SEQ ID NO:288, SEQ ID NO:289, SEQ ID NO:290, SEQ ID NO:291, SEQ ID NO:292, SEQ ID NO:293, SEQ ID NO:294, SEQ ID NO:295, SEQ ID NO:296, SEQ ID NO:297, SEQ ID NO:298, SEQ ID NO:299, SEQ ID NO:300, SEQ ID NO:301, SEQ ID NO:302, SEQ ID NO:303, SEQ ID NO:304, SEQ ID NO:305, SEQ ID NO:306, SEQ ID NO:307, SEQ ID NO:308, SEQ ID NO:309, SEQ ID NO:310, SEQ ID NO:311, SEQ ID NO:312, SEQ ID NO:313, SEQ ID NO:314, SEQ ID NO:315, SEQ ID NO:316, SEQ ID NO:317, SEQ ID NO:318, SEQ ID NO:319, SEQ ID NO:320, SEQ ID NO:321, SEQ ID NO:322, SEQ ID NO:323, SEQ ID NO:324, SEQ ID NO:325, SEQ ID NO:326, SEQ ID NO:327, SEQ ID NO:328, SEQ ID NO:329, SEQ ID NO:330, SEQ ID NO:331, SEQ ID NO:332, SEQ ID NO:2697, SEQ ID NO:2645, SEQ ID NO:2707, SEQ ID NO:2679, SEQ ID NO:2717, SEQ ID NO:2646, SEQ ID NO:2667, SEQ ID NO:2706, SEQ ID NO:2740, SEQ ID

NO:2669, SEQ ID NO:2674, SEQ ID NO:2743, SEQ ID NO:2716, SEQ ID NO:2727, SEQ ID NO:2721, SEQ ID NO:2641, SEQ ID NO:2671, SEQ ID NO:2752, SEQ ID NO:2737, SEQ ID NO:2719, SEQ ID NO:2684, SEQ ID NO:2677, SEQ ID NO:2748, SEQ ID NO:2703, SEQ ID NO:2711, SEQ ID NO:2663, SEQ ID NO:2657, SEQ ID NO:2683, SEQ ID NO:2686, SEQ ID NO:2687, SEQ ID NO:2644, SEQ ID NO:2664, SEQ ID NO:2747, SEQ ID NO:2744, SEQ ID NO:2678, SEQ ID NO:2731, SEQ ID NO:2713, SEQ ID NO:2736, SEQ ID NO:2708, SEQ ID NO:2670, SEQ ID NO:2661, SEQ ID NO:2680, SEQ ID NO:2754, SEQ ID NO:2728, SEQ ID NO:2742, SEQ ID NO:2668, SEQ ID NO:2750, SEQ ID NO:2746, SEQ ID NO:2738, SEQ ID NO:2627, SEQ ID NO:2739, SEQ ID NO:2647, SEQ ID NO:2628, SEQ ID NO:2638, SEQ ID NO:2725, SEQ ID NO:2714, SEQ ID NO:2635, SEQ ID NO:2751, SEQ ID NO:2629, SEQ ID NO:2695, SEQ ID NO:2741, SEQ ID NO:2691, SEQ ID NO:2726, SEQ ID NO:2722, SEQ ID NO:2689, SEQ ID NO:2734, SEQ ID NO:2631, SEQ ID NO:2656, SEQ ID NO:2696, SEQ ID NO:2676, SEQ ID NO:2701, SEQ ID NO:2730, SEQ ID NO:2710, SEQ ID NO:2632, SEQ ID NO:2724, SEQ ID NO:2698, SEQ ID NO:2662, SEQ ID NO:2753, SEQ ID NO:2704, SEQ ID NO:2675, SEQ ID NO:2700, SEQ ID NO:2640, SEQ ID NO:2723, SEQ ID NO:2658, SEQ ID NO:2688, SEQ ID NO:2735, SEQ ID NO:2702, SEQ ID NO:2681, SEQ ID NO:2755, SEQ ID NO:2715, SEQ ID NO:2732, SEQ ID NO:2652, SEQ ID NO:2651, SEQ ID NO:2718, SEQ ID NO:2673, SEQ ID NO:2733, SEQ ID NO:2712, SEQ ID NO:2659, SEQ ID NO:2654, SEQ ID NO:2636, SEQ ID NO:2639, SEQ ID NO:2690, SEQ ID NO:2705, SEQ ID NO:2685, SEQ ID NO:2692, SEQ ID NO:2693, SEQ ID NO:2648, SEQ ID NO:2650, SEQ ID NO:2720, SEQ ID NO:2660, SEQ ID NO:2666, SEQ ID NO:2699, SEQ ID NO:2633, SEQ ID NO:2672, SEQ ID NO:2642, SEQ ID NO:2682, SEQ ID NO:2655, SEQ ID NO:2630, SEQ ID NO:2745, SEQ ID NO:2643, SEQ ID NO:2694, SEQ ID NO:2749, SEQ ID NO:2665, SEQ ID NO:2649, SEQ ID NO:2637, SEQ ID NO:2634, SEQ ID NO:2709, SEQ ID NO:2653, SEQ ID NO:2729. In one variation, the method further includes detecting the expression level of one or more additional genes in the patient to diagnose or monitor kidney transplant rejection in a patient, wherein the one or more additional genes includes a nucleotide sequence selected from SEQ ID NO: 75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:79, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:89, SEQ ID NO:99, SEQ ID NO:100, SEQ ID NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151.

In another embodiment, the methods of diagnosing or monitoring transplant rejection include detecting the expression level of at least two of the genes. In another variation, methods of diagnosing or monitoring transplant rejection include detecting the expression level of at least ten of the genes. In a further variation, the methods of diagnosing or monitoring transplant rejection include detecting the expression level of at least one hundred of the genes. In still a further variation, the methods of diagnosing or monitoring transplant rejection include detecting the expression level of all the listed genes.

In another variation, transplant rejection may be selected from heart transplant rejection, kidney transplant rejection, liver transplant rejection, pancreas transplant rejection, pancreatic islet

transplant rejection, lung transplant rejection, bone marrow transplant rejection, stem cell transplant rejection, xenotransplant rejection, and mechanical organ replacement rejection.

In another embodiment, the methods of detecting transplant rejection include detecting the expression level by measuring the RNA level expressed by one or more genes. The method may further include isolating RNA from the patient prior to detecting the RNA level expressed by the one or more genes.

In one variation, the RNA level is detected by PCR. In a still further variation, the PCR uses primers consisting of nucleotide sequences selected from the group consisting of SEQ ID NO:665, SEQ ID NO:666, SEQ ID NO:667, SEQ ID NO:668, SEQ ID NO:669, SEQ ID NO:670, SEQ ID NO:671, SEQ ID NO:672, SEQ ID NO:673, SEQ ID NO:674, SEQ ID NO:675, SEQ ID NO:676, SEQ ID NO:677, SEQ ID NO:678, SEQ ID NO:679, SEQ ID NO:680, SEQ ID NO:681, SEQ ID NO:682, SEQ ID NO:683, SEQ ID NO:684, SEQ ID NO:685, SEQ ID NO:686, SEQ ID NO:687, SEQ ID NO:688, SEQ ID NO:689, SEQ ID NO:690, SEQ ID NO:691, SEQ ID NO:692, SEQ ID NO:693, SEQ ID NO:694, SEQ ID NO:695, SEQ ID NO:696, SEQ ID NO:697, SEQ ID NO:698, SEQ ID NO:699, SEQ ID NO:700, SEQ ID NO:701, SEQ ID NO:702, SEQ ID NO:703, SEQ ID NO:704, SEQ ID NO:705, SEQ ID NO:706, SEQ ID NO:707, SEQ ID NO:708, SEQ ID NO:709, SEQ ID NO:710, SEQ ID NO:711, SEQ ID NO:712, SEQ ID NO:713, SEQ ID NO:714, SEQ ID NO:715, SEQ ID NO:716, SEQ ID NO:717, SEQ ID NO:718, SEQ ID NO:719, SEQ ID NO:720, SEQ ID NO:721, SEQ ID NO:722, SEQ ID NO:723, SEQ ID NO:724, SEQ ID NO:725, SEQ ID NO:726, SEQ ID NO:727, SEQ ID NO:728, SEQ ID NO:729, SEQ ID NO:730, SEQ ID NO:731, SEQ ID NO:732, SEQ ID NO:733, SEQ ID NO:734, SEQ ID NO:735, SEQ ID NO:736, SEQ ID NO:737, SEQ ID NO:738, SEQ ID NO:739, SEQ ID NO:740, SEQ ID NO:741, SEQ ID NO:742, SEQ ID NO:743, SEQ ID NO:744, SEQ ID NO:745, SEQ ID NO:746, SEQ ID NO:747, SEQ ID NO:748, SEQ ID NO:749, SEQ ID NO:750, SEQ ID NO:751, SEQ ID NO:752, SEQ ID NO:753, SEQ ID NO:754, SEQ ID NO:755, SEQ ID NO:756, SEQ ID NO:757, SEQ ID NO:758, SEQ ID NO:759, SEQ ID NO:760, SEQ ID NO:761, SEQ ID NO:762, SEQ ID NO:763, SEQ ID NO:764, SEQ ID NO:765, SEQ ID NO:766, SEQ ID NO:767, SEQ ID NO:768, SEQ ID NO:769, SEQ ID NO:770, SEQ ID NO:771, SEQ ID NO:772, SEQ ID NO:773, SEQ ID NO:774, SEQ ID NO:775, SEQ ID NO:776, SEQ ID NO:777, SEQ ID NO:778, SEQ ID NO:779, SEQ ID NO:780, SEQ ID NO:781, SEQ ID NO:782, SEQ ID NO:783, SEQ ID NO:784, SEQ ID NO:785, SEQ ID NO:786, SEQ ID NO:787, SEQ ID NO:788, SEQ ID NO:789, SEQ ID NO:790, SEQ ID NO:791, SEQ ID NO:792, SEQ ID NO:793, SEQ ID NO:794, SEQ ID NO:795, SEQ ID NO:796, SEQ ID NO:797, SEQ ID NO:798, SEQ ID NO:799, SEQ ID NO:800, SEQ ID NO:801, SEQ ID NO:802, SEQ ID NO:803, SEQ ID NO:804, SEQ ID NO:805, SEQ ID NO:806, SEQ ID NO:807, SEQ ID NO:808, SEQ ID NO:809, SEQ ID NO:810, SEQ ID NO:811, SEQ ID NO:812, SEQ ID NO:813, SEQ ID NO:814, SEQ ID NO:815, SEQ ID NO:816, SEQ ID NO:817, SEQ ID NO:818, SEQ ID NO:819, SEQ ID NO:820, SEQ ID NO:821, SEQ ID NO:822, SEQ ID NO:823, SEQ ID NO:824, SEQ ID NO:825, SEQ ID NO:826, SEQ ID NO:827, SEQ ID NO:828, SEQ ID NO:829, SEQ ID NO:830, SEQ ID NO:831, SEQ ID NO:832, SEQ ID NO:833, SEQ ID NO:834, SEQ ID NO:835, SEQ ID NO:836, SEQ ID NO:837, SEQ ID NO:838, SEQ ID NO:839, SEQ ID NO:840, SEQ ID NO:841, SEQ ID NO:842, SEQ ID NO:843, SEQ ID NO:844, SEQ ID NO:845, SEQ ID NO:846, SEQ

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NO:2253, SEQ ID NO:2254, SEQ ID NO:2255, SEQ ID NO:2256, SEQ ID NO:2257, SEQ ID NO:2258, SEQ ID NO:2259, SEQ ID NO:2260, SEQ ID NO:2261, SEQ ID NO:2262, SEQ ID NO:2263, SEQ ID NO:2264, SEQ ID NO:2265, SEQ ID NO:2266, SEQ ID NO:2267, SEQ ID NO:2268, SEQ ID NO:2269, SEQ ID NO:2270, SEQ ID NO:2271, SEQ ID NO:2272, SEQ ID NO:2273, SEQ ID NO:2274, SEQ ID NO:2275, SEQ ID NO:2276, SEQ ID NO:2277, SEQ ID NO:2278, SEQ ID NO:2279, SEQ ID NO:2280, SEQ ID NO:2281, SEQ ID NO:2282, SEQ ID NO:2283, SEQ ID NO:2284, SEQ ID NO:2285, SEQ ID NO:2286, SEQ ID NO:2287, SEQ ID NO:2288, SEQ ID NO:2289, SEQ ID NO:2290, SEQ ID NO:2291, SEQ ID NO:2292, SEQ ID NO:2293, SEQ ID NO:2294, SEQ ID NO:2295, SEQ ID NO:2296, SEQ ID NO:2297, SEQ ID NO:2298, SEQ ID NO:2299, SEQ ID NO:2300, SEQ ID NO:2301, SEQ ID NO:2302, SEQ ID NO:2303, SEQ ID NO:2304, SEQ ID NO:2305, SEQ ID NO:2306, SEQ ID NO:2307, SEQ ID NO:2308, SEQ ID NO:2309, SEQ ID NO:2310, SEQ ID NO:2311, SEQ ID NO:2312, SEQ ID NO:2313, SEQ ID NO:2314, SEQ ID NO:2315, SEQ ID NO:2316, SEQ ID NO:2317, SEQ ID NO:2318, SEQ ID NO:2319, SEQ ID NO:2320, SEQ ID NO:2321, SEQ ID NO:2322, SEQ ID NO:2323, SEQ ID NO:2324, SEQ ID NO:2325, SEQ ID NO:2326, SEQ ID NO:2327, SEQ ID NO:2328, SEQ ID NO:2329, SEQ ID NO:2330, SEQ ID NO:2331, SEQ ID NO:2332, SEQ ID NO:2333, SEQ ID NO:2334, SEQ ID NO:2335, SEQ ID NO:2336, SEQ ID NO:2337, SEQ ID NO:2338, SEQ ID NO:2339, SEQ ID NO:2340, SEQ ID NO:2341, SEQ ID NO:2342, SEQ ID NO:2343, SEQ ID NO:2344, SEQ ID NO:2345, SEQ ID NO:2346, SEQ ID NO:2347, SEQ ID NO:2348, SEQ ID NO:2349, SEQ ID NO:2350, SEQ ID NO:2351, SEQ ID NO:2352, SEQ ID NO:2353, SEQ ID NO:2354, SEQ ID NO:2355, SEQ ID NO:2356, SEQ ID NO:2357, SEQ ID NO:2358, SEQ ID NO:2359, SEQ ID NO:2360, SEQ ID NO:2361, SEQ ID NO:2362, SEQ ID NO:2363, SEQ ID NO:2364, SEQ ID NO:2365, SEQ ID NO:2366, SEQ ID NO:2367, SEQ ID NO:2368, SEQ ID NO:2369, SEQ ID NO:2370, SEQ ID NO:2371, SEQ ID NO:2372, SEQ ID NO:2373, SEQ ID NO:2374, SEQ ID NO:2375, SEQ ID NO:2376, SEQ ID NO:2377, SEQ ID NO:2378, SEQ ID NO:2379, SEQ ID NO:2380, SEQ ID NO:2381, SEQ ID NO:2382, SEQ ID NO:2383, SEQ ID NO:2384, SEQ ID NO:2385, SEQ ID NO:2386, SEQ ID NO:2387, SEQ ID NO:2388, SEQ ID NO:2389, SEQ ID NO:2390, SEQ ID NO:2391, SEQ ID NO:2392, SEQ ID NO:2393, SEQ ID NO:2394, SEQ ID NO:2395, SEQ ID NO:2396, SEQ ID NO:2397, SEQ ID NO:2398, SEQ ID NO:2399. The RNA level may be detected by hybridization to the probes. In a further variation, the RNA level is detected by hybridization to an oligonucleotide. Examples of oligonucleotide include oligonucleotides having a nucleotide sequence selected from SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID

NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:78, SEQ ID NO:79, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:92, SEQ ID NO:93, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:97, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:100, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108, SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:114, SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:117, SEQ ID NO:118, SEQ ID NO:119, SEQ ID NO:120, SEQ ID NO:121, SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:192, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, SEQ ID NO:242, SEQ ID NO:243, SEQ ID NO:244, SEQ ID NO:245, SEQ ID NO:246, SEQ ID NO:247, SEQ ID NO:248, SEQ ID NO:249, SEQ ID NO:250, SEQ ID NO:251, SEQ ID NO:252, SEQ ID NO:253, SEQ ID NO:254, SEQ ID NO:255, SEQ ID NO:256, SEQ ID NO:257, SEQ ID NO:258, SEQ ID NO:259, SEQ ID NO:260, SEQ ID NO:261, SEQ ID NO:262, SEQ ID NO:263, SEQ ID NO:264, SEQ ID NO:265, SEQ ID NO:266, SEQ ID NO:267, SEQ ID NO:268, SEQ ID NO:269, SEQ ID NO:270, SEQ ID NO:271, SEQ ID NO:272, SEQ ID NO:273, SEQ ID NO:274, SEQ ID NO:275, SEQ ID NO:276, SEQ ID NO:277, SEQ ID NO:278, SEQ ID NO:279, SEQ ID NO:280,

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oligonucleotide has a nucleotide sequence consisting of SEQ ID NO: 107. The oligonucleotide may be DNA, RNA, cDNA, PNA, genomic DNA, or synthetic oligonucleotides.

In another embodiment, the methods of detecting transplant rejection include detecting the expression level by measuring one or more proteins expressed by the one or more genes. In one variation, the one or more proteins include an amino acid sequence selected from SEQ ID NO:2400, SEQ ID NO:2401, SEQ ID NO:2402, SEQ ID NO:2403, SEQ ID NO:2404, SEQ ID NO:2405, SEQ ID NO:2407, SEQ ID NO:2408, SEQ ID NO:2409, SEQ ID NO:2410, SEQ ID NO:2411, SEQ ID NO:2412, SEQ ID NO:2413, SEQ ID NO:2414, SEQ ID NO:2415, SEQ ID NO:2416, SEQ ID NO:2417, SEQ ID NO:2418, SEQ ID NO:2419, SEQ ID NO:2420, SEQ ID NO:2421, SEQ ID NO:2422, SEQ ID NO:2423, SEQ ID NO:2424, SEQ ID NO:2425, SEQ ID NO:2426, SEQ ID NO:2427, SEQ ID NO:2428, SEQ ID NO:2429, SEQ ID NO:2430, SEQ ID NO:2432, SEQ ID NO:2433, SEQ ID NO:2434, SEQ ID NO:2435, SEQ ID NO:2436, SEQ ID NO:2437, SEQ ID NO:2438, SEQ ID NO:2439, SEQ ID NO:2440, SEQ ID NO:2441, SEQ ID NO:2442, SEQ ID NO:2443, SEQ ID NO:2444, SEQ ID NO:2445, SEQ ID NO:2446, SEQ ID NO:2447, SEQ ID NO:2448, SEQ ID NO:2449, SEQ ID NO:2450, SEQ ID NO:2451, SEQ ID NO:2452, SEQ ID NO:2453, SEQ ID NO:2454, SEQ ID NO:2455, SEQ ID NO:2456, SEQ ID NO:2457, SEQ ID NO:2458, SEQ ID NO:2459, SEQ ID NO:2460, SEQ ID NO:2461, SEQ ID NO:2462, SEQ ID NO:2463, SEQ ID NO:2464, SEQ ID NO:2465, SEQ ID NO:2466, SEQ ID NO:2467, SEQ ID NO:2468, SEQ ID NO:2469, SEQ ID NO:2470, SEQ ID NO:2478, SEQ ID NO:2479, SEQ ID NO:2480, SEQ ID NO:2481, SEQ ID NO:2482, SEQ ID NO:2483, SEQ ID NO:2485, SEQ ID NO:2486, SEQ ID NO:2488, SEQ ID NO:2491, SEQ ID NO:2492, SEQ ID NO:2493, SEQ ID NO:2494, SEQ ID NO:2495, SEQ ID NO:2496, SEQ ID NO:2497, SEQ ID NO:2502, SEQ ID NO:2503, SEQ ID NO:2504, SEQ ID NO:2505, SEQ ID NO:2506, SEQ ID NO:2507, SEQ ID NO:2508, SEQ ID NO:2509, SEQ ID NO:2510, SEQ ID NO:2511, SEQ ID NO:2512, SEQ ID NO:2513, SEQ ID NO:2514, SEQ ID NO:2515, SEQ ID NO:2516, SEQ ID NO:2517, SEQ ID NO:2518, SEQ ID NO:2519, SEQ ID NO:2520, SEQ ID NO:2521, SEQ ID NO:2528, SEQ ID NO:2529, SEQ ID NO:2530, SEQ ID NO:2531, SEQ ID NO:2532, SEQ ID NO:2533, SEQ ID NO:2534, SEQ ID NO:2535, SEQ ID NO:2536, SEQ ID NO:2537, SEQ ID NO:2538, SEQ ID NO:2539, SEQ ID NO:2540, SEQ ID NO:2541, SEQ ID NO:2542, SEQ ID NO:2543, SEQ ID NO:2544, SEQ ID NO:2545, SEQ ID NO:2546, SEQ ID NO:2547, SEQ ID NO:2548, SEQ ID NO:2549, SEQ ID NO:2550, SEQ ID NO:2551, SEQ ID NO:2552, SEQ ID NO:2553, SEQ ID NO:2554, SEQ ID NO:2555, SEQ ID NO:2556, SEQ ID NO:2557, SEQ ID NO:2558, SEQ ID NO:2559, SEQ ID NO:2560, SEQ ID NO:2561, SEQ ID NO:2562, SEQ ID NO:2563, SEQ ID NO:2564, SEQ ID NO:2565, SEQ ID NO:2566, SEQ ID NO:2567, SEQ ID NO:2568, SEQ ID NO:2569, SEQ ID NO:2570, SEQ ID NO:2571, SEQ ID NO:2572, SEQ ID NO:2573, SEQ ID NO:2574, SEQ ID NO:2575, SEQ ID NO:2576, SEQ ID NO:2577, SEQ ID NO:2578, SEQ ID NO:2579, SEQ ID NO:2580, SEQ ID NO:2581, SEQ ID NO:2582, SEQ ID NO:2583, SEQ ID NO:2584, SEQ ID NO:2585, SEQ ID NO:2586, SEQ ID NO:2587, SEQ ID NO:2588, SEQ ID NO:2589, SEQ ID NO:2590, SEQ ID NO:2591, SEQ ID NO:2592, SEQ ID NO:2593, SEQ ID NO:2594, SEQ ID NO:2595, SEQ ID NO:2596, SEQ ID NO:2597, SEQ ID NO:2598, SEQ ID

NO:2599, SEQ ID NO:2600, SEQ ID NO:2601, SEQ ID NO:2602, SEQ ID NO:2603, SEQ ID NO:2604, SEQ ID NO:2605, SEQ ID NO:2606, SEQ ID NO:2607, SEQ ID NO:2608, SEQ ID NO:2609, SEQ ID NO:2610, SEQ ID NO:2611, SEQ ID NO:2612, SEQ ID NO:2613, SEQ ID NO:2614, SEQ ID NO:2615, SEQ ID NO:2616, SEQ ID NO:2617, SEQ ID NO:2618, SEQ ID NO:2619, SEQ ID NO:2620, SEQ ID NO:2621, SEQ ID NO:2622, SEQ ID NO:2623, SEQ ID NO:2624, SEQ ID NO:2625, SEQ ID NO:2626, SEQ ID NO:2925, SEQ ID NO:2926, SEQ ID NO:2927, SEQ ID NO:2928, SEQ ID NO:2929, SEQ ID NO:2930, SEQ ID NO:2932, SEQ ID NO:2933, SEQ ID NO:2935, SEQ ID NO:2936, SEQ ID NO:2937, SEQ ID NO:2938, SEQ ID NO:2939, SEQ ID NO:2941, SEQ ID NO:2942, SEQ ID NO:2943, SEQ ID NO:2945, SEQ ID NO:2946, SEQ ID NO:2947, SEQ ID NO:2948, SEQ ID NO:2949, SEQ ID NO:2950, SEQ ID NO:2951, SEQ ID NO:2952, SEQ ID NO:2953, SEQ ID NO:2954, SEQ ID NO:2955, SEQ ID NO:2956, SEQ ID NO:2957, SEQ ID NO:2959, SEQ ID NO:2960, SEQ ID NO:2961, SEQ ID NO:2962, SEQ ID NO:2963, SEQ ID NO:2964, SEQ ID NO:2965, SEQ ID NO:2966, SEQ ID NO:2967, SEQ ID NO:2968, SEQ ID NO:2969, SEQ ID NO:2970, SEQ ID NO:2971, SEQ ID NO:2972, SEQ ID NO:2973, SEQ ID NO:2974, SEQ ID NO:2975, SEQ ID NO:2976, SEQ ID NO:2977, SEQ ID NO:2978, SEQ ID NO:2979, SEQ ID NO:2980, SEQ ID NO:2981, SEQ ID NO:2982, SEQ ID NO:2983, SEQ ID NO:2984, SEQ ID NO:2985, SEQ ID NO:2986, SEQ ID NO:2987, SEQ ID NO:2988, SEQ ID NO:2989, SEQ ID NO:2990, SEQ ID NO:2991, SEQ ID NO:2992, SEQ ID NO:2993, SEQ ID NO:2994, SEQ ID NO:2995, SEQ ID NO:2996, SEQ ID NO:2997, SEQ ID NO:2998, SEQ ID NO:2999, SEQ ID NO:3000, SEQ ID NO:3001, SEQ ID NO:3002, SEQ ID NO:3003, SEQ ID NO:3004, SEQ ID NO:3005, SEQ ID NO:3006, SEQ ID NO:3007, SEQ ID NO:3008, SEQ ID NO:3009, SEQ ID NO:3010, SEQ ID NO:3011, SEQ ID NO:3012, SEQ ID NO:3013, SEQ ID NO:3014, SEQ ID NO:3015. In a further variation, the the method includes detecting one or more additional proteins expressed by SEQ ID NO:2406, SEQ ID NO:2431, SEQ ID NO:2471, SEQ ID NO:2472, SEQ ID NO:2473, SEQ ID NO:2474, SEQ ID NO:2475, SEQ ID NO:2476, SEQ ID NO:2477, SEQ ID NO:2484, SEQ ID NO:2487, SEQ ID NO:2489, SEQ ID NO:2490, SEQ ID NO:2498, SEQ ID NO:2499, SEQ ID NO:2500, SEQ ID NO:2501, SEQ ID NO:2522, SEQ ID NO:2523, SEQ ID NO:2524, SEQ ID NO:2525, SEQ ID NO:2526, SEQ ID NO:2527. In still another variation, one or more proteins may be selected from SEQ ID NO:2400, SEQ ID NO:2401, SEQ ID NO:2402, SEQ ID NO:2403, SEQ ID NO:2404, SEQ ID NO:2405, SEQ ID NO:2407, SEQ ID NO:2408, SEQ ID NO:2409, SEQ ID NO:2410, SEQ ID NO:2411, SEQ ID NO:2412, SEQ ID NO:2413, SEQ ID NO:2414, SEQ ID NO:2415, SEQ ID NO:2416, SEQ ID NO:2417, SEQ ID NO:2418, SEQ ID NO:2419, SEQ ID NO:2420, SEQ ID NO:2421, SEQ ID NO:2422, SEQ ID NO:2423, SEQ ID NO:2424, SEQ ID NO:2425, SEQ ID NO:2426, SEQ ID NO:2427, SEQ ID NO:2428, SEQ ID NO:2429, SEQ ID NO:2430, SEQ ID NO:2432, SEQ ID NO:2433, SEQ ID NO:2434, SEQ ID NO:2435, SEQ ID NO:2436, SEQ ID NO:2437, SEQ ID NO:2438, SEQ ID NO:2439, SEQ ID NO:2440, SEQ ID NO:2441, SEQ ID NO:2442, SEQ ID NO:2443, SEQ ID NO:2444, SEQ ID NO:2445, SEQ ID NO:2446, SEQ ID NO:2447, SEQ ID NO:2448, SEQ ID NO:2449, SEQ ID NO:2450, SEQ ID NO:2451, SEQ ID NO:2452, SEQ ID NO:2453, SEQ ID NO:2454, SEQ ID NO:2455, SEQ ID NO:2456, SEQ ID

NO:2457, SEQ ID NO:2458, SEQ ID NO:2459, SEQ ID NO:2460, SEQ ID NO:2461, SEQ ID NO:2462, SEQ ID NO:2463, SEQ ID NO:2464, SEQ ID NO:2465, SEQ ID NO:2466, SEQ ID NO:2467, SEQ ID NO:2468, SEQ ID NO:2469, SEQ ID NO:2470, SEQ ID NO:2478, SEQ ID NO:2479, SEQ ID NO:2480, SEQ ID NO:2481, SEQ ID NO:2482, SEQ ID NO:2483, SEQ ID NO:2485, SEQ ID NO:2486, SEQ ID NO:2488, SEQ ID NO:2491, SEQ ID NO:2492, SEQ ID NO:2493, SEQ ID NO:2494, SEQ ID NO:2495, SEQ ID NO:2496, SEQ ID NO:2497, SEQ ID NO:2502, SEQ ID NO:2503, SEQ ID NO:2504, SEQ ID NO:2505, SEQ ID NO:2506, SEQ ID NO:2507, SEQ ID NO:2508, SEQ ID NO:2509, SEQ ID NO:2510, SEQ ID NO:2511, SEQ ID NO:2512, SEQ ID NO:2513, SEQ ID NO:2514, SEQ ID NO:2515, SEQ ID NO:2516, SEQ ID NO:2517, SEQ ID NO:2518, SEQ ID NO:2519, SEQ ID NO:2520, SEQ ID NO:2521, SEQ ID NO:2528, SEQ ID NO:2529, SEQ ID NO:2530, SEQ ID NO:2531, SEQ ID NO:2532, SEQ ID NO:2533, SEQ ID NO:2534, SEQ ID NO:2535, SEQ ID NO:2536, SEQ ID NO:2537, SEQ ID NO:2538, SEQ ID NO:2539, SEQ ID NO:2540, SEQ ID NO:2541, SEQ ID NO:2542, SEQ ID NO:2543, SEQ ID NO:2544, SEQ ID NO:2545, SEQ ID NO:2546, SEQ ID NO:2547, SEQ ID NO:2548, SEQ ID NO:2549, SEQ ID NO:2550, SEQ ID NO:2551, SEQ ID NO:2552, SEQ ID NO:2553, SEQ ID NO:2554, SEQ ID NO:2555, SEQ ID NO:2556, SEQ ID NO:2557, SEQ ID NO:2558, SEQ ID NO:2559, SEQ ID NO:2560, SEQ ID NO:2561, SEQ ID NO:2562, SEQ ID NO:2563, SEQ ID NO:2564, SEQ ID NO:2565, SEQ ID NO:2566, SEQ ID NO:2567, SEQ ID NO:2568, SEQ ID NO:2569, SEQ ID NO:2570, SEQ ID NO:2571, SEQ ID NO:2572, SEQ ID NO:2573, SEQ ID NO:2574, SEQ ID NO:2575, SEQ ID NO:2576, SEQ ID NO:2577, SEQ ID NO:2578, SEQ ID NO:2579, SEQ ID NO:2580, SEQ ID NO:2581, SEQ ID NO:2582, SEQ ID NO:2583, SEQ ID NO:2584, SEQ ID NO:2585, SEQ ID NO:2586, SEQ ID NO:2587, SEQ ID NO:2588, SEQ ID NO:2589, SEQ ID NO:2590, SEQ ID NO:2591, SEQ ID NO:2592, SEQ ID NO:2593, SEQ ID NO:2594, SEQ ID NO:2595, SEQ ID NO:2596, SEQ ID NO:2597, SEQ ID NO:2598, SEQ ID NO:2599, SEQ ID NO:2600, SEQ ID NO:2601, SEQ ID NO:2602, SEQ ID NO:2603, SEQ ID NO:2604, SEQ ID NO:2605, SEQ ID NO:2606, SEQ ID NO:2607, SEQ ID NO:2608, SEQ ID NO:2609, SEQ ID NO:2610, SEQ ID NO:2611, SEQ ID NO:2612, SEQ ID NO:2613, SEQ ID NO:2614, SEQ ID NO:2615, SEQ ID NO:2616, SEQ ID NO:2617, SEQ ID NO:2618, SEQ ID NO:2619, SEQ ID NO:2620, SEQ ID NO:2621, SEQ ID NO:2622, SEQ ID NO:2623, SEQ ID NO:2624, SEQ ID NO:2625, SEQ ID NO:2626, SEQ ID NO:2925, SEQ ID NO:2926, SEQ ID NO:2927, SEQ ID NO:2928, SEQ ID NO:2929, SEQ ID NO:2930, SEQ ID NO:2932, SEQ ID NO:2933, SEQ ID NO:2935, SEQ ID NO:2936, SEQ ID NO:2937, SEQ ID NO:2938, SEQ ID NO:2939, SEQ ID NO:2941, SEQ ID NO:2942, SEQ ID NO:2943, SEQ ID NO:2945, SEQ ID NO:2946, SEQ ID NO:2947, SEQ ID NO:2948, SEQ ID NO:2949, SEQ ID NO:2950, SEQ ID NO:2951, SEQ ID NO:2952, SEQ ID NO:2953, SEQ ID NO:2954, SEQ ID NO:2955, SEQ ID NO:2956, SEQ ID NO:2957, SEQ ID NO:2959, SEQ ID NO:2960, SEQ ID NO:2961, SEQ ID NO:2962, SEQ ID NO:2963, SEQ ID NO:2964, SEQ ID NO:2965, SEQ ID NO:2966, SEQ ID NO:2967, SEQ ID NO:2968, SEQ ID NO:2969, SEQ ID NO:2970, SEQ ID NO:2971, SEQ ID NO:2972, SEQ ID NO:2973, SEQ ID NO:2974, SEQ ID NO:2975, SEQ ID NO:2976, SEQ ID NO:2977, SEQ ID NO:2978, SEQ ID NO:2979, SEQ ID NO:2980, SEQ ID

NO:2981, SEQ ID NO:2982, SEQ ID NO:2983, SEQ ID NO:2984, SEQ ID NO:2985, SEQ ID NO:2986, SEQ ID NO:2987, SEQ ID NO:2988, SEQ ID NO:2989, SEQ ID NO:2990, SEQ ID NO:2991, SEQ ID NO:2992, SEQ ID NO:2993, SEQ ID NO:2994, SEQ ID NO:2995, SEQ ID NO:2996, SEQ ID NO:2997, SEQ ID NO:2998, SEQ ID NO:2999, SEQ ID NO:3000, SEQ ID NO:3001, SEQ ID NO:3002, SEQ ID NO:3003, SEQ ID NO:3004, SEQ ID NO:3005, SEQ ID NO:3006, SEQ ID NO:3007, SEQ ID NO:3008, SEQ ID NO:3009, SEQ ID NO:3010, SEQ ID NO:3011, SEQ ID NO:3012, SEQ ID NO:3013, SEQ ID NO:3014, SEQ ID NO:3015, and one or more proteins may be selected from SEQ ID NO:2406, SEQ ID NO:2431, SEQ ID NO:2471, SEQ ID NO:2472, SEQ ID NO:2473, SEQ ID NO:2474, SEQ ID NO:2475, SEQ ID NO:2476, SEQ ID NO:2477, SEQ ID NO:2484, SEQ ID NO:2487, SEQ ID NO:2489, SEQ ID NO:2490, SEQ ID NO:2498, SEQ ID NO:2499, SEQ ID NO:2500, SEQ ID NO:2501, SEQ ID NO:2522, SEQ ID NO:2523, SEQ ID NO:2524, SEQ ID NO:2525, SEQ ID NO:2526, SEQ ID NO:2527.

In another embodiment, the method of diagnosing or monitoring cardiac transplant rejection in a patient includes detecting the expression level of one or more genes in the patient to diagnose or monitor cardiac transplant rejection in the patient by measuring one or more proteins expressed by the one or more genes. The one or more proteins may include an amino acid sequence selected from SEQ ID NO:2400, SEQ ID NO:2401, SEQ ID NO:2402, SEQ ID NO:2403, SEQ ID NO:2404, SEQ ID NO:2405, SEQ ID NO:2407, SEQ ID NO:2408, SEQ ID NO:2409, SEQ ID NO:2410, SEQ ID NO:2411, SEQ ID NO:2412, SEQ ID NO:2413, SEQ ID NO:2414, SEQ ID NO:2415, SEQ ID NO:2416, SEQ ID NO:2417, SEQ ID NO:2418, SEQ ID NO:2419, SEQ ID NO:2420, SEQ ID NO:2421, SEQ ID NO:2422, SEQ ID NO:2423, SEQ ID NO:2424, SEQ ID NO:2425, SEQ ID NO:2426, SEQ ID NO:2427, SEQ ID NO:2428, SEQ ID NO:2429, SEQ ID NO:2430, SEQ ID NO:2432, SEQ ID NO:2433, SEQ ID NO:2434, SEQ ID NO:2435, SEQ ID NO:2436, SEQ ID NO:2437, SEQ ID NO:2438, SEQ ID NO:2439, SEQ ID NO:2440, SEQ ID NO:2441, SEQ ID NO:2442, SEQ ID NO:2443, SEQ ID NO:2444, SEQ ID NO:2445, SEQ ID NO:2446, SEQ ID NO:2447, SEQ ID NO:2448, SEQ ID NO:2449, SEQ ID NO:2450, SEQ ID NO:2451, SEQ ID NO:2452, SEQ ID NO:2453, SEQ ID NO:2454, SEQ ID NO:2455, SEQ ID NO:2456, SEQ ID NO:2457, SEQ ID NO:2458, SEQ ID NO:2459, SEQ ID NO:2460, SEQ ID NO:2461, SEQ ID NO:2462, SEQ ID NO:2463, SEQ ID NO:2464, SEQ ID NO:2465, SEQ ID NO:2466, SEQ ID NO:2467, SEQ ID NO:2468, SEQ ID NO:2469, SEQ ID NO:2470, SEQ ID NO:2471, SEQ ID NO:2476, SEQ ID NO:2477, SEQ ID NO:2478, SEQ ID NO:2479, SEQ ID NO:2480, SEQ ID NO:2481, SEQ ID NO:2482, SEQ ID NO:2483, SEQ ID NO:2484, SEQ ID NO:2485, SEQ ID NO:2486, SEQ ID NO:2488, SEQ ID NO:2489, SEQ ID NO:2490, SEQ ID NO:2491, SEQ ID NO:2492, SEQ ID NO:2493, SEQ ID NO:2494, SEQ ID NO:2495, SEQ ID NO:2496, SEQ ID NO:2497, SEQ ID NO:2498, SEQ ID NO:2499, SEQ ID NO:2500, SEQ ID NO:2501, SEQ ID NO:2502, SEQ ID NO:2503, SEQ ID NO:2504, SEQ ID NO:2505, SEQ ID NO:2506, SEQ ID NO:2507, SEQ ID NO:2508, SEQ ID NO:2509, SEQ ID NO:2510, SEQ ID NO:2511, SEQ ID NO:2512, SEQ ID NO:2513, SEQ ID NO:2514, SEQ ID NO:2515, SEQ ID NO:2516, SEQ ID NO:2517, SEQ ID NO:2518, SEQ ID NO:2519, SEQ ID NO:2520, SEQ ID NO:2521, SEQ ID NO:2528, SEQ ID NO:2529, SEQ ID NO:2530, SEQ ID NO:2531, SEQ ID NO:2532, SEQ ID

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In another embodiment, the method of diagnosing or monitoring kidney transplant rejection in a patient includes detecting the expression level of one or more genes in the patient to diagnose or monitor kidney transplant rejection in the patient by measuring one or more proteins encoded by the one or more genes. In one variation, the one or more proteins include an amino acid sequence selected from SEQ ID NO:2400, SEQ ID NO:2401, SEQ ID NO:2402, SEQ ID NO:2403, SEQ ID NO:2404, SEQ ID NO:2405, SEQ ID NO:2406, SEQ ID NO:2407, SEQ ID NO:2408, SEQ ID NO:2409, SEQ ID NO:2410, SEQ ID NO:2411, SEQ ID NO:2412, SEQ ID NO:2413, SEQ ID NO:2414, SEQ ID NO:2415, SEQ ID NO:2416, SEQ ID NO:2417, SEQ ID NO:2418, SEQ ID NO:2419, SEQ ID NO:2420, SEQ ID NO:2421, SEQ ID NO:2422, SEQ ID NO:2423, SEQ ID NO:2424, SEQ ID NO:2425, SEQ ID NO:2426, SEQ ID NO:2427, SEQ ID NO:2428, SEQ ID NO:2429, SEQ ID NO:2430, SEQ ID NO:2432, SEQ ID NO:2433, SEQ ID NO:2434, SEQ ID NO:2435, SEQ ID

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Protein detection may be accomplished by measuring serum. In another variation, the protein is a cell surface protein. In a further variation, the measuring includes using a fluorescent activated cell sorter.

In another embodiment, the invention is directed to a substantially purified oligonucleotide having the nucleotide sequence selected from SEQ ID NO:2, SEQ ID NO :3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:78, SEQ ID NO:79, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:92, SEQ ID NO:93, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:97, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:100, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108, SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:114, SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:117, SEQ ID NO:118, SEQ ID NO:119, SEQ ID NO:120, SEQ ID NO:121, SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:192, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ

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In another embodiment, there is provided a method of diagnosing or monitoring transplant rejection in a patient wherein the expression level of one or more genes in a patient's bodily fluid is detected. In a further variation, the bodily fluid is peripheral blood.

In another embodiment, there is provided a method of diagnosing or monitoring transplant rejection in a patient, comprising detecting the expression level of four or more genes in the patient to diagnose or monitor transplant rejection in the patient wherein the four or more genes include a nucleotide sequence selected from SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID

NO:78, SEQ ID NO:79, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:92, SEQ ID NO:93, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:97, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:100, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108, SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:114, SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:117, SEQ ID NO:118, SEQ ID NO:119, SEQ ID NO:120, SEQ ID NO:121, SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:192, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, SEQ ID NO:242, SEQ ID NO:243, SEQ ID NO:244, SEQ ID NO:245, SEQ ID NO:246, SEQ ID NO:247, SEQ ID NO:248, SEQ ID NO:249, SEQ ID NO:250, SEQ ID NO:251, SEQ ID NO:252, SEQ ID NO:253, SEQ ID NO:254, SEQ ID NO:255, SEQ ID NO:256, SEQ ID NO:257, SEQ ID NO:258, SEQ ID NO:259, SEQ ID NO:260, SEQ ID NO:261, SEQ ID NO:262, SEQ ID NO:263, SEQ ID NO:264, SEQ ID NO:265, SEQ ID NO:266, SEQ ID NO:267, SEQ ID NO:268, SEQ ID NO:269, SEQ ID NO:270, SEQ ID NO:271, SEQ ID NO:272, SEQ ID NO:273, SEQ ID NO:274, SEQ ID NO:275, SEQ ID NO:276, SEQ ID NO:277, SEQ ID NO:278, SEQ ID NO:279, SEQ ID NO:280, SEQ ID NO:281, SEQ ID NO:282, SEQ ID NO:283, SEQ ID NO:284, SEQ ID NO:285, SEQ ID NO:286, SEQ ID NO:287, SEQ ID NO:288, SEQ ID NO:289, SEQ ID NO:290, SEQ ID NO:291, SEQ ID NO:292, SEQ ID NO:293, SEQ ID NO:294, SEQ ID NO:295, SEQ ID NO:296, SEQ ID NO:297, SEQ ID NO:298, SEQ ID NO:299, SEQ ID NO:300, SEQ ID NO:301, SEQ ID NO:302, SEQ ID NO:303, SEQ ID NO:304, SEQ ID NO:305, SEQ ID

NO:306, SEQ ID NO:307, SEQ ID NO:308, SEQ ID NO:309, SEQ ID NO:310, SEQ ID NO:311, SEQ ID NO:312, SEQ ID NO:313, SEQ ID NO:314, SEQ ID NO:315, SEQ ID NO:316, SEQ ID NO:317, SEQ ID NO:318, SEQ ID NO:319, SEQ ID NO:320, SEQ ID NO:321, SEQ ID NO:322, SEQ ID NO:323, SEQ ID NO:324, SEQ ID NO:325, SEQ ID NO:326, SEQ ID NO:327, SEQ ID NO:328, SEQ ID NO:329, SEQ ID NO:330, SEQ ID NO:331, SEQ ID NO:332, SEQ ID NO:2697, SEQ ID NO:2645, SEQ ID NO:2707, SEQ ID NO:2679, SEQ ID NO:2717, SEQ ID NO:2646, SEQ ID NO:2667, SEQ ID NO:2706, SEQ ID NO:2740, SEQ ID NO:2669, SEQ ID NO:2674, SEQ ID NO:2743, SEQ ID NO:2716, SEQ ID NO:2727, SEQ ID NO:2721, SEQ ID NO:2641, SEQ ID NO:2671, SEQ ID NO:2752, SEQ ID NO:2737, SEQ ID NO:2719, SEQ ID NO:2684, SEQ ID NO:2677, SEQ ID NO:2748, SEQ ID NO:2703, SEQ ID NO:2711, SEQ ID NO:2663, SEQ ID NO:2657, SEQ ID NO:2683, SEQ ID NO:2686, SEQ ID NO:2687, SEQ ID NO:2644, SEQ ID NO:2664, SEQ ID NO:2747, SEQ ID NO:2744, SEQ ID NO:2678, SEQ ID NO:2731, SEQ ID NO:2713, SEQ ID NO:2736, SEQ ID NO:2708, SEQ ID NO:2670, SEQ ID NO:2661, SEQ ID NO:2680, SEQ ID NO:2754, SEQ ID NO:2728, SEQ ID NO:2742, SEQ ID NO:2668, SEQ ID NO:2750, SEQ ID NO:2746, SEQ ID NO:2738, SEQ ID NO:2627, SEQ ID NO:2739, SEQ ID NO:2647, SEQ ID NO:2628, SEQ ID NO:2638, SEQ ID NO:2725, SEQ ID NO:2714, SEQ ID NO:2635, SEQ ID NO:2751, SEQ ID NO:2629, SEQ ID NO:2695, SEQ ID NO:2741, SEQ ID NO:2691, SEQ ID NO:2726, SEQ ID NO:2722, SEQ ID NO:2689, SEQ ID NO:2734, SEQ ID NO:2631, SEQ ID NO:2656, SEQ ID NO:2696, SEQ ID NO:2676, SEQ ID NO:2701, SEQ ID NO:2730, SEQ ID NO:2710, SEQ ID NO:2632, SEQ ID NO:2724, SEQ ID NO:2698, SEQ ID NO:2662, SEQ ID NO:2753, SEQ ID NO:2704, SEQ ID NO:2675, SEQ ID NO:2700, SEQ ID NO:2640, SEQ ID NO:2723, SEQ ID NO:2658, SEQ ID NO:2688, SEQ ID NO:2735, SEQ ID NO:2702, SEQ ID NO:2681, SEQ ID NO:2755, SEQ ID NO:2715, SEQ ID NO:2732, SEQ ID NO:2652, SEQ ID NO:2651, SEQ ID NO:2718, SEQ ID NO:2673, SEQ ID NO:2733, SEQ ID NO:2712, SEQ ID NO:2659, SEQ ID NO:2654, SEQ ID NO:2636, SEQ ID NO:2639, SEQ ID NO:2690, SEQ ID NO:2705, SEQ ID NO:2685, SEQ ID NO:2692, SEQ ID NO:2693, SEQ ID NO:2648, SEQ ID NO:2650, SEQ ID NO:2720, SEQ ID NO:2660, SEQ ID NO:2666, SEQ ID NO:2699, SEQ ID NO:2633, SEQ ID NO:2672, SEQ ID NO:2642, SEQ ID NO:2682, SEQ ID NO:2655, SEQ ID NO:2630, SEQ ID NO:2745, SEQ ID NO:2643, SEQ ID NO:2694, SEQ ID NO:2749, SEQ ID NO:2665, SEQ ID NO:2649, SEQ ID NO:2637, SEQ ID NO:2634, SEQ ID NO:2709, SEQ ID NO:2653, SEQ ID NO:2729.

In another embodiment, there is provided a method of diagnosing or monitoring kidney transplant rejection in a patient by detecting one or more proteins in a bodily fluid of the patient to diagnose or monitor transplant rejection in the patient wherein the one or more proteins have a protein sequence selected from SEQ ID NO:76, SEQ ID NO:2663, SEQ ID NO:98, SEQ ID NO:2696, SEQ ID NO: 2736, SEQ ID N0:2751, SEQ ID NO:2631, SEQ ID NO:2675, SEQ ID NO:2700, and SEQ ID NO:2693.

In a further embodiment, there is provided a system for detecting gene expression in body fluid including at least two isolated polynucleotides wherein the isolated polynucleotides detect expression of a gene wherein the gene includes a nucleotide sequence selected from SEQ ID NO:2,

SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:92, SEQ ID NO:93, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:98, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108, SEQ ID NO:109, SEQ ID NO:114, SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:117, SEQ ID NO:118, SEQ ID NO:119, SEQ ID NO:120, SEQ ID NO:121, SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:192, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, SEQ ID NO:242, SEQ ID NO:243, SEQ ID NO:244, SEQ ID NO:245, SEQ ID NO:246, SEQ ID NO:247, SEQ ID NO:248, SEQ ID NO:249, SEQ ID NO:250, SEQ ID NO:251, SEQ ID NO:252, SEQ ID NO:253, SEQ ID NO:254, SEQ ID NO:255, SEQ ID NO:256, SEQ ID NO:257, SEQ ID NO:258, SEQ ID NO:259, SEQ ID NO:260, SEQ ID NO:261, SEQ ID NO:262,

SEQ ID NO:263, SEQ ID NO:264, SEQ ID NO:265, SEQ ID NO:266, SEQ ID NO:267, SEQ ID NO:268, SEQ ID NO:269, SEQ ID NO:270, SEQ ID NO:271, SEQ ID NO:272, SEQ ID NO:273, SEQ ID NO:274, SEQ ID NO:275, SEQ ID NO:276, SEQ ID NO:277, SEQ ID NO:278, SEQ ID NO:279, SEQ ID NO:280, SEQ ID NO:281, SEQ ID NO:282, SEQ ID NO:283, SEQ ID NO:284, SEQ ID NO:285, SEQ ID NO:286, SEQ ID NO:287, SEQ ID NO:288, SEQ ID NO:289, SEQ ID NO:290, SEQ ID NO:291, SEQ ID NO:292, SEQ ID NO:293, SEQ ID NO:294, SEQ ID NO:295, SEQ ID NO:296, SEQ ID NO:297, SEQ ID NO:298, SEQ ID NO:299, SEQ ID NO:300, SEQ ID NO:301, SEQ ID NO:302, SEQ ID NO:303, SEQ ID NO:304, SEQ ID NO:305, SEQ ID NO:306, SEQ ID NO:307, SEQ ID NO:308, SEQ ID NO:309, SEQ ID NO:310, SEQ ID NO:311, SEQ ID NO:312, SEQ ID NO:313, SEQ ID NO:314, SEQ ID NO:315, SEQ ID NO:316, SEQ ID NO:317, SEQ ID NO:318, SEQ ID NO:319, SEQ ID NO:320, SEQ ID NO:321, SEQ ID NO:322, SEQ ID NO:323, SEQ ID NO:324, SEQ ID NO:325, SEQ ID NO:326, SEQ ID NO:327, SEQ ID NO:328, SEQ ID NO:329, SEQ ID NO:330, SEQ ID NO:331, SEQ ID NO:332, SEQ ID NO:2697, SEQ ID NO:2645, SEQ ID NO:2707, SEQ ID NO:2679, SEQ ID NO:2717, SEQ ID NO:2646, SEQ ID NO:2667, SEQ ID NO:2706, SEQ ID NO:2740, SEQ ID NO:2669, SEQ ID NO:2674, SEQ ID NO:2743, SEQ ID NO:2716, SEQ ID NO:2727, SEQ ID NO:2721, SEQ ID NO:2641, SEQ ID NO:2671, SEQ ID NO:2752, SEQ ID NO:2737, SEQ ID NO:2719, SEQ ID NO:2684, SEQ ID NO:2677, SEQ ID NO:2748, SEQ ID NO:2703, SEQ ID NO:2711, SEQ ID NO:2663, SEQ ID NO:2657, SEQ ID NO:2683, SEQ ID NO:2686, SEQ ID NO:2687, SEQ ID NO:2644, SEQ ID NO:2664, SEQ ID NO:2747, SEQ ID NO:2744, SEQ ID NO:2678, SEQ ID NO:2731, SEQ ID NO:2713, SEQ ID NO:2736, SEQ ID NO:2708, SEQ ID NO:2670, SEQ ID NO:2661, SEQ ID NO:2680, SEQ ID NO:2754, SEQ ID NO:2728, SEQ ID NO:2742, SEQ ID NO:2668, SEQ ID NO:2750, SEQ ID NO:2746, SEQ ID NO:2738, SEQ ID NO:2627, SEQ ID NO:2739, SEQ ID NO:2647, SEQ ID NO:2628, SEQ ID NO:2638, SEQ ID NO:2725, SEQ ID NO:2714, SEQ ID NO:2635, SEQ ID NO:2751, SEQ ID NO:2629, SEQ ID NO:2695, SEQ ID NO:2741, SEQ ID NO:2691, SEQ ID NO:2726, SEQ ID NO:2722, SEQ ID NO:2689, SEQ ID NO:2734, SEQ ID NO:2631, SEQ ID NO:2656, SEQ ID NO:2696, SEQ ID NO:2676, SEQ ID NO:2701, SEQ ID NO:2730, SEQ ID NO:2710, SEQ ID NO:2632, SEQ ID NO:2724, SEQ ID NO:2698, SEQ ID NO:2662, SEQ ID NO:2753, SEQ ID NO:2704, SEQ ID NO:2675, SEQ ID NO:2700, SEQ ID NO:2640, SEQ ID NO:2723, SEQ ID NO:2658, SEQ ID NO:2688, SEQ ID NO:2735, SEQ ID NO:2702, SEQ ID NO:2681, SEQ ID NO:2755, SEQ ID NO:2715, SEQ ID NO:2732, SEQ ID NO:2652, SEQ ID NO:2651, SEQ ID NO:2718, SEQ ID NO:2673, SEQ ID NO:2733, SEQ ID NO:2712, SEQ ID NO:2659, SEQ ID NO:2654, SEQ ID NO:2636, SEQ ID NO:2639, SEQ ID NO:2690, SEQ ID NO:2705, SEQ ID NO:2685, SEQ ID NO:2692, SEQ ID NO:2693, SEQ ID NO:2648, SEQ ID NO:2650, SEQ ID NO:2720, SEQ ID NO:2660, SEQ ID NO:2666, SEQ ID NO:2699, SEQ ID NO:2633, SEQ ID NO:2672, SEQ ID NO:2642, SEQ ID NO:2682, SEQ ID NO:2655, SEQ ID NO:2630, SEQ ID NO:2745, SEQ ID NO:2643, SEQ ID NO:2694, SEQ ID NO:2749, SEQ ID NO:2665, SEQ ID NO:2649, SEQ ID NO:2637, SEQ ID NO:2634, SEQ ID NO:2709, SEQ ID NO:2653, SEQ ID NO:2729 and the gene is differentially expressed in body fluid in an individual rejecting a transplanted

organ compared to the expression of the gene in leukocytes in an individual not rejecting a transplanted organ.

In another embodiment, there is provided a system for detecting gene expression in body fluid including at least two isolated polynucleotides wherein the isolated polynucleotides detect expression of a gene wherein the gene includes a nucleotide sequence selected from SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:78, SEQ ID NO:79, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:92, SEQ ID NO:93, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:97, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:100, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108, SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:114, SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:117, SEQ ID NO:118, SEQ ID NO:119, SEQ ID NO:120, SEQ ID NO:121, SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:192, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ

ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, SEQ ID NO:242, SEQ ID NO:243, SEQ ID NO:244, SEQ ID NO:245, SEQ ID NO:246, SEQ ID NO:247, SEQ ID NO:248, SEQ ID NO:249, SEQ ID NO:250, SEQ ID NO:251, SEQ ID NO:252, SEQ ID NO:253, SEQ ID NO:254, SEQ ID NO:255, SEQ ID NO:256, SEQ ID NO:257, SEQ ID NO:258, SEQ ID NO:259, SEQ ID NO:260, SEQ ID NO:261, SEQ ID NO:262, SEQ ID NO:263, SEQ ID NO:264, SEQ ID NO:265, SEQ ID NO:266, SEQ ID NO:267, SEQ ID NO:268, SEQ ID NO:269, SEQ ID NO:270, SEQ ID NO:271, SEQ ID NO:272, SEQ ID NO:273, SEQ ID NO:274, SEQ ID NO:275, SEQ ID NO:276, SEQ ID NO:277, SEQ ID NO:278, SEQ ID NO:279, SEQ ID NO:280, SEQ ID NO:281, SEQ ID NO:282, SEQ ID NO:283, SEQ ID NO:284, SEQ ID NO:285, SEQ ID NO:286, SEQ ID NO:287, SEQ ID NO:288, SEQ ID NO:289, SEQ ID NO:290, SEQ ID NO:291, SEQ ID NO:292, SEQ ID NO:293, SEQ ID NO:294, SEQ ID NO:295, SEQ ID NO:296, SEQ ID NO:297, SEQ ID NO:298, SEQ ID NO:299, SEQ ID NO:300, SEQ ID NO:301, SEQ ID NO:302, SEQ ID NO:303, SEQ ID NO:304, SEQ ID NO:305, SEQ ID NO:306, SEQ ID NO:307, SEQ ID NO:308, SEQ ID NO:309, SEQ ID NO:310, SEQ ID NO:311, SEQ ID NO:312, SEQ ID NO:313, SEQ ID NO:314, SEQ ID NO:315, SEQ ID NO:316, SEQ ID NO:317, SEQ ID NO:318, SEQ ID NO:319, SEQ ID NO:320, SEQ ID NO:321, SEQ ID NO:322, SEQ ID NO:323, SEQ ID NO:324, SEQ ID NO:325, SEQ ID NO:326, SEQ ID NO:327, SEQ ID NO:328, SEQ ID NO:329, SEQ ID NO:330, SEQ ID NO:331, SEQ ID NO:332, SEQ ID NO:2697, SEQ ID NO:2645, SEQ ID NO:2707, SEQ ID NO:2679, SEQ ID NO:2717, SEQ ID NO:2646, SEQ ID NO:2667, SEQ ID NO:2706, SEQ ID NO:2740, SEQ ID NO:2669, SEQ ID NO:2674, SEQ ID NO:2743, SEQ ID NO:2716, SEQ ID NO:2727, SEQ ID NO:2721, SEQ ID NO:2641, SEQ ID NO:2671, SEQ ID NO:2752, SEQ ID NO:2737, SEQ ID NO:2719, SEQ ID NO:2684, SEQ ID NO:2677, SEQ ID NO:2748, SEQ ID NO:2703, SEQ ID NO:2711, SEQ ID NO:2663, SEQ ID NO:2657, SEQ ID NO:2683, SEQ ID NO:2686, SEQ ID NO:2687, SEQ ID NO:2644, SEQ ID NO:2664, SEQ ID NO:2747, SEQ ID NO:2744, SEQ ID NO:2678, SEQ ID NO:2731, SEQ ID NO:2713, SEQ ID NO:2736, SEQ ID NO:2708, SEQ ID NO:2670, SEQ ID NO:2661, SEQ ID NO:2680, SEQ ID NO:2754, SEQ ID NO:2728, SEQ ID NO:2742, SEQ ID NO:2668, SEQ ID NO:2750, SEQ ID NO:2746, SEQ ID NO:2738, SEQ ID NO:2627, SEQ ID NO:2739, SEQ ID NO:2647, SEQ ID NO:2628, SEQ ID NO:2638, SEQ ID NO:2725, SEQ ID NO:2714, SEQ ID NO:2635, SEQ ID NO:2751, SEQ ID NO:2629, SEQ ID NO:2695, SEQ ID NO:2741, SEQ ID NO:2691, SEQ ID NO:2726, SEQ ID NO:2722, SEQ ID NO:2689, SEQ ID NO:2734, SEQ ID NO:2631, SEQ ID NO:2656, SEQ ID NO:2696, SEQ ID NO:2676, SEQ ID NO:2701, SEQ ID NO:2730, SEQ ID NO:2710, SEQ ID NO:2632, SEQ ID NO:2724, SEQ ID NO:2698, SEQ ID NO:2662, SEQ ID NO:2753, SEQ ID NO:2704, SEQ ID NO:2675, SEQ ID NO:2700, SEQ ID NO:2640, SEQ ID NO:2723, SEQ ID NO:2658, SEQ ID NO:2688, SEQ ID NO:2735, SEQ ID NO:2702, SEQ ID NO:2681, SEQ ID NO:2755, SEQ ID

NO: 2715, SEQ ID NO: 2732, SEQ ID NO: 2652, SEQ ID NO: 2651, SEQ ID NO: 2718, SEQ ID NO: 2673, SEQ ID NO: 2733, SEQ ID NO: 2712, SEQ ID NO: 2659, SEQ ID NO: 2654, SEQ ID NO: 2636, SEQ ID NO: 2639, SEQ ID NO: 2690, SEQ ID NO: 2705, SEQ ID NO: 2685, SEQ ID NO: 2692, SEQ ID NO: 2693, SEQ ID NO: 2648, SEQ ID NO: 2650, SEQ ID NO: 2720, SEQ ID NO: 2660, SEQ ID NO: 2666, SEQ ID NO: 2699, SEQ ID NO: 2633, SEQ ID NO: 2672, SEQ ID NO: 2642, SEQ ID NO: 2682, SEQ ID NO: 2655, SEQ ID NO: 2630, SEQ ID NO: 2745, SEQ ID NO: 2643, SEQ ID NO: 2694, SEQ ID NO: 2749, SEQ ID NO: 2665, SEQ ID NO: 2649, SEQ ID NO: 2637, SEQ ID NO: 2634, SEQ ID NO: 2709, SEQ ID NO: 2653, SEQ ID NO: 2729 and the gene expression is related to the rate of hematopoiesis or the distribution of hematopoeitic cells along their maturation pathway.

In another embodiment, there is provided a composition for assessing the immune status of an individual comprising a nucleotide sequence for detecting a nucleic acid wherein said nucleic acid is expressed at different levels depending upon the rate of hematopoiesis or the distribution of hematopoietic cells along their maturation pathway in said individual and comprises a nucleotide sequence chosen from SEQ ID NO: 52, SEQ ID NO: 67, SEQ ID NO: 19, SEQ ID NO: 39, SEQ ID NO: 63, SEQ ID NO: 26, SEQ ID NO: 68, SEQ ID NO: 13, SEQ ID NO: 200, and SEQ ID NO: 36

Embodiments of the invention are also directed to methods of diagnosing or monitoring transplant rejection in a patient by detecting the expression level of one or more genes including a nucleotide sequence selected from SEQ ID NOS: 3016-3117. SEQ ID NOS: 3108-3117 are useful in detecting CMV infection.

Brief Description of the Sequence Listing

SEQ ID's 1-332 are 50mer oligonucleotides corresponding to gene expression markers for diagnosis and monitoring of allograft rejection and other disorders.
SEQ ID's 333-664 are Reference mRNA sequences for genes identified by probes 1-332.
SEQ ID's 665-995 are a first set of Left PCR primers for genes 1-332.
SEQ ID's 996-1326 are a first set of Right PCR primers for genes 1-332.

SEQ ID's 1327-1657 are Taqman probes for the first set PCR primers for genes 1-332.
SEQ ID's 1658-1903 are a second alternative set of left PCR primers for selected genes 1-332.

SEQ ID's 1904-2151 are a second alternative set of right PCR primers for selected genes1-332.

SEQ ID's 2152-2399 are Taqman probes for the second alternative set of PCR primers for selected genes 1-332.
SEQ ID's 2400-2626 are Proteins encoded by mRNA's from genes identified in 1-332.
SEQ ID's 2627-2795 are 50mer oligonucleotide array probes used to identify genes in Figure 7 and Tables 6 and 8.
SEQ ID's 2796-2924 are reference mRNA sequences for genes in Table 8 which show altered expression in renal transplantation and rejection.
SEQ ID's 2925-3015 are proteins coded by genes which show altered expression in Table 8.
SEQ ID's 3016-3081 are50mer oligonucleotide array probes and used to identify genes in the Examples.
SEQ ID's 3082-3107 are genes and primers discussed in the Examples.
SEQ ID's 3108-3117 are mRNAs from human genes in which regulation is altered upon CMV infection.

Brief Description of the Figures

Figure 1: Figure 1 is a schematic flow chart illustrating a schematic instruction set for characterization of the nucleotide sequence and/or the predicted protein sequence of novel nucleotide sequences.
Figure 2: Figure 2 depicts the components of an automated RNA preparation machine.

Figure 3 shows the results of six hybridizations on a mini array graphed (n=6 for each column). The error bars are the SEM. This experiment shows that the average signal from AP prepared RNA is 47% of the average signal from GS prepared RNA for both Cy3 and Cy5.

Figure 4 shows the average background subtracted signal for each of nine leukocyte-specific genes on a mini array. This average is for 3-6 of the above-described hybridizations for each gene. The error bars are the SEM.

Figure 5 shows the ratio of Cy3 to Cy5 signal for a number of genes. After normalization, this ratio corrects for variability among hybridizations and allows comparison between experiments done at different times. The ratio is calculated as the Cy3 background subtracted signal divided by the Cy5 background subtracted signal. Each bar is the average for 3-6 hybridizations. The error bars are SEM.

Figure 6 shows data median Cy3 background subtracted signals for control RNAs using mini arrays.

Figure 7: Cardiac Allograft rejection diagnostic genes.

A. Example of rejection and no-rejection samples expression data for 5 marker genes. For each sample, the associated rejection grades are shown as are the expression ratios for 5 differentially expressed genes. The genes are identified by the SEQ ID number for the oligonucleotide. The average fold difference between grade 0 and grade 3A samples is calculated at the bottom.

B. CART classification model. Decision tree for a 3 gene classification model for diagnosis of cardiac rejection. In the first step, expression of gene 223 is used to divide the patients to 2 branches. The remaining samples in each branch are then further divided by one remaining gene. The samples are classified as either rejection or no rejection. 1 no rejection sample is misclassified as a rejection sample.

C. Surrogates for the CART classification model. For each of the 3 splitter genes in the CART rejection model described in the example, 5 top surrogate genes are listed that were identified by the CART algorithm.

Figure 8: Validation of differential expression of a gene discovered using microarrays using real-time PCR

Figure 8A. The Ct for each patient sample on multiple assays is shown along with the Ct in the R50 control RNA. Triangles represent –RT (reverse transcriptase) controls.

Figure 8B. The fold difference between the expression of Granzyme B and an Actin reference is shown for 3 samples from patients with and without CMV disease.

Figure 9: Endpoint testing of PCR primers

Electrophoresis and microfluidics are used to assess the product of gene specific PCR primers.

β-GUS gel image. Lane 3 is the image for primers F178 and R242. Lanes 2 and 1 correspond to the no-template control and –RT control, respectively.

The electropherogram of β-GUS primers F178 and R242, a graphical representation of Lane 3 from the gel image.

β-Actin gel image. Lane 3 is the image for primers F75 and R178. Lanes 2 and 1 correspond to the no-template control and –RT control, respectively.

The electropherogram of β-Actin primers F75 and R178, a graphical representation of Lave 3 from the gel image.

Figure 10: PCR Primer efficiency testing. A standard curve of Ct versus log of the starting RNA amount is shown for 2 genes.

Figure 11: Real-time PCR control gene analysis

11 candidate control genes were tested using real-time PCR on 6 whole blood samples (PAX) paired with 6 mononuclear samples (CPT) from the same patient. Each sample was tested twice. For each gene, the variability of the gene across the samples is shown on the vertical axis (top graph). The average Ct value for each gene is also shown (bottom graph). 2ug RNA was used for PAX samples and 0.5 ug total RNA was used for the mononuclear samples (CPT).

Figure 12: Rejection marker discovery by co-expression with established marker

Microarrays were used to measure expression of genes SEQ ID 85 and 302 in samples derived from 240 transplant recipients. For each sample, the expression measurement for 85 is plotted against 302.

Figure 13: ROC (receiver operator characteristics) curve for a 3-gene PCR assay for diagnosis of rejection (see example 17). The Sensitivity and False Positive Rate for each test cutoff is shown.

Brief Description of the Tables

Table 1: Table 1 lists diseases or conditions amenable to study by leukocyte profiling.

Table 2: Transplant Markers

A. Transplant Genes: Genes useful for monitoring of allograft rejection are listed in this here. The gene symbol and name are given. SEQ ID 50mer is the sequence ID of a 50mer oligonucleotide that is specific for the gene. The NCBI Unigene number (HS) from (Build 160, 16 Feb 2003) is given as is an accession number (ACC) from (Genbank Release 135, 15 April 2003) for an RNA or cDNA is Genbank that corresponds to the gene. The sequence identified by the ACC number is in the sequence listing (SEQ ID RNA/cDNA).

B. Microarray Data: SEQ ID 50mer, Gene, Gene Name, ACC and SEQ ID RNA/cDNA are given for each gene as in A (above). Each identified gene has a Non-Parametric Score and Median Rank in NR given from the non-parametric analysis of the data. The genes are ranked from highest to lowest scoring. Down Regulated genes are noted with a 1 in this column.

C. PCR Primers: Primers and probes for real-time PCR assays for each gene are given along with their SEQ ID #s. Each gene has 1 or 2 sets of a forward and reverse PCR primer and a hybridization probe for detection in TaqMan or similar assays.

D. PCR Data: Real-time PCR data was generated on a set of transplant samples using sybr green technology as described in the text. For each gene the number of samples (n) used in the analysis is given. An odds ratio and the p-values for a Fisher test and t-test are given for the comparison of acute rejection samples is given (see text).

E. Transplant proteins: For each gene, the corresponding protein in the RefSeq data base (Genbank Release 135, 18 April 2003) is given (RefSeq Peptide Accession #) along the the SEQ ID for that protein for the sequence listing.

Table 3: Viral gene for arrays. Viral genomes were used to design oligonucleotides for the microarrays. The accession numbers for the viral genomes used are given, along with the gene name and location of the region used for oligonucleotide design.

Table 4. Dependent variables for discovery of gene expression markers of cardiac allograft rejection. A stable Grade 0 is a Grade 0 biopsy in a patient who does not experience rejection with the subsequent biopsy. HG or highest grade means that the higher of the biopsy grades from the centralized and local pathologists was used for a definition of the dependent variable.

Table 5: Real-time PCR assay reporter and quencher dyes. Various combinations of reporter and quencher dyes are useful for real-time PCR assays. Reporter and quencher dyes work optimally in specific combinations defined by their spectra. For each reporter, appropriate choices for quencher dyes are given.

Table 6: Rejection marker PCR assay results

Results of real-time PCR assays are listed for the comparison of rejection samples to no rejection samples. The fold change is given for expression of each gene in rejection/no rejection samples. The p-value for the t-test comparing the rejection and no rejection classes is given.

Table 7: Summary results of array rejection significance analysis. Summary results are given for correlation analysis of leukocyte gene expression to acute rejection using significance analysis for microarrays (SAM). Five analyses are described. The ISHLT grades used to define the rejection and no rejection classes are given. In each case the highest grade from three pathology reading was taken for analysis. All samples are used for two analyses. The other analyses reduce redundancy of patients used in the analysis by using only one sample per patient ("Non-redundant") or using only one sample per patient within a given class ("Non-redundant within class"). The number of samples used in the analysis is given and the lowest false detection rate (FDR) achieved is noted.

Table 8: Renal tissue rejection array significance analysis. Genes are listed that were identified as upregulated using microarrays on renal tissue with acute rejection versus controls. Significance analysis for microarrays (SAM) was used to determine the false detection rate for each gene (FDR). Genes with known expression in leukocytes are noted in the table.

Table 9: Rejection marker sequence analysis. For 63 of the allograft rejection markers listed in Table 2, an analysis of the gene sequence was done. The genes and proteins are identified by accession numbers. The cellular localization of each gene is described as either secreted, nuclear, mitochondrial, cytoplasmic or cellular membrane. The function of the gene is also described.

Table 10: Gene expression markers for immature cells of a variety of lineages are given in Table 10 by way of example

Table 11: Changes in the rate of hematopoiesis have been correlated to a number of disease states and other pathologies. Examples of such conditions are listed in Table 11.

Table 12: This table lists the oligonucleotides and associated genes identified as having value for the diagnosis and monitoring of CMV infection. The first column gives the SEQ ID that corresponds to the oligonuclotide in the sequence listing. The unigene number, genebank accession and GI number are also given for each sequence when known. The name of the gene associated with the accession number is noted. The strand is noted as –1 or 1, meaning that the probe was designed from the complement of the sequence (-1) or directly from the sequence (1). Next, the nucleotide sequence of each probe is also given. For each gene, the false detection rate (FDR) from the significance analsysis described in

example 7 is given if applicable. WBC is the white blood cell count. WPT is the number of weeks past transplant.

Detailed Description of the Invention

Definitions

Unless defined otherwise, all scientific and technical terms are understood to have the same meaning as commonly used in the art to which they pertain. For the purpose of the present invention, the following terms are defined below.

In the context of the invention, the term "gene expression system" refers to any system, device or means to detect gene expression and includes diagnostic agents, candidate libraries, oligonucleotide sets or probe sets.

The term "monitoring" is used herein to describe the use of gene sets to provide useful information about an individual or an individual's health or disease status. "Monitoring" can include, determination of prognosis, risk-stratification, selection of drug therapy, assessment of ongoing drug therapy, prediction of outcomes, determining response to therapy, diagnosis of a disease or disease complication, following progression of a disease or providing any information relating to a patients health status over time, selecting patients most likely to benefit from experimental therapies with known molecular mechanisms of action, selecting patients most likely to benefit from approved drugs with known molecular mechanisms where that mechanism may be important in a small subset of a disease for which the medication may not have a label, screening a patient population to help decide on a more invasive/expensive test, for example a cascade of tests from a non-invasive blood test to a more invasive option such as biopsy, or testing to assess side effects of drugs used to treat another indication..

The term "diagnostic oligonucleotide set" generally refers to a set of two or more oligonucleotides that, when evaluated for differential expression of their products, collectively yields predictive data. Such predictive data typically relates to diagnosis, prognosis, monitoring of therapeutic outcomes, and the like. In general, the components of a diagnostic oligonucleotide set are distinguished from nucleotide sequences that are evaluated by analysis of the DNA to directly determine the genotype of an individual as it correlates with a specified trait or phenotype, such as a disease, in that it is the pattern of expression of the components of the diagnostic nucleotide set, rather than mutation or polymorphism of the DNA sequence that provides predictive value. It will be understood that a particular component (or member) of a diagnostic nucleotide set can, in some cases, also present one or more mutations, or polymorphisms that are amenable to direct genotyping by any of a variety of well known analysis methods, e.g., Southern blotting, RFLP, AFLP, SSCP, SNP, and the like.

A "disease specific target oligonucleotide sequence" is a gene or other oligonucleotide that encodes a polypeptide, most typically a protein, or a subunit of a multi-subunit protein, that is a therapeutic target for a disease, or group of diseases.

A "candidate library" or a "candidate oligonucleotide library" refers to a collection of oligonucleotide sequences (or gene sequences) that by one or more criteria have an increased probability of being associated with a particular disease or group of diseases. The criteria can be, for

example, a differential expression pattern in a disease state or in activated or resting leukocytes in vitro as reported in the scientific or technical literature, tissue specific expression as reported in a sequence database, differential expression in a tissue or cell type of interest, or the like. Typically, a candidate library has at least 2 members or components; more typically, the library has in excess of about 10, or about 100, or about 1000, or even more, members or components.

The term "disease criterion" is used herein to designate an indicator of a disease, such as a diagnostic factor, a prognostic factor, a factor indicated by a medical or family history, a genetic factor, or a symptom, as well as an overt or confirmed diagnosis of a disease associated with several indicators such as those selected from the above list. A disease criterian includes data describing a patient's health status, including retrospective or prospective health data, e.g. in the form of the patient's medical history, laboratory test results, diagnostic test result, clinical events, medications, lists, response(s) to treatment and risk factors, etc.

The terms "molecular signature" or "expression profile" refers to the collection of expression values for a plurality (e.g., at least 2, but frequently about 10, about 100, about 1000, or more) of members of a candidate library. In many cases, the molecular signature represents the expression pattern for all of the nucleotide sequences in a library or array of candidate or diagnostic nucleotide sequences or genes. Alternatively, the molecular signature represents the expression pattern for one or more subsets of the candidate library. The term "oligonucleotide" refers to two or more nucleotides. Nucleotides may be DNA or RNA, naturally occurring or synthetic.

The term "healthy individual," as used herein, is relative to a specified disease or disease criterion. That is, the individual does not exhibit the specified disease criterion or is not diagnosed with the specified disease. It will be understood, that the individual in question, can, of course, exhibit symptoms, or possess various indicator factors for another disease.

Similarly, an "individual diagnosed with a disease" refers to an individual diagnosed with a specified disease (or disease criterion). Such an individual may, or may not, also exhibit a disease criterion associated with, or be diagnosed with another (related or unrelated) disease.

An "array" is a spatially or logically organized collection, e.g., of oligonucleotide sequences or nucleotide sequence products such as RNA or proteins encoded by an oligonucleotide sequence. In some embodiments, an array includes antibodies or other binding reagents specific for products of a candidate library.

When referring to a pattern of expression, a "qualitative" difference in gene expression refers to a difference that is not assigned a relative value. That is, such a difference is designated by an "all or nothing" valuation. Such an all or nothing variation can be, for example, expression above or below a threshold of detection (an on/off pattern of expression). Alternatively, a qualitative difference can refer to expression of different types of expression products, e.g., different alleles (e.g., a mutant or polymorphic allele), variants (including sequence variants as well as post-translationally modified variants), etc.

In contrast, a "quantitative" difference, when referring to a pattern of gene expression, refers to a difference in expression that can be assigned a value on a graduated scale, (e.g., a 0-5 or 1-10 scale, a + - +++ scale, a grade 1- grade 5 scale, or the like; it will be understood that the numbers

selected for illustration are entirely arbitrary and in no-way are meant to be interpreted to limit the invention).

Gene Expression Systems of the Invention

The invention is directed to a gene expression system having one or more DNA molecules wherein the one or more DNA molecules has a nucleotide sequence which detects expression of a gene corresponding to the oligonucleotides depicted in the Sequence Listing. In one format, the oligonucleotide detects expression of a gene that is differentially expressed in leukocytes. The gene expression system may be a candidate library, a diagnostic agent, a diagnostic oligonucleotide set or a diagnostic probe set. The DNA molecules may be genomic DNA, protein nucleic acid (PNA), cDNA or synthetic oligonucleotides. Following the procedures taught herein, one can identity sequences of interest for analyzing gene expression in leukocytes. Such sequences may be predictive of a disease state.

Diagnostic oligonucleotides of the invention

The invention relates to diagnostic nucleotide set(s) comprising members of the leukocyte candidate library listed in Table 2, Table 8, and in the Sequence Listing, for which a correlation exists between the health status of an individual, the individual's expression of RNA or protein products corresponding to the nucleotide sequence, and the diagnosis and prognosis of transplant rejection. In some instances, only one oligonucleotide is necessary for such detection. Members of a diagnostic oligonucleotide set may be identified by any means capable of detecting expression of RNA or protein products, including but not limited to differential expression screening, PCR, RT-PCR, SAGE analysis, high-throughput sequencing, microarrays, liquid or other arrays, protein-based methods (e.g., western blotting, proteomics, and other methods described herein), and data mining methods, as further described herein.

In one embodiment, a diagnostic oligonucleotide set comprises at least two oligonucleotide sequences listed in Table 2, Table 8, or the Sequence Listing which are differentially expressed in leukocytes in an individual with at least one disease criterion for at least one leukocyte-implicated disease relative to the expression in individual without the at least one disease criterion, wherein expression of the two or more nucleotide sequences is correlated with at least one disease criterion, as described below.

In another embodiment, a diagnostic nucleotide set comprises at least one oligonucleotide having an oligonucleotide sequence listed in Table 2, Table 8, or the Sequence Listing which is differentially expressed, and further wherein the differential expression/correlation has not previously been described. In some embodiments, the diagnostic nucleotide set is immobilized on an array.

In another embodiment, diagnostic nucleotides (or nucleotide sets) are related to the members of the leukocyte candidate library listed in Table 2, Table 8, or in the Sequence Listing, for which a correlation exists between the health status, diagnosis and prognosis of transplant rejection (or disease criterion) of an individual. The diagnostic nucleotides are partially or totally contained in (or derived from) full-length gene sequences (or predicted full-length gene sequences) for the members of the candidate library listed in Table 2, Table 8, and the sequence listing. In some cases, oligonucleotide sequences are designed from EST or Chromosomal sequences from a public database. In these cases

the full-length gene sequences may not be known. Full-length sequences in these cases can be predicted using gene prediction algorithms. Alternatively the full-length can be determined by cloning and sequencing the full-length gene or genes that contain the sequence of interest using standard molecular biology approaches described here. The same is true for oligonucleotides designed from our sequencing of cDNA libraries where the cDNA does not match any sequence in the public databases.

The diagnostic nucleotides may also be derived from other genes that are coexpressed with the correlated sequence or full-length gene. Genes may share expression patterns because they are regulated in the same molecular pathway. Because of the similarity of expression behavior genes are identified as surrogates in that they can substitute for a diagnostic gene in a diagnostic gene set. Example 4 demonstrates the discovery of surrogates from the data and the sequence listing identifies and gives the sequence for surrogates for cardiac diagnostic genes.

As used herein the term "gene cluster" or "cluster" refers to a group of genes related by expression pattern. In other words, a cluster of genes is a group of genes with similar regulation across different conditions, such as graft non-rejection verus graft rejection. The expression profile for each gene in a cluster should be correlated with the expression profile of at least one other gene in that cluster. Correlation may be evaluated using a variety of statistical methods. As used herein the term "surrogate" refers to a gene with an expression profile such that it can substitute for a diagnostic gene in a diagnostic assay. Such genes are often members of the same gene cluster as the diagnostic gene. For each member of a diagnostic gene set, a set of potential surrogates can be identified through identification of genes with similar expression patterns as described below.

Many statistical analyses produce a correlation coefficient to describe the relatedness between two gene expression patterns. Patterns may be considered correlated if the correlation coefficient is greater than or equal to 0.8. In preferred embodiments, the correlation coefficient should be greater than 0.85, 0.9 or 0.95. Other statistical methods produce a measure of mutual information to describe the relatedness between two gene expression patterns. Patterns may be considered correlated if the normalized mutual information value is greater than or equal to 0.7. In preferred embodiments, the normalized mutual information value should be greater than 0.8, 0.9 or 0.95. Patterns may also be considered similar if they cluster closely upon hierarchical clustering of gene expression data (Eisen et al. 1998). Similar patterns may be those genes that are among the 1, 2, 5, 10, 20, 50 or 100 nearest neighbors in a hierarchical clustering or have a similarity score (Eisen et al. 1998) of > 0.5, 0.7, 0.8, 0.9, 0.95 or 0.99. Similar patterns may also be identified as those genes found to be surrogates in a classification tree by CART (Breiman et al. 1994). Often, but not always, members of a gene cluster have similar biological functions in addition to similar gene expression patterns.

Correlated genes, clusters and surrogates are identified for the diagnostic genes of the invention. These surrogates may be used as diagnostic genes in an assay instead of, or in addition to, the diagnostic genes for which they are surrogates.

The invention also provides diagnostic probe sets. It is understood that a probe includes any reagent capable of specifically identifying a nucleotide sequence of the diagnostic nucleotide set, including but not limited to amplified DNA, amplified RNA, cDNA, synthetic oligonucleotide, partial

or full-length nucleic acid sequences. In addition, the probe may identify the protein product of a diagnostic nucleotide sequence, including, for example, antibodies and other affinity reagents.

It is also understood that each probe can correspond to one gene, or multiple probes can correspond to one gene, or both, or one probe can correspond to more than one gene.

Homologs and variants of the disclosed nucleic acid molecules may be used in the present invention. Homologs and variants of these nucleic acid molecules will possess a relatively high degree of sequence identity when aligned using standard methods. The sequences encompassed by the invention have at least 40-50, 50-60, 70-80, 80-85, 85-90, 90-95 or 95-100% sequence identity to the sequences disclosed herein.

It is understood that for expression profiling, variations in the disclosed sequences will still permit detection of gene expression. The degree of sequence identity required to detect gene expression varies depending on the length of the oligomer. For a 60 mer, 6-8 random mutations or 6-8 random deletions in a 60 mer do not affect gene expression detection. Hughes, TR, et al. "Expression profiling using microarrays fabricated by an ink-jet oligonucleotide synthesizer. Nature Biotechnology, 19:343-347(2001). As the length of the DNA sequence is increased, the number of mutations or deletions permitted while still allowing gene expression detection is increased.

As will be appreciated by those skilled in the art, the sequences of the present invention may contain sequencing errors. That is, there may be incorrect nucleotides, frameshifts, unknown nucleotides, or other types of sequencing errors in any of the sequences; however, the correct sequences will fall within the homology and stringency definitions herein.

The minimum length of an oligonucleotide probe necessary for specific hybridization in the human genome can be estimated using two approaches. The first method uses a statistical argument that the probe will be unique in the human genome by chance. Briefly, the number of independent perfect matches (Po) expected for an oligonucleotide of length L in a genome of complexity C can be calculated from the equation (Laird CD, Chromosoma 32:378 (1971):

$Po=(1/4)^{L} * 2C$

In the case of mammalian genomes, $2C = \sim 3.6 \times 10^{9}$, and an oligonucleotide of 14-15 nucleotides is expected to be represented only once in the genome. However, the distribution of nucleotides in the coding sequence of mammalian genomes is nonrandom (Lathe, R. J. Mol. Biol. 183:1 (1985) and longer oligonucleotides may be preferred in order to in increase the specificity of hybridization. In practical terms, this works out to probes that are 19-40 nucleotides long (Sambrook J et al., infra). The second method for estimating the length of a specific probe is to use a probe long enough to hybridize under the chosen conditions and use a computer to search for that sequence or close matches to the sequence in the human genome and choose a unique match. Probe sequences are chosen based on the desired hybridization properties as described in Chapter 11 of Sambrook et al, infra. The PRIMER3 program is useful for designing these probes (S. Rozen and H. Skaletsky 1996,1997; Primer3 code available at the web site located at genome.wi.mit.edu/genome_software/other/primer3.html). The sequences of these probes are then compared pair wise against a database of the human genome sequences using a program such as BLAST or MEGABLAST (Madden, T.L et al.(1996) Meth. Enzymol. 266:131-141). Since most of the

human genome is now contained in the database, the number of matches will be determined. Probe sequences are chosen that are unique to the desired target sequence.

In some embodiments, a diagnostic probe set is immobilized on an array. The array is optionally comprises one or more of: a chip array, a plate array, a bead array, a pin array, a membrane array, a solid surface array, a liquid array, an oligonucleotide array, a polynucleotide array or a cDNA array, a microtiter plate, a pin array, a bead array, a membrane or a chip.

In some embodiments, the leukocyte-implicated disease is selected from the diseases listed in Table 1. In other embodiments, In some embodiments, the disease is atherosclerosis or cardiac allograft rejection. In other embodiments, the disease is congestive heart failure, angina, and myocardial infarction.

In some embodiments, diagnostic nucleotides of the invention are used as a diagnostic gene set in combination with genes that are know to be associated with a disease state ("known markers"). The use of the diagnostic nucleotides in combination with the known markers can provide information that is not obtainable through the known markers alone. The known markers include those identified by the prior art listing provided.

Hematopoeisis

The present invention is also directed to methods of measurement of the rate of hematopoiesis using the diagnostic oligonucleotides of the invention and measurement of the rates of hematopoesis by any technique as a method for the monitoring and diagnosis of transplant rejection. Precursor and immature cells often have cell specific phenotypic markers. These are genes and/or proteins that expressed in a restricted manner in immature or precursor cells. This expression decreases with maturation. Gene expression markers for immature cells of a variety of lineages are given in Table 10 below by way of example.

Table 10:

Gene	Cell type
CD10	B-lymphoblasts
RAG1	B-lymphoblasts
RAG2	B-lymphoblasts
NF-E2	Platelets/Megakaryocyte/Erythroid
GATA-1	Platelets/Megakaryocyte
GP IIb	Platelets
pf4	Platelets
EPO-R	Erythroblast
Band 4.1	Erythrocyte
ALAS2	Erythroid specific heme biosynthesis
hemoglobin chains	Erythocyte
2,3-BPG mutase	Erythrocyte
CD16b	Neutrophil
LAP	Neutrophil
CD16	NK cells
CD159a	NK cells

By measuring the levels of these and other genes in peripheral blood samples, an assessment of the number and proportion of immature or precursor cells can be made. Of particular use is RNA quantification in erythrocytes and platelets. These cells are anucleated in their mature forms. During

development, platelets pinch off of a megakaryocyte and take a compliment of RNA without a nucleus. This RNA is quickly consumed by the platelet. Erythrocytes start as nucleated cells, but the nucleus extrudes toward the end of the maturation process. These cells have RNA which is rapidly consumed within the first 2 days of the cells 120 day life span.

For these anucleated cell types, gene expression markers must be specific only to the cell line (and not the immature form) to be useful as measures of cellular production rates. Genes specific to the lineage vs. other blood cell types will serve as markers of cellular production rates when measured on the RNA level. This is because RNA is specific to immature forms in these cases. For example, hemoglobin is specific to erythrocytes, but hemoglobin RNA is specific to newly produced erythrocytes. Therefore, if the rate of production of erythrocytes increases, so will the level of a lineage specific RNA (e.g., hemoglobin).

Hematopoietic growth factors and cytokines have incomplete lineage specificity. G-CSF is administered to patient with low granulocyte counts and the effect is a stimulation of all lineages (granulocytes, erythrocytes, platelets, etc...). Hemolytic anemia leads to increased production of multiple cell lineages although the only lineage in increased demand is the erythrocyte. Because of this lack of specificity of hematopoietic responses, erythrocyte and platelet production rates may serve as surrogates of increased production of lymphocyte lineages. Using RBCs and platelets production rates as surrogates for lymphocyte lineages may be useful because of the lack of a nucleus in these cells and the ease of measuring cellular production rates by simply measuring lineage specific RNA levels.

Hematopoieis rates can be measured using gene expression profiling of peripheral blood. RBC and platelet specific genes provide unique opportunity for this because of their lack of a nucleus and kinetics. New cells = new / much more RNA from these cell types in peripheral blood. Immature lymphocytes may be even more specific for immune activation and rejection. Cell specific markers of lymphocyte precursors were identified (aka lymphoblasts) see below. Granulocyte precursors and markers of megakaryocytes or premature forms of any blood cells may be useful in this regard.

Applications for measuring the rate of hematopoiesis

Changes in the rate of hematopoiesis have been correlated to a number of disease states and other pathologies. Examples of such conditions are listed in Table 11. One of skill in the art would be aware of other such conditions. In addition, one aspect of the present invention is the identification of the linkage between changes in the rate of hematopoiesis. The methods of the present invention directed to measuring the rates of hematopoiesis can therefore be applied to the diagnosis and monitoring of a number of disease states and other pathologies. In addition, these methods can be beneficial in determining appropriate therapies for patients.

Table: 11

Disorder / condition	Cell type	Cell production	Therapy
Anemia – Iron Deficiency	Erythrocyte	Decreased	Iron
Anemia – B12, Folate deficiency	Erythrocyte	Decreased	B12, Folate
Anemia – Aplastic	Erythrocyte	Decreased	Epogen, transfusion

Anemia – hemolytic	Erythrocyte	Increased	Immunosuppression, Splenectomy
Anemia – Renal failure	Erythrocyte	Decreased	Erythropoietin
Anemia – Chronic disease	Erythrocyte	Decreased	Treat underlying cause
Polycythemia rubra vera	Erythrocyte	Increased	
Idiophic Thrrombocytopenic purpura	Platelet	Increased	Immunosuppression, Splenectomy
Thrombotic Thrombocytopenic purpura	Platelet	Increased or decreased	Immunosuppression, plasmapheresis
Essential thrombocytosis	Platelet	Increased	
Leukemia	All lineages, variable	Increase, decreased or abnomal	Chemotherapy, BMT
Cytopenias due to immunosupression	All lineages, variable	Decreased	Epo, neupogen
Cytopenias due to Chemotherapy	All lineages, variable	Decreased	Epo, GCSF, GMCSF
GVHD	All lineages, variable	Decreased	Immunosuppression
Myelodysplasia	All lineages, variable	Decreased, increased or abnormal	Chemo?
Allograft rejection	Lymphocytes, All lineages	Increased	Immunosuppression
Autoimmune diseases (many)	Lymphocytes, All lineages	Increased	Immunosuppression

The methods of the present invention are also useful for monitoring treatment regimens of diseases or other pathologies which are correlated with changes in the rate of hematopoiesis. Furthermore, the methods may be used to monitor treatment with agents that affect the rate of hematopoiesis. One of skill in the art is aware of many such agents. The following agents are examples of such.

Erythropoietin is a growth factor that is used to treat a variety of anemias that are due to decreased red cell production. Monitoring of red cell production by gene expression or other means may improve dosing and provide a means for earlier assessment of response to therapy for this expensive drug.

Neupogen (G-CSF) is used for the treatment of low neutrophil counts (neutropenia) usually related to immunosuppression or chemotherapy. Monitoring neutrophil production by gene expression testing or another means may improve dosing, patient selection, and shorten duration of therapy.

Prednisone / Immunosuppression – One of most common side effects of immunosuppression is suppression of hematopoiesis. This may occur in any cell lineage. Gene expression monitoring or other measures of hematopoietic rates could be used to monitor regularly for cytopenias in a particular cell line and the information could be used to modify dosing, modify therapy or add a specific hematologic growth factor. Following cell counts themselves is less sensitive and results in the need for prolonged trials of therapies at a given dose before efficacy and toxicity can be assessed.

Monitoring of chemotherapeutic agents –Most chemotherapy agents suppress the bone marrow for some or all lineages. Gene expression testing or other means of assessing hematopoietic rates could be used to monitor regularly for cytopenias in a particular cell line and use information to modify dosing, modify therapy or add a specific hematologic growth factor.

General Molecular Biology References

In the context of the invention, nucleic acids and/or proteins are manipulated according to well known molecular biology techniques. Detailed protocols for numerous such procedures are described in, e.g., in Ausubel et al. Current Protocols in Molecular Biology (supplemented through 2000) John Wiley & Sons, New York ("Ausubel"); Sambrook et al. Molecular Cloning - A Laboratory Manual (2nd Ed.), Vol. 1-3, Cold Spring Harbor Laboratory, Cold Spring Harbor, New York, 1989 ("Sambrook"), and Berger and Kimmel Guide to Molecular Cloning Techniques, Methods in Enzymology volume 152 Academic Press, Inc., San Diego, CA ("Berger").

In addition to the above references, protocols for in vitro amplification techniques, such as the polymerase chain reaction (PCR), the ligase chain reaction (LCR), Q-replicase amplification, and other RNA polymerase mediated techniques (e.g., NASBA), useful e.g., for amplifying cDNA probes of the invention, are found in Mullis et al. (1987) U.S. Patent No. 4,683,202; PCR Protocols A Guide to Methods and Applications (Innis et al. eds) Academic Press Inc. San Diego, CA (1990) ("Innis"); Arnheim and Levinson (1990) C&EN 36; The Journal Of NIH Research (1991) 3:81; Kwoh et al. (1989) Proc Natl Acad Sci USA 86, 1173; Guatelli et al. (1990) Proc Natl Acad Sci USA 87:1874; Lomell et al. (1989) J Clin Chem 35:1826; Landegren et al. (1988) Science 241:1077; Van Brunt (1990) Biotechnology 8:291; Wu and Wallace (1989) Gene 4: 560; Barringer et al. (1990) Gene 89:117, and Sooknanan and Malek (1995) Biotechnology 13:563. Additional methods, useful for cloning nucleic acids in the context of the present invention, include Wallace et al. U.S. Pat. No. 5,426,039. Improved methods of amplifying large nucleic acids by PCR are summarized in Cheng et al. (1994) Nature 369:684 and the references therein.

Certain polynucleotides of the invention, e.g., oligonucleotides can be synthesized utilizing various solid-phase strategies involving mononucleotide- and/or trinucleotide-based phosphoramidite coupling chemistry. For example, nucleic acid sequences can be synthesized by the sequential addition of activated monomers and/or trimers to an elongating polynucleotide chain. See e.g., Caruthers, M.H. et al. (1992) Meth Enzymol 211:3.

In lieu of synthesizing the desired sequences, essentially any nucleic acid can be custom ordered from any of a variety of commercial sources, such as The Midland Certified Reagent Company, The Great American Gene Company ExpressGen, Inc., Operon Technologies, Inc. and many others.

Similarly, commercial sources for nucleic acid and protein microarrays are available, and include, e.g., Agilent Technologies, Palo Alto, CA Affymetrix, Santa Clara,CA ; and others.

One area of relevance to the present invention is hybridization of oligonucleotides. Those of skill in the art differentiate hybridization conditions based upon the stringency of hybridization. For example, highly stringent conditions could include hybridization to filter-bound DNA in 0.5 M $NaHPO_4$, 7% sodium dodecyl sulfate (SDS), 1 mM EDTA at 65° C, and washing in 0.1XSSC/0.1%

SDS at 68° C. (Ausubel F. M. et al., eds., 1989, Current Protocols in Molecular Biology, Vol. I, Green Publishing Associates, Inc., and John Wiley & sons, Inc., New York, at p. 2.10.3). Moderate stringency conditions could include, e.g., washing in 0.2XSSC/0.1% SDS at 42°C. (Ausubel et al., 1989, supra).

The invention also includes nucleic acid molecules, preferably DNA molecules, that hybridize to, and are therefore the complements of, the DNA sequences of the present invention. Such hybridization conditions may be highly stringent or less highly stringent, as described above. In instances wherein the nucleic acid molecules are deoxyoligonucleotides ("oligos"), highly stringent conditions may refer, e.g., to washing in 6xSSC/0.05% sodium pyrophosphate at 37°C. (for 14-base oligos), 48°C. (for 17-base oligos), 55°C. (for 20-base oligos), and 60°C. (for 23-base oligos). These nucleic acid molecules may act as target nucleotide sequence antisense molecules, useful, for example, in target nucleotide sequence regulation and/or as antisense primers in amplification reactions of target nucleotide sequence nucleic acid sequences. Further, such sequences may be used as part of ribozyme and/or triple helix sequences, also useful for target nucleotide sequence regulation. Still further, such molecules may be used as components of diagnostic methods whereby the presence of a disease-causing allele, may be detected.

Identification of diagnostic nucleotide sets

Candidate library

Libraries of candidates that are differentially expressed in leukocytes are substrates for the identification and evaluation of diagnostic oligonucleotide sets and disease specific target nucleotide sequences.

The term leukocyte is used generically to refer to any nucleated blood cell that is not a nucleated erythrocyte. More specifically, leukocytes can be subdivided into two broad classes. The first class includes granulocytes, including, most prevalently, neutrophils, as well as eosinophils and basophils at low frequency. The second class, the non-granular or mononuclear leukocytes, includes monocytes and lymphocytes (e.g., T cells and B cells). There is an extensive literature in the art implicating leukocytes, e.g., neutrophils, monocytes and lymphocytes in a wide variety of disease processes, including inflammatory and rheumatic diseases, neurodegenerative diseases (such as Alzheimer's dementia), cardiovascular disease, endocrine diseases, transplant rejection, malignancy and infectious diseases, and other diseases listed in Table 1. Mononuclear cells are involved in the chronic immune response, while granulocytes, which make up approximately 60% of the leukocytes, have a non-specific and stereotyped response to acute inflammatory stimuli and often have a life span of only 24 hours.

In addition to their widespread involvement and/or implication in numerous disease related processes, leukocytes are particularly attractive substrates for clinical and experimental evaluation for a variety of reasons. Most importantly, they are readily accessible at low cost from essentially every potential subject. Collection is minimally invasive and associated with little pain, disability or recovery time. Collection can be performed by minimally trained personnel (e.g., phlebotomists, medical technicians, etc.) in a variety of clinical and non-clinical settings without significant

technological expenditure. Additionally, leukocytes are renewable, and thus available at multiple time points for a single subject.

Assembly of an initial candidate library

The initial candidate library was assembled from a combination of "mining" publication and sequence databases and construction of a differential expression library. Candidate oligonucleotide sequences in the library may be represented by a full-length or partial nucleic acid sequence, deoxyribonucleic acid (DNA) sequence, cDNA sequence, RNA sequence, synthetic oligonucleotides, etc. The nucleic acid sequence can be at least 19 nucleotides in length, at least 25 nucleotides, at least 40 nucleotides, at least 100 nucleotides, or larger. Alternatively, the protein product of a candidate nucleotide sequence may be represented in a candidate library using standard methods, as further described below. In selecting and validatating diagnostic oligonucleotides, an initial library of 8,031 candidate oligonucleotide sequences using nucleic acid sequences of 50 nucleotides in length was constructed as described below.

Candidate nucleotide library of the invention

We identified members of an initial candidate nucleotide library that are differentially expressed in activated leukocytes and resting leukocytes. From that initial candidate nucleotide library, a pool of candidates was selected as listed in Table 2, Table 8, and the seuqnce listing. Accordingly, the invention provides the candidate leukocyte nucleotide library comprising the nucleotide sequences listed in Table 2, Table 8, and in the sequence listing. In another embodiment, the invention provides an candidate library comprising at least one nucleotide sequence listed in Tables 2 and 8 and the sequence listing. In another embodiment, the invention provides an candidate library comprising at least two nucleotide sequences listed in Tables 2 and 8 and the sequence listing. In another embodiment, the at least two nucleotide sequence are at least 19 nucleotides in length, at least 35 nucleotides, at least 40 nucleotides or at least 100 nucleotides. In some embodiments, the nucleotide sequences comprises deoxyribonucleic acid (DNA) sequence, ribonucleic acid (RNA) sequence, synthetic oligonucleotide sequence, or genomic DNA sequence. It is understood that the nucleotide sequences may each correspond to one gene, or that several nucleotide sequences may correspond to one gene, or both.

The invention also provides probes to the candidate nucleotide library. In one embodiment of the invention, the probes comprise at least two nucleotide sequences listed in Table 2, Table 8, or the sequence listing which are differentially expressed in leukocytes in an individual with a least one disease criterion for at least one leukocyte-related disease and in leukocytes in an individual without the at least one disease criterion, wherein expression of the two or more nucleotide sequences is correlated with at least one disease criterion. It is understood that a probe may detect either the RNA expression or protein product expression of the candidate nucleotide library. Alternatively, or in addition, a probe can detect a genotype associated with a candidate nucleotide sequence, as further described below. In another embodiment, the probes for the candidaten ucleotide library are immobilized on an array.

The candidate nucleotide library of the invention is useful in identifying diagnostic nucleotide sets of the invention and is itself a diagnostic nucleotide set of the invention, as described below. The candidate nucleotide sequences may be further characterized, and may be identified as a disease target

nucleotide sequence and/or a novel nucleotide sequence, as described below. The candidate nucleotide sequences may also be suitable for use as imaging reagents, as described below.

Detection of non-leukocyte expressed genes

When measuring gene expression levels in a blood sample, RNAs may be measured that are not derived from leukocytes. Examples are viral genes, free RNAs that have been released from damaged non-leukocyte cell types or RNA from circulating non-leukocyte cell types. For example, in the process of acute allograft rejection, tissue damage may result in release of allograft cells or RNAs derived from allograft cells into the circulation. In the case of cardiac allografts, such transcripts may be specific to muscle (myoglobin) or to cardiac muscle (Troponin I, Toponin T, CK-MB). Presence of cardiac specific mRNAs in peripheral blood may indicate ongoing or recent cardiac cellular damage (resulting from acute rejection). Therefore, such genes may be excellent diagnostic markers for allograft rejection.

Generation of Expression Patterns

RNA, DNA or protein sample procurement

Following identification or assembly of a library of differentially expressed candidate nucleotide sequences, leukocyte expression profiles corresponding to multiple members of the candidate library are obtained. Leukocyte samples from one or more subjects are obtained by standard methods. Most typically, these methods involve trans-cutaneous venous sampling of peripheral blood. While sampling of circulating leukocytes from whole blood from the peripheral vasculature is generally the simplest, least invasive, and lowest cost alternative, it will be appreciated that numerous alternative sampling procedures exist, and are favorably employed in some circumstances. No pertinent distinction exists, in fact, between leukocytes sampled from the peripheral vasculature, and those obtained, e.g., from a central line, from a central artery, or indeed from a cardiac catheter, or during a surgical procedure which accesses the central vasculature. In addition, other body fluids and tissues that are, at least in part, composed of leukocytes are also desirable leukocyte samples. For example, fluid samples obtained from the lung during bronchoscopy may be rich in leukocytes, and amenable to expression profiling in the context of the invention, e.g., for the diagnosis, prognosis, or monitoring of lung transplant rejection, inflammatory lung diseases or infectious lung disease. Fluid samples from other tissues, e.g., obtained by endoscopy of the colon, sinuses, esophagus, stomach, small bowel, pancreatic duct, biliary tree, bladder, ureter, vagina, cervix or uterus, etc., are also suitable. Samples may also be obtained other sources containing leukocytes, e.g., from urine, bile, cerebrospinal fluid, feces, gastric or intestinal secretions, semen, or solid organ or joint biopsies.

Most frequently, mixed populations of leukocytes, such as are found in whole blood are utilized in the methods of the present invention. A crude separation, e.g., of mixed leukocytes from red blood cells, and/or concentration, e.g., over a sucrose, percoll or ficoll gradient, or by other methods known in the art, can be employed to facilitate the recovery of RNA or protein expression products at sufficient concentrations, and to reduce non-specific background. In some instances, it can be desirable to purify sub-populations of leukocytes, and methods for doing so, such as density or affinity gradients, flow cytometry, fluorescence Activated Cell Sorting (FACS), immuno-magnetic separation, "panning," and the like, are described in the available literature and below.

Obtaining DNA, RNA and protein samples for expression profiling

Expression patterns can be evaluated at the level of DNA, or RNA or protein products. For example, a variety of techniques are available for the isolation of RNA from whole blood. Any technique that allows isolation of mRNA from cells (in the presence or absence of rRNA and tRNA) can be utilized. In brief, one method that allows reliable isolation of total RNA suitable for subsequent gene expression analysis, is described as follows. Peripheral blood (either venous or arterial) is drawn from a subject, into one or more sterile, endotoxin free, tubes containing an anticoagulant (e.g., EDTA, citrate, heparin, etc.). Typically, the sample is divided into at least two portions. One portion, e.g., of 5-8 ml of whole blood is frozen and stored for future analysis, e.g., of DNA or protein. A second portion, e.g., of approximately 8 ml whole blood is processed for isolation of total RNA by any of a variety of techniques as described in, e.g, Sambook, Ausubel, below, as well as U.S. Patent Numbers: 5,728,822 and 4,843,155.

Typically, a subject sample of mononuclear leukocytes obtained from about 8 ml of whole blood, a quantity readily available from an adult human subject under most circumstances, yields 5-20 μg of total RNA. This amount is ample, e.g., for labeling and hybridization to at least two probe arrays. Labeled probes for analysis of expression patterns of nucleotides of the candidate libraries are prepared from the subject's sample of RNA using standard methods. In many cases, cDNA is synthesized from total RNA using a polyT primer and labeled, e.g., radioactive or fluorescent, nucleotides. The resulting labeled cDNA is then hybridized to probes corresponding to members of the candidate nucleotide library, and expression data is obtained for each nucleotide sequence in the library. RNA isolated from subject samples (e.g., peripheral blood leukocytes, or leukocytes obtained from other biological fluids and samples) is next used for analysis of expression patterns of nucleotides of the candidate libraries.

In some cases, however, the amount of RNA that is extracted from the leukocyte sample is limiting, and amplification of the RNA is desirable. Amplification may be accomplished by increasing the efficiency of probe labeling, or by amplifying the RNA sample prior to labeling. It is appreciated that care must be taken to select an amplification procedure that does not introduce any bias (with respect to gene expression levels) during the amplification process.

Several methods are available that increase the signal from limiting amounts of RNA, e.g. use of the Clontech (Glass Fluorescent Labeling Kit) or Stratagene (Fairplay Microarray Labeling Kit), or the Micromax kit (New England Nuclear, Inc.). Alternatively, cDNA is synthesized from RNA using a T7- polyT primer, in the absence of label, and DNA dendrimers from Genisphere (3DNA Submicro) are hybridized to the poly T sequence on the primer, or to a different "capture sequence" which is complementary to a fluorescently labeled sequence. Each 3DNA molecule has 250 fluorescent molecules and therefore can strongly label each cDNA.

Alternatively, the RNA sample is amplified prior to labeling. For example, linear amplification may be performed, as described in U.S. Patent No. 6,132,997. A T7-polyT primer is used to generate the cDNA copy of the RNA. A second DNA strand is then made to complete the substrate for amplification. The T7 promoter incorporated into the primer is used by a T7 polymerase to produce numerous antisense copies of the original RNA. Fluorescent dye labeled nucleotides are

directly incorporated into the RNA. Alternatively, amino allyl labeled nucleotides are incorporated into the RNA, and then fluorescent dyes are chemically coupled to the amino allyl groups, as described in Hughes. Other exemplary methods for amplification are described below.

It is appreciated that the RNA isolated must contain RNA derived from leukocytes, but may also contain RNA from other cell types to a variable degree. Additionally, the isolated RNA may come from subsets of leukocytes, e.g. monocytes and/or T-lymphocytes, as described above. Such consideration of cell type used for the derivation of RNA depend on the method of expression profiling used. Subsets of leukocytes can be obtained by fluorescence activated cell sorting (FACS), microfluidics cell seperation systems or a variety of other methods. Cell sorting may be necessary for the discovery of diagnostic gene sets, for the implementation of gene sets as products or both. Cell sorting can be achieved with a variety of technologies (See Galbraith et al. 1999, Cantor et al. 1975, see also the technology of Guava Technologies, Hayward, CA).

DNA samples may be obtained for analysis of the presence of DNA mutations, single nucleotide polymorphisms (SNPs), or other polymorphisms. DNA is isolated using standard techniques, e.g. *Maniatus, supra*.

Expression of products of candidate nucleotides may also be assessed using proteomics. Protein(s) are detected in samples of patient serum or from leukocyte cellular protein. Serum is prepared by centrifugation of whole blood, using standard methods. Proteins present in the serum may have been produced from any of a variety of leukocytes and non-leukocyte cells, and include secreted proteins from leukocytes. Alternatively, leukocytes or a desired sub-population of leukocytes are prepared as described above. Cellular protein is prepared from leukocyte samples using methods well known in the art, e.g., Trizol (Invitrogen Life Technologies, cat # 15596108; Chomczynski, P. and Sacchi, N. (1987) Anal. Biochem. 162, 156; Simms, D., Cizdziel, P.E., and Chomczynski, P. (1993) Focus® 15, 99; Chomczynski, P., Bowers-Finn, R., and Sabatini, L. (1987) J. of NIH Res. 6, 83; Chomczynski, P. (1993) Bio/Techniques 15, 532; Bracete, A.M., Fox, D.K., and Simms, D. (1998) Focus 20, 82; Sewall, A. and McRae, S. (1998) Focus 20, 36; Anal Biochem 1984 Apr;138(1):141-3, A method for the quantitative recovery of protein in dilute solution in the presence of detergents and lipids; Wessel D, Flugge UI. (1984) Anal Biochem. 1984 Apr;138(1):141-143.

The assay itself may be a cell sorting assay in which cells are sorted and/or counted based on cell surface expression of a protein marker. (See Cantor et al. 1975, Galbraith et al. 1999)

Obtaining expression patterns

Expression patterns, or profiles, of a plurality of nucleotides corresponding to members of the candidate library are then evaluated in one or more samples of leukocytes. Typically, the leukocytes are derived from patient peripheral blood samples, although, as indicated above, many other sample sources are also suitable. These expression patterns constitute a set of relative or absolute expression values for a some number of RNAs or protein products corresponding to the plurality of nucleotide sequences evaluated, which is referred to herein as the subject's "expression profile" for those nucleotide sequences. While expression patterns for as few as one independent member of the candidate library can be obtained, it is generally preferable to obtain expression patterns corresponding to a larger number of nucleotide sequences, e.g., about 2, about 5, about 10, about 20, about 50, about

100, about 200, about 500, or about 1000, or more. The expression pattern for each differentially expressed component member of the library provides a finite specificity and sensitivity with respect to predictive value, e.g., for diagnosis, prognosis, monitoring, and the like.

Clinical Studies, Data and Patient Groups

For the purpose of discussion, the term subject, or subject sample of leukocytes, refers to an individual regardless of health and/or disease status. A subject can be a patient, a study participant, a control subject, a screening subject, or any other class of individual from whom a leukocyte sample is obtained and assessed in the context of the invention. Accordingly, a subject can be diagnosed with a disease, can present with one or more symptom of a disease, or a predisposing factor, such as a family (genetic) or medical history (medical) factor, for a disease, or the like. Alternatively, a subject can be healthy with respect to any of the aforementioned factors or criteria. It will be appreciated that the term "healthy" as used herein, is relative to a specified disease, or disease factor, or disease criterion, as the term "healthy" cannot be defined to correspond to any absolute evaluation or status. Thus, an individual defined as healthy with reference to any specified disease or disease criterion, can in fact be diagnosed with any other one or more disease, or exhibit any other one or more disease criterion.

Furthermore, while the discussion of the invention focuses, and is exemplified using human sequences and samples, the invention is equally applicable, through construction or selection of appropriate candidate libraries, to non-human animals, such as laboratory animals, e.g., mice, rats, guinea pigs, rabbits; domesticated livestock, e.g., cows, horses, goats, sheep, chicken, etc.; and companion animals, e.g., dogs, cats, etc.

Methods for obtaining expression data

Numerous methods for obtaining expression data are known, and any one or more of these techniques, singly or in combination, are suitable for determining expression profiles in the context of the present invention. For example, expression patterns can be evaluated by northern analysis, PCR, RT-PCR, Taq Man analysis, FRET detection, monitoring one or more molecular beacon, hybridization to an oligonucleotide array, hybridization to a cDNA array, hybridization to a polynucleotide array, hybridization to a liquid microarray, hybridization to a microelectric array, molecular beacons, cDNA sequencing, clone hybridization, cDNA fragment fingerprinting, serial analysis of gene expression (SAGE), subtractive hybridization, differential display and/or differential screening (*see*, e.g., Lockhart and Winzeler (2000) Nature 405:827-836, and references cited therein).

For example, specific PCR primers are designed to a member(s) of an candidate nucleotide library. cDNA is prepared from subject sample RNA by reverse transcription from a poly-dT oligonucleotide primer, and subjected to PCR. Double stranded cDNA may be prepared using primers suitable for reverse transcription of the PCR product, followed by amplification of the cDNA using in vitro transcription. The product of in vitro transcription is a sense-RNA corresponding to the original member(s) of the candidate library. PCR product may be also be evaluated in a number of ways known in the art, including real-time assessment using detection of labeled primers, e.g. TaqMan or molecular beacon probes. Technology platforms suitable for analysis of PCR products include the ABI 7700, 5700, or 7000 Sequence Detection Systems (Applied Biosystems, Foster City, CA), the MJ Research Opticon (MJ Research, Waltham, MA), the Roche Light Cycler (Roche Diagnositics, Indianapolis, IN),

the Stratagene MX4000 (Stratagene, La Jolla, CA), and the Bio-Rad iCycler (Bio-Rad Laboratories, Hercules, CA). Alternatively, molecular beacons are used to detect presence of a nucleic acid sequence in an unamplified RNA or cDNA sample, or following amplification of the sequence using any method, e.g. IVT (In Vitro transcription) or NASBA (nucleic acid sequence based amplification). Molecular beacons are designed with sequences complementary to member(s) of an candidate nucleotide library, and are linked to fluorescent labels. Each probe has a different fluorescent label with non-overlapping emission wavelengths. For example, expression of ten genes may be assessed using ten different sequence-specific molecular beacons.

Alternatively, or in addition, molecular beacons are used to assess expression of multiple nucleotide sequences at once. Molecular beacons with sequence complimentary to the members of a diagnostic nucleotide set are designed and linked to fluorescent labels. Each fluorescent label used must have a non-overlapping emission wavelength. For example, 10 nucleotide sequences can be assessed by hybridizing 10 sequence specific molecular beacons (each labeled with a different fluorescent molecule) to an amplified or un-amplified RNA or cDNA sample. Such an assay bypasses the need for sample labeling procedures.

Alternatively, or in addition bead arrays can be used to assess expression of multiple sequences at once. See, e.g, LabMAP 100, Luminex Corp, Austin, Texas). Alternatively, or in addition electric arrays are used to assess expression of multiple sequences, as exemplified by the e-Sensor technology of Motorola (Chicago, Ill.) or Nanochip technology of Nanogen (San Diego, CA.)

Of course, the particular method elected will be dependent on such factors as quantity of RNA recovered, practitioner preference, available reagents and equipment, detectors, and the like. Typically, however, the elected method(s) will be appropriate for processing the number of samples and probes of interest. Methods for high-throughput expression analysis are discussed below.

Alternatively, expression at the level of protein products of gene expression is performed. For example, protein expression, in a sample of leukocytes, can be evaluated by one or more method selected from among: western analysis, two-dimensional gel analysis, chromatographic separation, mass spectrometric detection, protein-fusion reporter constructs, colorimetric assays, binding to a protein array and characterization of polysomal mRNA. One particularly favorable approach involves binding of labeled protein expression products to an array of antibodies specific for members of the candidate library. Methods for producing and evaluating antibodies are widespread in the art, *see*, e.g., Coligan, *supra*; and Harlow and Lane (1989) Antibodies: A Laboratory Manual, Cold Spring Harbor Press, NY ("Harlow and Lane"). Additional details regarding a variety of immunological and immunoassay procedures adaptable to the present invention by selection of antibody reagents specific for the products of candidate nucleotide sequences can be found in, e.g., Stites and Terr (eds.)(1991) Basic and Clinical Immunology, 7th ed., and Paul, *supra*. Another approach uses systems for performing desorption spectrometry. Commercially available systems, e.g., from Ciphergen Biosystems, Inc. (Fremont, CA) are particularly well suited to quantitative analysis of protein expression. Indeed, Protein Chip® arrays (*see*, e.g., the web site ciphergen.com) used in desorption spectrometry approaches provide arrays for detection of protein expression. Alternatively, affinity reagents, e.g., antibodies, small molecules, etc.) are developed that recognize epitopes of the protein

product. Affinity assays are used in protein array assays, e.g. to detect the presence or absence of particular proteins. Alternatively, affinity reagents are used to detect expression using the methods described above. In the case of a protein that is expressed on the cell surface of leukocytes, labeled affinity reagents are bound to populations of leukocytes, and leukocytes expressing the protein are identified and counted using fluorescent activated cell sorting (FACS).

It is appreciated that the methods of expression evaluation discussed herein, although discussed in the context of discovery of diagnostic nucleotide sets, are equally applicable for expression evaluation when using diagnostic nucleotide sets for, e.g. diagnosis of diseases, as further discussed below.

High Throughput Expression Assays

A number of suitable high throughput formats exist for evaluating gene expression. Typically, the term high throughput refers to a format that performs at least about 100 assays, or at least about 500 assays, or at least about 1000 assays, or at least about 5000 assays, or at least about 10,000 assays, or more per day. When enumerating assays, either the number of samples or the number of candidate nucleotide sequences evaluated can be considered. For example, a northern analysis of, e.g., about 100 samples performed in a gridded array, e.g., a dot blot, using a single probe corresponding to an candidate nucleotide sequence can be considered a high throughput assay. More typically, however, such an assay is performed as a series of duplicate blots, each evaluated with a distinct probe corresponding to a different member of the candidate library. Alternatively, methods that simultaneously evaluate expression of about 100 or more candidate nucleotide sequences in one or more samples, or in multiple samples, are considered high throughput.

Numerous technological platforms for performing high throughput expression analysis are known. Generally, such methods involve a logical or physical array of either the subject samples, or the candidate library, or both. Common array formats include both liquid and solid phase arrays. For example, assays employing liquid phase arrays, e.g., for hybridization of nucleic acids, binding of antibodies or other receptors to ligand, etc., can be performed in multiwell, or microtiter, plates. Microtiter plates with 96, 384 or 1536 wells are widely available, and even higher numbers of wells, e.g, 3456 and 9600 can be used. In general, the choice of microtiter plates is determined by the methods and equipment, e.g., robotic handling and loading systems, used for sample preparation and analysis. Exemplary systems include, e.g., the ORCA™ system from Beckman-Coulter, Inc. (Fullerton, CA) and the Zymate systems from Zymark Corporation (Hopkinton, MA).

Alternatively, a variety of solid phase arrays can favorably be employed in to determine expression patterns in the context of the invention. Exemplary formats include membrane or filter arrays (e.g, nitrocellulose, nylon), pin arrays, and bead arrays (e.g., in a liquid "slurry"). Typically, probes corresponding to nucleic acid or protein reagents that specifically interact with (e.g., hybridize to or bind to) an expression product corresponding to a member of the candidate library are immobilized, for example by direct or indirect cross-linking, to the solid support. Essentially any solid support capable of withstanding the reagents and conditions necessary for performing the particular expression assay can be utilized. For example, functionalized glass, silicon, silicon dioxide, modified silicon, any of a variety of polymers, such as (poly)tetrafluoroethylene, (poly)vinylidenedifluoride,

polystyrene, polycarbonate, or combinations thereof can all serve as the substrate for a solid phase array.

In a preferred embodiment, the array is a "chip" composed, e.g., of one of the above specified materials. Polynucleotide probes, e.g., RNA or DNA, such as cDNA, synthetic oligonucleotides, and the like, or binding proteins such as antibodies, that specifically interact with expression products of individual components of the candidate library are affixed to the chip in a logically ordered manner, i.e., in an array. In addition, any molecule with a specific affinity for either the sense or anti-sense sequence of the marker nucleotide sequence (depending on the design of the sample labeling), can be fixed to the array surface without loss of specific affinity for the marker and can be obtained and produced for array production, for example, proteins that specifically recognize the specific nucleic acid sequence of the marker, ribozymes, peptide nucleic acids (PNA), or other chemicals or molecules with specific affinity.

Detailed discussion of methods for linking nucleic acids and proteins to a chip substrate, are found in, e.g., US Patent No. 5,143,854 "LARGE SCALE PHOTOLITHOGRAPHIC SOLID PHASE SYNTHESIS OF POLYPEPTIDES AND RECEPTOR BINDING SCREENING THEREOF" to Pirrung et al., issued, September 1, 1992; US Patent No. 5,837,832 "ARRAYS OF NUCLEIC ACID PROBES ON BIOLOGICAL CHIPS" to Chee et al., issued November 17, 1998; US Patent No. 6,087,112 "ARRAYS WITH MODIFIED OLIGONUCLEOTIDE AND POLYNUCLEOTIDE COMPOSITIONS" to Dale, issued July 11, 2000; US Patent No. 5,215,882 "METHOD OF IMMOBILIZING NUCLEIC ACID ON A SOLID SUBSTRATE FOR USE IN NUCLEIC ACID HYBRIDIZATION ASSAYS" to Bahl et al., issued June 1, 1993; US Patent No. 5,707,807 "MOLECULAR INDEXING FOR EXPRESSED GENE ANALYSIS" to Kato, issued January 13, 1998; US Patent No. 5,807,522 "METHODS FOR FABRICATING MICROARRAYS OF BIOLOGICAL SAMPLES" to Brown et al., issued September 15, 1998; US Patent No. 5,958,342 "JET DROPLET DEVICE" to Gamble et al., issued Sept. 28, 1999; US Patent 5,994,076 "METHODS OF ASSAYING DIFFERENTIAL EXPRESSION" to Chenchik et al., issued Nov. 30, 1999; US Patent No. 6,004,755 "QUANTITATIVE MICROARRAY HYBRIDIZATION ASSAYS" to Wang, issued Dec. 21, 1999; US Patent No. 6,048,695 "CHEMICALLY MODIFIED NUCLEIC ACIDS AND METHOD FOR COUPLING NUCLEIC ACIDS TO SOLID SUPPORT" to Bradley et al., issued April 11, 2000; US Patent No. 6,060,240 "METHODS FOR MEASURING RELATIVE AMOUNTS OF NUCLEIC ACIDS IN A COMPLEX MIXTURE AND RETRIEVAL OF SPECIFIC SEQUENCES THEREFROM" to Kamb et al., issued May 9, 2000; US Patent No. 6,090,556 "METHOD FOR QUANTITATIVELY DETERMINING THE EXPRESSION OF A GENE" to Kato, issued July 18, 2000; and US Patent 6,040,138 "EXPRESSION MONITORING BY HYBRIDIZATION TO HIGH DENSITY OLIGONUCLEOTIDE ARRAYS" to Lockhart et al., issued March 21, 2000 each of which are hereby incorporated by reference in their entirety.

For example, cDNA inserts corresponding to candidate nucleotide sequences, in a standard TA cloning vector are amplified by a polymerase chain reaction for approximately 30-40 cycles. The amplified PCR products are then arrayed onto a glass support by any of a variety of well known techniques, e.g., the VSLIPS™ technology described in US Patent No. 5,143,854. RNA, or cDNA

corresponding to RNA, isolated from a subject sample of leukocytes is labeled, e.g., with a fluorescent tag, and a solution containing the RNA (or cDNA) is incubated under conditions favorable for hybridization, with the "probe" chip. Following incubation, and washing to eliminate non-specific hybridization, the labeled nucleic acid bound to the chip is detected qualitatively or quantitatively, and the resulting expression profile for the corresponding candidate nucleotide sequences is recorded. It is appreciated that the probe used for diagnostic purposes may be identical to the probe used during diagnostic nucleotide sequence discovery and validation. Alternatively, the probe sequence may be different than the sequence used in diagnostic nucleotide sequence discovery and validation. Multiple cDNAs from a nucleotide sequence that are non-overlapping or partially overlapping may also be used.

In another approach, oligonucleotides corresponding to members of an candidate nucleotide library are synthesized and spotted onto an array. Alternatively, oligonucleotides are synthesized onto the array using methods known in the art, e.g. Hughes, et al. *supra*. The oligonucleotide is designed to be complementary to any portion of the candidate nucleotide sequence. In addition, in the context of expression analysis for, e.g. diagnostic use of diagnostic nucleotide sets, an oligonucleotide can be designed to exhibit particular hybridization characteristics, or to exhibit a particular specificity and/or sensitivity, as further described below.

Hybridization signal may be amplified using methods known in the art, and as described herein, for example use of the Clontech kit (Glass Fluorescent Labeling Kit), Stratagene kit (Fairplay Microarray Labeling Kit), the Micromax kit (New England Nuclear, Inc.), the Genisphere kit (3DNA Submicro), linear amplification, e.g. as described in U.S. Patent No. 6,132,997 or described in Hughes, TR, et al., Nature Biotechnology, 19:343-347 (2001) and/or Westin et al. Nat Biotech. 18:199-204.

Alternatively, fluorescently labeled cDNA are hybridized directly to the microarray using methods known in the art. For example, labeled cDNA are generated by reverse transcription using Cy3- and Cy5-conjugated deoxynucleotides, and the reaction products purified using standard methods. It is appreciated that the methods for signal amplification of expression data useful for identifying diagnostic nucleotide sets are also useful for amplification of expression data for diagnostic purposes.

Microarray expression may be detected by scanning the microarray with a variety of laser or CCD-based scanners, and extracting features with numerous software packages, for example, Imagene (Biodiscovery), Feature Extraction (Agilent), Scanalyze (Eisen, M. 1999. SCANALYZE User Manual; Stanford Univ., Stanford, CA. Ver 2.32.), GenePix (Axon Instruments).

In another approach, hybridization to microelectric arrays is performed, e.g. as described in Umek et al (2001) J Mol Diagn. 3:74-84. An affinity probe, e.g. DNA, is deposited on a metal surface. The metal surface underlying each probe is connected to a metal wire and electrical signal detection system. Unlabelled RNA or cDNA is hybridized to the array, or alternatively, RNA or cDNA sample is amplified before hybridization, e.g. by PCR. Specific hybridization of sample RNA or cDNA results in generation of an electrical signal, which is transmitted to a detector. See Westin (2000) Nat Biotech. 18:199-204 (describing anchored multiplex amplification of a microelectronic chip array); Edman (1997) NAR 25:4907-14; Vignali (2000) J Immunol Methods 243:243-55.

In another approach, a microfluidics chip is used for RNA sample preparation and analysis. This approach increases efficiency because sample preparation and analysis are streamlined. Briefly,

microfluidics may be used to sort specific leukocyte sub-populations prior to RNA preparation and analysis. Microfluidics chips are also useful for, e.g., RNA preparation, and reactions involving RNA (reverse transcription, RT-PCR). Briefly, a small volume of whole, anti-coagulated blood is loaded onto a microfluidics chip, for example chips available from Caliper (Mountain View, CA) or Nanogen (San Diego, CA.) A microfluidics chip may contain channels and reservoirs in which cells are moved and reactions are performed. Mechanical, electrical, magnetic, gravitational, centrifugal or other forces are used to move the cells and to expose them to reagents. For example, cells of whole blood are moved into a chamber containing hypotonic saline, which results in selective lysis of red blood cells after a 20-minute incubation. Next, the remaining cells (leukocytes) are moved into a wash chamber and finally, moved into a chamber containing a lysis buffer such as guanidine isothyocyanate. The leukocyte cell lysate is further processed for RNA isolation in the chip, or is then removed for further processing, for example, RNA extraction by standard methods. Alternatively, the microfluidics chip is a circular disk containing ficoll or another density reagent. The blood sample is injected into the center of the disc, the disc is rotated at a speed that generates a centrifugal force appropriate for density gradient separation of mononuclear cells, and the separated mononuclear cells are then harvested for further analysis or processing.

It is understood that the methods of expression evaluation, above, although discussed in the context of discovery of diagnostic nucleotide sets, are also applicable for expression evaluation when using diagnostic nucleotide sets for, e.g. diagnosis of diseases, as further discussed below.

Evaluation of expression patterns

Expression patterns can be evaluated by qualitative and/or quantitative measures. Certain of the above described techniques for evaluating gene expression (as RNA or protein products) yield data that are predominantly qualitative in nature. That is, the methods detect differences in expression that classify expression into distinct modes without providing significant information regarding quantitative aspects of expression. For example, a technique can be described as a qualitative technique if it detects the presence or absence of expression of an candidate nucleotide sequence, i.e., an on/off pattern of expression. Alternatively, a qualitative technique measures the presence (and/or absence) of different alleles, or variants, of a gene product.

In contrast, some methods provide data that characterizes expression in a quantitative manner. That is, the methods relate expression on a numerical scale, e.g., a scale of 0-5, a scale of 1-10, a scale of + - +++, from grade 1 to grade 5, a grade from a to z, or the like. It will be understood that the numerical, and symbolic examples provided are arbitrary, and that any graduated scale (or any symbolic representation of a graduated scale) can be employed in the context of the present invention to describe quantitative differences in nucleotide sequence expression. Typically, such methods yield information corresponding to a relative increase or decrease in expression.

Any method that yields either quantitative or qualitative expression data is suitable for evaluating expression of candidate nucleotide sequence in a subject sample of leukocytes. In some cases, e.g., when multiple methods are employed to determine expression patterns for a plurality of candidate nucleotide sequences, the recovered data, e.g., the expression profile, for the nucleotide sequences is a combination of quantitative and qualitative data.

In some applications, expression of the plurality of candidate nucleotide sequences is evaluated sequentially. This is typically the case for methods that can be characterized as low- to moderate-throughput. In contrast, as the throughput of the elected assay increases, expression for the plurality of candidate nucleotide sequences in a sample or multiple samples of leukocytes, is assayed simultaneously. Again, the methods (and throughput) are largely determined by the individual practitioner, although, typically, it is preferable to employ methods that permit rapid, e.g. automated or partially automated, preparation and detection, on a scale that is time-efficient and cost-effective.

It is understood that the preceding discussion, while directed at the assessment of expression of the members of candidate libraries, is also applies to the assessment of the expression of members of diagnostic nucleotide sets, as further discussed below.

Genotyping

In addition to, or in conjunction with the correlation of expression profiles and clinical data, it is often desirable to correlate expression patterns with the subject's genotype at one or more genetic loci. The selected loci can be, for example, chromosomal loci corresponding to one or more member of the candidate library, polymorphic alleles for marker loci, or alternative disease related loci (not contributing to the candidate library) known to be, or putatively associated with, a disease (or disease criterion). Indeed, it will be appreciated, that where a (polymorphic) allele at a locus is linked to a disease (or to a predisposition to a disease), the presence of the allele can itself be a disease criterion.

Numerous well known methods exist for evaluating the genotype of an individual, including southern analysis, restriction fragment length polymorphism (RFLP) analysis, polymerase chain reaction (PCR), amplification length polymorphism (AFLP) analysis, single stranded conformation polymorphism (SSCP) analysis, single nucleotide polymorphism (SNP) analysis (e.g., via PCR, Taqman or molecular beacons), among many other useful methods. Many such procedures are readily adaptable to high throughput and/or automated (or semi-automated) sample preparation and analysis methods. Most, can be performed on nucleic acid samples recovered via simple procedures from the same sample of leukocytes as yielded the material for expression profiling. Exemplary techniques are described in, e.g., Sambrook, and Ausubel, *supra*.

Identification of the diagnostic nucleotide sets of the invention

Identification of diagnostic nucleotide sets and disease specific target nucleotide sequence proceeds by correlating the leukocyte expression profiles with data regarding the subject's health status to produce a data set designated a "molecular signature." Examples of data regarding a patient's health status, also termed "disease criteria(ion)", is described below and in the Section titled "selected diseases," below. Methods useful for correlation analysis are further described elsewhere in the specification.

Generally, relevant data regarding the subject's health status includes retrospective or prospective health data, e.g., in the form of the subject's medical history, as provided by the subject, physician or third party, such as, medical diagnoses, laboratory test results, diagnostic test results, clinical events, or medication lists, as further described below. Such data may include information regarding a patient's response to treatment and/or a particular medication and data regarding the presence of previously characterized "risk factors." For example, cigarette smoking and obesity are

previously identified risk factors for heart disease. Further examples of health status information, including diseases and disease criteria, is described in the section titled Selected diseases, below.

Typically, the data describes prior events and evaluations (i.e., retrospective data). However, it is envisioned that data collected subsequent to the sampling (i.e., prospective data) can also be correlated with the expression profile. The tissue sampled, e.g., peripheral blood, bronchial lavage, etc., can be obtained at one or more multiple time points and subject data is considered retrospective or prospective with respect to the time of sample procurement.

Data collected at multiple time points, called "longitudinal data", is often useful, and thus, the invention encompasses the analysis of patient data collected from the same patient at different time points. Analysis of paired samples, such as samples from a patient at different time, allows identification of differences that are specifically related to the disease state since the genetic variability specific to the patient is controlled for by the comparison. Additionally, other variables that exist between patients may be controlled for in this way, for example, the presence or absence of inflammatory diseases (e.g., rheumatoid arthritis) the use of medications that may effect leukocyte gene expression, the presence or absence of co-morbid conditions, etc. Methods for analysis of paired samples are further described below. Moreover, the analysis of a pattern of expression profiles (generated by collecting multiple expression profiles) provides information relating to changes in expression level over time, and may permit the determination of a rate of change, a trajectory, or an expression curve. Two longitudinal samples may provide information on the change in expression of a gene over time, while three longitudinal samples may be necessary to determine the "trajectory" of expression of a gene. Such information may be relevant to the diagnosis of a disease. For example, the expression of a gene may vary from individual to individual, but a clinical event, for example , a heart attack, may cause the level of expression to double in each patient. In this example, clinically interesting information is gleaned from the change in expression level, as opposed to the absolute level of expression in each individual.

When a single patient sample is obtained, it may still be desirable to compare the expression profile of that sample to some reference expression profile. In this case, one can determine the change of expression between the patient's sample and a reference expression profile that is appropriate for that patient and the medical condition in question. For example, a reference expression profile can be determined for all patients without the disease criterion in question who have similar characteristics, such as age, sex, race, diagnoses etc.

Generally, small sample sizes of 20-100 samples are used to identify a diagnostic nucleotide set. Larger sample sizes are generally necessary to validate the diagnostic nucleotide set for use in large and varied patient populations, as further described below. For example, extension of gene expression correlations to varied ethnic groups, demographic groups, nations, peoples or races may require expression correlation experiments on the population of interest.

Expression Reference Standards

Expression profiles derived from a patient (i.e., subjects diagnosed with, or exhibiting symptoms of, or exhibiting a disease criterion, or under a doctor's care for a disease) sample are compared to a control or standard expression RNA to facilitate comparison of expression profiles (e.g.

of a set of candidate nucleotide sequences) from a group of patients relative to each other (i.e., from one patient in the group to other patients in the group, or to patients in another group).

The reference RNA used should have desirable features of low cost and simplicity of production on a large scale. Additionally, the reference RNA should contain measurable amounts of as many of the genes of the candidate library as possible.

For example, in one approach to identifying diagnostic nucleotide sets, expression profiles derived from patient samples are compared to a expression reference "standard." Standard expression reference can be, for example, RNA derived from resting cultured leukocytes or commercially available reference RNA, such as Universal reference RNA from Stratagene. *See* Nature, V406, 8-17-00, p. 747-752. Use of an expression reference standard is particularly useful when the expression of large numbers of nucleotide sequences is assayed, e.g. in an array, and in certain other applications, e.g. qualitative PCR, RT-PCR, etc., where it is desirable to compare a sample profile to a standard profile, and/or when large numbers of expression profiles, e.g. a patient population, are to be compared. Generally, an expression reference standard should be available in large quantities, should be a good substrate for amplification and labeling reactions, and should be capable of detecting a large percentage of candidate nucleic acids using suitable expression profiling technology.

Alternatively, or in addition, the expression profile derived from a patient sample is compared with the expression of an internal reference control gene, for example, β-actin or CD4. The relative expression of the profiled genes and the internal reference control gene (from the same individual) is obtained. An internal reference control may also be used with a reference RNA. For example, an expression profile for "gene 1" and the gene encoding CD4 can be determined in a patient sample and in a reference RNA. The expression of each gene can be expressed as the "relative" ratio of expression the gene in the patient sample compared with expression of the gene in the reference RNA. The expression ratio (sample/reference) for gene 1 may be divided by the expression ration for CD4 (sample/reference) and thus the relative expression of gene 1 to CD4 is obtained.

The invention also provides a buffy coat control RNA useful for expression profiling, and a method of using control RNA produced from a population of buffy coat cells, the white blood cell layer derived from the centrifugation of whole blood. Buffy coat contains all white blood cells, including granulocytes, mononuclear cells and platelets. The invention also provides a method of preparing control RNA from buffy coat cells for use in expression profile analysis of leukocytes. Buffy coat fractions are obtained, e.g. from a blood bank or directly from individuals, preferably from a large number of individuals such that bias from individual samples is avoided and so that the RNA sample represents an average expression of a healthy population. Buffy coat fractions from about 50 or about 100, or more individuals are preferred. 10 ml buffy coat from each individual is used. Buffy coat samples are treated with an erthythrocyte lysis buffer, so that erthythrocytes are selectively removed. The leukocytes of the buffy coat layer are collected by centrifugation. Alternatively, the buffy cell sample can be further enriched for a particular leukocyte sub-populations, e.g. mononuclear cells, T-lymphocytes, etc. To enrich for mononuclear cells, the buffy cell pellet, above, is diluted in PBS (phosphate buffered saline) and loaded onto a non-polystyrene tube containing a polysucrose and sodium diatrizoate solution adjusted to a density of 1.077+/-0.001 g/ml. To enrich for T-lymphocytes,

45 ml of whole blood is treated with RosetteSep (Stem Cell Technologies), and incubated at room temperature for 20 minutes. The mixture is diluted with an equal volume of PBS plus 2% FBS and mixed by inversion. 30 ml of diluted mixture is layered on top of 15 ml DML medium (Stem Cell Technologies). The tube is centrifuged at 1200 x g, and the enriched cell layer at the plasma : medium interface is removed, washed with PBS + 2% FBS, and cells collected by centrifugation at 1200 x g. The cell pellet is treated with 5 ml of erythrocyte lysis buffer (EL buffer, Qiagen) for 10 minutes on ice, and enriched T-lymphoctes are collected by centrifugation.

In addition or alternatively, the buffy cells (whole buffy coat or sub-population, e.g. mononuclear fraction) can be cultured *in vitro* and subjected to stimulation with cytokines or activating chemicals such as phorbol esters or ionomycin. Such stimuli may increase expression of nucleotide sequences that are expressed in activated immune cells and might be of interest for leukocyte expression profiling experiments.

Following sub-population selection and/or further treatment, e.g. stimulation as described above, RNA is prepared using standard methods. For example, cells are pelleted and lysed with a phenol/guanidinium thiocyanate and RNA is prepared. RNA can also be isolated using a silica gel-based purification column or the column method can be used on RNA isolated by the phenol/guanidinium thiocyanate method. RNA from individual buffy coat samples can be pooled during this process, so that the resulting reference RNA represents the RNA of many individuals and individual bias is minimized or eliminated. In addition, a new batch of buffy coat reference RNA can be directly compared to the last batch to ensure similar expression pattern from one batch to another, using methods of collecting and comparing expression profiles described above/below. One or more expression reference controls are used in an experiment. For example, RNA derived from one or more of the following sources can be used as controls for an experiment: stimulated or unstimulated whole buffy coat, stimulated or unstimulated peripheral mononuclear cells, or stimulated or unstimulated T-lymphocytes.

Alternatively, the expression reference standard can be derived from any subject or class of subjects including healthy subjects or subjects diagnosed with the same or a different disease or disease criterion. Expression profiles from subjects in two distinct classes are compared to determine which subset of nucleotide sequences in the candidate library best distinguish between the two subject classes, as further discussed below. It will be appreciated that in the present context, the term "distinct classes" is relevant to at least one distinguishable criterion relevant to a disease of interest, a "disease criterion." The classes can, of course, demonstrate significant overlap (or identity) with respect to other disease criteria, or with respect to disease diagnoses, prognoses, or the like. The mode of discovery involves, e.g., comparing the molecular signature of different subject classes to each other (such as patient to control, patients with a first diagnosis to patients with a second diagnosis, etc.) or by comparing the molecular signatures of a single individual taken at different time points. The invention can be applied to a broad range of diseases, disease criteria, conditions and other clinical and/or epidemiological questions, as further discussed above/below.

It is appreciated that while the present discussion pertains to the use of expression reference controls while identifying diagnostic nucleotide sets, expression reference controls are also useful

during use of diagnostic nucleotide sets, e.g. use of a diagnostic nucleotide set for diagnosis of a disease, as further described below.

Analysis of expression profiles

In order to facilitate ready access, e.g., for comparison, review, recovery, and/or modification, the molecular signatures/expression profiles are typically recorded in a database. Most typically, the database is a relational database accessible by a computational device, although other formats, e.g., manually accessible indexed files of expression profiles as photographs, analogue or digital imaging readouts, spreadsheets, etc. can be used. Further details regarding preferred embodiments are provided below. Regardless of whether the expression patterns initially recorded are analog or digital in nature and/or whether they represent quantitative or qualitative differences in expression, the expression patterns, expression profiles (collective expression patterns), and molecular signatures (correlated expression patterns) are stored digitally and accessed via a database. Typically, the database is compiled and maintained at a central facility, with access being available locally and/or remotely.

As additional samples are obtained, and their expression profiles determined and correlated with relevant subject data, the ensuing molecular signatures are likewise recorded in the database. However, rather than each subsequent addition being added in an essentially passive manner in which the data from one sample has little relation to data from a second (prior or subsequent) sample, the algorithms optionally additionally query additional samples against the existing database to further refine the association between a molecular signature and disease criterion. Furthermore, the data set comprising the one (or more) molecular signatures is optionally queried against an expanding set of additional or other disease criteria. The use of the database in integrated systems and web embodiments is further described below.

Analysis of expression profile data from arrays

Expression data is analyzed using methods well known in the art, including the software packages Imagene (Biodiscovery, Marina del Rey, CA), Feature Extraction Software (Agilent, Palo Alto, CA), and Scanalyze (Stanford University). In the discussion that follows, a "feature" refers to an individual spot of DNA on an array. Each gene may be represented by more than one feature. For example, hybridized microarrays are scanned and analyzed on an Axon Instruments scanner using GenePix 3.0 software (Axon Instruments, Union City, CA). The data extracted by GenePix is used for all downstream quality control and expression evaluation. The data is derived as follows. The data for all features flagged as "not found" by the software is removed from the dataset for individual hybridizations. The "not found" flag by GenePix indicates that the software was unable to discriminate the feature from the background. Each feature is examined to determine the value of its signal. The median pixel intensity of the background (B_n) is subtracted from the median pixel intensity of the feature (F_n) to produce the background-subtracted signal (hereinafter, "BGSS"). The BGSS is divided by the standard deviation of the background pixels to provide the signal-to-noise ratio (hereinafter, "S/N"). Features with a S/N of three or greater in both the Cy3 channel (corresponding to the sample RNA) and Cy5 channel (corresponding to the reference RNA) are used for further analysis (hereinafter denoted "useable features"). Alternatively, different S/Ns are used for selecting expression data for an analysis. For example, only expression data with signal to noise ratios > 3 might be used in an

analysis. Alternatively, features with S/N values < 3 may be flagged as such and included in the analysis. Such flagged data sets include more values and may allow one to discover expression markers that would be missed otherwise. However, such data sets may have a higher variablilty than filtered data, which may decrease significance of findings or performance of correlation statistics.

For each usable feature (i), the expression level (e) is expressed as the logarithm of the ratio (R) of the Background Subtracted Signal (hereinafter "BGSS") for the Cy3 (sample RNA) channel divided by the BGSS for the Cy5 channel (reference RNA). This "log ratio" value is used for comparison to other experiments.

$$R_i = \frac{BGSS_{sample}}{BGSS_{reference}} \tag{0.1}$$

$$e_i = \log r_i \tag{0.2}$$

Variation in signal across hybridizations may be caused by a number of factors affecting hybridization, DNA spotting, wash conditions, and labeling efficiency.

A single reference RNA may be used with all of the experimental RNAs, permitting multiple comparisons in addition to individual comparisons. By comparing sample RNAs to the same reference, the gene expression levels from each sample are compared across arrays, permitting the use of a consistent denominator for our experimental ratios.

Alternative methods of analyzing the data may involve 1) using the sample channel without normalization by the reference channel, 2) using an intensity-dependent normalization based on the reference which provides a greater correction when the signal in the reference channel is large, 3) using the data without background subtraction or subtracting an empirically derived function of the background intensity rather than the background itself.

Scaling

The data may be scaled (normalized) to control for labeling and hybridization variability within the experiment, using methods known in the art. Scaling is desirable because it facilitates the comparison of data between different experiments, patients, etc. Generally the BGSS are scaled to a factor such as the median, the mean, the trimmed mean, and percentile. Additional methods of scaling include: to scale between 0 and 1, to subtract the mean, or to subtract the median.

Scaling is also performed by comparison to expression patterns obtained using a common reference RNA, as described in greater detail above. As with other scaling methods, the reference RNA facilitates multiple comparisons of the expression data, e.g., between patients, between samples, etc. Use of a reference RNA provides a consistent denominator for experimental ratios.

In addition to the use of a reference RNA, individual expression levels may be adjusted to correct for differences in labeling efficiency between different hybridization experiments, allowing direct comparison between experiments with different overall signal intensities, for example. A scaling factor (a) may be used to adjust individual expression levels as follows. The median of the scaling

factor (a), for example, BGSS, is determined for the set of all features with a S/N greater than three. Next, the $BGSS_i$ (the BGSS for each feature "i") is divided by the median for all features (a), generating a scaled ratio. The scaled ration is used to determine the expression value for the feature (e_i), or the log ratio.

$$S_i = \frac{BGSS_i}{a} \tag{0.3}$$

$$e_i = \log\left(\frac{Cy3S_i}{Cy5S_i}\right) \tag{0.4}$$

In addition, or alternatively, control features are used to normalize the data for labeling and hybridization variability within the experiment. Control feature may be cDNA for genes from the plant, *Arabidopsis thaliana*, that are included when spotting the mini-array. Equal amounts of RNA complementary to control cDNAs are added to each of the samples before they were labeled. Using the signal from these control genes, a normalization constant (L) is determined according to the following formula:

$$L_j = \frac{\frac{\sum_{i=1}^{N} BGSS_{j,i}}{N}}{\frac{\sum_{j=1}^{K} \frac{\sum_{i=1}^{N} BGSS_{j,i}}{N}}{K}}$$

where $BGSS_i$ is the signal for a specific feature, N is the number of *A. thaliana* control features, K is the number of hybridizations, and L_j is the normalization constant for each individual hybridization.

Using the formula above, the mean for all control features of a particular hybridization and dye (e.g., Cy3) is calculated. The control feature means for all Cy3 hybridizations are averaged, and the control feature mean in one hybridization divided by the average of all hybridizations to generate a normalization constant for that particular Cy3 hybridization (L_j), which is used as a in equation (0.3). The same normalization steps may be performed for Cy3 and Cy5 values.

An alternative scaling method can also be used. The log of the ratio of Green/Red is determined for all features. The median log ratio value for all features is determined. The feature values are then scaled using the following formula: Log_Scaled_Feature_Ratio = Log_Feature_Ratio – Median_Log_Ratio.

Many additional methods for normalization exist and can be applied to the data. In one method, the average ratio of Cy3 BGSS / Cy5 BGSS is determined for all features on an array. This ratio is then scaled to some arbitrary number, such as 1 or some other number. The ratio for each probe is then multiplied by the scaling factor required to bring the average ratio to the chosen level. This is

performed for each array in an analysis. Alternatively, the ratios are normalized to the average ratio across all arrays in an analysis. Other methods of normalization include forcing the distribution of signal strengths of the various arrays into greater agreement by transforming them to match certain points (quartiles, or deciles, etc.) in a standard distribution, or in the most extreme case using the rank of the signal of each oligonucleotide relative to the other oligonucleotides on the array.

If multiple features are used per gene sequence or oligonucleotide, these repeats can be used to derive an average expression value for each gene. If some of the replicate features are of poor qualitay and don't meet requirements for analysis, the remaining features can be used to represent the gene or gene sequence.

Correlation analysis

Correlation analysis is performed to determine which array probes have expression behavior that best distinguishes or serves as markers for relevant groups of samples representing a particular clinical condition. Correlation analysis, or comparison among samples representing different disease criteria (e.g., clinical conditions), is performed using standard statistical methods. Numerous algorithms are useful for correlation analysis of expression data, and the selection of algorithms depends in part on the data analysis to be performed. For example, algorithms can be used to identify the single most informative gene with expression behavior that reliably classifies samples, or to identify all the genes useful to classify samples. Alternatively, algorithms can be applied that determine which set of 2 or more genes have collective expression behavior that accurately classifies samples. The use of multiple expression markers for diagnostics may overcome the variability in expression of a gene between individuals, or overcome the variability intrinsic to the assay. Multiple expression markers may include redundant markers (surrogates), in that two or more genes or probes may provide the same information with respect to diagnosis. This may occur, for example, when two or more genes or gene probes are coordinately expressed. For diagnostic application, it may be appropriate to utilize a gene and one or more of its surrogates in the assay. This redundancy may overcome failures (technical or biological) of a single marker to distinguish samples. Alternatively, one or more surrogates may have properties that make them more suitable for assay development, such as a higher baseline level of expression, better cell specificity, a higher fold change between sample groups or more specific sequence for the design of PCR primers or complimentary probes. It will be appreciated that while the discussion above pertains to the analysis of RNA expression profiles the discussion is equally applicable to the analysis of profiles of proteins or other molecular markers.

Prior to analysis, expression profile data may be formatted or prepared for analysis using methods known in the art. For example, often the log ratio of scaled expression data for every array probe is calculated using the following formula:

log (Cy 3 BGSS/ Cy5 BGSS), where Cy 3 signal corresponds to the expression of the gene in the clinical sample, and Cy5 signal corresponds to expression of the gene in the reference RNA.

Data may be further filtered depending on the specific analysis to be done as noted below. For example, filtering may be aimed at selecting only samples with expression above a certain level, or probes with variability above a certain level between sample sets.

The following non-limiting discussion consider several statistical methods known in the art. Briefly, the t-test and ANOVA are used to identify single genes with expression differences between or among populations, respectively. Multivariate methods are used to identify a set of two or more genes for which expression discriminates between two disease states more specifically than expression of any single gene.

t-test

The simplest measure of a difference between two groups is the Student's t test. See, e.g., Welsh et al. (2001) Proc Natl Acad Sci USA 98:1176-81 (demonstrating the use of an unpaired Student's t-test for the discovery of differential gene expression in ovarian cancer samples and control tissue samples). The t- test assumes equal variance and normally distributed data. This test identifies the probability that there is a difference in expression of a single gene between two groups of samples. The number of samples within each group that is required to achieve statistical significance is dependent upon the variation among the samples within each group. The standard formula for a t-test is:

$$t(e_i) = \frac{\bar{e}_{i,c} - \bar{e}_{i,t}}{\sqrt{(s^2_{i,c}/n_c) + (s^2_{i,t}/n_t)}}, \qquad (0.5)$$

where $\bar{e}_i$ is the difference between the mean expression level of gene i in groups c and t, $s_{i,c}$ is the variance of gene x in group c and $s_{i,t}$ is the variance of gene x in group t. n_c and n_t are the numbers of samples in groups c and t.

The combination of the t statistic and the degrees of freedom [$\min(n_t, n_c)$-1] provides a p value, the probability of rejecting the null hypothesis. A p-value of ≤0.01, signifying a 99 percent probability the mean expression levels are different between the two groups (a 1% chance that the mean expression levels are in fact not different and that the observed difference occurred by statistical chance), is often considered acceptable.

When performing tests on a large scale, for example, on a large dataset of about 8000 genes, a correction factor must be included to adjust for the number of individual tests being performed. The most common and simplest correction is the Bonferroni correction for multiple tests, which divides the p-value by the number of tests run. Using this test on an 8000 member dataset indicates that a p value of ≤0.00000125 is required to identify genes that are likely to be truly different between the two test conditions.

Significance analysis for microarrays (SAM)

Significance analysis for microarrays (SAM) (Tusher 2001) is a method through which genes with a correlation between their expression values and the response vector are statistically discovered and assigned a statistical significance. The ratio of false significant to significant genes is the False Discovery Rate (FDR). This means that for each threshold there are a set of genes which are called significant, and the FDR gives a confidence level for this claim. If a gene is called differentially

expressed between 2 classes by SAM, with a FDR of 5%, there is a 95% chance that the gene is actually differentially expressed between the classes. SAM takes intoaccount the variability and large number of variables of microarrays. SAM will identiy genes that are most globally differentially expressed between the classes. Thus, important genes for identifying and classifying outlier samples or patients may not be identified by SAM.

Non-Parametric Tests

Wilcoxon's signed ranks method is one example of a non-parametric test and is utilized for paired comparisons. See e.g., Sokal and Rohlf (1987) Introduction to Biostatistics 2nd edition, WH Freeman, New York. At least 6 pairs are necessary to apply this statistic. This test is useful for analysis of paired expression data (for example, a set of patients who have cardiac transplant biopsy on 2 occasions and have a grade 0 on one occasion and a grade 3A on another). The Fisher Exact Test with a threshold and the Mann-Whitney Test are other non-parametric tests that may be used.

ANOVA

Differences in gene expression across multiple related groups may be assessed using an Analysis of Variance (ANOVA), a method well known in the art (Michelson and Schofield, 1996).

Multivariate analysis

Many algorithms suitable for multivariate analysis are known in the art. Generally, a set of two or more genes for which expression discriminates between two disease states more specifically than expression of any single gene is identified by searching through the possible combinations of genes using a criterion for discrimination, for example the expression of gene X must increase from normal 300 percent, while the expression of genes Y and Z must decrease from normal by 75 percent. Ordinarily, the search starts with a single gene, then adds the next best fit at each step of the search. Alternatively, the search starts with all of the genes and genes that do not aid in the discrimination are eliminated step-wise.

Paired samples

Paired samples, or samples collected at different time-points from the same patient, are often useful, as described above. For example, use of paired samples permits the reduction of variation due to genetic variation among individuals. In addition, the use of paired samples has a statistical significance, in that data derived from paired samples can be calculated in a different manner that recognizes the reduced variability. For example, the formula for a t-test for paired samples is:

$$t(e_x) = \frac{\overline{D}_{ex}}{\sqrt{\frac{\sum D^2 - (\sum D)^2 / b}{b-1}}}, \qquad (0.5)$$

where D is the difference between each set of paired samples and b is the number of sample pairs. $\overline{D}$ is the mean of the differences between the members of the pairs. In this test, only the differences between the paired samples are considered, then grouped together (as opposed to taking all possible differences between groups, as would be the case with an ordinary t-test). Additional statistical tests useful with paired data, e.g., ANOVA and Wilcoxon's signed rank test, are discussed above.

Diagnostic classification

Once a discriminating set of genes is identified, the diagnostic classifier (a mathematical function that assigns samples to diagnostic categories based on expression data) is applied to unknown sample expression levels.

Methods that can be used for this analysis include the following non-limiting list:

CLEAVER is an algorithm used for classification of useful expression profile data. See Raychaudhuri et al. (2001) Trends Biotechnol 19:189-193. CLEAVER uses positive training samples (e.g., expression profiles from samples known to be derived from a particular patient or sample diagnostic category, disease or disease criteria), negative training samples (e.g., expression profiles from samples known not to be derived from a particular patient or sample diagnostic category, disease or disease criteria) and test samples (e.g., expression profiles obtained from a patient), and determines whether the test sample correlates with the particular disease or disease criteria, or does not correlate with a particular disease or disease criteria. CLEAVER also generates a list of the 20 most predictive genes for classification.

Artificial neural networks (hereinafter, "ANN") can be used to recognize patterns in complex data sets and can discover expression criteria that classify samples into more than 2 groups. The use of artificial neural networks for discovery of gene expression diagnostics for cancers using expression data generated by oligonucleotide expression microarrays is demonstrated by Khan et al. (2001) Nature Med. 7:673-9. Khan found that 96 genes provided 0% error rate in classification of the tumors. The most important of these genes for classification was then determined by measuring the sensitivity of the classification to a change in expression of each gene. Hierarchical clustering using the 96 genes results in correct grouping of the cancers into diagnostic categories.

Golub uses cDNA microarrays and a distinction calculation to identify genes with expression behavior that distinguishes myeloid and lymphoid leukemias. See Golub et al. (1999) Science 286:531-7. Self organizing maps were used for new class discovery. Cross validation was done with a "leave one out" analysis. 50 genes were identified as useful markers. This was reduced to as few as 10 genes with equivalent diagnostic accuracy.

Hierarchical and non-hierarchical clustering methods are also useful for identifying groups of genes that correlate with a subset of clinical samples such as with transplant rejection grade. Alizadeh used hierarchical clustering as the primary tool to distinguish different types of diffuse B-cell lymphomas based on gene expression profile data. See Alizadeh et al. (2000) Nature 403:503-11. Alizadeh used hierarchical clustering as the primary tool to distinguish different types of diffuse B-cell lymphomas based on gene expression profile data. A cDNA array carrying 17856 probes was used for these experiments, 96 samples were assessed on 128 arrays, and a set of 380 genes was identified as being useful for sample classification.

Perou demonstrates the use of hierarchical clustering for the molecular classification of breast tumor samples based on expression profile data. See Perou el al. (2000) Nature 406:747-52. In this work, a cDNA array carrying 8102 gene probes was used. 1753 of these genes were found to have high variation between breast tumors and were used for the analysis.

Hastie describes the use of gene shaving for discovery of expression markers. Hastie et al. (2000) Genome Biol. 1(2):RESEARCH 0003.1-0003.21. The gene shaving algorithm identifies sets of genes with similar or coherent expression patterns, but large variation across conditions (RNA samples, sample classes, patient classes). In this manner, genes with a tight expression pattern within a transplant rejection grade, but also with high variability across rejection grades are grouped together. The algorithm takes advantage of both characteristics in one grouping step. For example, gene shaving can identify useful marker genes with co-regulated expression. Sets of useful marker genes can be reduced to a smaller set, with each gene providing some non-redundant value in classification. This algorithm was used on the data set described in Alizadeh et al., supra, and the set of 380 informative gene markers was reduced to 234.

Supervised harvesting of expression trees (Hastie 2001) identifies genes or clusters that best distinguish one class from all the others on the data set. The method is used to identify the genes/clusters that can best separate one class versus all the others for datasets that include two or more classes or all classes from each other. This algorithm can be used for discovery or testing of a diagnostic gene set.

CART is a decision tree classification algorithm (Breiman 1984). From gene expression and or other data, CART can develop a decision tree for the classification of samples. Each node on the decision tree involves a query about the expression level of one or more genes or variables. Samples that are above the threshold go down one branch of the decision tree and samples that are not go down the other branch. See example 4 for further description of its use in classification analysis and examples of its usefulness in discovering and implementing a diagnostic gene set. CART identifies surrogates for each splitter (genes that are the next best substitute for a useful gene in classification.

Multiple Additive Regression Trees (Friedman, JH 1999, MART) is similar to CART in that it is a classification algorithm that builds decision trees to distinguish groups. MART builds numerous trees for any classification problem and the resulting model involves a combination of the multiple trees. MART can select variables as it build models and thus can be used on large data sets, such as those derived from an 8000 gene microarray. Because MART uses a combination of many trees and does not take too much information from any one tree, it resists over training. MART identifies a set of genes and an algorithm for their use as a classifier.

A Nearest Shrunken Centroids Classifier can be applied to microarray or other data sets by the methods described by Tibshirani et al. 2002. This algorithms also identified gene sets for classification and determines their 10 fold cross validation error rates for each class of samples. The algorithm determines the error rates for models of any size, from one gene to all genes in the set. The error rates for either or both sample classes can are minimized when a particular number of genes are used. When this gene number is determined, the algorithm associated with the selected genes can be identified and employed as a classifier on prospective sample.

Once a set of genes and expression criteria for those genes have been established for classification, cross validation is done. There are many approaches, including a 10 fold cross validation analysis in which 10% of the training samples are left out of the analysis and the classification algorithm is built with the remaining 90%. The 10% are then used as a test set for the

algorithm. The process is repeated 10 times with 10% of the samples being left out as a test set each time. Through this analysis, one can derive a cross validation error which helps estimate the robustness of the algorithm for use on prospective (test) samples.

Clinical data are gathered for every patient sample used for expression analysis. Clinical variables can be quantitative or non-quantitative. A clinical variable that is quantitiative can be used as a variable for significance or classification analysis. Non-quantitative clinical variables, such as the sex of the patient, can also be used in a significance analysis or classification analysis with some statistical tool. It is appreciated that the most useful diagnostic gene set for a condition may be optimal when considered along with one or more predictive clinical variables. Clinical data can also be used as supervising vectors for a correlation analysis. That is to say that the clinical data associated with each sample can be used to divide the samples into meaningful diagnostic categories for analysis. For example, samples can be divided into 2 or more groups based on the presence or absence of some diagnostic criterion (a). In addition, clinical data can be utilized to select patients for a correlation analysis or to exclude them based on some undesirable characteristic, such as an ongoing infection, a medicine or some other issue. Clincial data can also be used to assess the pre-test probability of an outcome. For example, patients who are female are much more likely to be diagnosed as having systemic lupus erythematosis than patients who are male.

Once a set of genes are identified that classify samples with acceptable accuracy. These genes are validated as a set using new samples that were not used to discover the gene set. These samples can be taken from frozen archieves from the discovery clinical study or can be taken from new patients prospectively. Validation using a "test set" of samples can be done using expression profiling of the gene set with microarrays or using real-time PCR for each gene on the test set samples. Alternatively, a different expression profiling technology can be used.

Immune Monitoring

Leukocyte gene expression can be used to monitor the immune system. Immune monitoring examines both the level of gene expression for a set of genes in a given cell type and for genes which are expressed in a cell type selective manner gene expression monitoring will also detect the presence or absence of new cell types, progenitor cells, differentiation of cells and the like. Gene expression patterns may be associated with activation or the resting state of cells of the immune system that are responsible for or responsive to a disease state. For example, in the process of transplant rejection, cells of the immune system are activated by the presence of the foreign tissue. Genes and gene sets that monitor and diagnose this process are providing a measure of the level and type of activation of the immune system. Genes and gene sets that are useful in monitoring the immune system may be useful for diagnosis and monitoring of all diseases that involve the immune system. Some examples are transplant rejection, rheumatoid arthritis, lupus, inflammatory bowel diseases, multiple sclerosis, HIV/AIDS, and viral, bacterial and fungal infection. All disorders and diseases disclosed herein are contemplated. Genes and gene sets that monitor immune activation are useful for monitoring response to immunosuppressive drug therapy, which is used to decrease immune activation. Genes are found to correlate with immune activation by correlation of expression patterns to the known presence of immune activation or quiescence in a sample as determined by some other test.

Selected Diseases

In principle, diagnostic nucleotide sets of the invention may be developed and applied to essentially any disease, or disease criterion, as long as at least one subset of nucleotide sequences is differentially expressed in samples derived from one or more individuals with a disease criteria or disease and one or more individuals without the disease criteria or disease, wherein the individual may be the same individual sampled at different points in time, or the individuals may be different individuals (or populations of individuals). For example, the subset of nucleotide sequences may be differentially expressed in the sampled tissues of subjects with the disease or disease criterion (e.g., a patient with a disease or disease criteria) as compared to subjects without the disease or disease criterion (e.g., patients without a disease (control patients)). Alternatively, or in addition, the subset of nucleotide sequence(s) may be differentially expressed in different samples taken from the same patient, e.g at different points in time, at different disease stages, before and after a treatment, in the presence or absence of a risk factor, etc.

Expression profiles corresponding to sets of nucleotide sequences that correlate not with a diagnosis, but rather with a particular aspect of a disease can also be used to identify the diagnostic nucleotide sets and disease specific target nucleotide sequences of the invention. For example, such an aspect, or disease criterion, can relate to a subject's medical or family history, e.g., childhood illness, cause of death of a parent or other relative, prior surgery or other intervention, medications, symptoms (including onset and/or duration of symptoms), etc. Alternatively, the disease criterion can relate to a diagnosis, e.g., hypertension, diabetes, atherosclerosis, or prognosis (e.g., prediction of future diagnoses, events or complications), e.g., acute myocardial infarction, restenosis following angioplasty, reperfusion injury, allograft rejection, rheumatoid arthritis or systemic lupus erythematosis disease activity or the like. In other cases, the disease criterion corresponds to a therapeutic outcome, e.g., transplant rejection, bypass surgery or response to a medication, restenosis after stent implantation, collateral vessel growth due to therapeutic angiogenesis therapy, decreased angina due to revascularization, resolution of symptoms associated with a myriad of therapies, and the like. Alternatively, the disease criteria corresponds with previously identified or classic risk factors and may correspond to prognosis or future disease diagnosis. As indicated above, a disease criterion can also correspond to genotype for one or more loci. Disease criteria (including patient data) may be collected (and compared) from the same patient at different points in time, from different patients, between patients with a disease (criterion) and patients respresenting a control population, etc. Longitudinal data, i.e., data collected at different time points from an individual (or group of individuals) may be used for comparisons of samples obtained from an individual (group of individuals) at different points in time, to permit identification of differences specifically related to the disease state, and to obtain information relating to the change in expression over time, including a rate of change or trajectory of expression over time. The usefulness of longitudinal data is further discussed in the section titled "Identification of diagnostic nucleotide sets of the invention".

It is further understood that diagnostic nucleotide sets may be developed for use in diagnosing conditions for which there is no present means of diagnosis. For example, in rheumatoid arthritis, joint destruction is often well under way before a patient experience symptoms of the condition. A

diagnostic nucleotide set may be developed that diagnoses rheumatic joint destruction at an earlier stage than would be possible using present means of diagnosis, which rely in part on the presentation of symptoms by a patient. Diagnostic nucleotide sets may also be developed to replace or augment current diagnostic procedures. For example, the use of a diagnostic nucleotide set to diagnose cardiac allograft rejection may replace the current diagnostic test, a graft biopsy.

It is understood that the following discussion of diseases is exemplary and non-limiting, and further that the general criteria discussed above, e.g. use of family medical history, are generally applicable to the specific diseases discussed below.

In addition to leukocytes, as described throughout, the general method is applicable to nucleotide sequences that are differentially expressed in any subject tissue or cell type, by the collection and assessment of samples of that tissue or cell type. However, in many cases, collection of such samples presents significant technical or medical problems given the current state of the art.

Organ transplant rejection and success

A frequent complication of organ transplantation is recognition of the transplanted organ as foreign by the immune system resulting in rejection. Diagnostic nucleotide sets can be identified and validated for monitoring organ transplant success, rejection and treatment. Medications currently exist that suppress the immune system, and thereby decrease the rate of and severity of rejection. However, these drugs also suppress the physiologic immune responses, leaving the patient susceptible to a wide variety of opportunistic infections and cancers. At present there is no easy, reliable way to diagnose transplant rejection. Organ biopsy is the preferred method, but this is expensive, painful and associated with significant risk and has inadequate sensitivity for focal rejection.

Diagnostic nucleotide sets of the present invention can be developed and validated for use as diagnostic tests for transplant rejection and success. It is appreciated that the methods of identifying diagnostic nucleotide sets are applicable to any organ transplant population. For example, diagnostic nucleotide sets are developed for cardiac allograft rejection and success.

In some cases, disease criteria correspond to acute stage rejection diagnosis based on organ biopsy and graded using the International Society for Heart and Lung Transplantation ("ISHLT") criteria. This grading system classifies endomyocardial biopsies on the histological level as Grade 0, 1A, 1B, 2, 3A, 3B, or 4. Grade 0 biopies have no evidence of rejection, while each successive grade has increased severity of leukocyte infiltration and/or damage to the graft myocardial cells. It is appreciated that there is variability in the Grading systems between medical centers and pathologists and between repeated readings of the same pathologist at different times. When using the biopsy grade as a disease criterion for leukocyte gene expression correlation analysis, it may be desirable to have a single pathologist read all biopsy slides or have multiple pathologists read all slides to determine the variablility in this disease criterion. It is also appreciated that cardiac biopsy, in part due to variability, is not 100% sensitive or 100% specific for diagnosing acute rejection. When using the cardiac biopsy grade as a disease criterion for the discovery of diagnostic gene sets, it may be desirable to divide patient samples into diagnostic categories based on the grades. Examples of such classes are those patients with: Grade 0 vs. Grades 1A-4, Grade 0 vs. Grades 1B-4, Grade 0 vs. Grades 2-4, Grade 0-1 vs. Grade 2-4, Grade 0-1 vs. Grade 3A-4, or Grade 0 vs. Grade 3A-4.

Other disease criteria correspond to the cardiac biopsy results and other criteria, such as the results of cardiac function testing by echocardiography, hemodynamics assessment by cardiac catheterization, CMV infection, weeks post transplant, medication regimen, demographics and/or results of other diagnostic tests.

Other disease criteria correspond to information from the patient's medical history and information regarding the organ donor. Alternatively, disease criteria include the presence or absence of cytomegalovirus (CMV) infection, Epstein-Barr virus (EBV) infection, allograft dysfunction measured by physiological tests of cardiac function (e.g., hemodynamic measurements from catheterization or echocardiograph data), and symptoms of other infections. Alternatively, disease criteria correspond to therapeutic outcome, e.g. graft failure, re-transplantation, death, hospitalization, need for intravenous immunosuppression, transplant vasculopathy, response to immunosuppressive medications, etc. Disease criteria may further correspond to a rejection episode of at least moderate histologic grade, which results in treatment of the patient with additional corticosteroids, anti-T cell antibodies, or total lymphoid irradiation; a rejection with histologic grade 2 or higher; a rejection with histologic grade <2; the absence of histologic rejection and normal or unchanged allograft function (based on hemodynamic measurements from catheterization or on echocardiographic data); the presence of severe allograft dysfunction or worsening allograft dysfunction during the study period (based on hemodynamic measurements from catheterization or on echocardiographic data).; documented CMV infection by culture, histology, or PCR, and at least one clinical sign or symptom of infection; specific graft biopsy rejection grades; rejection of mild to moderate histologic severity prompting augmentation of the patient's chronic immunosuppressive regimen; rejection of mild to moderate severity with allograft dysfunction prompting plasmaphoresis or a diagnosis of "humoral" rejection; infections other than CMV, especially infection with Epstein Barr virus (EBV); lymphoproliferative disorder (also called post-transplant lymphoma); transplant vasculopathy diagnosed by increased intimal thickness on intravascular ultrasound (IVUS), angiography, or acute myocardial infarction; graft failure or retransplantation; and all cause mortality. Further specific examples of clinical data useful as disease criteria are provided in Example 3.

In another example, diagnostic nucleotide sets are developed and validated for use in diagnosis and monitoring of kidney allograft recipients. Disease criteria correspond to, e.g., results of biopsy analysis for kidney allograft rejection, serum creatine level, creatinine clearance, radiological imaging results for the kidney and urinalysis results. Another disease criterion corresponds to the need for hemodialysis, retransplantation, death or other renal replacement therapy. Diagnostic nucleotide sets are developed and validated for use in diagnosis and treatment of bone marrow transplant and liver transplantation pateints, respectively. Disease criteria for bone marrow transplant correspond to the diagnosis and monitoring of graft rejection and/or graft versus host disease, the recurrence of cancer, complications due to immunosuppression, hematologic abnormalities, infection, hospitalization and/or death. Disease criteria for liver transplant rejection include levels of serum markers for liver damage and liver function such as AST (aspartate aminotransferase), ALT (alanine aminotransferase), Alkaline phosphatase, GGT, (gamma-glutamyl transpeptidase) Bilirubin, Albumin and Prothrombin time. Further disease criteria correspond to hepatic encephalopathy, medication usage, ascites, graft failure,

retransplantation, hospitalization, complications of immunosuppression, results of diagnostic tests, results of radiological testing, death and histological rejection on graft biopsy. In addition, urine can be utilized for at the target tissue for profiling in renal transplant, while biliary and intestinal secretions and feces may be used favorably for hepatic or intestinal organ allograft rejection. Diagnostic nuclotide sets can also be discovered and developed for the diagnosis and monitoring of chronic renal allograft rejection .

In the case of renal allografts, gene expression markers may be identified that are secreted proteins. These proteins may be detected in the urine of allograft recipients using standard immunoassays. Proteins are more likely to be present in the urine if they are of low molecular weight. Lower molecular weight proteins are more likely to pass through the glomerular membrane and into the urine.

In another example, diagnostic nucleotide sets are developed and validated for use in diagnosis and treatment of xenograft recipients. This can include the transplantation of any organ from a non-human animal to a human or between non-human animals. Considerations for discovery and application of diagnostics and therapeutics and for disease criterion are substantially similar to those for allograft transplantation between humans.

In another example, diagnostic nucleotide sets are developed and validated for use in diagnosis and treatment of artificial organ recipients. This includes, but is not limited to mechanical circulatory support, artificial hearts, left ventricular assist devices, renal replacement therapies, organ prostheses and the like. Disease criteria are thrombosis (blood clots), infection, death, hospitalization, and worsening measures of organ function (e.g., hemodynamics, creatinine, liver function testing, renal function testing, functional capacity).

In another example, diagnostic nucleotide sets are developed and validated for use in matching donor organs to appropriate recipients. Diagnostic gene set can be discovered that correlate with successful matching of donor organ to recipient. Disease criteria include graft failure, acute and chronic rejection, death, hospitalization, immunosuppressive drug use, and complications of immunosuppression. Gene sets may be assayed from the donor or recipient's peripheral blood, organ tissue or some other tissue.

In another example, diagnostic nucleotide sets are developed and validated for use in diagnosis and induction of patient immune tolerance (decrease rejection of an allograft by the host immune system). Disease criteria include rejection, assays of immune activation, need for immunosupression and all disease criteria noted above for transplantation of each organ.

Viral diseases

Diagnostic leukocyte nucleotide sets may be developed and validated for use in diagnosing viral disease, as well as diagnosing and monitoring transplant rejection. In another aspect, viral nucleotide sequences may be added to a leukocyte nucleotide set for use in diagnosis of viral diseases, as well as diagnosing and monitoring transplant rejection. Alternatively, viral nucleotide sets and leukocyte nucleotides sets may be used sequentially.

Epstein-Barr virus (EBV)

EBV causes a variety of diseases such as mononucleosis, B-cell lymphoma, and pharyngeal carcinoma. It infects mononuclear cells and circulating atypical lymphocytes are a common manifestation of infection. Peripheral leukocyte gene expression is altered by infection. Transplant recipients and patients who are immunosuppressed are at increased risk for EBV-associated lymphoma.

Diagnostic nucleotide sets may be developed and validated for use in diagnosis and monitoring of EBV, as well as diagnosing and monitoring transplant rejection. In one aspect, the diagnostic nucleotide set is a leukocyte nucleotide set. Alternatively, EBV nucleotide sequences are added to a leukocyte nucleotide set, for use in diagnosing EBV. Disease criteria correspond with diagnosis of EBV, and, in patients who are EBV-sero-positive, presence (or prospective occurrence) of EBV-related illnesses such as mononucleosis, and EBV-associated lymphoma. Diagnostic nucleotide sets are useful for diagnosis of EBV, and prediction of occurrence of EBV-related illnesses.

Cytomegalovirus (CMV)

Cytomegalovirus cause inflammation and disease in almost any tissue, particularly the colon, lung, bone marrow and retina, and is a very important cause of disease in immunosuppressed patients, e.g. transplant, cancer, AIDS. Many patients are infected with or have been exposed to CMV, but not all patients develop clinical disease from the virus. Also, CMV negative recipients of allografts that come from CMV positive donors are at high risk for CMV infection. As immunosuppressive drugs are developed and used, it is increasingly important to identify patients with current or impending clinical CMV disease, because the potential benefit of immunosuppressive therapy must be balanced with the increased rate of clinical CMV infection and disease that may result from the use of immunosuppression therapy. CMV may also play a role in the occurrence of atherosclerosis or restenosis after angioplasty. CMV expression also correlates to transplant rejection, and is useful in diagnosing and monitoring transplant rejection.

Diagnostic nucleotide sets are developed for use in diagnosis and monitoring of CMV infection or re-activation of CMV infection. In one aspect, the diagnostic nucleotide set is a leukocyte nucleotide set. In another aspect, CMV nucleotide sequences are added to a leukocyte nucleotide set, for use in diagnosing CMV. Disease criteria correspond to diagnosis of CMV (e.g., sero-positive state) and presence of clinically active CMV. Disease criteria may also correspond to prospective data, e.g. the likelihood that CMV will become clinically active or impending clinical CMV infection. Antiviral medications are available and diagnostic nucleotide sets can be used to select patients for early treatment, chronic suppression or prophylaxis of CMV activity.

Hepatitis B and C

These chronic viral infections affect about 1.25 and 2.7 million patients in the US, respectively. Many patients are infected, but suffer no clinical manifestations. Some patients with infection go on to suffer from chronic liver failure, cirrhosis and hepatic carcinoma.

Diagnostic nucleotide sets are developed for use in diagnosis and monitoring of HBV or HCV infection. In one aspect, the diagnostic nucleotide set is a leukocyte nucleotide set. In another aspect, viral nucleotide sequences are added to a leukocyte nucleotide set, for use in diagnosing the virus and monitoring progression of liver disease. Disease criteria correspond to diagnosis of the virus (e.g.,

sero-positive state or other disease symptoms). Alternatively, disease criteria correspond to liver damage, e.g., elevated alkaline phosphatase, ALT, AST or evidence of ongoing hepatic damage on liver biopsy. Alternatively, disease criteria correspond to serum liver tests (AST, ALT, Alkaline Phosphatase, GGT, PT, bilirubin), liver biopsy, liver ultrasound, viral load by serum PCR, cirrhosis, hepatic cancer, need for hospitalization or listing for liver transplant. Diagnostic nucleotide sets are used to diagnose HBV and HCV, and to predict likelihood of disease progression. Antiviral therapeutic usage, such as Interferon gamma and Ribavirin, can also be disease criteria.

HIV

HIV infects T cells and certainly causes alterations in leukocyte expression. Diagnostic nucleotide sets are developed for diagnosis and monitoring of HIV. In one aspect, the diagnostic nucleotide set is a leukocyte nucleotide set. In another aspect, viral nucleotide sequences are added to a leukocyte nucleotide set, for use in diagnosing the virus. Disease criteria correspond to diagnosis of the virus (e.g., sero-positive state). In addition, disease criteria correspond to viral load, CD4 T cell counts, opportunistic infection, response to antiretroviral therapy, progression to AIDS, rate of progression and the occurrence of other HIV related outcomes (e.g., malignancy, CNS disturbance). Response to antiretrovirals may also be disease criteria.

Pharmacogenomics

Pharmocogenomics is the study of the individual propensity to respond to a particular drug therapy (combination of therapies). In this context, response can mean whether a particular drug will work on a particular patient, e.g. some patients respond to one drug but not to another drug. Response can also refer to the likelihood of successful treatment or the assessment of progress in treatment. Titration of drug therapy to a particular patient is also included in this description, e.g. different patients can respond to different doses of a given medication. This aspect may be important when drugs with side-effects or interactions with other drug therapies are contemplated.

Diagnostic nucleotide sets are developed and validated for use in assessing whether a patient will respond to a particular therapy and/or monitoring response of a patient to drug therapy(therapies). Disease criteria correspond to presence or absence of clinical symptoms or clinical endpoints, presence of side-effects or interaction with other drug(s). The diagnostic nucleotide set may further comprise nucleotide sequences that are targets of drug treatment or markers of active disease.

Validation and accuracy of diagnostic nucleotide sets

Prior to widespread application of the diagnostic probe sets of the invention the predictive value of the probe set is validated. When the diagnostic probe set is discovered by microarray based expression analysis, the differential expression of the member genes may be validated by a less variable and more quantitive and accurate technology such as real time PCR. In this type of experiment the amplification product is measured during the PCR reaction. This enables the researcher to observe the amplification before any reagent becomes rate limiting for amplification. In kinetic PCR the measurement is of C_T (threshold cycle) or C_P (crossing point). This measurement (C_T=C_P) is the point at which an amplification curve crosses a threshold fluorescence value. The threshold is set to a point within the area where all of the reactions were in their linear phase of amplification. When measuring

C_T, a lower C_T value is indicative of a higher amount of starting material since an earlier cycle number means the threshold was crossed more quickly.

Several fluorescence methodologies are available to measure amplification product in real-time PCR. Taqman (Applied BioSystems, Foster City, CA) uses fluorescence resonance energy transfer (FRET) to inhibit signal from a probe until the probe is degraded by the sequence specific binding and Taq 3′ exonuclease activity. Molecular Beacons (Stratagene, La Jolla, CA) also use FRET technology, whereby the fluorescence is measured when a hairpin structure is relaxed by the specific probe binding to the amplified DNA. The third commonly used chemistry is Sybr Green, a DNA-binding dye (Molecular Probes, Eugene, OR). The more amplified product that is produced, the higher the signal. The Sybr Green method is sensitive to non-specific amplification products, increasing the importance of primer design and selection. Other detection chemistries can also been used, such as ethedium bromide or other DNA-binding dyes and many modifications of the fluorescent dye/quencher dye Taqman chemistry, for example scorpions.

Real-time PCR validation can be done as described in Example 12.

Typically, the oligonucleotide sequence of each probe is confirmed, e.g. by DNA sequencing using an oligonucleotide-specific primer. Partial sequence obtained is generally sufficient to confirm the identity of the oligonucleotide probe. Alternatively, a complementary polynucleotide is fluorescently labeled and hybridized to the array, or to a different array containing a resynthesized version of the oligo nucleotide probe, and detection of the correct probe is confirmed.

Typically, validation is performed by statistically evaluating the accuracy of the correspondence between the molecular signature for a diagnostic probe set and a selected indicator. For example, the expression differential for a nucleotide sequence between two subject classes can be expressed as a simple ratio of relative expression. The expression of the nucleotide sequence in subjects with selected indicator can be compared to the expression of that nucleotide sequence in subjects without the indicator, as described in the following equations.

$\sum E_x ai/N = E_x A$ the average expression of nucleotide sequence x in the members of group A;

$\sum E_x bi/M = E_x B$ the average expression of nucleotide sequence x in the members of group B;

$E_x A/ ExB = \Delta E_x AB$ the average differential expression of nucleotide sequence x between groups A and B:

where $\sum$ indicates a sum; Ex is the expression of nucleotide sequence x relative to a standard; ai are the individual members of group A, group A has N members; bi are the individual members of group B, group B has M members.

The expression of at least two nucleotide sequences, e.g., nucleotide sequence X and nucleotide sequence Y are measured relative to a standard in at least one subject of group A (e.g., with a disease) and group B (e.g., without the disease). Ideally, for purposes of validation the indicator is independent from (i.e., not assigned based upon) the expression pattern. Alternatively, a minimum threshold of gene expression for nucleotide sequences X and Y, relative to the standard, are designated for assignment to group A. For nucleotide sequence x, this threshold is designated ΔEx, and for nucleotide sequence y, the threshold is designated ΔEy.

The following formulas are used in the calculations below:

Sensitivity = (true positives/true positives + false negatives)

Specificity = (true negatives/true negatives + false positives)

If, for example, expression of nucleotide sequence x above a threshold: $x > \Delta Ex$, is observed for 80/100 subjects in group A and for 10/100 subjects in group B, the sensitivity of nucleotide sequence x for the assignment to group A, at the given expression threshold ΔEx, is 80%, and the specificity is 90%.

If the expression of nucleotide sequence y is > ΔEy in 80/100 subjects in group A, and in 10/100 subjects in group B, then, similarly the sensitivity of nucleotide sequence y for the assignment to group A at the given threshold ΔEy is 80% and the specificity is 90%. If in addition, 60 of the 80 subjects in group A that meet the expression threshold for nucleotide sequence y also meet the expression threshold ΔEx and that 5 of the 10 subjects in group B that meet the expression threshold for nucleotide sequence y also meet the expression threshold ΔEx, the sensitivity of the test ($x>\Delta Ex$ and $y>\Delta Ey$)for assignment of subjects to group A is 60% and the specificity is 95%.

Alternatively, if the criteria for assignment to group A are change to: Expression of $x > \Delta Ex$ or expression of $y > \Delta Ey$, the sensitivity approaches 100% and the specificity is 85%.

Clearly, the predictive accuracy of any diagnostic probe set is dependent on the minimum expression threshold selected. The expression of nucleotide sequence X (relative to a standard) is measured in subjects of groups A (with disease) and B (without disease). The minimum threshold of nucleotide sequence expression for x, required for assignment to group A is designated ΔEx 1.

If 90/100 patients in group A have expression of nucleotide sequence $x > \Delta Ex$ 1 and 20/100 patients in group B have expression of nucleotide sequence $x > \Delta Ex$ 1, then the sensitivity of the expression of nucleotide sequence x (using ΔEx 1 as a minimum expression threshold) for assignment of patients to group A will be 90% and the specificity will be 80%.

Altering the minimum expression threshold results in an alteration in the specificity and sensitivity of the nucleotide sequences in question. For example, if the minimum expression threshold of nucleotide sequence x for assignment of subjects to group A is lowered to ΔEx 2, such that 100/100 subjects in group A and 40/100 subjects in group B meet the threshold, then the sensitivity of the test for assignment of subjects to group A will be 100% and the specificity will be 60%.

Thus, for 2 nucleotide sequences X and Y: the expression of nucleotide sequence x and nucleotide sequence y (relative to a standard) are measured in subjects belonging to groups A (with disease) and B (without disease). Minimum thresholds of nucleotide sequence expression for nucleotide sequences X and Y (relative to common standards) are designated for assignment to group A. For nucleotide sequence x, this threshold is designated ΔEx1 and for nucleotide sequence y, this threshold is designated ΔEy1.

If in group A, 90/100 patients meet the minimum requirements of expression ΔEx1 and ΔEy1, and in group B, 10/100 subjects meet the minimum requirements of expression ΔEx1 and ΔEy1, then the sensitivity of the test for assignment of subjects to group A is 90% and the specificity is 90%.

Increasing the minimum expression thresholds for X and Y to ΔEx2 and ΔEy2, such that in group A, 70/100 subjects meet the minimum requirements of expression ΔEx2 and ΔEy2, and in group

B, 3/100 subjects meet the minimum requirements of expression ΔEx2 and ΔEy2. Now the sensitivity of the test for assignment of subjects to group A is 70% and the specificity is 97%.

If the criteria for assignment to group A is that the subject in question meets either threshold, ΔEx2 or ΔEy2, and it is found that 100/100 subjects in group A meet the criteria and 20/100 subjects in group B meet the criteria, then the sensitivity of the test for assignment to group A is 100% and the specificity is 80%.

Individual components of a diagnostic probe set each have a defined sensitivity and specificity for distinguishing between subject groups. Such individual nucleotide sequences can be employed in concert as a diagnostic probe set to increase the sensitivity and specificity of the evaluation. The database of molecular signatures is queried by algorithms to identify the set of nucleotide sequences (i.e., corresponding to members of the probe set) with the highest average differential expression between subject groups. Typically, as the number of nucleotide sequences in the diagnostic probe set increases, so does the predictive value, that is, the sensitivity and specificity of the probe set. When the probe sets are defined they may be used for diagnosis and patient monitoring as discussed below. The diagnostic sensitivity and specificity of the probe sets for the defined use can be determined for a given probe set with specified expression levels as demonstrated above. By altering the expression threshold required for the use of each nucleotide sequence as a diagnostic, the sensitivity and specificity of the probe set can be altered by the practitioner. For example, by lowering the magnitude of the expression differential threshold for each nucleotide sequence in the set, the sensitivity of the test will increase, but the specificity will decrease. As is apparent from the foregoing discussion, sensitivity and specificity are inversely related and the predictive accuracy of the probe set is continuous and dependent on the expression threshold set for each nucleotide sequence. Although sensitivity and specificity tend to have an inverse relationship when expression thresholds are altered, both parameters can be increased as nucleotide sequences with predictive value are added to the diagnostic nucleotide set. In addition a single or a few markers may not be reliable expression markers across a population of patients. This is because of the variability in expression and measurement of expression that exists between measurements, individuals and individuals over time. Inclusion of a large number of candidate nucleotide sequences or large numbers of nucleotide sequences in a diagnostic nucleotide set allows for this variability as not all nucleotide sequences need to meet a threshold for diagnosis. Generally, more markers are better than a single marker. If many markers are used to make a diagnosis, the likelihood that all expression markers will not meet some thresholds based upon random variability is low and thus the test will give fewer false negatives.

It is appreciated that the desired diagnostic sensitivity and specificity of the diagnostic nucleotide set may vary depending on the intended use of the set. For example, in certain uses, high specificity and high sensitivity are desired. For example, a diagnostic nucleotide set for predicting which patient population may experience side effects may require high sensitivity so as to avoid treating such patients. In other settings, high sensitivity is desired, while reduced specificity may be tolerated. For example, in the case of a beneficial treatment with few side effects, it may be important to identify as many patients as possible (high sensitivity) who will respond to the drug, and treatment of some patients who will not respond is tolerated. In other settings, high specificity is desired and

reduced sensitivity may be tolerated. For example, when identifying patients for an early-phase clinical trial, it is important to identify patients who may respond to the particular treatment. Lower sensitivity is tolerated in this setting as it merely results in reduced patients who enroll in the study or requires that more patients are screened for enrollment.

Methods of using diagnostic nucleotide sets.

The invention also provide methods of using the diagnostic nucleotide sets to: diagnose disease; assess severity of disease; predict future occurrence of disease; predict future complications of disease; determine disease prognosis; evaluate the patient's risk, or "stratify" a group of patients; assess response to current drug therapy; assess response to current non-pharmacological therapy; determine the most appropriate medication or treatment for the patient; predict whether a patient is likely to respond to a particular drug; and determine most appropriate additional diagnostic testing for the patient, among other clinically and epidemiologically relevant applications.

The nucleotide sets of the invention can be utilized for a variety of purposes by physicians, healthcare workers, hospitals, laboratories, patients, companies and other institutions. As indicated previously, essentially any disease, condition, or status for which at least one nucleotide sequence is differentially expressed in leukocyte populations (or sub-populations) can be evaluated, e.g., diagnosed, monitored, etc. using the diagnostic nucleotide sets and methods of the invention. In addition to assessing health status at an individual level, the diagnostic nucleotide sets of the present invention are suitable for evaluating subjects at a "population level," e.g., for epidemiological studies, or for population screening for a condition or disease.

Collection and preparation of sample

RNA, protein and/or DNA is prepared using methods well-known in the art, as further described herein. It is appreciated that subject samples collected for use in the methods of the invention are generally collected in a clinical setting, where delays may be introduced before RNA samples are prepared from the subject samples of whole blood, e.g. the blood sample may not be promptly delivered to the clinical lab for further processing. Further delay may be introduced in the clinical lab setting where multiple samples are generally being processed at any given time. For this reason, methods which feature lengthy incubations of intact leukocytes at room temperature are not preferred, because the expression profile of the leukocytes may change during this extended time period. For example, RNA can be isolated from whole blood using a phenol/guanidine isothiocyanate reagent or another direct whole-blood lysis method, as described in, e.g., U.S. Patent Nos. 5,346,994 and 4,843,155. This method may be less preferred under certain circumstances because the large majority of the RNA recovered from whole blood RNA extraction comes from erythrocytes since these cells outnumber leukocytes 1000:1. Care must be taken to ensure that the presence of erythrocyte RNA and protein does not introduce bias in the RNA expression profile data or lead to inadequate sensitivity or specificity of probes.

Alternatively, intact leukocytes may be collected from whole blood using a lysis buffer that selectively lyses erythrocytes, but not leukocytes, as described, e.g., in (U.S. Patent Nos. 5,973,137, and 6,020,186). Intact leukocytes are then collected by centrifugation, and leukocyte RNA is isolated using standard protocols, as described herein. However, this method does not allow isolation of sub-

populations of leukocytes, e.g. mononuclear cells, which may be desired. In addition, the expression profile may change during the lengthy incubation in lysis buffer, especially in a busy clinical lab where large numbers of samples are being prepared at any given time.

Alternatively, specific leukocyte cell types can be separated using density gradient reagents (Boyum, A, 1968.). For example, mononuclear cells may be separated from whole blood using density gradient centrifugation, as described, e.g., in U.S. Patents Nos. 4190535, 4350593, 4751001, 4818418, and 5053134. Blood is drawn directly into a tube containing an anticoagulant and a density reagent (such as Ficoll or Percoll). Centrifugation of this tube results in separation of blood into an erythrocyte and granulocyte layer, a mononuclear cell suspension, and a plasma layer. The mononuclear cell layer is easily removed and the cells can be collected by centrifugation, lysed, and frozen. Frozen samples are stable until RNA can be isolated. Density centrifugation, however, must be conducted at room temperature, and if processing is unduly lengthy, such as in a busy clinical lab, the expression profile may change.

Alternatively, cells can be separated using fluorescence activated cell sorting (FACS) or some other technique, which divides cells into subsets based on gene or protein expression. This may be desirable to enrich the sample for cells of interest, but it may also introduce cell manipulations and time delays, which result in alteration of gene expression profiles (Cantor et al. 1975; Galbraith et al. 1999).

The quality and quantity of each clinical RNA sample is desirably checked before amplification and labeling for array hybridization, using methods known in the art. For example, one microliter of each sample may be analyzed on a Bioanalyzer (Agilent 2100 Palo Alto, CA. USA) using an RNA 6000 nano LabChip (Caliper, Mountain View, CA. USA). Degraded RNA is identified by the reduction of the 28S to 18S ribosomal RNA ratio and/or the presence of large quantities of RNA in the 25-100 nucleotide range.

It is appreciated that the RNA sample for use with a diagnostic nucleotide set may be produced from the same or a different cell population, sub-population and/or cell type as used to identify the diagnostic nucleotide set. For example, a diagnostic nucleotide set identified using RNA extracted from mononuclear cells may be suitable for analysis of RNA extracted from whole blood or mononuclear cells, depending on the particular characteristics of the members of the diagnostic nucleotide set. Generally, diagnostic nucleotide sets must be tested and validated when used with RNA derived from a different cell population, sub-population or cell type than that used when obtaining the diagnostic gene set. Factors such as the cell-specific gene expression of diagnostic nucleotide set members, redundancy of the information provided by members of the diagnostic nucleotide set, expression level of the member of the diagnostic nucleotide set, and cell-specific alteration of expression of a member of the diagnostic nucleotide set will contribute to the usefullness of using a different RNA source than that used when identifying the members of the diagnostic nucleotide set. It is appreciated that it may be desirable to assay RNA derived from whole blood, obviating the need to isolate particular cell types from the blood.

Rapid method of RNA extraction suitable for production in a clinical setting of high quality RNA for expression profiling

In a clinical setting, obtaining high quality RNA preparations suitable for expression profiling, from a desired population of leukocytes poses certain technical challenges, including: the lack of capacity for rapid, high-throughput sample processing in the clinical setting, and the possibility that delay in processing (in a busy lab or in the clinical setting) may adversely affect RNA quality, e.g. by a permitting the expression profile of certain nucleotide sequences to shift. Also, use of toxic and expensive reagents, such as phenol, may be disfavored in the clinical setting due to the added expense associated with shipping and handling such reagents.

A useful method for RNA isolation for leukocyte expression profiling would allow the isolation of monocyte and lymphocyte RNA in a timely manner, while preserving the expression profiles of the cells, and allowing inexpensive production of reproducible high-quality RNA samples. Accordingly, the invention provides a method of adding inhibitor(s) of RNA transcription and/or inhibitor(s) of protein synthesis, such that the expression profile is "frozen" and RNA degradation is reduced. A desired leukocyte population or sub-population is then isolated, and the sample may be frozen or lysed before further processing to extract the RNA. Blood is drawn from subject population and exposed to ActinomycinD (to a final concentration of 10 ug/ml) to inhibit transcription, and cycloheximide (to a final concentration of 10 ug/ml) to inhibit protein synthesis. The inhibitor(s) can be injected into the blood collection tube in liquid form as soon as the blood is drawn, or the tube can be manufactured to contain either lyophilized inhibitors or inhibitors that are in solution with the anticoagulant. At this point, the blood sample can be stored at room temperature until the desired leukocyte population or sub-population is isolated, as described elsewhere. RNA is isolated using standard methods, e.g., as described above, or a cell pellet or extract can be frozen until further processing of RNA is convenient.

The invention also provides a method of using a low-temperature density gradient for separation of a desired leukocyte sample. In another embodiment, the invention provides the combination of use of a low-temperature density gradient and the use of transcriptional and/or protein synthesis inhibitor(s). A desired leukocyte population is separated using a density gradient solution for cell separation that maintains the required density and viscosity for cell separation at 0-4°C. Blood is drawn into a tube containing this solution and may be refrigerated before and during processing as the low temperatures slow cellular processes and minimize expression profile changes. Leukocytes are separated, and RNA is isolated using standard methods. Alternately, a cell pellet or extract is frozen until further processing of RNA is convenient. Care must be taken to avoid rewarming the sample during further processing steps.

Alternatively, the invention provides a method of using low-temperature density gradient separation, combined with the use of actinomycin A and cyclohexamide, as described above.

Assessing expression for diagnostics

Expression profiles for the set of diagnostic nucleotide sequences in a subject sample can be evaluated by any technique that determines the expression of each component nucleotide sequence. Methods suitable for expression analysis are known in the art, and numerous examples are discussed in

the Sections titled "Methods of obtaining expression data" and "high throughput expression Assays", above.

In many cases, evaluation of expression profiles is most efficiently, and cost effectively, performed by analyzing RNA expression. Alternatively, the proteins encoded by each component of the diagnostic nucleotide set are detected for diagnostic purposes by any technique capable of determining protein expression, e.g., as described above. Expression profiles can be assessed in subject leukocyte sample using the same or different techniques as those used to identify and validate the diagnostic nucleotide set. For example, a diagnostic nucleotide set identified as a subset of sequences on a cDNA microarray can be utilized for diagnostic (or prognostic, or monitoring, etc.) purposes on the same array from which they were identified. Alternatively, the diagnostic nucleotide sets for a given disease or condition can be organized onto a dedicated sub-array for the indicated purpose. It is important to note that if diagnostic nucleotide sets are discovered using one technology, e.g. RNA expression profiling, but applied as a diagnostic using another technology, e.g. protein expression profiling, the nucleotide sets must generally be validated for diagnostic purposes with the new technology. In addition, it is appreciated that diagnostic nucleotide sets that are developed for one use, e.g. to diagnose a particular disease, may later be found to be useful for a different application, e.g. to predict the likelihood that the particular disease will occur. Generally, the diagnostic nucleotide set will need to be validated for use in the second circumstance. As discussed herein, the sequence of diagnostic nucleotide set members may be amplified from RNA or cDNA using methods known in the art providing specific amplification of the nucleotide sequences.

General Protein Methods

Protein products of the nucleotide sequences of the invention may include proteins that represent functionally equivalent gene products. Such an equivalent gene product may contain deletions, additions or substitutions of amino acid residues within the amino acid sequence encoded by the nucleotide sequences described, above, but which result in a silent change, thus producing a functionally equivalent nucleotide sequence product. Amino acid substitutions may be made on the basis of similarity in polarity, charge, solubility, hydrophobicity, hydrophilicity, and/or the amphipathic nature of the residues involved.

For example, nonpolar (hydrophobic) amino acids include alanine, leucine, isoleucine, valine, proline, phenylalanine, tryptophan, and methionine; polar neutral amino acids include glycine, serine, threonine, cysteine, tyrosine, asparagine, and glutamine; positively charged (basic) amino acids include arginine, lysine, and histidine; and negatively charged (acidic) amino acids include aspartic acid and glutamic acid. "Functionally equivalent", as utilized herein, refers to a protein capable of exhibiting a substantially similar in vivo activity as the endogenous gene products encoded by the nucleotide described, above.

The gene products (protein products of the nucleotide sequences) may be produced by recombinant DNA technology using techniques well known in the art. Thus, methods for preparing the gene polypeptides and peptides of the invention by expressing nucleic acid encoding nucleotide sequences are described herein. Methods which are well known to those skilled in the art can be used to construct expression vectors containing nucleotide sequence protein coding sequences and

appropriate transcriptional/translational control signals. These methods include, for example, in vitro recombinant DNA techniques, synthetic techniques and in vivo recombination/genetic recombination. See, for example, the techniques described in Sambrook et al., 1989, supra, and Ausubel et al., 1989, supra. Alternatively, RNA capable of encoding nucleotide sequence protein sequences may be chemically synthesized using, for example, synthesizers. See, for example, the techniques described in "Oligonucleotide Synthesis", 1984, Gait, M. J. ed., IRL Press, Oxford, which is incorporated by reference herein in its entirety

A variety of host-expression vector systems may be utilized to express the nucleotide sequence coding sequences of the invention. Such host-expression systems represent vehicles by which the coding sequences of interest may be produced and subsequently purified, but also represent cells which may, when transformed or transfected with the appropriate nucleotide coding sequences, exhibit the protein encoded by the nucleotide sequence of the invention in situ. These include but are not limited to microorganisms such as bacteria (e.g., E. coli, B. subtilis) transformed with recombinant bacteriophage DNA, plasmid DNA or cosmid DNA expression vectors containing nucleotide sequence protein coding sequences; yeast (e.g. Saccharomyces, Pichia) transformed with recombinant yeast expression vectors containing the nucleotide sequence protein coding sequences; insect cell systems infected with recombinant virus expression vectors (e.g., baculovirus) containing the nucleotide sequence protein coding sequences; plant cell systems infected with recombinant virus expression vectors (e.g., cauliflower mosaic virus, CaMV; tobacco mosaic virus, TMV) or transformed with recombinant plasmid expression vectors (e.g., Ti plasmid) containing nucleotide sequence protein coding sequences; or mammalian cell systems (e.g. COS, CHO, BHK, 293, 3T3) harboring recombinant expression constructs containing promoters derived from the genome of mammalian cells (e.g., metallothionein promoter) or from mammalian viruses (e.g., the adenovirus late promoter; the vaccinia virus 7.5 K promoter).

In bacterial systems, a number of expression vectors may be advantageously selected depending upon the use intended for the nucleotide sequence protein being expressed. For example, when a large quantity of such a protein is to be produced, for the generation of antibodies or to screen peptide libraries, for example, vectors which direct the expression of high levels of fusion protein products that are readily purified may be desirable. Such vectors include, but are not limited, to the E. coli expression vector pUR278 (Ruther et al., 1983, EMBO J. 2:1791), in which the nucleotide sequence protein coding sequence may be ligated individually into the vector in frame with the lac Z coding region so that a fusion protein is produced; pIN vectors (Inouye & Inouye, 1985, Nucleic Acids Res. 13:3101-3109; Van Heeke & Schuster, 1989, J. Biol. Chem. 264:5503-5509); and the likes of pGEX vectors may also be used to express foreign polypeptides as fusion proteins with glutathione S-transferase (GST). In general, such fusion proteins are soluble and can easily be purified from lysed cells by adsorption to glutathione-agarose beads followed by elution in the presence of free glutathione. The pGEX vectors are designed to include thrombin or factor Xa protease cleavage sites so that the cloned target nucleotide sequence protein can be released from the GST moiety. Other systems useful in the invention include use of the FLAG epitope or the 6-HIS systems.

In an insect system, Autographa californica nuclear polyhedrosis virus (AcNPV) is used as a vector to express foreign nucleotide sequences. The virus grows in Spodoptera frugiperda cells. The nucleotide sequence coding sequence may be cloned individually into non-essential regions (for example the polyhedrin gene) of the virus and placed under control of an AcNPV promoter (for example the polyhedrin promoter). Successful insertion of nucleotide sequence coding sequence will result in inactivation of the polyhedrin gene and production of non-occluded recombinant virus (i.e., virus lacking the proteinaceous coat coded for by the polyhedrin gene). These recombinant viruses are then used to infect Spodoptera frugiperda cells in which the inserted nucleotide sequence is expressed. (E.g., see Smith et al., 1983, J. Virol. 46: 584; Smith, U.S. Pat. No. 4,215,051).

In mammalian host cells, a number of viral-based expression systems may be utilized. In cases where an adenovirus is used as an expression vector, the nucleotide sequence coding sequence of interest may be ligated to an adenovirus transcription/translation control complex, e.g., the late promoter and tripartite leader sequence. This chimeric nucleotide sequence may then be inserted in the adenovirus genome by in vitro or in vivo recombination. Insertion in a non-essential region of the viral genome (e.g., region E1 or E3) will result in a recombinant virus that is viable and capable of expressing nucleotide sequence encoded protein in infected hosts. (E.g., See Logan & Shenk, 1984, Proc. Natl. Acad. Sci. USA 81:3655-3659). Specific initiation signals may also be required for efficient translation of inserted nucleotide sequence coding sequences. These signals include the ATG initiation codon and adjacent sequences. In cases where an entire nucleotide sequence, including its own initiation codon and adjacent sequences, is inserted into the appropriate expression vector, no additional translational control signals may be needed. However, in cases where only a portion of the nucleotide sequence coding sequence is inserted, exogenous translational control signals, including, perhaps, the ATG initiation codon, must be provided. Furthermore, the initiation codon must be in phase with the reading frame of the desired coding sequence to ensure translation of the entire insert. These exogenous translational control signals and initiation codons can be of a variety of origins, both natural and synthetic. The efficiency of expression may be enhanced by the inclusion of appropriate transcription enhancer elements, transcription terminators, etc. (see Bittner et al., 1987, Methods in Enzymol. 153:516-544).

In addition, a host cell strain may be chosen which modulates the expression of the inserted sequences, or modifies and processes the product of the nucleotide sequence in the specific fashion desired. Such modifications (e.g., glycosylation) and processing (e.g., cleavage) of protein products may be important for the function of the protein. Different host cells have characteristic and specific mechanisms for the post-translational processing and modification of proteins. Appropriate cell lines or host systems can be chosen to ensure the correct modification and processing of the foreign protein expressed. To this end, eukaryotic host cells which possess the cellular machinery for proper processing of the primary transcript, glycosylation, and phosphorylation of the gene product may be used. Such mammalian host cells include but are not limited to CHO, VERO, BHK, HeLa, COS, MDCK, 293, 3T3, WI38, etc.

For long-term, high-yield production of recombinant proteins, stable expression is preferred. For example, cell lines which stably express the nucleotide sequence encoded protein may be

engineered. Rather than using expression vectors which contain viral origins of replication, host cells can be transformed with DNA controlled by appropriate expression control elements (e.g., promoter, enhancer, sequences, transcription terminators, polyadenylation sites, etc.), and a selectable marker. Following the introduction of the foreign DNA, engineered cells may be allowed to grow for 1-2 days in an enriched media, and then are switched to a selective media. The selectable marker in the recombinant plasmid confers resistance to the selection and allows cells to stably integrate the plasmid into their chromosomes and grow to form foci which in turn can be cloned and expanded into cell lines. This method may advantageously be used to engineer cell lines which express nucleotide sequence encoded protein. Such engineered cell lines may be particularly useful in screening and evaluation of compounds that affect the endogenous activity of the nucleotide sequence encoded protein.

A number of selection systems may be used, including but not limited to the herpes simplex virus thymidine kinase (Wigler, et al., 1977, Cell 11:223), hypoxanthine-guanine phosphoribosyltransferase (Szybalska & Szybalski, 1962, Proc. Natl. Acad. Sci. USA 48:2026), and adenine phosphoribosyltransferase (Lowy, et al., 1980, Cell 22:817) genes can be employed in tk-, hgprt- or aprt- cells, respectively. Also, antimetabolite resistance can be used as the basis of selection for dhfr, which confers resistance to methotrexate (Wigler, et al., 1980, Natl. Acad. Sci. USA 77:3567; O'Hare, et al., 1981, Proc. Natl. Acad. Sci. USA 78:1527); gpt, which confers resistance to mycophenolic acid (Mulligan & Berg, 1981, Proc. Natl. Acad. Sci. USA 78:2072); neo, which confers resistance to the aminoglycoside G-418 (Colberre-Garapin, et al., 1981, J. Mol. Biol. 150:1); and hygro, which confers resistance to hygromycin (Santerre, et al., 1984, Gene 30:147) genes.

An alternative fusion protein system allows for the ready purification of non-denatured fusion proteins expressed in human cell lines (Janknecht, et al., 1991, Proc. Natl. Acad. Sci. USA 88: 8972-8976). In this system, the nucleotide sequence of interest is subcloned into a vaccinia recombination plasmid such that the nucleotide sequence's open reading frame is translationally fused to an amino-terminal tag consisting of six histidine residues. Extracts from cells infected with recombinant vaccinia virus are loaded onto Ni.sup.2 +-nitriloacetic acid-agarose columns and histidine-tagged proteins are selectively eluted with imidazole-containing buffers.

Where recombinant DNA technology is used to produce the protein encoded by the nucleotide sequence for such assay systems, it may be advantageous to engineer fusion proteins that can facilitate labeling, immobilization and/or detection.

Antibodies

Indirect labeling involves the use of a protein, such as a labeled antibody, which specifically binds to the protein encoded by the nucleotide sequence. Such antibodies include but are not limited to polyclonal, monoclonal, chimeric, single chain, Fab fragments and fragments produced by an Fab expression library.

The invention also provides for antibodies to the protein encoded by the nucleotide sequences. Described herein are methods for the production of antibodies capable of specifically recognizing one or more nucleotide sequence epitopes. Such antibodies may include, but are not limited to polyclonal antibodies, monoclonal antibodies (mAbs), humanized or chimeric antibodies, single chain antibodies, Fab fragments, F(ab')2 fragments, fragments produced by a Fab expression library, anti-idiotypic (anti-

Id) antibodies, and epitope-binding fragments of any of the above. Such antibodies may be used, for example, in the detection of a nucleotide sequence in a biological sample, or, alternatively, as a method for the inhibition of abnormal gene activity, for example, the inhibition of a disease target nucleotide sequence, as further described below. Thus, such antibodies may be utilized as part of cardiovascular or other disease treatment method, and/or may be used as part of diagnostic techniques whereby patients may be tested for abnormal levels of nucleotide sequence encoded proteins, or for the presence of abnormal forms of the such proteins.

For the production of antibodies to a nucleotide sequence, various host animals may be immunized by injection with a protein encoded by the nucleotide sequence, or a portion thereof. Such host animals may include but are not limited to rabbits, mice, and rats, to name but a few. Various adjuvants may be used to increase the immunological response, depending on the host species, including but not limited to Freund's (complete and incomplete), mineral gels such as aluminum hydroxide, surface active substances such as lysolecithin, pluronic polyols, polyanions, peptides, oil emulsions, keyhole limpet hemocyanin, dinitrophenol, and potentially useful human adjuvants such as BCG (bacille Calmette-Guerin) and Corynebacterium parvum.

Polyclonal antibodies are heterogeneous populations of antibody molecules derived from the sera of animals immunized with an antigen, such as gene product, or an antigenic functional derivative thereof. For the production of polyclonal antibodies, host animals such as those described above, may be immunized by injection with gene product supplemented with adjuvants as also described above.

Monoclonal antibodies, which are homogeneous populations of antibodies to a particular antigen, may be obtained by any technique which provides for the production of antibody molecules by continuous cell lines in culture. These include, but are not limited to the hybridoma technique of Kohler and Milstein, (1975, Nature 256:495-497; and U.S. Pat. No. 4,376,110), the human B-cell hybridoma technique (Kosbor et al., 1983, Immunology Today 4:72; Cole et al., 1983, Proc. Natl. Acad. Sci. USA 80:2026-2030), and the EBV-hybridoma technique (Cole et al., 1985, Monoclonal Antibodies And Cancer Therapy, Alan R. Liss, Inc., pp. 77-96). Such antibodies may be of any immunoglobulin class including IgG, IgM, IgE, IgA, IgD and any subclass thereof. The hybridoma producing the mAb of this invention may be cultivated in vitro or in vivo.

In addition, techniques developed for the production of "chimeric antibodies" (Morrison et al., 1984, Proc. Natl. Acad. Sci., 81:6851-6855; Neuberger et al., 1984, Nature, 312:604-608; Takeda et al., 1985, Nature, 314:452-454) by splicing the genes from a mouse antibody molecule of appropriate antigen specificity together with genes from a human antibody molecule of appropriate biological activity can be used. A chimeric antibody is a molecule in which different portions are derived from different animal species, such as those having a variable region derived from a murine mAb and a human immunoglobulin constant region.

Alternatively, techniques described for the production of single chain antibodies (U.S. Pat. No. 4,946,778; Bird, 1988, Science 242:423-426; Huston et al., 1988, Proc. Natl. Acad. Sci. USA 85:5879-5883; and Ward et al., 1989, Nature 334:544-546) can be adapted to produce nucleotide sequence-single chain antibodies. Single chain antibodies are formed by linking the heavy and light chain fragments of the Fv region via an amino acid bridge, resulting in a single chain polypeptide.

Antibody fragments which recognize specific epitopes may be generated by known techniques For example, such fragments include but are not limited to: the F(ab')2 fragments which can be produced by pepsin digestion of the antibody molecule and the Fab fragments which can be generated by reducing the disulfide bridges of the F(ab')2 fragments. Alternatively, Fab expression libraries may be constructed (Huse et al., 1989, Science, 246:1275-1281) to allow rapid and easy identification of monoclonal Fab fragments with the desired specificity.

Disease specific target nucleotide sequences

The invention also provides disease specific target nucleotide sequences, and sets of disease specific target nucleotide sequences. The diagnostic nucleotide sets, subsets thereof, novel nucleotide sequences, and individual members of the diagnostic nucleotide sets identified as described above are also disease specific target nucleotide sequences. In particular, individual nucleotide sequences that are differentially regulated or have predictive value that is strongly correlated with a disease or disease criterion are especially favorable as disease specific target nucleotide sequences. Sets of genes that are co-regulated may also be identified as disease specific target nucleotide sets. Such nucleotide sequences and/or nucleotide sequence products are targets for modulation by a variety of agents and techniques. For example, disease specific target nucleotide sequences (or the products of such nucleotide sequences, or sets of disease specific target nucleotide sequences) can be inhibited or activated by, e.g., target specific monoclonal antibodies or small molecule inhibitors, or delivery of the nucleotide sequence or gene product of the nucleotide sequence to patients. Also, sets of genes can be inhibited or activated by a variety of agents and techniques. The specific usefulness of the target nucleotide sequence(s) depends on the subject groups from which they were discovered, and the disease or disease criterion with which they correlate.

Imaging

The invention also provides for imaging reagents. The differentially expressed leukocyte nucleotide sequences, diagnostic nucleotide sets, or portions thereof, and novel nucleotide sequences of the invention are nucleotide sequences expressed in cells with or without disease. Leukocytes expressing a nucleotide sequence(s) that is differentially expressed in a disease condition may localize within the body to sites that are of interest for imaging purposes. For example, a leukocyte expressing a nucleotide sequence(s) that are differentially expressed in an individual having atherosclerosis may localize or accumulate at the site of an atherosclerotic placque. Such leukocytes, when labeled, may provide a detection reagent for use in imaging regions of the body where labeled leukocyte accumulate or localize, for example, at the atherosclerotic plaque in the case of atherosclerosis. For example, leukocytes are collected from a subject, labeled in vitro, and reintroduced into a subject. Alternatively, the labeled reagent is introduced into the subject individual, and leukocyte labeling occurs within the patient.

Imaging agents that detect the imaging targets of the invention are produced by well-known molecular and immunological methods (for exemplary protocols, *see*, e.g., Ausubel, Berger, and Sambrook, as well as Harlow and Lane, *supra*).

For example, a full-length nucleic acid sequence, or alternatively, a gene fragment encoding an immunogenic peptide or polypeptide fragments, is cloned into a convenient expression vector, for

example, a vector including an in-frame epitope or substrate binding tag to facilitate subsequent purification. Protein is then expressed from the cloned cDNA sequence and used to generate antibodies, or other specific binding molecules, to one or more antigens of the imaging target protein. Alternatively, a natural or synthetic polypeptide (or peptide) or small molecule that specifically binds (or is specifically bound to) the expressed imaging target can be identified through well established techniques (*see*, e.g., Mendel et al. (2000) Anticancer Drug Des 15:29-41; Wilson (2000) Curr Med Chem 7:73-98; Hamby and Showwalter (1999) Pharmacol Ther 82:169-93; and Shimazawa et al. (1998) Curr Opin Struct Biol 8:451-8). The binding molecule, e.g., antibody, small molecule ligand, etc., is labeled with a contrast agent or other detectable label, e.g., gadolinium, iodine, or a gamma-emitting source. For in-vivo imaging of a disease process that involved leukocytes, the labeled antibody is infused into a subject, e.g., a human patient or animal subject, and a sufficient period of time is passed to permit binding of the antibody to target cells. The subject is then imaged with appropriate technology such as MRI (when the label is gadolinium) or with a gamma counter (when the label is a gamma emitter).

Identification of nucleotide sequence involved in leukocyte adhesion

The invention also encompasses a method of identifying nucleotide sequences involved in leukocyte adhesion. The interaction between the endothelial cell and leukocyte is a fundamental mechanism of all inflammatory disorders, including the diagnosis and prognosis of allograft rejection the diseases listed in Table 1. For example, the first visible abnormality in atherosclerosis is the adhesion to the endothelium and diapedesis of mononuclear cells (e.g., T-cell and monocyte). Insults to the endothelium (for example, cytokines, tobacco, diabetes, hypertension and many more) lead to endothelial cell activation. The endothelium then expresses adhesion molecules, which have counter receptors on mononuclear cells. Once the leukocyte receptors have bound the endothelial adhesion molecules, they stick to the endothelium, roll a short distance, stop and transmigrate across the endothelium. A similar set of events occurs in both acute and chronic inflammation. When the leukocyte binds the endothelial adhesion molecule, or to soluble cytokines secreted by endothelial or other cells, a program of gene expression is activated in the leukocyte. This program of expression leads to leukocyte rolling, firm adhesion and transmigration into the vessel wall or tissue parenchyma. Inhibition of this process is highly desirable goal in anti-inflammatory drug development. In addition, leukocyte nucleotide sequences and epithelial cell nucleotide sequences, that are differentially expressed during this process may be disease-specific target nucleotide sequences.

Human endothelial cells, e.g. derived from human coronary arteries, human aorta, human pulmonary artery, human umbilical vein or microvascular endothelial cells, are cultured as a confluent monolayer, using standard methods. Some of the endothelial cells are then exposed to cytokines or another activating stimuli such as oxidized LDL, hyperglycemia, shear stress, or hypoxia (Moser et al. 1992). Some endothelial cells are not exposed to such stimuli and serve as controls. For example, the endothelial cell monolayer is incubated with culture medium containing 5 U/ml of human recombinant IL-1alpha or 10 ng/ml TNF (tumor necrosis factor), for a period of minutes to overnight. The culture medium composition is changed or the flask is sealed to induce hypoxia. In addition, tissue culture plate is rotated to induce sheer stress.

Human T-cells and/or monocytes are cultured in tissue culture flasks or plates, with LGM-3 media from Clonetics. Cells are incubated at 37 degree C, 5% CO2 and 95% humidity. These leukocytes are exposed to the activated or control endothelial layer by adding a suspension of leukocytes on to the endothelial cell monolayer. The endothelial cell monolayer is cultured on a tissue culture treated plate/ flask or on a microporous membrane. After a variable duration of exposures, the endothelial cells and leukocytes are harvested separately by treating all cells with trypsin and then sorting the endothelial cells from the leukocytes by magnetic affinity reagents to an endothelial cell specific marker such as PECAM-1 (Stem Cell Technologies). RNA is extracted from the isolated cells by standard techniques. Leukocyte RNA is labeled as described above, and hybridized to leukocyte candidate nucleotide library. Epithelial cell RNA is also labeled and hybridized to the leukocyte candidate nucleotide library. Alternatively, the epithelial cell RNA is hybridized to a epithelial cell candidate nucleotide library, prepared according to the methods described for leukocyte candidate libraries, above.

Hybridization to candidate nucleotide libraries will reveal nucleotide sequences that are up-regulated or down-regulated in leukocyte and/or epithelial cells undergoing adhesion. The differentially regulated nucleotide sequences are further characterized, e.g. by isolating and sequencing the full-length sequence, analysis of the DNA and predicted protein sequence, and functional characterization of the protein product of the nucleotide sequence, as described above. Further characterization may result in the identification of leukocyte adhesion specific target nucleotide sequences, which may be candidate targets for regulation of the inflammatory process. Small molecule or antibody inhibitors can be developed to inhibit the target nucleotide sequence function. Such inhibitors are tested for their ability to inhibit leukocyte adhesion in the in vitro test described above.

Integrated systems

Integrated systems for the collection and analysis of expression profiles, and molecular signatures, as well as for the compilation, storage and access of the databases of the invention, typically include a digital computer with software including an instruction set for sequence searching and analysis, and, optionally, high-throughput liquid control software, image analysis software, data interpretation software, a robotic control armature for transferring solutions from a source to a destination (such as a detection device) operably linked to the digital computer, an input device (e.g., a computer keyboard) for entering subject data to the digital computer, or to control analysis operations or high throughput sample transfer by the robotic control armature. Optionally, the integrated system further comprises an image scanner for digitizing label signals from labeled assay components, e.g., labeled nucleic acid hybridized to a candidate library microarray. The image scanner can interface with image analysis software to provide a measurement of the presence or intensity of the hybridized label, i.e., indicative of an on/off expression pattern or an increase or decrease in expression.

Readily available computational hardware resources using standard operating systems are fully adequate, e.g., a PC (Intel x86 or Pentium chip- compatible DOS,™ OS2,™ WINDOWS,™ WINDOWS NT,™ WINDOWS95,™ WINDOWS98,™ LINUX, or even Macintosh, Sun or PCs will suffice) for use in the integrated systems of the invention. Current art in software technology is similarly adequate (i.e., there are a multitude of mature programming languages and source code

suppliers) for design, e.g., of an upgradeable open-architecture object-oriented heuristic algorithm, or instruction set for expression analysis, as described herein. For example, software for aligning or otherwise manipulating ,molecular signatures can be constructed by one of skill using a standard programming language such as Visual basic, Fortran, Basic, Java, or the like, according to the methods herein.

Various methods and algorithms, including genetic algorithms and neural networks, can be used to perform the data collection, correlation, and storage functions, as well as other desirable functions, as described herein. In addition, digital or analog systems such as digital or analog computer systems can control a variety of other functions such as the display and/or control of input and output files.

For example, standard desktop applications such as word processing software (e.g., Corel WordPerfect™ or Microsoft Word™) and database software (e.g., spreadsheet software such as Corel Quattro Pro™, Microsoft Excel™, or database programs such as Microsoft Access™ or Paradox™) can be adapted to the present invention by inputting one or more character string corresponding, e.g., to an expression pattern or profile, subject medical or historical data, molecular signature, or the like, into the software which is loaded into the memory of a digital system, and carrying out the operations indicated in an instruction set, e.g., as exemplified in Figure 2. For example, systems can include the foregoing software having the appropriate character string information, e.g., used in conjunction with a user interface in conjunction with a standard operating system such as a Windows, Macintosh or LINUX system. For example, an instruction set for manipulating strings of characters, either by programming the required operations into the applications or with the required operations performed manually by a user (or both). For example, specialized sequence alignment programs such as PILEUP or BLAST can also be incorporated into the systems of the invention, e.g., for alignment of nucleic acids or proteins (or corresponding character strings).

Software for performing the statistical methods required for the invention, e.g., to determine correlations between expression profiles and subsets of members of the diagnostic nucleotide libraries, such as programmed embodiments of the statistical methods described above, are also included in the computer systems of the invention. Alternatively, programming elements for performing such methods as principle component analysis (PCA) or least squares analysis can also be included in the digital system to identify relationships between data. Exemplary software for such methods is provided by Partek, Inc., St. Peter, Mo; at the web site partek.com.

Any controller or computer optionally includes a monitor which can include, e.g., a flat panel display (e.g., active matrix liquid crystal display, liquid crystal display), a cathode ray tube ("CRT") display, or another display system which serves as a user interface, e.g., to output predictive data. Computer circuitry, including numerous integrated circuit chips, such as a microprocessor, memory, interface circuits, and the like, is often placed in a casing or box which optionally also includes a hard disk drive, a floppy disk drive, a high capacity removable drive such as a writeable CD-ROM, and other common peripheral elements.

Inputting devices such as a keyboard, mouse, or touch sensitive screen, optionally provide for input from a user and for user selection, e.g., of sequences or data sets to be compared or otherwise

manipulated in the relevant computer system. The computer typically includes appropriate software for receiving user instructions, either in the form of user input into a set parameter or data fields (e.g., to input relevant subject data), or in the form of preprogrammed instructions, e.g., preprogrammed for a variety of different specific operations. The software then converts these instructions to appropriate language for instructing the system to carry out any desired operation.

The integrated system may also be embodied within the circuitry of an application specific integrated circuit (ASIC) or programmable logic device (PLD). In such a case, the invention is embodied in a computer readable descriptor language that can be used to create an ASIC or PLD. The integrated system can also be embodied within the circuitry or logic processors of a variety of other digital apparatus, such as PDAs, laptop computer systems, displays, image editing equipment, etc.

The digital system can comprise a learning component where expression profiles, and relevant subject data are compiled and monitored in conjunction with physical assays, and where correlations, e.g., molecular signatures with predictive value for a disease, are established or refined. Successful and unsuccessful combinations are optionally documented in a database to provide justification/preferences for user-base or digital system based selection of diagnostic nucleotide sets with high predictive accuracy for a specified disease or condition.

The integrated systems can also include an automated workstation. For example, such a workstation can prepare and analyze leukocyte RNA samples by performing a sequence of events including: preparing RNA from a human blood sample; labeling the RNA with an isotopic or non-isotopic label; hybridizing the labeled RNA to at least one array comprising all or part of the candidate library; and detecting the hybridization pattern. The hybridization pattern is digitized and recorded in the appropriate database.

Automated RNA preparation tool

The invention also includes an automated RNA preparation tool for the preparation of mononuclear cells from whole blood samples, and preparation of RNA from the mononuclear cells. In a preferred embodiment, the use of the RNA preparation tool is fully automated, so that the cell separation and RNA isolation would require no human manipulations. Full automation is advantageous because it minimizes delay, and standardizes sample preparation across different laboratories. This standardization increases the reproducibility of the results.

Figure 2 depicts the processes performed by the RNA preparation tool of the invention. A primary component of the device is a centrifuge (A). Tubes of whole blood containing a density gradient solution, transcription/translation inhibitors, and a gel barrier that separates erythrocytes from mononuclear cells and serum after centrifugation are placed in the centrifuge (B). The barrier is permeable to erythrocytes and granulocytes during centrifugation, but does not allow mononuclear cells to pass through (or the barrier substance has a density such that mononuclear cells remain above the level of the barrier during the centrifugation). After centrifugation, the erythrocytes and granulocytes are trapped beneath the barrier, facilitating isolation of the mononuclear cell and serum layers. A mechanical arm removes the tube and inverts it to mix the mononuclear cell layer and the serum (C). The arm next pours the supernatant into a fresh tube (D), while the erythrocytes and granulocytes remained below the barrier. Alternatively, a needle is used to aspirate the supernatant and

transfer it to a fresh tube. The mechanical arms of the device opens and closes lids, dispenses PBS to aid in the collection of the mononuclear cells by centrifugation, and moves the tubes in and out of the centrifuge. Following centrifugation, the supernatant is poured off or removed by a vacuum device (E), leaving an isolated mononuclear cell pellet. Purification of the RNA from the cells is performed automatically, with lysis buffer and other purification solutions (F) automatically dispensed and removed before and after centrifugation steps. The result is a purified RNA solution. In another embodiment, RNA isolation is performed using a column or filter method. In yet another embodiment, the invention includes an on-board homogenizer for use in cell lysis.

Other automated systems

Automated and/or semi-automated methods for solid and liquid phase high-throughput sample preparation and evaluation are available, and supported by commercially available devices. For example, robotic devices for preparation of nucleic acids from bacterial colonies, e.g., to facilitate production and characterization of the candidate library include, for example, an automated colony picker (e.g., the Q-bot, Genetix, U.K.) capable of identifying, sampling, and inoculating up to 10,000/4 hrs different clones into 96 well microtiter dishes. Alternatively, or in addition, robotic systems for liquid handling are available from a variety of sources, e.g., automated workstations like the automated synthesis apparatus developed by Takeda Chemical Industries, LTD. (Osaka, Japan) and many robotic systems utilizing robotic arms (Zymate II, Zymark Corporation, Hopkinton, Mass.; Orca, Beckman Coulter, Inc. (Fullerton, CA)) which mimic the manual operations performed by a scientist. Any of the above devices are suitable for use with the present invention, e.g., for high-throughput analysis of library components or subject leukocyte samples. The nature and implementation of modifications to these devices (if any) so that they can operate as discussed herein will be apparent to persons skilled in the relevant art.

High throughput screening systems that automate entire procedures, e.g., sample and reagent pipetting, liquid dispensing, timed incubations, and final readings of the microplate in detector(s) appropriate for the relevant assay are commercially available. (*see, e.g.*, Zymark Corp., Hopkinton, MA; Air Technical Industries, Mentor, OH; Beckman Instruments, Inc. Fullerton, CA; Precision Systems, Inc., Natick, MA, *etc.*). These configurable systems provide high throughput and rapid start up as well as a high degree of flexibility and customization. Similarly, arrays and array readers are available, e.g., from Affymetrix, PE Biosystems, and others.

The manufacturers of such systems provide detailed protocols the various high throughput. Thus, for example, Zymark Corp. provides technical bulletins describing screening systems for detecting the modulation of gene transcription, ligand binding, and the like.

A variety of commercially available peripheral equipment, including, e.g., optical and fluorescent detectors, optical and fluorescent microscopes, plate readers, CCD arrays, phosphorimagers, scintillation counters, phototubes, photodiodes, and the like, and software is available for digitizing, storing and analyzing a digitized video or digitized optical or other assay results, e.g., using PC (Intel x86 or pentium chip- compatible DOS™, OS2™ WINDOWS™, WINDOWS NT™ or WINDOWS95™ based machines), MACINTOSH™, or UNIX based (*e.g.*, SUN™ work station) computers.

Embodiment in a web site.

The methods described above can be implemented in a localized or distributed computing environment. For example, if a localized computing environment is used, an array comprising a candidate nucleotide library, or diagnostic nucleotide set, is configured in proximity to a detector, which is, in turn, linked to a computational device equipped with user input and output features.

In a distributed environment, the methods can be implemented on a single computer with multiple processors or, alternatively, on multiple computers. The computers can be linked, e.g. through a shared bus, but more commonly, the computer(s) are nodes on a network. The network can be generalized or dedicated, at a local level or distributed over a wide geographic area. In certain embodiments, the computers are components of an intra-net or an internet.

The predictive data corresponding to subject molecular signatures (e.g., expression profiles, and related diagnostic, prognostic, or monitoring results) can be shared by a variety of parties. In particular, such information can be utilized by the subject, the subject's health care practitioner or provider, a company or other institution, or a scientist. An individual subject's data, a subset of the database or the entire database recorded in a computer readable medium can be accessed directly by a user by any method of communication, including, but not limited to, the internet. With appropriate computational devices, integrated systems, communications networks, users at remote locations, as well as users located in proximity to, e.g., at the same physical facility, the database can access the recorded information. Optionally, access to the database can be controlled using unique alphanumeric passwords that provide access to a subset of the data. Such provisions can be used, e.g., to ensure privacy, anonymity, etc.

Typically, a client (e.g., a patient, practitioner, provider, scientist, or the like) executes a Web browser and is linked to a server computer executing a Web server. The Web browser is, for example, a program such as IBM's Web Explorer, Internet explorer, NetScape or Mosaic, or the like. The Web server is typically, but not necessarily, a program such as IBM's HTTP Daemon or other WWW daemon (e.g., LINUX-based forms of the program). The client computer is bi-directionally coupled with the server computer over a line or via a wireless system. In turn, the server computer is bi-directionally coupled with a website (server hosting the website) providing access to software implementing the methods of this invention.

A user of a client connected to the Intranet or Internet may cause the client to request resources that are part of the web site(s) hosting the application(s) providing an implementation of the methods described herein. Server program(s) then process the request to return the specified resources (assuming they are currently available). A standard naming convention has been adopted, known as a Uniform Resource Locator ("URL"). This convention encompasses several types of location names, presently including subclasses such as Hypertext Transport Protocol ("http"), File Transport Protocol ("ftp"), gopher, and Wide Area Information Service ("WAIS"). When a resource is downloaded, it may include the URLs of additional resources. Thus, the user of the client can easily learn of the existence of new resources that he or she had not specifically requested.

Methods of implementing Intranet and/or Intranet embodiments of computational and/or data access processes are well known to those of skill in the art and are documented, e.g., in ACM Press, pp.

383-392; ISO-ANSI, Working Draft, "Information Technology-Database Language SQL", Jim Melton, Editor, International Organization for Standardization and American National Standards Institute, Jul. 1992; ISO Working Draft, "Database Language SQL-Part 2:Foundation (SQL/Foundation)", CD9075-2:199.chi.SQL, Sep. 11, 1997; and Cluer et al. (1992) A General Framework for the Optimization of Object-Oriented Queries, Proc SIGMOD International Conference on Management of Data, San Diego, California, Jun. 2-5, 1992, SIGMOD Record, vol. 21, Issue 2, Jun., 1992; Stonebraker, M., Editor;. Other resources are available, e.g., from Microsoft, IBM, Sun and other software development companies.

Using the tools described above, users of the reagents, methods and database as discovery or diagnostic tools can query a centrally located database with expression and subject data. Each submission of data adds to the sum of expression and subject information in the database. As data is added, a new correlation statistical analysis is automatically run that incorporates the added clinical and expression data. Accordingly, the predictive accuracy and the types of correlations of the recorded molecular signatures increases as the database grows.

For example, subjects, such as patients, can access the results of the expression analysis of their leukocyte samples and any accrued knowledge regarding the likelihood of the patient's belonging to any specified diagnostic (or prognostic, or monitoring, or risk group), i.e., their expression profiles, and/or molecular signatures. Optionally, subjects can add to the predictive accuracy of the database by providing additional information to the database regarding diagnoses, test results, clinical or other related events that have occurred since the time of the expression profiling. Such information can be provided to the database via any form of communication, including, but not limited to, the internet. Such data can be used to continually define (and redefine) diagnostic groups. For example, if 1000 patients submit data regarding the occurrence of myocardial infarction over the 5 years since their expression profiling, and 300 of these patients report that they have experienced a myocardial infarction and 700 report that they have not, then the 300 patients define a new "group A." As the algorithm is used to continually query and revise the database, a new diagnostic nucleotide set that differentiates groups A and B (i.e., with and without myocardial infarction within a five year period) is identified. This newly defined nucleotide set is then be used (in the manner described above) as a test that predicts the occurrence of myocardial infarction over a five-year period. While submission directly by the patient is exemplified above, any individual with access and authority to submit the relevant data e.g., the patient's physician, a laboratory technician, a health care or study administrator, or the like, can do so.

As will be apparent from the above examples, transmission of information via the internet (or via an intranet) is optionally bi-directional. That is, for example, data regarding expression profiles, subject data, and the like are transmitted via a communication system to the database, while information regarding molecular signatures, predictive analysis, and the like, are transmitted from the database to the user. For example, using appropriate configurations of an integrated system including a microarray comprising a diagnostic nucleotide set, a detector linked to a computational device can directly transmit (locally or from a remote workstation at great distance, e.g., hundreds or thousands of miles distant from the database) expression profiles and a corresponding individual identifier to a

central database for analysis according to the methods of the invention. According to, e.g., the algorithms described above, the individual identifier is assigned to one or more diagnostic (or prognostic, or monitoring, etc.) categories. The results of this classification are then relayed back, via, e.g., the same mode of communication, to a recipient at the same or different internet (or intranet) address.

Kits

The present invention is optionally provided to a user as a kit. Typically, a kit contains one or more diagnostic nucleotide sets of the invention. Alternatively, the kit contains the candidate nucleotide library of the invention. Most often, the kit contains a diagnostic nucleotide probe set, or other subset of a candidate library, e.g., as a cDNA or antibody microarray packaged in a suitable container. The kit may further comprise, one or more additional reagents, e.g., substrates, labels, primers, for labeling expression products, tubes and/or other accessories, reagents for collecting blood samples, buffers, e.g., erythrocyte lysis buffer, leukocyte lysis buffer, hybridization chambers, cover slips, etc., as well as a software package, e.g., including the statistical methods of the invention, e.g., as described above, and a password and/or account number for accessing the compiled database. The kit optionally further comprises an instruction set or user manual detailing preferred methods of using the diagnostic nucleotide sets in the methods of the invention. In one embodiment, the kit may include contents useful for the discovery of diagnostic nucleotide sets using microarrays. The kit may include sterile, endotoxin and RNAse free blood collection tubes. The kit may also include alcohol swabs, tourniquet, blood collection set, and/or PBS (phosphate buffer saline; needed when method of example 2 is used to derived mononuclear RNA). The kit may also include cell lysis buffer. The kit may include RNA isolation kit, substrates for labeling of RNA (may vary for various expression profiling techniques). The kit may also include materials for fluorescence microarray expression profiling, including one or more of the following: reverse transcriptase and 10x RT buffer, T7(dT)24 primer (primer with T7 promoter at 5' end), DTT, deoxynucleotides, optionally 100mM each, RNAse inhibitor, second strand cDNA buffer, DNA polymerase, Rnase H, T7 RNA polymerase ribonucleotides, in vitro transcription buffer, and/or Cy3 and Cy5 labeled ribonucleotides. The kit may also include microarrays containing candidate gene libraries, cover slips for slides, and/or hybridization chambers. The kit may further include software package for identification of diagnostic gene set from data, that contains statistical methods, and/or allows alteration in desired sensitivity and specificity of gene set. The software may further facilitate access to and data analysis by centrally a located database server. The software may further include a password and account number to access central database server. In addition, the kit may include a kit user manual.

In another embodiment, the kit may include contents useful for the application of diagnostic nucleotide sets using microarrays. The kit may include sterile, endotoxin and/or RNAse free blood collection tubes. The kit may also include, alcohol swabs, tourniquet, and/or a blood collection set. The kit may further include PBS (phosphate buffer saline; needed when method of example 2 is used to derived mononuclear RNA), cell lysis buffer, and/or an RNA isolation kit. In addition, the kit may include substrates for labeling of RNA (may vary for various expression profiling techniques). For fluorescence microarray expression profiling, components may include reverse transcriptase and 10x

RT buffer, T7(dT)24 primer (primer with T7 promoter at 5' end), DTT, deoxynucleotides (optionally 100mM each), RNAse inhibitor, second strand cDNA buffer, DNA polymerase, Rnase H, T7 RNA polymerase, ribonucleotides, in vitro transcription buffer, and/or Cy3 and Cy5 labeled ribonucleotides. The kit may further include microarrays containing candidate gene libraries. The kit may also include cover slips for slides, and/or hybridization chambers. The kit may include a software package for identification of diagnostic gene set from data. The software package may contain statistical methods, allow alteration in desired sensitivity and specificity of gene set, and/or facilitate access to and data analysis by centrally located database server. The software package may include a password and account number to access central database server. In addition, the kit may include a kit user manual.

In another embodiment, the kit may include contents useful for the application of diagnostic nucleotide sets using real-time PCR. This kit may include terile, endotoxin and/or RNAse free blood collection tubes. The kit may further include alcohol swabs, tourniquet, and/or a blood collection set. The kit may also include PBS (phosphate buffer saline; needed when method of example 2 is used to derived mononuclear RNA). In addition, the kit may include cell lysis buffer and/or an RNA isolation kit. The kit may laso include substrates for real time RT-PCR, which may vary for various real-time PCR techniques, including poly dT primers, random hexamer primers, reverse Transcriptase and RT buffer, DTT, deoxynucleotides 100 mM, RNase H, primer pairs for diagnostic and control gene set, 10x PCR reaction buffer, and/or Taq DNA polymerase. The kit may also include fluorescent probes for diagnostic and control gene set (alternatively, fluorescent dye that binds to only double stranded DNA). The kit may further include reaction tubes with or without barcode for sample tracking, 96-well plates with barcode for sample identification, one barcode for entire set, or individual barcode per reaction tube in plate. The kit may also include a software package for identification of diagnostic gene set from data, and /or statistical methods. The software package may allow alteration in desired sensitivity and specificity of gene set, and/or facilitate access to and data analysis by centrally located database server. The kit may include a password and account number to access central database server. Finally, the kit may include a kit user manual.

This invention will be better understood by reference to the following non-limiting Examples:

LIST OF EXAMPLE TITLES

Example 1: Preparation of a leukocyte cDNA array comprising a candidate gene library

Example 2: Preparation of RNA from mononuclear cells for expression profiling

Example 3: Preparation of Universal Control RNA for use in leukocyte expression profiling

Example 4. RNA Labeling and hybridization to a leukocyte cDNA array of candidate nucleotide sequences.

Example 5: Clinical study for the Identification of diagnostic gene sets useful in diagnosis and treatment of Cardiac allograft rejection

Example 6: Identification of diagnostic nucleotide sets for kidney and liver allograft rejection

Example 7: Identification of diagnostic nucleotide sets for diagnosis of cytomegalovirus

Example 8: Design of oligonucleotide probes

Example 9: Production of an array of 8,000 spotted 50 mer oligonucleotides.

Example 10: Identification of diagnostic nucleotide sets for diagnosis of Cardiac Allograft Rejection using microarrays

Example 11: Amplification, labeling, and hybridization of total RNA to an oligonucleotide microarray

Example 12: Real-time PCR validation of array expression results

Example 13: Real-time PCR expression markers of acute allograft rejection

Example 14: Identification of diagnostic nucleotide sets for diagnosis of Cardiac Allograft Rejection using microarrays

Example 15: Correlation and Classification Analysis

Example 16: Acute allograft rejection: biopsy tissue gene expression profiling

Example 17: Microarray and PCR gene expression panels for diagnosis and monitoring of acute allograft rejection

Example 18: Assay sample preparation

Example 19: Allograft rejection diagnostic gene sequence analysis

Example 20: Detection of proteins expressed by diagnostic gene sequences

Example 21: Detecting changes in the rate of hematopoiesis

Examples

Example 1: Preparation of a leukocyte cDNA array comprising a candidate gene library

Candidate genes and gene sequences for leukocyte expression profiling are identified through methods described elsewhere in this document. Candidate genes are used to obtain or design probes for peripheral leukocyte expression profiling in a variety of ways.

A cDNA microarray carrying 384 probes was constructed using sequences selected from the initial candidate library. cDNAs is selected from T-cell libraries, PBMC libraries and buffy coat libraries.

96-Well PCR

Plasmids are isolated in 96-well format and PCR was performed in 96-well format. A master mix is made that contain the reaction buffer, dNTPs, forward and reverse primer and DNA polymerase was made. 99 ul of the master mix was aliquoted into 96-well plate. 1 ul of plasmid (1-2 ng/ul) of plasmid was added to the plate. The final reaction concentration was 10 mM Tris pH 8.3, 3.5 mM MgCl2, 25 mM KCl, 0.4 mM dNTPs, 0.4 uM M13 forward primer, 0.4 M13 reverse primer, and 10 U of Taq Gold (Applied Biosystems). The PCR conditions were:

Step 1 95C for 10 min

Step 2 95C for 15 sec

Step 3 56C for 30 sec

Step 4 72C for 2 min 15 seconds

Step 5 go to Step 2 39 times

Step 6 72C for 10 minutes

Step 7 4C for ever.

PCR Purification

PCR purification is done in a 96-well format. The ArrayIt (Telechem International, Inc.) PCR purification kit is used and the provided protocol was followed without modification. Before the

sample is evaporated to dryness, the concentration of PCR products was determined using a spectrophotometer. After evaporation, the samples are re-suspended in 1x Micro Spotting Solution (ArrayIt) so that the majority of the samples were between 0.2-1.0 ug/ul.

Array Fabrication

Spotted cDNA microarrays are then made from these PCR products by ArrayIt using their protocols, which may be found at the ArrayIt website. Each fragment was spotted 3 times onto each array. Candidate genes and gene sequences for leukocyte expression profiling are identified through methods described elsewhere in this document. Those candidate genes are used for peripheral leukocyte expression profiling. The candidate libraries can used to obtain or design probes for expression profiling in a variety of ways.

Oligonucleotide probes are prepared using the gene sequences of Table 2, Table 8, and the sequence listing. Oligo probes are designed on a contract basis by various companies (for example, Compugen, Mergen, Affymetrix, Telechem), or designed from the candidate sequences using a variety of parameters and algorithms as indicated at located at the MIT web site. Briefly, the length of the oligonucleotide to be synthesized is determined, preferably greater than 18 nucleotides, generally 18-24 nucleotides, 24-70 nucleotides and, in some circumstances, more than 70 nucleotides. The sequence analysis algorithms and tools described above are applied to the sequences to mask repetitive elements, vector sequences and low complexity sequences. Oligonucleotides are selected that are specific to the candidate nucleotide sequence (based on a Blast n search of the oligonucleotide sequence in question against gene sequences databases, such as the Human Genome Sequence, UniGene, dbEST or the non-redundant database at NCBI), and have <50% G content and 25--70% G+C content. Desired oligonucleotides are synthesized using well-known methods and apparatus, or ordered from a company (for example Sigma). Oligonucleotides are spotted onto microarrays. Alternatively, oligonucleotides are synthesized directly on the array surface, using a variety of techniques (Hughes et al. 2001, Yershov et al. 1996, Lockhart et al 1996).

Example 2: Preparation of RNA from mononuclear cells for expression profiling

Blood was isolated from the subject for leukocyte expression profiling using the following methods: Two tubes were drawn per patient. Blood was drawn from either a standard peripheral venous blood draw or directly from a large-bore intra-arterial or intravenous catheter inserted in the femoral artery, femoral vein, subclavian vein or internal jugular vein. Care was taken to avoid sample contamination with heparin from the intravascular catheters, as heparin can interfere with subsequent RNA reactions. For each tube, 8 ml of whole blood was drawn into a tube (CPT, Becton-Dickinson order #362753) containing the anticoagulant Citrate, 25°C density gradient solution (e.g. Ficoll, Percoll) and a polyester gel barrier that upon centrifugation was permeable to RBCs and granulocytes but not to mononuclear cells. The tube was inverted several times to mix the blood with the anticoagulant. The tubes were centrifuged at 1750xg in a swing-out rotor at room temperature for 20 minutes. The tubes were removed from the centrifuge and inverted 5-10 times to mix the plasma with the mononuclear cells, while trapping the RBCs and the granulocytes beneath the gel barrier. The plasma/mononuclear cell mix was decanted into a 15ml tube and 5ml of phosphate-buffered saline (PBS) is added. The 15ml tubes were spun for 5 minutes at 1750xg to pellet the cells. The supernatant was discarded and

1.8 ml of RLT lysis buffer is added to the mononuclear cell pellet. The buffer and cells were pipetted up and down to ensure complete lysis of the pellet. The cell lysate was frozen and stored until it is convenient to proceed with isolation of total RNA.

Total RNA was purified from the lysed mononuclear cells using the Qiagen Rneasy Miniprep kit, as directed by the manufacturer (10/99 version) for total RNA isolation, including homogenization (Qiashredder columns) and on-column DNase treatment. The purified RNA was eluted in 50ul of water. The further use of RNA prepared by this method is described in Examples 10 and 11.

Some samples were prepared by a different protocol, as follows:

Two 8 ml blood samples were drawn from a peripheral vein into a tube (CPT, Becton-Dickinson order #362753) containing anticoagulant (Citrate), 25°C density gradient solution (Ficoll) and a polyester gel barrier that upon centrifugation is permeable to RBCs and granulocytes but not to mononuclear cells. The mononuclear cells and plasma remained above the barrier while the RBCs and granulocytes were trapped below. The tube was inverted several times to mix the blood with the anticoagulant, and the tubes were subjected to centrifugation at 1750xg in a swing-out rotor at room temperature for 20 min. The tubes were removed from the centrifuge, and the clear plasma layer above the cloudy mononuclear cell layer was aspirated and discarded. The cloudy mononuclear cell layer was aspirated, with care taken to rinse all of the mononuclear cells from the surface of the gel barrier with PBS (phosphate buffered saline). Approximately 2 mls of mononuclear cell suspension was transferred to a 2ml microcentrifuge tube, and centrifuged for 3min. at 16,000 rpm in a microcentrifuge to pellet the cells. The supernatant was discarded and 1.8 ml of RLT lysis buffer (Qiagen) were added to the mononuclear cell pellet, which lysed the cells and inactivated Rnases. The cells and lysis buffer were pipetted up and down to ensure complete lysis of the pellet. Cell lysate was frozen and stored until it was convenient to proceed with isolation of total RNA.

RNA samples were isolated from 8 mL of whole blood. Yields ranged from 2 ug to 20ug total RNA for 8mL blood. A260/A280 spectrophotometric ratios were between 1.6 and 2.0, indicating purity of sample. 2ul of each sample were run on an agarose gel in the presence of ethidium bromide. No degradation of the RNA sample and no DNA contamination was visible.

In some cases, specific subsets of mononuclear cells were isolated from peripheral blood of human subjects. When this was done, the StemSep cell separation kits (manual version 6.0.0) were used from StemCell Technologies (Vancouver, Canada). This same protocol can be applied to the isolation of T cells, CD4 T cells, CD8 T cells, B cells, monocytes, NK cells and other cells. Isolation of cell types using negative selection with antibodies may be desirable to avoid activation of target cells by antibodies.

Example 3: Preparation of Universal Control RNA for use in leukocyte expression profiling

Control RNA was prepared using total RNA from Buffy coats and/or total RNA from enriched mononuclear cells isolated from Buffy coats, both with and without stimulation with ionomycin and PMA. The following control RNAs were prepared:

Control 1: Buffy Coat Total RNA

Control 2: Mononuclear cell Total RNA

Control 3: Stimulated buffy coat Total RNA

Control 4: Stimulated mononuclear Total RNA

Control 5: 50% Buffy coat Total RNA / 50% Stimulated buffy coat Total RNA

Control 6: 50% Mononuclear cell Total RNA / 50% Stimulated Mononuclear Total RNA

Some samples were prepared using the following protocol: Buffy coats from 38 individuals were obtained from Stanford Blood Center. Each buffy coat is derived from ~350 mL whole blood from one individual. 10 ml buffy coat was removed from the bag, and placed into a 50 ml tube. 40 ml of Buffer EL (Qiagen) was added, the tube was mixed and placed on ice for 15 minutes, then cells were pelleted by centrifugation at 2000xg for 10 minutes at 4°C. The supernatant was decanted and the cell pellet was re-suspended in 10 ml of Qiagen Buffer EL. The tube was then centrifuged at 2000xg for 10 minutes at 4°C. The cell pellet was then re-suspended in 20 ml TRIZOL (GibcoBRL) per Buffy coat sample, the mixture was shredded using a rotary homogenizer, and the lysate was then frozen at –80°C prior to proceeding to RNA isolation.

Other control RNAs were prepared from enriched mononuclear cells prepared from Buffy coats. Buffy coats from Stanford Blood Center were obtained, as described above. 10 ml buffy coat was added to a 50 ml polypropylene tube, and 10 ml of phosphate buffer saline (PBS) was added to each tube. A polysucrose (5.7 g/dL) and sodium diatrizoate (9.0 g/dL) solution at a 1.077 +/-0.0001 g/ml density solution of equal volume to diluted sample was prepared (Histopaque 1077, Sigma cat. no 1077-1). This and all subsequent steps were performed at room temperature. 15 ml of diluted buffy coat/PBS was layered on top of 15 ml of the histopaque solution in a 50 ml tube. The tube was centrifuged at 400xg for 30 minutes at room temperature. After centrifugation, the upper layer of the solution to within 0.5 cm of the opaque interface containing the mononuclear cells was discarded. The opaque interface was transferred into a clean centrifuge tube. An equal volume of PBS was added to each tube and centrifuged at 350xg for 10 minutes at room temperature. The supernatant was discarded. 5 ml of Buffer EL (Qiagen) was used to resuspend the remaining cell pellet and the tube was centrifuged at 2000xg for 10 minutes at room temperature. The supernatant was discarded. The pellet was resuspended in 20 ml of TRIZOL (GibcoBRL) for each individual buffy coat that was processed. The sample was homogenized using a rotary homogenizer and frozen at -80C until RNA was isolated. RNA was isolated from frozen lysed Buffy coat samples as follows: frozen samples were thawed, and 4 ml of chloroform was added to each buffy coat sample. The sample was mixed by vortexing and centrifuged at 2000xg for 5 minutes. The aqueous layer was moved to new tube and then repurified by using the RNeasy Maxi RNA clean up kit, according to the manufacturer's instruction (Qiagen, PN 75162). The yield, purity and integrity were assessed by spectrophotometer and gel electrophoresis.

Some samples were prepared by a different protocol, as follows. The further use of RNA prepared using this protocol is described in Example 11.

50 whole blood samples were randomly selected from consented blood donors at the Stanford Medical School Blood Center. Each buffy coat sample was produced from ~350 mL of an individual's donated blood. The whole blood sample was centrifuged at ~4,400 x g for 8 minutes at room temperature, resulting in three distinct layers: a top layer of plasma, a second layer of buffy coat, and a third layer of red blood cells. 25 ml of the buffy coat fraction was obtained and diluted with an equal volume of PBS (phosphate buffered saline). 30 ml of diluted buffy coat was layered onto 15 ml of sodium diatrizoate

solution adjusted to a density of 1.077+/-0.001 g/ml (Histopaque 1077, Sigma) in a 50mL plastic tube. The tube was spun at 800 g for 10 minutes at room temperature. The plasma layer was removed to the 30 ml mark on the tube, and the mononuclear cell layer removed into a new tube and washed with an equal volume of PBS, and collected by centrifugation at 2000 g for 10 minutes at room temperature. The cell pellet was resuspended in 10 ml of Buffer EL (Qiagen) by vortexing and incubated on ice for 10 minutes to remove any remaining erthythrocytes. The mononuclear cells were spun at 2000 g for 10 minutes at 4 degrees Celsius. The cell pellet was lysed in 25 ml of a phenol/guanidinium thiocyanate solution (TRIZOL Reagent, Invitrogen). The sample was homogenized using a PowerGene 5 rotary homogenizer (Fisher Scientific) and Omini disposable generator probes (Fisher Scientific). The Trizol lysate was frozen at –80 degrees C until the next step.

The samples were thawed out and incubated at room temperature for 5 minutes. 5 ml chloroform was added to each sample, mixed by vortexing, and incubated at room temperature for 3 minutes. The aqueous layers were transferred to new 50 ml tubes. The aqueous layer containing total RNA was further purified using the Qiagen RNeasy Maxi kit (PN 75162), per the manufacturer's protocol (October 1999). The columns were eluted twice with 1 ml Rnase-free water, with a minute incubation before each spin. Quantity and quality of RNA was assessed using standard methods. Generally, RNA was isolated from batches of 10 buffy coats at a time, with an average yield per buffy coat of 870 μg, and an estimated total yield of 43.5 mg total RNA with a 260/280 ratio of 1.56 and a 28S/18S ratio of 1.78.

Quality of the RNA was tested using the Agilent 2100 Bioanalyzer using RNA 6000 microfluidics chips. Analysis of the electrophorgrams from the Bioanalyzer for five different batches demonstrated the reproducibility in quality between the batches.

Total RNA from all five batches were combined and mixed in a 50 ml tube, then aliquoted as follows: 2 x 10 ml aliquots in 15 ml tubes, and the rest in 100 μl aliquots in 1.5 ml microcentrifuge tubes. The aliquots gave highly reproducible results with respect to RNA purity, size and integrity. The RNA was stored at –80°C.

Test hybridization of Reference RNA.

When compared with BC38 and Stimulated mononuclear reference samples, the R50 performed as well, if not better than the other reference samples as shown in Figure 3. In an analysis of hybridizations, where the R50 targets were fluorescently labeled with Cy-5 using methods described herein and the amplified and labeled aRNA was hybridized (as in example 11) to the olignoucleotide array described in example 9. The R50 detected 97.3% of probes with a Signal to Noise ratio (S/N) of greater than three and 99.9 % of probes with S/N greater than one.

Example 4. RNA Labeling and hybridization to a leukocyte cDNA array of candidate nucleotide sequences.

Comparison of Guanine-Silica to Acid-Phenol RNA Purification (GSvsAP)

These data are from a set of 12 hybridizations designed to identify differences between the signal strength from two different RNA purification methods. The two RNA methods used were guanidine-silica (GS, Qiagen) and acid-phenol (AP, Trizol, Gibco BRL). Ten tubes of blood were drawn from each of four people. Two were used for the AP prep, the other eight were used for the GS prep. The

protocols for the leukocyte RNA preps using the AP and GS techniques were completed as described here:

Guanidine-silica (GS) method:

For each tube, 8ml blood was drawn into a tube containing the anticoagulant Citrate, 25°C density gradient solution and a polyester gel barrier that upon centrifugation is permeable to RBCs and granulocytes but not to mononuclear cells. The mononuclear cells and plasma remained above the barrier while the RBCs and granulocytes were trapped below. CPT tubes from Becton-Dickinson (#362753) were used for this purpose. The tube was inverted several times to mix the blood with the anticoagulant. The tubes were immediately centrifuged @1750xg in a swinging bucket rotor at room temperature for 20 min. The tubes were removed from the centrifuge and inverted 5-10 times. This mixed the plasma with the mononuclear cells, while the RBCs and the granulocytes remained trapped beneath the gel barrier. The plasma/mononuclear cell mix was decanted into a 15ml tube and 5ml of phosphate-buffered saline (PBS) was added. The 15ml tubes are spun for 5 minutes at 1750xg to pellet the cells. The supernatant was discarded and 1.8 ml of RLT lysis buffer (guanidine isothyocyanate) was added to the mononuclear cell pellet. The buffer and cells were pipetted up and down to ensure complete lysis of the pellet. The cell lysate was then processed exactly as described in the Qiagen Rneasy Miniprep kit protocol (10/99 version) for total RNA isolation (including steps for homogenization (Qiashredder columns) and on-column DNase treatment. The purified RNA was eluted in 50ul of water.

Acid-phenol (AP) method:

For each tube, 8ml blood was drawn into a tube containing the anticoagulant Citrate, 25°C density gradient solution and a polyester gel barrier that upon centrifugation is permeable to RBCs and granulocytes but not to mononuclear cells. The mononuclear cells and plasma remained above the barrier while the RBCs and granulocytes were trapped below. CPT tubes from Becton-Dickinson (#362753) were used for this purpose. The tube was inverted several times to mix the blood with the anticoagulant. The tubes were immediately centrifuged @1750xg in a swinging bucket rotor at room temperature for 20 min. The tubes were removed from the centrifuge and inverted 5-10 times. This mixed the plasma with the mononuclear cells, while the RBCs and the granulocytes remained trapped beneath the gel barrier. The plasma/mononuclear cell mix was decanted into a 15ml tube and 5ml of phosphate-buffered saline (PBS) was added. The 15ml tubes are spun for 5 minutes @1750xg to pellet the cells. The supernatant was discarded and the cell pellet was lysed using 0.6 mL Phenol/guanidine isothyocyanate (e.g. Trizol reagent, GibcoBRL). Subsequent total RNA isolation proceeded using the manufacturers protocol.

RNA from each person was labeled with either Cy3 or Cy5, and then hybridized in pairs to the mini-array. For instance, the first array was hybridized with GS RNA from one person (Cy3) and GS RNA from a second person (Cy5).

Techniques for labeling and hybridization for all experiments discussed here were completed as detailed above. Arrays were prepared as described in example 1.

RNA isolated from subject samples, or control Buffy coat RNA, were labeled for hybridization to a cDNA array. Total RNA (up to 100 μg) was combined with 2 μl of 100 μM solution of an Oligo

(dT)12-18 (GibcoBRL) and heated to 70°C for 10 minutes and place on ice. Reaction buffer was added to the tube, to a final concentration of 1xRT buffer (GibcoBRL), 10 mM DTT (GibcoBRL), 0.1 mM unlabeled dATP, dTTP, and dGTP, and 0.025 mM unlabeled dCTP, 200 pg of CAB (A. thaliana photosystem I chlorophyll a/b binding protein), 200 pg of RCA (A. thaliana RUBISCO activase), 0.25 mM of Cy-3 or Cy-5 dCTP, and 400 U Superscript II RT (GibcoBRL).

The volumes of each component of the labeling reaction were as follows: 20 µl of 5xRT buffer; 10 µl of 100 mM DTT; 1 µl of 10 mM dNTPs without dCTP; 0.5 µl of 5 mM CTP; 13 µl of H20; 0.02 µl of 10 ng/µl CAB and RCA; 1 µl of 40 Units/µl RNAseOUT Recombinatnt Ribonuclease Inhibitor (GibcoBRL); 2.5 µl of 1.0 mM Cy-3 or Cy-5 dCTP; and 2.0 µl of 200 Units/µl of Superscript II RT. The sample was vortexed and centrifuged. The sample was incubated at 4°C for 1 hour for first strand cDNA synthesis, then heated at 70°C for 10 minutes to quench enzymatic activity. 1 µl of 10 mg/ml of Rnase A was added to degrade the RNA strand, and the sample was incubated at 37°C for 30 minutes. Next, the Cy-3 and Cy-5 cDNA samples were combined into one tube. Unincorporated nucleotides were removed using QIAquick RCR purification protocol (Qiagen), as directed by the manufacturer. The sample was evaporated to dryness and resuspended in 5 µl of water. The sample was mixed with hybridization buffer containing 5xSSC, 0.2% SDS, 2 mg/ml Cot-1 DNA (GibcoBRL), 1 mg/ml yeast tRNA (GibcoBRL), and 1.6 ng/µl poly dA40-60 (Pharmacia). This mixture was placed on the microarray surface and a glass cover slip was placed on the array (Corning). The microarray glass slide was placed into a hybridization chamber (ArrayIt). The chamber was then submerged in a water bath overnight at 62° C. The microarray was removed from the cassette and the cover slip was removed by repeatedly submerging it to a wash buffer containing 1xSSC, and 0.1% SDS. The microarray slide was washed in 1xSSC/0.1% SDS for 5 minutes. The slide was then washed in 0.1%SSC/0.1% SDS for 5 minutes. The slide was finally washed in 0.1xSSC for 2 minutes. The slide was spun at 1000 rpm for 2 minutes to dry out the slide, then scanned on a microarray scanner (Axon Instruments, Union City, CA.).

Six hybridizations with 20 µg of RNA were performed for each type of RNA preparation (GS or AP). Since both the Cy3 and the Cy5 labeled RNA are from test preparations, there are six data points for each GS prepped, Cy3-labeled RNA and six for each GS-prepped, Cy5-labeled RNA. The mini array hybridizations were scanned on and Axon Instruments scanner using GenPix 3.0 software. The data presented were derived as follows. First, all features flagged as "not found" by the software were removed from the dataset for individual hybridizations. These features are usually due to high local background or other processing artifacts. Second, the median fluorescence intensity minus the background fluorescence intensity was used to calculate the mean background subtracted signal for each dye for each hybridization. In Figure 3, the mean of these means across all six hybridizations is graphed (n=6 for each column). The error bars are the SEM. This experiment shows that the average signal from AP prepared RNA is 47% of the average signal from GS prepared RNA for both Cy3 and Cy5.

Generation of expression data for leukocyte genes from peripheral leukocyte samples

Six hybridizations were performed with RNA purified from human blood leukocytes using the protocols given above. Four of the six were prepared using the GS method and 2 were prepared using

the AP method. Each preparation of leukocyte RNA was labeled with Cy3 and 10 μg hybridized to the mini-array. A control RNA was batch labeled with Cy5 and 10 μg hybridized to each mini-array together with the Cy3-labeled experimental RNA.

The control RNA used for these experiments was Control 1: Buffy Coat RNA, as described above. The protocol for the preparation of that RNA is reproduced here:

Buffy Coat RNA Isolation:

Buffy coats were obtained from Stanford Blood Center (in total 38 individual buffy coats were used. Each buffy coat is derived from ~350 mL whole blood from one individual. 10 ml buffy coat was taken and placed into a 50 ml tube and 40 ml of a hypoclorous acid (HOCl) solution (Buffer EL from Qiagen) was added. The tube was mixed and placed on ice for 15 minutes. The tube was then centrifuged at 2000xg for 10 minutes at 4°C. The supernatant was decanted and the cell pellet was re-suspended in 10 ml of hypochlorous acid solution (Qiagen Buffer EL). The tube was then centrifuged at 2000xg for 10 minutes at 4°C. The cell pellet was then re-suspended in 20 ml phenol/guanidine thiocyanate solution (TRIZOL from GibcoBRL) for each individual buffy coat that was processed. The mixture was then shredded using a rotary homogenizer. The lysate was then frozen at –80°C prior to proceeding to RNA isolation.

The arrays were then scanned and analyzed on an Axon Instruments scanner using GenePix 3.0 software. The data presented were derived as follows. First, all features flagged as "not found" by the software were removed from the dataset for individual hybridizations. Second, control features were used to normalize the data for labeling and hybridization variability within the experiment. The control features are cDNA for genes from the plant, *Arabidopsis thaliana*, that were included when spotting the mini-array. Equal amounts of RNA complementary to two of these cDNAs were added to each of the samples before they were labeled. A third was pre-labeled and equal amounts were added to each hybridization solution before hybridization. Using the signal from these genes, we derived a normalization constant (L_j) according to the following formula:

$$L_j = \frac{\frac{\sum_{i=1}^{N} BGSS_{j,i}}{N}}{\frac{\sum_{j=1}^{K} \frac{\sum_{i=1}^{N} BGSS_{j,i}}{N}}{K}}$$

where $BGSS_i$ is the signal for a specific feature as identified in the GenePix software as the median background subtracted signal for that feature, N is the number of *A. thaliana* control features, K is the number of hybridizations, and L is the normalization constant for each individual hybridization. Using the formula above, the mean over all control features of a particular hybridization and dye (eg Cy3) was calculated. Then these control feature means for all Cy3 hybridizations were averaged. The

control feature mean in one hybridization divided by the average of all hybridizations gives a normalization constant for that particular Cy3 hybridization.

The same normalization steps were performed for Cy3 and Cy5 values, both fluorescence and background. Once normalized, the background Cy3 fluorescence was subtracted from the Cy3 fluorescence for each feature. Values less than 100 were eliminated from further calculations since low values caused spurious results.

Figure 4 shows the average background subtracted signal for each of nine leukocyte-specific genes on the mini array. This average is for 3-6 of the above-described hybridizations for each gene. The error bars are the SEM.

The ratio of Cy3 to Cy5 signal is shown for a number of genes. This ratio corrects for variability among hybridizations and allows comparison between experiments done at different times. The ratio is calculated as the Cy3 background subtracted signal divided by the Cy5 background subtracted signal. Each bar is the average for 3-6 hybridizations. The error bars are SEM.

Together, these results show that we can measure expression levels for genes that are expressed specifically in sub-populations of leukocytes. These expression measurements were made with only 10 μg of leukocyte total RNA that was labeled directly by reverse transcription. The signal strength can be increased by improved labeling techniques that amplify either the starting RNA or the signal fluorescence. In addition, scanning techniques with higher sensitivity can be used.

Genes in Figures 4 and 5:

Gene Name/Description	GenBank Accession Number	Gene Name Abbreviatio
T cell-specific tyrosine kinase Mrna	L10717	TKTCS
Interleukin 1 alpha (IL 1) mRNA, complete cds	NM_000575	IL1A
T-cell surface antigen CD2 (T11) mRNA, complete cds	M14362	CD2
Interleukin-13 (IL-13) precursor gene, complete cds	U31120	IL-13
Thymocyte antigen CD1a mRNA, complete cds	M28825	CD1a
CD6 mRNA for T cell glycoprotein CDS	NM_006725	CD6
MHC class II HLA-DQA1 mRNA, complete cds	U77589	HLA-DQA1
Granulocyte colony-stimulating factor	M28170	CD19
Homo sapiens CD69 antigen	NM_001781	CD69

Example 5: Clinical study to identify diagnostic gene sets useful in diagnosis and treatment of cardiac allograft recipients

An observational study was conducted in which a prospective cohort of cardiac transplant recipients were analyzed for associations between clinical events or rejection grades and expression of a leukocyte candidate nucleotide sequence library. Patients were identified at 4 cardiac transplantation

centers while on the transplant waiting list or during their routing post-transplant care. All adult cardiac transplant recipients (new or re-transplants) who received an organ at the study center during the study period or within 3 months of the start of the study period were eligible. The first year after transplantation is the time when most acute rejection occurs and it is thus important to study patients during this period. Patients provided informed consent prior to study procedures.

Peripheral blood leukocyte samples were obtained from all patients at the following time points: prior to transplant surgery (when able), the same day as routinely scheduled screening biopsies, upon evaluation for suspected acute rejection (urgent biopsies), on hospitalization for an acute complication of transplantation or immunosuppression, and when Cytomegalovirus (CMV) infection was suspected or confirmed. Samples were obtained through a standard peripheral vein blood draw or through a catheter placed for patient care (for example, a central venous catheter placed for endocardial biopsy). When blood was drawn from a intravenous line, care was taken to avoid obtaining heparin with the sample as it can interfere with downstream reactions involving the RNA. Mononuclear cells were prepared from whole blood samples as described in Example 2. Samples were processed within 2 hours of the blood draw and DNA and serum were saved in addition to RNA. Samples were stored at –80° C or on dry ice and sent to the site of RNA preparation in a sealed container with ample dry ice. RNA was isolated from subject samples as described in Example 2 and hybridized to a candidate library of differentially expressed leukocyte nucleotide sequences, as further described in Examples 9-10. Methods used for amplification, labeling, hybridization and scanning are described in Example 11. Analysis of human transplant patient mononuclear cell RNA hybridized to a microarray and identification of diagnostic gene sets is shown in Example 10.

From each patient, clinical information was obtained at the following time points: prior to transplant surgery (when available), the same day as routinely scheduled screening biopsies, upon evaluation for suspected acute rejection (e.g., urgent biopsies), on hospitalization for an acute complication of transplantation or immunosuppression, and when Cytomegalovirus (CMV) infection was suspected or confirmed. Data was collected directly from the patient, from the patient's medical record, from diagnostic test reports or from computerized hospital databases. It was important to collect all information pertaining to the study clinical correlates (diagnoses and patient events and states to which expression data is correlated) and confounding variables (diagnoses and patient events and states that may result in altered leukocyte gene expression. Examples of clinical data collected are: patient sex, date of birth, date of transplant, race, requirement for prospective cross match, occurrence of pre-transplant diagnoses and complications, indication for transplantation, severity and type of heart disease, history of left ventricular assist devices, all known medical diagnoses, blood type, HLA type, viral serologies (including CMV, Hepatitis B and C, HIV and others), serum chemistries, white and red blood cell counts and differentials, CMV infections (clinical manifestations and methods of diagnosis), occurrence of new cancer, hemodynamic parameters measured by catheterization of the right or left heart (measures of graft function), results of echocardiography, results of coronary angiograms, results of intravascular ultrasound studies (diagnosis of transplant vasculopathy), medications, changes in medications, treatments for rejection, and medication levels. Information was also collected regarding the organ donor, including demographics, blood type, HLA type, results of screening cultures, results

of viral serologies, primary cause of brain death, the need for inotropic support, and the organ cold ischemia time.

Of great importance was the collection of the results of endocardial biopsy for each of the patients at each visit. Biopsy results were all interpreted and recorded using the international society for heart and lung transplantation (ISHLT) criteria, described below. Biopsy pathological grades were determined by experienced pathologists at each center.

ISHLT Criteria

Grade	Finding	Rejection Severity
0	No lymphocytic infiltrates	None
1A	Focal (perivascular or interstitial lymphocytic infiltrates without necrosis)	Borderline mild
1B	Diffuse but sparse lymphocytic infiltrates without necrosis	Mild
2	One focus only with aggressive lymphocytic infiltrate and/or myocyte damage	Mild, focal moderate
3A	Multifocal aggressive lymphocytic infiltrates and/or myocardial damage	Moderate
3B	Diffuse inflammatory lymphocytic infiltrates with necrosis	Borderline Severe
4	Diffuse aggressive polymorphous lymphocytic infiltrates with edema hemorrhage and vasculitis, with necrosis	Severe

Because variability exists in the assignment of ISHLT grades, it was important to have a centralized and blinded reading of the biopsy slides by a single pathologist. This was arranged for all biopsy slides associated with samples in the analysis. Slides were obtained and assigned an encoded number. A single pathologist then read all slides from all centers and assigned an ISHLT grade. Grades from the single pathologist were then compared to the original grades derived from the pathologists at the study centers. For the purposes of correlation analysis of leukocyte gene expression to biopsy grades, the centralized reading information was used in a variety of ways (see Example 10 for more detail). In some analyses, only the original reading was used as an outcome. In other analyses, the result from the centralized reader was used as an outcome. In other analyses, the highest of the 2 grades was used. For example, if the original assigned grade was 0 and the centralized reader assigned a 1A, then 1A was the grade used as an outcome. In some analyses, the highest grade was used and then samples associated with a Grade 1A reading were excluded from the analysis. In some analyses, only grades with no disagreement between the 2 readings were used as outcomes for correlation analysis.

Clinical data was entered and stored in a database. The database was queried to identify all patients and patient visits that meet desired criteria (for example, patients with > grade II biopsy results, no CMV infection and time since transplant < 12 weeks).

The collected clinical data (disease criteria) is used to define patient or sample groups for correlation of expression data. Patient groups are identified for comparison, for example, a patient group that possesses a useful or interesting clinical distinction, versus a patient group that does not possess the distinction. Examples of useful and interesting patient distinctions that can be made on the basis of collected clinical data are listed here:

1. Rejection episode of at least moderate histologic grade, which results in treatment of the patient with additional corticosteroids, anti-T cell antibodies, or total lymphoid irradiation.
2. Rejection with histologic grade 2 or higher.
3. Rejection with histologic grade <2.
4. The absence of histologic rejection and normal or unchanged allograft function (based on hemodynamic measurements from catheterization or on echocardiographic data).
5. The presence of severe allograft dysfunction or worsening allograft dysfunction during the study period (based on hemodynamic measurements from catheterization or on echocardiographic data).
6. Documented CMV infection by culture, histology, or PCR, and at least one clinical sign or symptom of infection.
7. Specific graft biopsy rejection grades
8. Rejection of mild to moderate histologic severity prompting augmentation of the patient's chronic immunosuppressive regimen
9. Rejection of mild to moderate severity with allograft dysfunction prompting plasmaphoresis or a diagnosis of "humoral" rejection
10. Infections other than CMV, esp. Epstein Barr virus (EBV)
11. Lymphoproliferative disorder (also called, post-transplant lymphoma)
12. Transplant vasculopathy diagnosed by increased intimal thickness on intravascular ultrasound (IVUS), angiography, or acute myocardial infarction.
13. Graft Failure or Retransplantation
14. All cause mortality
15. Grade 1A or higher rejection as defined by the initial biopsy reading.
16. Grade 1B or higher rejection as defined by the initial biopsy reading.
17. Grade 1A or higher rejection as defined by the centralized biopsy reading.
18. Grade 1B or higher rejection as defined by the centralized biopsy reading.
19. Grade 1A or higher rejection as defined by the highest of the initial and centralized biopsy reading.
20. Grade 1B or higher rejection as defined by the highest of the initial and centralized biopsy reading.
21. Any rejection > Grade 2 occurring in patient at any time in the post-transplant course.

Expression profiles of subject samples are examined to discover sets of nucleotide sequences with differential expression between patient groups, for example, by methods describes above and below. Non-limiting examples of patient leukocyte samples to obtain for discovery of various diagnostic nucleotide sets are as follows:

Leukocyte set to avoid biopsy or select for biopsy:
Samples : Grade 0 vs. Grades 1-4

Leukocyte set to monitor therapeutic response:
Examine successful vs. unsuccessful drug treatment.

Samples:
Successful: Time 1: rejection, Time 2: drug therapy Time 3: no rejection
Unsuccessful: Time 1: rejection, Time 2: drug therapy; Time 3: rejection

Leukocyte set to predict subsequent acute rejection.
Biopsy may show no rejection, but the patient may develop rejection shortly thereafter. Look at profiles of patients who subsequently do and do not develop rejection.

Samples:
Group 1 (Subsequent rejection): Time 1: Grade 0; Time 2: Grade>0
Group 2 (No subsequent rejection): Time 1: Grade 0; Time 2: Grade 0

Focal rejection may be missed by biopsy. When this occurs the patient may have a Grade 0, but actually has rejection. These patients may go on to have damage to the graft etc.

Samples:
Non-rejectors: no rejection over some period of time
Rejectors: an episode of rejection over same period

Leukocyte set to diagnose subsequent or current graft failure:

Samples:
Echocardiographic or catheterization data to define worsening function over time and correlate to profiles.

Leukocyte set to diagnose impending active CMV:

Samples:
Look at patients who are CMV IgG positive. Compare patients with subsequent (to a sample) clinical CMV infection verses no subsequent clinical CMV infection.

Leukocyte set to diagnose current active CMV:

Samples:
Analyze patients who are CMV IgG positive. Compare patients with active current clinical CMV infection vs. no active current CMV infection.

Upon identification of a nucleotide sequence or set of nucleotide sequences that distinguish patient groups with a high degree of accuracy, that nucleotide sequence or set of nucleotide sequences is validated, and implemented as a diagnostic test. The use of the test depends on the patient groups that are used to discover the nucleotide set. For example, if a set of nucleotide sequences is discovered that have collective expression behavior that reliably distinguishes patients with no histological rejection or graft dysfunction from all others, a diagnostic is developed that is used to screen patients for the need for biopsy. Patients identified as having no rejection do not need biopsy, while others are subjected to a biopsy to further define the extent of disease. In another example, a diagnostic nucleotide set that determines continuing graft rejection associated with myocyte necrosis (> grade I) is used to determine that a patient is not receiving adequate treatment under the current treatment regimen. After increased

or altered immunosuppressive therapy, diagnostic profiling is conducted to determine whether continuing graft rejection is progressing. In yet another example, a diagnostic nucleotide set(s) that determine a patient's rejection status and diagnose cytomegalovirus infection is used to balance immunosuppressive and anti-viral therapy.

The methods of this example are also applicable to cardiac xenograft monitoring.

Example 6: Identification of diagnostic nucleotide sets for kidney and liver allograft rejection

Diagnostic tests for rejection are identified using patient leukocyte expression profiles to identify a molecular signature correlated with rejection of a transplanted kidney or liver. Blood, or other leukocyte source, samples are obtained from patients undergoing kidney or liver biopsy following liver or kidney transplantation, respectively. Such results reveal the histological grade, i.e., the state and severity of allograft rejection. Expression profiles are obtained from the samples as described above, and the expression profile is correlated with biopsy results. In the case of kidney rejection, clinical data is collected corresponding to urine output, level of creatine clearance, and level of serum creatine (and other markers of renal function). Clinical data collected for monitoring liver transplant rejection includes, biochemical characterization of serum markers of liver damage and function such as SGOT, SGPT, Alkaline phosphatase, GGT, Bilirubin, Albumin and Prothrombin time.

Leukocyte nucleotide sequence expression profiles are collected and correlated with important clinical states and outcomes in renal or hepatic transplantation. Examples of useful clinical correlates are given here:

1. Rejection episode of at least moderate histologic grade, which results in treatment of the patient with additional corticosteriods, anti-T cell antibodies, or total lymphoid irradiation.
2. The absence of histologic rejection and normal or unchanged allograft function (based on tests of renal or liver function listed above).
3. The presence of severe allograft dysfunction or worsening allograft dysfunction during the study period (based on tests of renal and hepatic function listed above).
4. Documented CMV infection by culture, histology, or PCR, and at least one clinical sign or symptom of infection.
5. Specific graft biopsy rejection grades
6. Rejection of mild to moderate histologic severity prompting augmentation of the patient's chronic immunosuppressive regimen
7. Infections other than CMV, esp. Epstein Barr virus (EBV)
8. Lymphoproliferative disorder (also called, post-transplant lymphoma)
9. Graft Failure or Retransplantation
10. Need for hemodialysis or other renal replacement therapy for renal transplant patients.
11. Hepatic encephalopathy for liver transplant recipients.
12. All cause mortality

Subsets of the candidate library (or of a previously identified diagnostic nucleotide set), are identified, according to the above procedures, that have predictive and/or diagnostic value for kidney or liver allograft rejection.

Example 7: Identification of a diagnostic nucleotide set for diagnosis of cytomegalovirus

Cytomegalovirus is a very important cause of disease in immunocompromised patients, for example, transplant patients, cancer patients, and AIDS patients. The virus can cause inflammation and disease in almost any tissue (particularly the colon, lung, bone marrow and retina). It is increasingly important to identify patients with current or impending clinical CMV disease, particularly when immunosuppressive drugs are to be used in a patient, e.g. for preventing transplant rejection. Leukocytes are profiled in patients with active CMV, impending CMV, or no CMV. Expression profiles correlating with diagnosis of active or impending CMV are identified. Subsets of the candidate library (or a previously identified diagnostic nucleotide set) are identified, according to the above procedures that have predictive value for the diagnosis of active or impending CMV. Diagnostic nucleotide set(s) identified with predictive value for the diagnosis of active or impending CMV may be combined, or used in conjunction with, cardiac, liver and/or kidney allograft-related diagnostic gene set(s) (described in Examples 6 and 10).

In addition, or alternatively, CMV nucleotide sequences are obtained, and a diagnostic nucleotide set is designed using CMV nucleotide sequence. The entire sequence of the organism is known and all CMV nucleotide sequences can be isolated and added to the library using the sequence information and the approach described below. Known expressed genes are preferred. Alternatively, nucleotide sequences are selected to represent groups of CMV genes that are coordinately expressed (immediate early genes, early genes, and late genes) (Spector et al. 1990, Stamminger et al. 1990).

Oligonucleotides were designed for CMV genes using the oligo design procedures of Example 8. Probes were designed using the 14 gene sequences shown here and were included on the array described in example 9:

Cytomegalovirus (CMV) Accession #X17403	HCMVTRL2 (IRL2)	1893..2240
	HCMVTRL7 (IRL7)	complement(6595..6843)
	HCMVUL21	complement(26497..27024)
	HCMVUL27	complement(32831..34657)
	HCMVUL33	43251..44423
	HCMVUL54	complement(76903..80631)
	HCMVUL75	complement(107901..110132)
	HCMVUL83	complement(119352..121037)
	HCMVUL106	complement(154947..155324)
	HCMVUL109	complement(157514..157810)
	HCMVUL113	161503..162800
	HCMVUL122	complement(169364..170599)
	HCMVUL123 (last exon at 3'-end)	complement(171006..172225)
	HCMVUS28	219200..220171

Diagnostic nucleotide set(s) for expression of CMV genes is used in combination with diagnostic leukocyte nucleotide sets for diagnosis of other conditions, e.g. organ allograft rejection.

Using the techniques described in example 2 mononuclear samples from 180 cardiac transplant recipients (enrolled in the study described in Example 5) were used for expression profiling with the leukocyte arrays. Of these samples 15 were associated with patients who had a diagnosis of primary or reactivation CMV made by culture, PCR or any specific diagnostic test.

After preparation of RNA, amplification, labeling, hybridization, scanning, feature extraction and data processing were done as described in Example 11 using the oligonucleotide microarrays described in Example 9.

The resulting log ratio of expression of Cy3 (patient sample)/ Cy5 (R50 reference RNA) was used for analysis. Significance analysis for microarrays (SAM, Tusher 2001, see Example 15) was applied to determine which genes were most significantly differentially expressed between these 15 CMV patients and the 165 non-CMV patients (Table 12). 12 genes were identified with a 0% FDR and 6 with a 0.1% FDR and are listed in Table 2. Some genes are represented by more than one oligonucleotide on the array and for 2 genes, multiple oligonucleotides from the same gene are called significant (SEQ IDs: 3061, 3064: eomesodermin and 3031, 3040, 104, 2736: small inducible cytokine A4).

Clinical variables were also included in the significance analysis. For example, the white blood cell count and the number of weeks post transplant (for the patient at the time the sample was obtained) were available for most of the 180 samples. The log of these variables was taken and the variables were then used in the significance analysis described above with the gene expression data. Both the white blood cell count (0.1% FDR) and the weeks post transplant (0% FDR) appeared to correlate with CMV status. CMV patients were more likely to have samples associated with later post transplant data and the lower white blood cell counts.

These genes and variables can be used alone or in association with other genes or variables or with other genes to build a diagnostic gene set or a classification algorithm using the approaches described herein.

Primers for real-time PCR validation were designed for some of these genes as described in Example 13 and listed in Table 2C and the sequence listing. Using the methods described in example 13, primers for Granzyme B were designed and used to validate expression findings from the arrays. 6 samples were tested (3 from patients with CMV and 3 from patients without CMV). The gene was found to be differentially expressed between the patients with and without CMV (see example 13 for full description). This same approach can be used to validate other diagnostic genes by real-time PCR. Diagnostic nucleotide sets can also be identified for a variety of other viral diseases (Table 1) using this same approach.

cDNA microarrays may be used to monitor viral expression. In addition, these methods may be used to monitor other viruses, such as Epstein-Barr virus, Herpes Simplex 1 and vesicular stomatitis virus.

Example 8- Design of oligonucleotide probes

By way of example, this section describes the design of four oligonucleotide probes using Array Designer Ver 1.1 (Premier Biosoft International, Palo Alto, CA). The major steps in the process are given first.

Obtain best possible sequence of mRNA from GenBank. If a full-length sequence reference sequence is not available, a partial sequence is used, with preference for the 3' end over the 5' end. When the

sequence is known to represent the antisense strand, the reverse complement of the sequence is used for probe design. For sequences represented in the subtracted leukocyte expression library that have no significant match in GenBank at the time of probe design, our sequence is used.

Mask low complexity regions and repetitive elements in the sequence using an algorithm such as RepeatMasker.

Use probe design software, such as Array Designer, version 1.1, to select a sequence of 50 residues with specified physical and chemical properties. The 50 residues nearest the 3' end constitute a search frame. The residues it contains are tested for suitability. If they don't meet the specified criteria, the search frame is moved one residue closer to the 5' end, and the 50 residues it now contains are tested. The process is repeated until a suitable 50-mer is found.

If no such 50-mer occurs in the sequence, the physical and chemical criteria are adjusted until a suitable 50-mer is found.

Compare the probe to dbEST, the UniGene cluster set, and the assembled human genome using the BLASTn search tool at NCBI to obtain the pertinent identifying information and to verify that the probe does not have significant similarity to more than one known gene.

Clone 40H12

Clone 40H12 was sequenced and compared to the nr, dbEST, and UniGene databases at NCBI using the BLAST search tool. The sequence matched accession number NM_002310, a 'curated RefSeq project' sequence, see Pruitt et al. (2000) Trends Genet. 16:44-47, encoding leukemia inhibitory factor receptor (LIFR) mRNA with a reported E value of zero. An E value of zero indicates there is, for all practical purposes, no chance that the similarity was random based on the length of the sequence and the composition and size of the database. This sequence, cataloged by accession number NM_002310, is much longer than the sequence of clone 40H12 and has a poly-A tail. This indicated that the sequence cataloged by accession number NM_002310 is the sense strand and a more complete representation of the mRNA than the sequence of clone 40H12, especially at the 3' end. Accession number "NM_002310" was included in a text file of accession numbers representing sense strand mRNAs, and sequences for the sense strand mRNAs were obtained by uploading a text file containing desired accession numbers as an Entrez search query using the Batch Entrez web interface and saving the results locally as a FASTA file. The following sequence was obtained, and the region of alignment of clone 40H12 is outlined:

CTCTCTCCCAGAACGTGTCTCTGCTGCAAGGCACCGGGCCCTTTCGCTCTGCAGAACTGCACTTGCAAGA
CCATTATCAACTCCTAATCCCAGCTCAGAAAGGGAGCCTCTGCGACTCATTCATCGCCCTCCAGGACTGA
CTGCATTGCACAGATGATGGATATTTACGTATGTTTGAAACGACCATCCTGGATGGTGGACAATAAAAGA
ATGAGGACTGCTTCAAATTTCCAGTGGCTGTTATCAACATTTATTCTTCTATATCTAATGAATCAAGTAA
ATAGCCAGAAAAAGGGGGCTCCTCATGATTTGAAGTGTGTAACTAACAATTTGCAAGTGTGGAACTGTTC
TTGGAAAGCACCCTCTGGAACAGGCCGTGGTACTGATTATGAAGTTTGCATTGAAAACAGGTCCCGTTCT
TGTTATCAGTTGGAGAAAACCAGTATTAAAATTCCAGCTCTTTCACATGGTGATTATGAAATAACAATAA
ATTCTCTACATGATTTTGGAAGTTCTACAAGTAAATTCACACTAAATGAACAAAACGTTTCCTTAATTCC
AGATACTCCAGAGATCTTGAATTTGTCTGCTGATTTCTCAACCTCTACATTATACCTAAAGTGGAACGAC
AGGGGTTCAGTTTTTCCACACCGCTCAAATGTTATCTGGGAAATTAAAGTTCTACGTAAAGAGAGTATGG
AGCTCGTAAAATTAGTGACCCACAACACAACTCTGAATGGCAAAGATACACTTCATCACTGGAGTTGGGC
CTCAGATATGCCCTTGGAATGTGCCATTCATTTTGTGGAAATTAGATGCTACATTGACAATCTTCATTTT
TCTGGTCTCGAAGAGTGGAGTGACTGGAGCCCTGTGAAGAACATTTCTTGGATACCTGATTCTCAGACTA
AGGTTTTTCCTCAAGATAAAGTGATACTTGTAGGCTCAGACATAACATTTTGTTGTGTGAGTCAAGAAAA

AGTGTTATCAGCACTGATTGGCCATACAAACTGCCCCTTGATCCATCTTGATGGGGAAAATGTTGCAATC
AAGATTCGTAATATTTCTGTTTCTGCAAGTAGTGGAACAAATGTAGTTTTTACAACCGAAGATAACATAT
TTGGAACCGTTATTTTTGCTGGATATCCACCAGATACTCCTCAACAACTGAATTGTGAGACACATGATTT
AAAAGAAATTATATGTAGTTGGAATCCAGGAAGGGTGACAGCGTTGGTGGGCCCACGTGCTACAAGCTAC
ACTTTAGTTGAAAGTTTTTCAGGAAAATATGTTAGACTTAAAAGAGCTGAAGCACCTACAAACGAAAGCT
ATCAATTATTATTTCAAATGCTTCCAAATCAAGAAATATATAATTTTACTTTGAATGCTCACAATCCGCT
GGGTCGATCACAATCAACAATTTTAGTTAATATAACTGAAAAAGTTTATCCCCATACTCCTACTTCATTC
AAAGTGAAGGATATTAATTCAACAGCTGTTAAACTTTCTTGGCATTTACCAGGCAACTTTGCAAAGATTA
ATTTTTTATGTGAAATTGAAATTAAGAAATCTAATTCAGTACAAGAGCAGCGGAATGTCACAATCAAAGG
AGTAGAAAATTCAAGTTATCTTGTTGCTCTGGACAAGTTAAATCCATACACTCTATATACTTTTCGGATT
CGTTGTTCTACTGAAACTTTCTGGAAATGGAGCAAATGGAGCAATAAAAAACAACATTTAACAACAGAAG
CCAGTCCTTCAAAGGGGCCTGATACTTGGAGAGAGTGGAGTTCTGATGGAAAAAATTTAATAATCTATTG
GAAGCCTTTACCCATTAATGAAGCTAATGGAAAAATACTTTCCTACAATGTATCGTGTTCATCAGATGAG
GAAACACAGTCCCTTTCTGAAATCCCTGATCCTCAGCACAAAGCAGAGATACGACTTGATAAGAATGACT
ACATCATCAGCGTAGTGGCTAAAAATTCTGTGGGCTCATCACCACCTTCCAAAATAGCGAGTATGGAAAT
TCCAAATGATGATCTCAAAATAGAACAAGTTGTTGGGATGGGAAAGGGGATTCTCCTCACCTGGCATTAC
GACCCCAACATGACTTGCGACTACGTCATTAAGTGGTGTAACTCGTCTCGGTCGGAACCATGCCTTATGG
ACTGGAGAAAAGTTCCCTCAAACAGCACTGAAACTGTAATAGAATCTGATGAGTTTCGACCAGGTATAAG
ATATAATTTTTTCCTGTATGGATGCAGAAATCAAGGATATCAATTATTACGCTCCATGATTGGATATATA
GAAGAATTGGCTCCCATTGTTGCACCAAATTTTACTGTTGAGGATACTTCTGCAGATTCGATATTAGTAA
AATGGGAAGACATTCCTGTGGAAGAACTTAGAGGCTTTTTAAGAGGATATTTGTTTTACTTTGGAAAAGG
AGAAAGAGACACATCTAAGATGAGGGTTTTAGAATCAGGTCGTTCTGACATAAAAGTTAAGAATATTACT
GACATATCCCAGAAGACACTGAGAATTGCTGATCTTCAAGGTAAAACAAGTTACCACCTGGTCTTGCGAG
CCTATACAGATGGTGGAGTGGGCCCGGAGAAGAGTATGTATGTGGTGACAAAGGAAAATTCTGTGGGATT
AATTATTGCCATTCTCATCCCAGTGGCAGTGGCTGTCATTGTTGGAGTGGTGACAAGTATCCTTTGCTAT
CGGAAACGAGAATGGATTAAAGAAACCTTCTACCCTGATATTCCAAATCCAGAAAACTGTAAAGCATTAC
AGTTTCAAAAGAGTGTCTGTGAGGGAAGCAGTGCTCTTAAAACATTGGAAATGAATCCTTGTACCCCAAA
TAATGTTGAGGTTCTGGAAACTCGATCAGCATTTCCTAAAATAGAAGATACAGAAATAATTTCCCCAGTA
GCTGAGCGTCCTGAAGATCGCTCTGATGCAGAGCCTGAAAACCATGTGGTTGTGTCCTATTGTCCACCCA
TCATTGAGGAAGAAATACCAAACCCAGCCGCAGATGAAGCTGGAGGGACTGCACAGGTTATTTACATTGA
TGTTCAGTCGATGTATCAGCCTCAAGCAAAACCAGAAGAAGAACAAGAAAATGACCCTGTAGGAGGGGCA
GGCTATAAGCCACAGATGCACCTCCCCATTAATTCTACTGTGGAAGATATAGCTGCAGAAGAGGACTTAG
ATAAAACTGCGGGTTACAGACCTCAGGCCAATGTAAATACATGGAATTTAGTGTCTCCAGACTCTCCTAG
ATCCATAGACAGCAACAGTGAGATTGTCTCATTTGGAAGTCCATGCTCCATTAATTCCCGACAATTTTTG
ATTCCTCCTAAAGATGAAGACTCTCCTAAATCTAATGGAGGAGGGTGGTCCTTTACAAACTTTTTTCAGA
ACAAACCAAACGATTAACAGTGTCACCGTGTCACTTCAGTCAGCCATCTCAATAAGCTCTTACTGCTAGT
GTTGCTACATCAGCACTGGGCATTCTTGGAGGGATCCTGTGAAGTATTGTTAGGAGGTGAACTTCACTAC
ATGTTAAGTTACACTGAAAGTTCATGTGCTTTTAATGTAGTCTAAAAGCCAAAGTATAGTGACTCAGAAT
CCTCAATCCACAAAACTCAAGATTGGGAGCTCTTTGTGATCAAGCCAAAGAATTCTCATGTACTCTACCT
TCAAGAAGCATTTCAAGGCTAATACCTACTTGTACGTACATGTAAAACAAATCCCGCCGCAACTGTTTTC
TGTTCTGTTGTTTGTGGTTTTCTCATATGTATACTTGGTGGAATTGTAAGTGGATTTGCAGGCCAGGGAG
AAAATGTCCAAGTAACAGGTGAAGTTTATTTGCCTGACGTTTACTCCTTTCTAGATGAAAACCAAGCACA
GATTTTAAAACTTCTAAGATTATTCTCCTCTATCCACAGCATTCACAAAAATTAATATAATTTTTAATGT
AGTGACAGCGATTTAGTGTTTTGTTTGATAAAGTATGCTTATTTCTGTGCCTACTGTATAATGGTTATCA
AACAGTTGTCTCAGGGGTACAAACTTTGAAAACAAGTGTGACACTGACCAGCCCAAATCATAATCATGTT
TTCTTGCTGTGATAGGTTTTGCTTGCCTTTTCATTATTTTTTAGCTTTTATGCTTGCTTCCATTATTTCA
GTTGGTTGCCCTAATATTTAAAATTTACACTTCTAAGACTAGAGACCCACATTTTTTAAAAATCATTTTA
TTTTGTGATACAGTGACAGCTTTATATGAGCAAATTCAATATTATTCATAAGCATGTAATTCCAGTGACT
TACTATGTGAGATGACTACTAAGCAATATCTAGCAGCGTTAGTTCCATATAGTTCTGATTGGATTTCGTT
CCTCCTGAGGAGACCATGCCGTTGAGCTTGGCTACCCAGGCAGTGGTGATCTTTGACACCTTCTGGTGGA
TGTTCCTCCCACTCATGAGTCTTTTCATCATGCCACATTATCTGATCCAGTCCTCACATTTTTAAATATA
AAACTAAAGAGAGAATGCTTCTTACAGGAACAGTTACCCAAGGGCTGTTTCTTAGTAACTGTCATAAACT
GATCTGGATCCATGGGCATACCTGTGTTCGAGGTGCAGCAATTGCTTGGTGAGCTGTGCAGAATTGATTG
CCTTCAGCACAGCATCCTCTGCCCACCCTTGTTTCTCATAAGCGATGTCTGGAGTGATTGTGGTTCTTGG
AAAAGCAGAAGGAAAAACTAAAAAGTGTATCTTGTATTTTCCCTGCCCTCAGGTTGCCTATGTATTTTAC
CTTTTCATATTTAAGGCAAAAGTACTTGAAAATTTTAAGTGTCCGAATAAGATATGTCTTTTTTGTTTGT
TTTTTTTGGTTGGTTGTTTGTTTTTTATCATCTGAGATTCTGTAATGTATTTGCAAATAATGGATCAATT
AATTTTTTTTGAAGCTCATATTGTATCTTTTTAAAAACCATGTTGTGGAAAAAAGCCAGAGTGACAAGTG
ACAAAATCTATTTAGGAACTCTGTGTATGAATCCTGATTTTAACTGCTAGGATTCAGCTAAATTTCTGAG
CTTTATGATCTGTGGAAATTTGGAATGAAATCGAATTCATTTTGTACATACATAGTATATTAAAACTATA

TAATAGTTCATAGAAATGTTCAGTAATGAAAAAATATATCCAATCAGAGCCATCCCGAAAAAAAAAAAAA
AA (SEQ ID NO: 3101)

The FASTA file, including the sequence of NM_002310, was masked using the RepeatMasker web interface (Smit, AFA & Green, P RepeatMasker at http://ftp.genome.washington.edu/RM/RepeatMasker.html, Smit and Green). Specifically, during masking, the following types of sequences were replaced with "N's": SINE/MIR & LINE/L2, LINE/L1 , LTR/MaLR, LTR/Retroviral , Alu, and other low informational content sequences such as simple repeats. Below is the sequence following masking:

CTCTCTCCCAGAACGTGTCTCTGCTGCAAGGCACCGGGCCCTTTCGCTCTGCAGAACTGCACTTGCAAG
ACCATTATCAACTCCTAATCCCAGCTCAGAAAGGGAGCCTCTGCGACTCATTCATCGCCCTCCAGGACT
GACTGCATTGCACAGATGATGGATATTTACGTATGTTTGAAACGACCATCCTGGATGGTGGACAATAAA
AGAATGAGGACTGCTTCAAATTTCCAGTGGCTGTTATCAACATTTATTCTTCTATATCTAATGAATCAA
GTAAATAGCCAGAAAAAGGGGGCTCCTCATGATTTGAAGTGTGTAACTAACAATTTGCAAGTGTGGAAC
TGTTCTTGGAAAGCACCCTCTGGAACAGGCCGTGGTACTGATTATGAAGTTTGCATTGAAAACAGGTCC
CGTTCTTGTTATCAGTTGGAGAAAACCAGTATTAAAATTCCAGCTCTTTCACATGGTGATTATGAAATA
ACAATAAATTCTCTACATGATTTTGGAAGTTCTACAAGTAAATTCACACTAAATGAACAAAACGTTTCC
TTAATTCCAGATACTCCAGAGATCTTGAATTTGTCTGCTGATTTCTCAACCTCTACATTATACCTAAAG
TGGAACGACAGGGGTTCAGTTTTTCCACACCGCTCAAATGTTATCTGGGAAATTAAAGTTCTACGTAAA
GAGAGTATGGAGCTCGTAAAATTAGTGACCCACAACACAACTCTGAATGGCAAAGATACACTTCATCAC
TGGAGTTGGGCCTCAGATATGCCCTTGGAATGTGCCATTCATTTTGTGGAAATTAGATGCTACATTGAC
AATCTTCATTTTTCTGGTCTCGAAGAGTGGAGTGACTGGAGCCCTGTGAAGAACATTTCTTGGATACCT
GATTCTCAGACTAAGGTTTTTCCTCAAGATAAAGTGATACTTGTAGGCTCAGACATAACATTTTGTTGT
GTGAGTCAAGAAAAAGTGTTATCAGCACTGATTGGCCATACAAACTGCCCCTTGATCCATCTTGATGGG
GAAAATGTTGCAATCAAGATTCGTAATATTTCTGTTTCTGCAAGTAGTGGAACAAATGTAGTTTTTACA
ACCGAAGATAACATATTTGGAACCGTTATTTTTGCTGGATATCCACCAGATACTCCTCAACAACTGAAT
TGTGAGACACATGATTTAAAAGAAATTATATGTAGTTGGAATCCAGGAAGGGTGACAGCGTTGGTGGGC
CCACGTGCTACAAGCTACACTTTAGTTGAAAGTTTTTCAGGAAAATATGTTAGACTTAAAAGAGCTGAA
GCACCTACAAACGAAAGCTATCAATTATTATTTCAAATGCTTCCAAATCAAGAAATATATAATTTTACT
TTGAATGCTCACAATCCGCTGGGTCGATCACAATCAACAATTTTAGTTAATATAACTGAAAAAGTTTAT
CCCCATACTCCTACTTCATTCAAAGTGAAGGATATTAATTCAACAGCTGTTAAACTTTCTTGGCATTTA
CCAGGCAACTTTGCAAAGATTAATTTTTTATGTGAAATTGAAATTAAGAAATCTAATTCAGTACAAGAG
CAGCGGAATGTCACAATCAAAGGAGTAGAAAATTCAAGTTATCTTGTTGCTCTGGACAAGTTAAATCCA
TACACTCTATATACTTTTCGGATTCGTTGTTCTACTGAAACTTTCTGGAAATGGAGCAAATGGAGCAAT
AAAAAACAACATTTAACAACAGAAGCCAGTCCTTCAAAGGGGCCTGATACTTGGAGAGAGTGGAGTTCT
GATGGAAAAAATTTAATAATCTATTGGAAGCCTTTACCCATTAATGAAGCTAATGGAAAAATACTTTCC
TACAATGTATCGTGTTCATCAGATGAGGAAACACAGTCCCTTTCTGAAATCCCTGATCCTCAGCACAAA
GCAGAGATACGACTTGATAAGAATGACTACATCATCAGCGTAGTGGCTAAAAATTCTGTGGGCTCATCA
CCACCTTCCAAAATAGCGAGTATGGAAATTCCAAATGATGATCTCAAAATAGAACAAGTTGTTGGGATG
GGAAAGGGGATTCTCCTCACCTGGCATTACGACCCCAACATGACTTGCGACTACGTCATTAAGTGGTGT
AACTCGTCTCGGTCGGAACCATGCCTTATGGACTGGAGAAAAGTTCCCTCAAACAGCACTGAAACTGTA

ATAGAATCTGATGAGTTTCGACCAGGTATAAGATATAATTTTTTCCTGTATGGATGCAGAAATCAAGGA
TATCAATTATTACGCTCCATGATTGGATATATAGAAGAATTGGCTCCCATTGTTGCACCAAATTTTACT
GTTGAGGATACTTCTGCAGATTCGATATTAGTAAAATGGGAAGACATTCCTGTGGAAGAACTTAGAGGC
TTTTTAAGAGGATATTTGTTTTACTTTGGAAAAGGAGAAAGAGACACATCTAAGATGAGGGTTTTAGAA
TCAGGTCGTTCTGACATAAAAGTTAAGAATATTACTGACATATCCCAGAAGACACTGAGAATTGCTGAT
CTTCAAGGTAAAACAAGTTACCACCTGGTCTTGCGAGCCTATACAGATGGTGGAGTGGGCCCGGAGAAG
AGTATGTATGTGGTGACAAAGGAAAATTCTGTGGGATTAATTATTGCCATTCTCATCCCAGTGGCAGTG
GCTGTCATTGTTGGAGTGGTGACAAGTATCCTTTGCTATCGGAAACGAGAATGGATTAAAGAAACCTTC
TACCCTGATATTCCAAATCCAGAAAACTGTAAAGCATTACAGTTTCAAAAGAGTGTCTGTGAGGGAAGC
AGTGCTCTTAAAACATTGGAAATGAATCCTTGTACCCCAAATAATGTTGAGGTTCTGGAAACTCGATCA
GCATTTCCTAAAATAGAAGATACAGAAATAATTTCCCCAGTAGCTGAGCGTCCTGAAGATCGCTCTGAT
GCAGAGCCTGAAAACCATGTGGTTGTGTCCTATTGTCCACCCATCATTGAGGAAGAAATACCAAACCCA
GCCGCAGATGAAGCTGGAGGGACTGCACAGGTTATTTACATTGATGTTCAGTCGATGTATCAGCCTCAA
GCAAAACCAGAAGAAGAACAAGAAAATGACCCTGTAGGAGGGGCAGGCTATAAGCCACAGATGCACCTC
CCCATTAATTCTACTGTGGAAGATATAGCTGCAGAAGAGGACTTAGATAAAACTGCGGGTTACAGACCT
CAGGCCAATGTAAATACATGGAATTTAGTGTCTCCAGACTCTCCTAGATCCATAGACAGCAACAGTGAG
ATTGTCTCATTTGGAAGTCCATGCTCCATTAATTCCCGACAATTTTTGATTCCTCCTAAAGATGAAGAC
TCTCCTAAATCTAATGGAGGAGGGTGGTCCTTTACAAACTTTTTTCAGAACAAACCAAACGATTAACAG
TGTCACCGTGTCACTTCAGTCAGCCATCTCAATAAGCTCTTACTGCTAGTGTTGCTACATCAGCACTGG
GCATTCTTGGAGGGATCCTGTGAAGTATTGTTAGGAGGTGAACTTCACTACATGTTAAGTTACACTGAA
AGTTCATGTGCTTTTAATGTAGTCTAAAAGCCAAAGTATAGTGACTCAGAATCCTCAATCCACAAAACT
CAAGATTGGGAGCTCTTTGTGATCAAGCCAAAGAATTCTCATGTACTCTACCTTCAAGAAGCATTTCAA
GGCTAATACCTACTTGTACGTACATGTAAAACAAATCCCGCCGCAACTGTTTTCTGTTCTGTTGTTTGT
GGTTTTCTCATATGTATACTTGGTGGAATTGTAAGTGGATTTGCAGGCCAGGGAGAAAATGTCCAAGTA
ACAGGTGAAGTTTATTTGCCTGACGTTTACTCCTTTCTAGATGAAAACCAAGCACAGATTTTAAAACTT
CTAAGATTATTCTCCTCTATCCACAGCATTCACNNNNNNNNNNNNNNNNNNNNNGTAGTGACAGCGAT
TTAGTGTTTTGTTTGATAAAGTATGCTTATTTCTGTGCCTACTGTATAATGGTTATCAAACAGTTGTCT
CAGGGGTACAAACTTTGAAAACAAGTGTGACACTGACCAGCCCAAATCATAATCATGTTTTCTTGCTGT
GATAGGTTTTGCTTGCCTTTTCATTATTTTTTAGCTTTTATGCTTGCTTCCATTATTTCAGTTGGTTGC
CCTAATATTTAAAATTTACACTTCTAAGACTAGAGACCCACATTTTTTAAAAATCATTTTATTTTGTGA
TACAGTGACAGCTTTATATGAGCAAATTCAATATTATTCATAAGCATGTAATTCCAGTGACTTACTATG
TGAGATGACTACTAAGCAATATCTAGCAGCGTTAGTTCCATATAGTTCTGATTGGATTTCGTTCCTCCT
GAGGAGACCATGCCGTTGAGCTTGGCTACCCAGGCAGTGGTGATCTTTGACACCTTCTGGTGGATGTTC
CTCCCACTCATGAGTCTTTTCATCATGCCACATTATCTGATCCAGTCCTCACATTTTTAAATATAAAAC
TAAAGAGAGAATGCTTCTTACAGGAACAGTTACCCAAGGGCTGTTTCTTAGTAACTGTCATAAACTGAT
CTGGATCCATGGGCATACCTGTGTTCGAGGTGCAGCAATTGCTTGGTGAGCTGTGCAGAATTGATTGCC
TTCAGCACAGCATCCTCTGCCCACCCTTGTTTCTCATAAGCGATGTCTGGAGTGATTGTGGTTCTTGGA
AAAGCAGAAGGAAAAACTAAAAAGTGTATCTTGTATTTTCCCTGCCCTCAGGTTGCCTATGTATTTTAC
CTTTTCATATTTAAGGCAAAAGTACTTGAAAATTTTAAGTGTCCGAATAAGATATGTCTTTTTTGTTTG
TTTTTTTTGGTTGGTTGTTTGTTTTTTATCATCTGAGATTCTGTAATGTATTTGCAAATAATGGATCAA

TTAATTTTTTTTGAAGCTCATATTGTATCTTTTTAAAAACCATGTTGTGGAAAAAAGCCAGAGTGACAA
GTGACAAAATCTATTTAGGAACTCTGTGTATGAATCCTGATTTTAACTGCTAGGATTCAGCTAAATTTC
TGAGCTTTATGATCTGTGGAAATTTGGAATGAAATCGAATTCATTTTGTACATACATAGTATATTAAAA
CTATATAATAGTTCATAGAAATGTTCAGTAATGAAAAAATATATCCAATCAGAGCCATCCCGAAAAAAA
AAAAAAAA (SEQ ID NO: 3102).

The length of this sequence was determined using batch, automated computational methods and the sequence, as sense strand, its length, and the desired location of the probe sequence near the 3' end of the mRNA was submitted to Array Designer Ver 1.1 (Premier Biosoft International, Palo Alto, CA). Search quality was set at 100%, number of best probes set at 1, length range set at 50 base pairs, Target Tm set at 75 C. degrees plus or minus 5 degrees, Hairpin max deltaG at 6.0 -kcal/mol., Self dimmer max deltaG at 6.0 –kcal/mol, Run/repeat (dinucleotide) max length set at 5, and Probe site minimum overlap set at 1. When none of the 49 possible probes met the criteria, the probe site would be moved 50 base pairs closer to the 5' end of the sequence and resubmitted to Array Designer for analysis. When no possible probes met the criteria, the variation on melting temperature was raised to plus and minus 8 degrees and the number of identical basepairs in a run increased to 6 so that a probe sequence was produced.

In the sequence above, using the criteria noted above, Array Designer Ver 1.1 designed a probe corresponding to oligonucleotide number 3037 and is indicated by underlining in the sequence above. It has a melting temperature of 68.4 degrees Celsius and a max run of 6 nucleotides and represents one of the cases where the criteria for probe design in Array Designer Ver 1.1 were relaxed in order to obtain an oligonucleotide near the 3' end of the mRNA (Low melting temperature was allowed).

Clone 463D12

Clone 463D12 was sequenced and compared to the nr, dbEST, and UniGene databases at NCBI using the BLAST search tool. The sequence matched accession number AI184553, an EST sequence with the definition line "qd60a05.x1 Soares_testis_NHT Homo sapiens cDNA clone IMAGE:1733840 3' similar to gb:M29550 PROTEIN PHOSPHATASE 2B CATALYTIC SUBUNIT 1 (HUMAN);, mRNA sequence." The E value of the alignment was 1.00×10^{-118}. The GenBank sequence begins with a poly-T region, suggesting that it is the antisense strand, read 5' to 3'. The beginning of this sequence is complementary to the 3' end of the mRNA sense strand. The accession number for this sequence was included in a text file of accession numbers representing antisense sequences. Sequences for antisense strand mRNAs were obtained by uploading a text file containing desired accession numbers as an Entrez search query using the Batch Entrez web interface and saving the results locally as a FASTA file. The following sequence was obtained, and the region of alignment of clone 463D12 is outlined:

TTTTTTTTTTTTTTCTTAAATAGCATTTATTTTCTCTCAAAAAGCCTATTATGTACTAACAAGTGTTCC
TCTAAATTAGAAAGGCATCACTACTAAAATTTTATACATATTTTTTATATAAGAGAAGGAATATTGGGT
TACAATCTGAATTTCTCTTTATGATTTCTCTTAAAGTATAGAACAGCTATTAAAATGACTAATATTGCT
AAAATGAAGGCTACTAAATTTCCCCAAGAATTTCGGTGGAATGCCCAAAAATGGTGTTAAGATATGCAG
AAGGGCCCATTTCAAGCAAAGCAATCTCTCCACCCCTTCATAAAAGATTTAAGCTAAAAAAAAAAAAAA

AAGAAGAAAATCCAACAGCTGAAGACATTGGGCTATTTATAAATCTTCTCCCAGTCCCCCAGACAGCCT
CACATGGGGGCTGTAAACAGCTAACTAAAATATCTTTGAGACTCTTATGTCCACACCCACTGACACAAG
GAGAGCTGTAACCACAGTGAAACTAGACTTTGCTTTCCTTTAGCAAGTATGTGCCTATGATAGTAAACT
GGAGTAAATGTAACAGTAATAAAACAAATTTTTTTTAAAAATAAAAATTATACCTTTTTCTCCAACAAA
CGGTAAAGACCACGTGAAGACATCCATAAAATTAGGCAACCAGTAAAGATGTGGAGAACCAGTAAACTG
TCGAAATTCATCACATTATTTTCATACTTTAATACAGCAGCTTTAATTATTGGAGAACATCAAAGTAAT
TAGGTGCCGAAAAACATTGTTATTAATGAAGGGAACCCCTGACGTTTGACCTTTTCTGTACCATCTATA
GCCCTGGACTTGA (SEQ ID NO: 3103)

The FASTA file, including the sequence of AA184553, was then masked using the RepeatMasker web interface, as shown below. The region of alignment of clone 463D12 is outlined.

TTTTTTTTTTTTTTCTTAAATAGCATTTATTTTCTCTCAAAAAGCCTATTATGTACTAACAAGTGTTCC
TCTAAATTAGAAAGGCATCACTACNNNNNNNNNNNNNNNNNNNNNNNNNNNNGAGAAGGAATATTGGGT
TACAATCTGAATTTCTCTTTATGATTTCTCTTAAAGTATAGAACAGCTATTAAAATGACTAATATTGCT
AAAATGAAGGCTACTAAATTTCCCCAAGAATTTCGGTGGAATGCCCAAAAATGGTGTTAAGATATGCAG
AAGGGCCCATTTCAAGCAAAGCAATCTCTCCACCCCTTCATAAAAGATTTAAGCTAAAAAAAAAAAAAA
AAGAAGAAAATCCAACAGCTGAAGACATTGGGCTATTTATAAATCTTCTCCCAGTCCCCCAGACAGCCT
CACATGGGGGCTGTAAACAGCTAACTAAAATATCTTTGAGACTCTTATGTCCACACCCACTGACACAAG
GAGAGCTGTAACCACAGTGAAACTAGACTTTGCTTTCCTTTAGCAAGTATGTGCCTATGATAGTAAACT
GGAGTAAATGTAACAGNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNCCTTTTTCTCCAACAAA
CGGTAAAGACCACGTGAAGACATCCATAAAATTAGGCAACCAGTAAAGATGTGGAGAACCAGTAAACTG
TCGAAATTCATCACATTATTTTCATACTTTAATACAGCAGCTTTAATTATTGGAGAACATCAAAGTAAT
TAGGTGCCGAAAAACATTGTTATTAATGAAGGGAACCCCTGACGTTTGACCTTTTCTGTACCATCTATA
GCCCTGGACTTGA Masked version of 463D12 sequence. (SEQ ID NO:3104)

The sequence was submitted to Array Designer as described above, however, the desired location of the probe was indicated at base pair 50 and if no probe met the criteria, moved in the 3' direction. The complementary sequence from Array Designer was used, because the original sequence was antisense. The oligonucleotide designed by Array Designer corresponds to oligonucleotide number 3054 and is complementary to the underlined sequence above. The probe has a melting temperature of 72.7 degrees centigrade and a max run of 4 nucleotides.

Clone 72D4

Clone 72D4 was sequenced and compared to the nr, dbEST, and UniGene databases at NCBI using the BLAST search tool. No significant matches were found in any of these databases. When compared to the human genome draft, significant alignments were found to three consecutive regions of the reference sequence NT_008060, as depicted below, suggesting that the insert contains three spliced exons of an unidentified gene.

Residue numbers on clone 72D4 sequence	Matching residue numbers on NT_008060
1 – 198	478646 – 478843

197 – 489	479876 – 480168
491 – 585	489271 – 489365

Because the reference sequence contains introns and may represent either the coding or noncoding strand for this gene, BioCardia's own sequence file was used to design the oligonucleotide. Two complementary probes were designed to ensure that the sense strand was represented. The sequence of the insert in clone 72D4 is shown below, with the three putative exons outlined.

CAGGTCACACAGCACATCAGTGGCTACATGTGAGCTCAGACCTGGGTCTGCTGCTGTCTGT
CTTCCCAATATCCATGACCTTGACTGATGCAGGTGTCTAGGGATACGTCCATCCCCGTCCT
GCTGGAGCCCAGAGCACGGAAGCCTGGCCCTCCGAGGAGACAGAAGGGAGTGTCGGACA
CCATGACGAGAGCTTGGCAGAATAAATAACTTCTTTAAACAATTTTACGGCATGAAGAAA
TCTGGACCAGTTTATTAAATGGGATTTCTGCCACAAACCTTGGAAGAATCACATCATCTTA
NNCCCAAGTGAAAACTGTGTTGCGTAACAAAGAACATGACTGCGCTCCACACATACATCA
TTGCCCGGCGAGGCGGGACACAAGTCAACGACGGAACACTTGAGACAGGCCTACAACTG
TGCACGGGTCAGAAGCAAGTTTAAGCCATACTTGCTGCAGTGAGACTACATTTCTGTCTAT
AGAAGATA CCTGACTTGATCTGTTTTTCAGCTCCAGTTCCCAGATGTGCGTGTTGTGGTCC
CCAAGTATCACCTTCCAATTTCTGGGAGCAGTGCTCTGGCCG GATCCTTGCCGCGCGGAT
AAAAAC (SEQ ID NO: 3106)

The sequence was submitted to RepeatMasker, but no repetitive sequences were found. The sequence shown above was used to design the two 50-mer probes using Array Designer as described above. The probes are shown in bold typeface in the sequence depicted below. The probe in the sequence is oligonucleotide number 3020 (SEQ ID NO: 3020) and the complementary probe is oligonucleotide number 318 (SEQ ID NO:318). A portion of the target sequence is listed below (SEQ ID: 3106).

CAGGTCACACAGCACATCAGTGGCTACATGTGAGCTCAGACCTGGGTCTGCTGCTGTCTGTCTTCCCAA
TATCCATGACCTTGACTGATGCAGGTGTCTAGGGATACGTCCATCCCCGTCCTGCTGGAGCCCAGAGCA
CGGAAGCCTGGCCCTCCGAGGAGACAGAAGGGAGTGTCGGACACCATGACGAGAGCTTGGCAGAATAAA
TAACTTCTTTAAACAATTTTACGGCATGAAGAAATCTGGACCAGTTTATTAAATGGGATTTCTGCCACA
AACCTTGGAAGAATCACATCATCTTANNCCCAAGTGAAAACTGTGTTGCGTAACAAAGAACATGACTGC
GCTCCACACATACATCATTGCCCGGCGAGGCGGGACACAAGTCAACGACGGAACACTTGAGACAGGCCT
ACAACTGTGCACGGGTCAGAAGCAAGTTTAAGCCATACTTGCTGCAGTGAGACTACATTTCTGTCTATA
GAAGATACCTGACTTGATCTGTTTTTCAGCTC**CAGTTCCCAGATGTGC**

←----**GTCAAGGGTCTACACG**

GTGTTGTGGTCCCCAAGTATCACCTTCCAATTTCTGGGAG--→

CACAACACCAGGGGTTCATAGTGGAAGGTTAAAG-5'

CAGTGCTCTGGCCGGATCCTTGCCGCGCGGATAAAAACT---→

Confirmation of probe sequence

Following probe design, each probe sequence was confirmed by comparing the sequence against dbEST, the UniGene cluster set, and the assembled human genome using BLASTn at NCBI. Alignments, accession numbers, gi numbers, UniGene cluster numbers and names were examined and the most common sequence used for the probe.

Example 9 - Production of an array of 8000 spotted 50mer oligonucleotides

We produced an array of *8000* spotted initial candidate 50mer oligonucleotides. Example 8 exemplifies the design and selection of probes for this array.

Sigma-Genosys (The Woodlands, TX) synthesized un-modified 50-mer oligonucleotides using standard phosphoramidite chemistry, with a starting scale of synthesis of 0.05 μmole (see, e.g., R. Meyers, ed. (1995) Molecular Biology and Biotechnology: A Comprehensive Desk Reference). Briefly, to begin synthesis, a 3' hydroxyl nucleoside with a dimethoxytrityl (DMT) group at the 5' end was attached to a solid support. The DMT group was removed with trichloroacetic acid (TCA) in order to free the 5'-hydroxyl for the coupling reaction. Next, tetrazole and a phosphoramidite derivative of the next nucleotide were added. The tetrazole protonates the nitrogen of the phosphoramidite, making it susceptible to nucleophilic attack. The DMT group at the 5'-end of the hydroxyl group blocks further addition of nucleotides in excess. Next, the inter-nucleotide linkage was converted to a phosphotriester bond in an oxidation step using an oxidizing agent and water as the oxygen donor. Excess nucleotides were filtered out and the cycle for the next nucleotide was started by the removal of the DMT protecting group. Following the synthesis, the oligo was cleaved from the solid support. The oligonucleotides were desalted, resuspended in water at a concentration of 100 or 200 μM, and placed in 96-deep well format. The oligonucleotides were re-arrayed into Whatman Uniplate 384-well polyproylene V bottom plates. The oligonucleotides were diluted to a final concentration 30 μM in 1X Micro Spotting Solution Plus (Telechem/arrayit.com, Sunnyvale, CA) in a total volume of 15 μl. In total, 8,031 oligonucleotides were arrayed into twenty-one 384-well plates.

Arrays were produced on Telechem/arrayit.com Super amine glass substrates (Telechem/arrayit.com), which were manufactured in 0.1 mm filtered clean room with exact dimensions of 25x76x0.96 mm. The arrays were printed using the Virtek Chipwriter with a Telechem 48 pin Micro Spotting Printhead. The Printhead was loaded with 48 Stealth SMP3B TeleChem Micro Spotting Pins, which were used to print oligonucleotides onto the slide with the spot size being 110-115 microns in diameter.

Example 10: Identification of diagnostic nucleotide sets for diagnosis of Cardiac Allograft Rejection

Genes were identified which have expression patterns useful for the diagnosis and monitoring of cardiac allograft rejection. Further, sets of genes that work together in a diagnostic algorithm for

allograft rejection were identified. Patients, patient clinical data and patient samples used in the discovery of markers below were derived from a clinical study described in example 5.
The collected clinical data is used to define patient or sample groups for correlation of expression data. Patient groups are identified for comparison, for example, a patient group that possesses a useful or interesting clinical distinction, verses a patient group that does not possess the distinction. Measures of cardiac allograft rejection are derived from the clinical data described above to divide patients (and patient samples) into groups with higher and lower rejection activity over some period of time or at any one point in time. Such data are rejection grade as determined from pathologist reading of the cardiac biopsies and data measuring progression of end-organ damage, including depressed left ventricular dysfunction (decreased cardiac output, decreased ejection fraction, clinical signs of low cardiac output) and usage of inotropic agents (Kobashigawa 1998).

Expression profiles correlating with occurrence of allograft rejection are identified, including expression profiles corresponding to end-organ damage and progression of end-organ damage. Expression profiles are identified predicting allograft rejection, and response to treatment or likelihood of response to treatment. Subsets of the candidate library (or a previously identified diagnostic nucleotide set) are identified, that have predictive value for the presence of allograft rejection or prediction of allograft rejection or end organ damage.
Mononuclear RNA samples were collected from patients who had recently undergone a cardiac allograft transplantation using the protocol described in example 2. The allograft rejection status at the time of sample collection was determined by examination of cardiac biopsies as described in example 5.
180 samples were included in the analysis. Each patient sample was associated with a biopsy and clinical data collected at the time of the sample. The cardiac biopsies were graded by a pathologist at the local center and by a centralized pathologist who read the biopsy slides from all four local centers in a blinded manner. Biopsy grades included 0, 1A, 1B, 2, 3A, and 3B. No grade 4 rejection was identified. Dependent variables were developed based on these grades using either the local center pathology reading or the higher of the two readings, local or centralized. The dependent variables used for correlation of gene expression profiles with cardiac allograft rejection are shown in Table 4. Dependent variables are used to create classes of samples corresponding to the presence or absence of rejection.
Clinical data were also used to determine criteria for including samples in the analysis. The strictest inclusion criteria required that samples be from patients who did not have a bacterial or viral infection, were at least two weeks post cardiac transplant and were not currently admitted to the hospital. A second inclusion criteria (inclusion 2) reduced the post-transplant criteria to 1 week and eliminated the hospital admission criteria.
After preparation of RNA (example 2), amplification, labeling, hybridization, scanning, feature extraction and data processing were done as described in Example 11, using the oligonucleotide microarrays described in Example 9. The resulting log ratio of expression of Cy3 (patient sample)/ Cy5 (R50 reference RNA) was used for analysis. This dataset is called the "static" data. A second

type of dataset, referenced, was derived from the first. These datasets compared the gene expression log ratio in each sample to a baseline sample from the same patient using the formula:

$$\text{ref log ratio} = (\text{log ratio}_{sample}) - (\text{log ratio}_{baseline})$$

Two referenced datasets were used, named "0 HG" and "Best 0". The baseline for 0 HG was a Grade 0 sample from the same patient as the sample, using the highest grade between the centralized and local pathologists. The baseline for Best 0 was a Grade 0 sample from the same patient as the sample, using both the local and centralized reader biopsy grade data. When possible a Grade 0 prior to the sample was used as the baseline in both referenced datasets.

The datasets were also divided into subsets to compare analysis between two subsets of roughly half of the data. The types of subsets constructed were as follows. First half/second half subsets were the first half of the samples and the second half of the samples from a dataset ordered by sample number. Odd/even subsets used the same source, a dataset ordered by sample number, but the odd subset consisted of every 2nd sample starting with the first and the even subset consisted of every 2nd sample starting with the second sample, Center 14/other subsets were the same datasets, divided by transplant hospital. The center 14 subset consisted of all samples from patients at center 14, while the other subset consisted of all samples from the other three centers (12,13, and 15).

Initially, significance analysis for microarrays (SAM, Tusher 2001, Example 15) was used to discover genes that were differentially expressed between the rejection and no-rejection groups. Ninety-six different combinations of dependent variables, inclusion criteria, static/referenced, and data subsets were used in SAM analysis to develop the primary lists of genes significantly differentially expressed between rejection and no-rejection. The most significant of these genes were chosen based on the following criteria. Tier 1 genes were those which appeared with an FDR of less than 20% in identical analyses in two independent subsets. Tier 2 genes were those which appeared in the top 20 genes on the list with an FDR less than 20% more than 50% of the time over all dependent variables with the inclusion criteria, and static/referenced constant. Tier 3 genes were those that appeared more than 50% of the time with an FDR less than 20% more than 50% of the time over all dependent variables with the inclusion criteria, and static/referenced constant. The genes that were identified by the analysis as statistically differentially expressed between rejection and no rejection are shown in Table 2.

SAM chooses genes as significantly different based on the magnitude of the difference between the groups and the variation among the samples within each group. An example of the difference between some Grade 0 and some Grade 3A samples for 9 genes is shown in Figure 7A.

Additionally, many of these same combinations were used in the Supervised Harvesting of Expression Trees (SHET, Hastie et al. 2001) algorithm (see example 15) to identify markers that the algorithm chose as the best to distinguish between the rejection and no rejection classes using a bias factor of 0.01. The top 20 or 30 terms were taken from the SHET output and among all comparisons in either the static or referenced data the results were grouped. Any gene found in the top 5 terms in more than 50% of the analyses was selected to be in group B1 (Table 2). The occurrences of each gene were tabulated over all SHET analysis (for either static or referenced data) and the 10 genes that occurred the most were selected to be in group B2 (Table 2).

An additional classification method used was CART (Salford Systems, San Diego, example 15). Either the static or referenced dataset was reduced to only the genes for which expression values (log ratios) were present in at least 80% of the samples. These data were used in CART with the default settings, using the Symmetric Gini algorithm. Each of the dependent variables was used with both the full sample set and the strict inclusion criteria. Two groups of genes were identified. Group C1 were those genes that were a primary splitter (1st decision node). Group C2 genes were the 10 genes that occurred as splitters the most often over all these analyses.

Two other classification models were developed and their best genes identified as markers of cardiac allograft rejection. Group D genes were identified from a set of 59 samples, referenced data, local biopsy reading grade, using logistic regression. Group E genes were identified from the primary static dataset using a K-nearest neighbor classification algorithm.

Both hierarchical clustering (Eisen et al. 1998) and CART were used to identify surrogates for each identified marker. Hierarchical clustering surrogates are genes co-expressed in these and were chosen from the nearest branches of the dendrogram. CART surrogates were identified by CART as the surrogates for those genes chosen as primary splitters at decision nodes.

Primers for real-time PCR validation were designed for each of the marker genes as described in Example 13.

CART was used to build a decision tree for classification of samples as rejection or no-rejection using the gene expression data from the arrays. The analysis identified sets of genes that can be used together to accurately identify samples derived from cardiac allograft transplant patients. The set of genes and the identified threshold expression levels for the decision tree are referred to as a "models". This model can be used to predict the rejection state of an unknown sample. The input data were the static expression data (log ratio) and the referenced expression data (log ratio referenced to the best available grade 0 from either the centralized reader or the local reader) for 139 of our top marker genes. These two types of expression data were entered into the CART software as independent variables. The dependent variable was rejection state, defined for this model as no rejection = grade 0 and rejection = grade 3A. Samples were eliminated from consideration in the training set if they were from patients with either bacterial or viral infection or were from patients who were less than two weeks post-transplant. The method used was Symmetric Gini, allowing linear combinations of independent variables. The costs were set to 1 for both false negatives and false positives and the priors were set equal for the two states. No penalties were assessed for missing data, however the marker genes selected have strong representation across the dataset. 10-fold cross validation was used to test the model. Settings not specified remained at the default values.

The model shown in Figure 7B is based on decisions about expression values at three nodes, each a different marker gene. The cost assigned to this model is 0.292, based on the priors being equal, the costs set to 1 for each type of error, and the results from the 10-fold cross validation.

In the training set, no rejection samples were misclassified (sensitivity = 100%) and only 1 no-rejection sample was misclassified (specificity = 94.4%). Following 10-fold cross validation, 2 rejection samples were misclassified (sensitivity = 87.5%) and 3 no-rejection samples were misclassified (specificity = 83.3%). The CART software assigns surrogate markers for each decision node.

These genes can be used alone or in association with other genes or variables to build a diagnostic gene set or a classification algorithm. These genes can be used in association with known gene markers for rejection (such as those identified in the prior art) to provide a diagnostic algorithm.

Example 11- Amplification, labeling, and hybridization of total RNA to an oligonucleotide microarray

Amplification, labeling, hybridization and scanning

Samples consisting of at least 0.5 to 2 μg of intact total RNA were further processed for array hybridization. When available, 2 μg of intact total RNA is used for amplification. Amplification and labeling of total RNA samples was performed in three successive enzymatic reactions. First, a single-stranded DNA copy of the RNA was made (hereinafter, "ss-cDNA"). Second, the ss-cDNA was used as a template for the complementary DNA strand, producing double-stranded cDNA (hereinafter, "ds-cDNA, or cDNA"). Third, linear amplification was performed by in vitro transcription from a bacterial T_7 promoter. During this step, fluorescent-conjugated nucleotides were incorporated into the amplified RNA (hereinafter, "aRNA").

The first strand cDNA was produced using the Invitrogen kit (Superscript II). The first strand cDNA was produced in a reaction composed of 50 mM Tris-HCl (pH 8.3), 75 mM KCl, and 3 mM $MgCl_2$ (1x First Strand Buffer, Invitrogen), 0.5 mM dGTP, 0.5 mM dATP, 0.5 mM dTTP, 0.5 mM dCTP, 10 mM DTT, 200 U reverse transcriptase (Superscript II, Invitrogen, #18064014), 15 U RNase inhibitor (RNAGuard, Amersham Pharmacia, #27-0815-01), 5 μM T7T24 primer (5'-GGCCAGTGAATTGTAATACGACTCACTATAGGGAGGCGGTTTTTTTTTTTTTTTTTTTT TTT-3'), (SEQ ID NO:3105) and 0.5 to 2 μg of selected sample total RNA. Several purified, recombinant control mRNAs from the plant Arabidopsis thaliana were added to the reaction mixture: 2-20 pg of the following genes CAB, RCA, LTP4, NAC1, RCP1,XCP2, RBCL, LTP6, TIM, and PRKase (Stratagene, #252201, #252202, #252204, #252208, #252207, #252206, #252203, #252205, #252209, #252210 respectively). The control RNAs allow the estimate of copy numbers for individual mRNAs in the clinical sample because corresponding sense oligonucleotide probes for each of these plant genes are present on the microarray. The final reaction volume of 20 μl was incubated at 42°C for 90 min. For synthesis of the second cDNA strand, DNA polymerase and RNase were added to the previous reaction, bringing the final volume to 150 μl. The previous contents were diluted and new substrates were added to a final concentration of 20 mM Tris-HCl (pH 7.0) (Fisher Scientific, Pittsburgh, PA #BP1756-100), 90 mMKCl (Teknova, Half Moon Bay, CA, #0313-500) , 4.6 mM $MgCl_2$ (Teknova, Half Moon Bay, CA, #0304-500), 10 mM$(NH_4)_2SO_4$ (Fisher Scientific #A702-500)(1x Second Strand buffer, Invitrogen), 0.266 mM dGTP, 0.266 mM dATP, 0.266 mM dTTP, 0.266 mM dCTP, 40 U *E. coli* DNA polymerase (Invitrogen, #18010-025), and 2 U RNaseH (Invitrogen, #18021-014). The second strand synthesis took place at 16°C for 150 minutes.

Following second-strand synthesis, the ds-cDNA was purified from the enzymes, dNTPs, and buffers before proceeding to amplification, using phenol-chloroform extraction followed by ethanol precipitation of the cDNA in the presence of glycogen.

Alternatively, a silica-gel column is used to purify the cDNA (e.g. Qiaquick PCR cleanup from Qiagen, #28104). The volume of the column purified cDNA was reduced by ethanol precipitation in the

presence of glycogen in which the cDNA was collected by centrifugation at >10,000 ×g for 30 minutes, the supernatant is aspirated, and 150 µl of 70% ethanol, 30% water was added to wash the DNA pellet. Following centrifugation, the supernatant was removed, and residual ethanol was evaporated at room temperature. Alternatively, the volume of the column purified cDNA is reduce in a vacuum evaporator where the supernatant is reduce to a final volume of 7.4 µl.

Linear amplification of the cDNA was performed by in vitro transcription of the cDNA. The cDNA pellet from the step described above was resuspended in 7.4 µl of water, and in vitro transcription reaction buffer was added to a final volume of 20 µl containing 7.5 mM GTP, 7.5 mM ATP, 7.5 mM TTP, 2.25 mM CTP, 1.025 mM Cy3-conjugated CTP (Perkin Elmer; Boston, MA, #NEL-580), 1x reaction buffer (Ambion, Megascript Kit, Austin, TX and #1334) and 1 % T_7 polymerase enzyme mix (Ambion, Megascript Kit, Austin, TX and #1334). This reaction was incubated at 37°C overnight. Following in vitro transcription, the RNA was purified from the enzyme, buffers, and excess NTPs using the RNeasy kit from Qiagen (Valencia, CA; # 74106) as described in the vendor's protocol. A second elution step was performed and the two eluates were combined for a final volume of 60 µl. RNA is quantified using an Agilent 2100 bioanalyzer with the RNA 6000 nano LabChip.

Reference RNA was prepared as described above, except Cy5-CTP was incorporated instead of Cy3CTP. Reference RNA from five reactions, each reaction started with 2 ug total RNA, was pooled together and quantitated as described above.

Hybridization to an array

RNA was prepared for hybridization as follows: for an 18mm×55mm array, 20 µg of amplified RNA (aRNA) was combined with 20 µg of reference aRNA. The combined sample and reference aRNA was concentrated by evaporating the water to 10 µl in a vacuum evaporator. The sample was fragmented by heating the sample at 95°C for 30 minutes to fragment the RNA into 50-200 bp pieces. Alternatively, the combined sample and reference aRNA was concentrated by evaporating the water to 5 µl in a vacuum evaporator. Five µl of 20 mM zinc acetate was added to the aRNA and the mix incubated at 60°C for 10 minutes. Following fragmentation, 40 µl of hybridization buffer was added to achieve final concentrations of 5×SSC and 0.20 %SDS with 0.1 µg/ul of Cot-1 DNA (Invitrogen) as a competitor DNA. The final hybridization mix was heated to 98°C, and then reduced to 50°C at 0.1°C per second.

Alternatively, formamide is included in the hybridization mixture to lower the hybridization temperature.

The hybridization mixture was applied to a pre-heated 65°C microarray, surface, covered with a glass coverslip (Corning, #2935-246), and placed on a pre-heated 65°C hybridization chamber (Telechem, AHC-10). 15 ul of 5xSSC was placed in each of the reservoir in the hybridization chamber and the chamber was sealed and placed in a water bath at 62°C for overnight (16-20 hrs). Following incubation, the slides were washed in 2×SSC, 0.1% SDS for five minutes at 30°C, then in 2×SSC for five minutes at 30°C, then in 2xSSC for another five minutes at 30°C, then in 0.2×SSC for two minutes

at room temperature. The arrays were spun at 1000×g for 2 minutes to dry them. The dry microarrays are then scanned by methods described above.

The microarrays were imaged on the Agilent (Palo Alto, CA) scanner G2565AA. The scan settings using the Agilent software were as follows: for the PMT Sensitivity (100% Red and 100% Green); Scan Resolution (10 microns); red and green dye channels; used the default scan region for all slides in the carousel; using the largest scan region; scan date for Instrument ID; and barcode for Slide ID. The full image produced by the Agilent scanner was flipped, rotated, and split into two images (one for each signal channel) using TIFFSplitter (Agilent, Palo Alto, CA). The two channels are the output at 532 nm (Cy3-labeled sample) and 633 nm (Cy5-labeled R50). The individual images were loaded into GenePix 3.0 (Axon Instruments, Union City, CA) for feature extraction, each image was assigned an excitation wavelength corresponding the file opened; Red equals 633 nm and Green equals 532 nm. The setting file (gal) was opened and the grid was laid onto the image so that each spot in the grid overlaped with >50% of the feature. Then the GenePix software was used to find the features without setting minimum threshold value for a feature. For features with low signal intensity, GenePix reports "not found". For all features, the diameter setting was adjusted to include only the feature if necessary.

The GenePix software determined the median pixel intensity for each feature (F_i) and the median pixel intensity of the local background for each feature (B_i) in both channels. The standard deviation (SDF_i and SDB_i) for each is also determined. Features for which GenePix could not discriminate the feature from the background were "flagged" as described below.

Following feature extraction into a " .gpr" file, the header information of the .gpr file was changed to carry accurate information into the database. An Excel macro was written to include the following information: Name of the original .tif image file, SlideID, Version of the feature extraction software, GenePix Array List file, GenePix Settings file, ScanID, Name of person who scanned the slide, Green PMT setting, Red PMT setting, ExtractID (date .gpr file was created, formatted as yyyy.mm.dd-hh.mm.ss), Results file name (same as the .gpr file name), StorageCD, and Extraction comments.

Pre-processing with Excel Templates

Following analysis of the image and extraction of the data, the data from each hybridization was pre-processed to extract data that was entered into the database and subsequently used for analysis. The complete GPR file produced by the feature extraction in GenePix was imported into an excel file pre-processing template or processed using a AWK script. Both programs used the same processing logic and produce identical results. The same excel template or AWK script was used to process each GPR file. The template performs a series of calculations on the data to differentiate poor features from others and to combine duplicate or triplicate feature data into a single data point for each probe.

The data columns used in the pre-processing were: Oligo ID, F633 Median (median value from all the pixels in the feature for the Cy5 dye), B633 Median (the median value of all the pixels in the local background of the selected feature for Cy5), B633 SD (the standard deviation of the values for the pixels in the local background of the selected feature for Cy5), F532 Median (median value from all the pixels in the feature for the Cy3 dye), B532 Median (the median value of all the pixels in the local background of the selected feature for Cy3), B532 SD (the standard deviation of the values for the pixels in the local background of the selected feature for Cy3), and Flags. The GenePix Flags column contains the flags set during feature extraction. "-75" indicates there were no features printed on the array in that position, "-50" indicates that GenePix could not differentiate the feature signal from the local background, and "-100" indicates that the user marked the feature as bad.

Once imported, the data associated with features with -75 flags was not used. Then the median of B633 SD and B532 SD were calculated over all features with a flag value of "0". The minimum values of B633 Median and B532 Median were identified, considering only those values associated with a flag value of "0". For each feature, the signal to noise ratio (S/N) was calculated for both dyes by taking the fluorescence signal minus the local background (BGSS) and dividing it by the standard deviation of the local background:

$$S/N = \frac{F_i - B_i}{SDB_i}$$

If the S/N was less than 3, then an adjusted background-subtracted signal was calculated as the fluorescence minus the minimum local background on the slide. An adjusted S/N was then calculated as the adjusted background subtracted signal divided by the median noise over all features for that channel. If the adjusted S/N was greater than three and the original S/N were less than three, a flag of 25 was set for the Cy5 channel, a flag of 23 was set for the Cy3 channel, and if both met these criteria, then a flag of 28 was set. If both the adjusted S/N and the original S/N were less than three, then a flag of 65 was set for Cy5, 63 set for Cy3, and 68 set if both dye channels had an adjusted S/N less than three. All signal to noise calculations, adjusted background-subtracted signal, and adjusted S/N were calculated for each dye channel. If the BGSS value was greater than or equal to 64000, a flag was set to indicate saturation; 55 for Cy5, 53 for Cy3, 58 for both.

The BGSS used for further calculations was the original BGSS if the original S/N was greater than or equal to three. If the original S/N ratio was less than three and the adjusted S/N ratio was greater than or equal to three, then the adjusted BGSS was used. If the adjusted S/N ratio was less than three, then the adjusted BGSS was used, but with knowledge of the flag status.

To facilitate comparison among arrays, the Cy3 and Cy5 data were scaled. The log of the ratio of Green/Red was determined for all features. The median log ratio value for good features (Flags 0, 23, 25, 28, 63) was determined. The feature values were scaled using the following formula:

Log_Scaled_Feature_Ratio = Log_Feature_Ratio – Median_Log_Ratio.

The flag setting for each feature was used to determine the expression ratio for each probe, a choice of one, two or three features. If all features had flag settings in the same category (categories=negatives,

0 to 28, 53-58, and 63-68), then the average of the three scaled, anti log feature ratios was calculated If the three features did not have flags in the same category, then the feature or features with the best quality flags were used (0>25>23>28>55>53>58>65>63>68). Features with negative flags were never used. When the best flags were two or three features in the same category, the anti log average was used. If a single feature had a better flag category than the other two then the anti log of that feature ratio was used.

Once the probe expression ratios were calculated from the one, two, or three features, the log of the scaled, averaged ratios was taken as described below and stored for use in analyzing the data. Whichever features were used to calculate the probe value, the flag from those features was carried forward and stored as the flag value for that probe. 2 different data sets can be used for analysis. Flagged data uses all values, including those with flags. Filtered data sets are created by removing flagged data from the set before analysis.

Example 12: Real-time PCR validation of array expression results

Leukocyte microarray gene expression was used to discover expression markers and diagnostic gene sets for clinical outcomes. It is desirable to validate the gene expression results for each gene using a more sensitive and quantitative technology such as real-time PCR. Further, it is possible for the diagnostic nucleotide sets to be implemented as a diagnostic test as a real-time PCR panel. Alternatively, the quantitative information provided by real-time PCR validation can be used to design a diagnostic test using any alternative quantitative or semi-quantitative gene expression technology. To validate the results of the microarray experiments we used real-time, or kinetic, PCR. In this type of experiment the amplification product is measured during the PCR reaction. This enables the researcher to observe the amplification before any reagent becomes rate limiting for amplification. In kinetic PCR the measurement is of C_T (threshold cycle) or C_P (crossing point). This measurement (C_T=C_P) is the point at which an amplification curve crosses a threshold fluorescence value. The threshold is set to a point within the area where all of the reactions were in their linear phase of amplification. When measuring C_T, a lower C_T value is indicative of a higher amount of starting material since an earlier cycle number means the threshold was crossed more quickly.

Several fluorescence methodologies are available to measure amplification product in real-time PCR. Taqman (Applied BioSystems, Foster City, CA) uses fluorescence resonance energy transfer (FRET) to inhibit signal from a probe until the probe is degraded by the sequence specific binding and Taq 3' exonuclease activity. Molecular Beacons (Stratagene, La Jolla, CA) also use FRET technology, whereby the fluorescence is measured when a hairpin structure is relaxed by the specific probe binding to the amplified DNA. The third commonly used chemistry is Sybr Green, a DNA-binding dye (Molecular Probes, Eugene, OR). The more amplified product that is produced, the higher the signal. The Sybr Green method is sensitive to non-specific amplification products, increasing the importance of primer design and selection. Other detection chemistries can also been used, such as ethedium bromide or other DNA-binding dyes and many modifications of the fluorescent dye/quencher dye Taqman chemistry.

Sample prep and cDNA synthesis

The inputs for real time PCR reaction are gene-specific primers, cDNA from specific patient samples, and standard reagents. The cDNA was produced from mononuclear RNA (prepared as in example 2) or whole blood RNA by reverse transcription using Oligo dT primers (Invitrogen, 18418-012) and random hexamers (Invitrogen, 48190-011) at a final concentration of 0.5ng/µl and 3ng/µl respectively. For the first strand reaction mix, 0.5 µg of mononuclear total RNA or 2 µg of whole blood RNA and 1 µl of the Oligo dT/ Random Hexamer Mix, were added to water to a final volume of 11.5 µl. The sample mix was then placed at 70°C for 10 minutes. Following the 70°C incubation, the samples were chilled on ice, spun down, and 88.5 µl of first strand buffer mix dispensed into the reaction tube. The final first strand buffer mix produced final concentrations of 1X first strand buffer (Invitrogen, Y00146, Carlsbad, CA), 10 mM DTT (Invitrogen, Y00147), 0.5 mM dATP (NEB, N0440S, Beverly, MA), 0.5 mM dGTP (NEB, N0442S), 0.5mM dTTP (NEB, N0443S), 0.5 mM dCTP (NEB, N0441S), 200U of reverse transcriptase (Superscript II, Invitrogen, 18064-014), and 18U of RNase inhibitor (RNAGaurd Amersham Pharmacia, 27-0815-01, Piscataway, NJ). The reaction was incubated at 42°C for 90 minutes. After incubation the enzyme was heat inactivated at 70°C for 15 minutes, 2 U of RNAse H added to the reaction tube, and incubated at 37°C for 20 minutes.

PRIMER DESIGN

Two methods were used to design primers. The first was to use the software, Primer Express™ and recommendations for primer design that are provided with the GeneAmp® 7700 Sequence Detection System supplied by Applied BioSystems (Foster City, CA). The second method used to design primers was the PRIMER3 ver 0.9 program that is available from the Whitehead Research Institute, Cambridge, Massachusetts at the Whitehead Research web site. The program can also be accessed on the World Wide Web at the web site at the Massechusetts Institute of Technology website. Primers and Taqman/hybridization probes were designed as described below using both programs.

The Primer Express literature explains that primers should be designed with a melting temperature between 58 and 60 degrees C. while the Taqman probes should have a melting temperature of 68 to 70 under the salt conditions of the supplied reagents. The salt concentration is fixed in the software. Primers should be between 15 and 30 basepairs long. The primers should produce and amplicon in size between 50 and 150 base pairs, have a C-G content between 20% and 80%, have no more than 4 identical base pairs next to one another, and no more than 2 C's and G's in the last 5 bases of the 3' end. The probe cannot have a G on the 5' end and the strand with the fewest G's should be used for the probe.

Primer3 has a large number of parameters. The defaults were used for all except for melting temperature and the optimal size of the amplicon was set at 100 bases. One of the most critical is salt concentration as it affects the melting temperature of the probes and primers. In order to produce , primers and probes with melting temperatures equivalent to Primer Express, a number of primers and probes designed by Primer Express were examined using PRIMER3. Using a salt concentration of 50 mM these primers had an average melting temperature of 3.7 degrees higher than predicted by Primer

Express. In order to design primers and probes with equivalent melting temperatures as Primer Express using PRIMER3, a melting temperature of 62.7 plus/minus 1.0 degree was used in PRIMER3 for primers and 72.7 plus/minus 1.0 degrees for probes with a salt concentration of 50 mM.

The C source code for Primer3 was downloaded and complied on a Sun Enterprise 250 server using the GCC complier. The program was then used from the command line using a input file that contained the sequence for which we wanted to design primers and probes along with the input parameters as described by help files that accompany the software. Using scripting it was possible to input a number of sequences and automatically generate a number of possible probes and primers.

Primers for β-Actin (Beta Actin, Genbank Locus: NM_001101)and β-GUS: glucuronidase, beta, (GUSB, Genbank Locus: NM_000181), two reference genes, were designed using both methods and are shown here as examples:

The first step was to mask out repetitive sequences found in the mRNA sequences using RepeatMasker program that can be accessed at: the web site University of Washington Genome Repeatmasker website. (Smit, A.F.A. & Green, P.).

The last 500 basepairs on the last 3' end of masked sequence was then submitted to PRIMER3 using the following exemplary input sequences:

PRIMER_SEQUENCE_ID=>ACTB Beta Actin (SEQID 3083)
SEQUENCE=TTGGCTTGACTCAGGATTTAAAAACTGGAACGGTGAAGGTGACAGCAGTCGGTTGGACGA
GCATCCCCCAAAGTTCACAATGTGGCCGAGGACTTTGATTGCACATTGTTGTTTTTTAATAGTCATTCC
AAATATGAGATGCATTGTTACAGGAAGTCCCTTGCCATCCTAAAAGCACCCCACTTCTCTCTAAGGAGA
ATGGCCCAGTCCTCTCCCAAGTCCACACAGGGGAGGGATAGCATTGCTTTCGTGTAAATTATGTAATGC
AAAATTTTTTTAATCTTCGCCTTAATCTTTTTTATTTTGTTTTATTTTGAATGATGAGCCTTCGTGCCC
CCCCTTCCCCCTTTTTTCCCCCAACTTGAGATGTATGAAGGCTTTTGGTCTCCCTGGGAGTGGGTGGAG
GCAGCCGGGCTTACCTGTACACTGACTTGAGACCAGTTGAATAAAAGTGCACACCTTA

PRIMER_SEQUENCE_ID=>GUSB (SEQID 3084)
SEQUENCE=GAAGAGTACCAGAAAAGTCTGCTAGAGCAGTACCATCTGGGTCTGGATCAAAAACGCAGA
AAATATGTGGTTGGAGAGCTCATTTGGAATTTTGCCGATTTCATGACTGAACAGTCACCGACGAGAGTG
CTGGGGAATAAAAAGGGGATCTTCACTCGGCAGAGACAACCAAAAAGTGCAGCGTTCCTTTTGCGAGAG
AGATACTGGAAGATTGCCAATGAAACCAGGTATCCCCACTCAGTAGCCAAGTCACAATGTTTGGAAAAC
AGCCCGTTTACTTGAGCAAGACTGATACCACCTGCGTGTCCCTTCCTCCCCGAGTCAGGGCGACTTCCA
CAGCAGCAGAACAAGTGCCTCCTGGACTGTTCACGGCAGACCAGAACGTTTCTGGCCTGGGTTTTGTGG
TCATCTATTCTAGCAGGGAACACTAAAGGTGGAAATAAAAGATTTTCTATTATGGAAATAAAGAGTTGG
CATGAAAGTCGCTACTG

After running PRIMER3, 100 sets of primers and probes were generated for ACTB and GUSB. From this set, nested primers were chosen based on whether both left primers could be paired with both right primers and a single Taqman probe could be used on an insert of the correct size. With more experience we have decided not use the mix and match approach to primer selection and just use several of the top pairs of predicted primers.

For ACTB this turned out to be:
Forward 75 CACAATGTGGCCGAGGACTT(SEQID 3085),
Forward 80 TGTGGCCGAGGACTTTGATT(SEQID 3086),
Reverse 178 TGGCTTTTAGGATGGCAAGG(SEQID 3087), and
Reverse 168 GGGGGCTTAGTTTGCTTCCT(SEQID 3088).

Upon testing, the F75 and R178 pair worked best.

For GUSB the following primers were chosen:
Forward 59 AAGTGCAGCGTTCCTTTTGC(SEQID 3089),
Forward 65 AGCGTTCCTTTTGCGAGAGA (SEQID 3090),
Reverse 158 CGGGCTGTTTTCCAAACATT (SEQID 3091), and
Reverse 197 GAAGGGACACGCAGGTGGTA (SEQID 3092).

No combination of these GUSB pairs worked well.

In addition to the primer pairs above, Primer Express predicted the following primers for GUSB: Forward 178 TACCACCTGCGTGTCCCTTC (SEQID 3093) and Reverse 242 GAGGCACTTGTTCTGCTGCTG (SEQID 3094). This pair of primers worked to amplify the GUSB mRNA.

The parameters used to predict these primers in Primer Express were:
Primer Tm: min 58, Max=60, opt 59, max difference=2 degrees
Primer GC: min=20% Max =80% no 3' G/C clamp
Primer: Length: min=9 max=40 opt=20
Amplicon: min Tm=0 max Tm=85
min = 50 bp max = 150 bp
Probe: Tm 10 degrees > primers, do not begin with a G on 5' end
Other: max base pair repeat = 3
max number of ambiguous residues = 0
secondary structure: max consecutive bp = 4, max total bp = 8
Uniqueness: max consecutive match = 9
max % match = 75
max 3' consecutive match = 7

Granzyme B is a marker of transplant rejection.

For Granzyme B the following sequence (NM_004131) (SEQID 3096) was used as input for Primer3 :

GGGGACTCTGGAGGCCCTCTTGTGTGTAACAAGGTGGCCCAGGGCATTGT
CTCCTATGGACGAAACAATGGCATGCCTCCACGAGCCTGCACCAAAGTCT
CAAGCTTTGTACACTGGATAAAGAAAACCATGAAACGCTACTAACTACAG
GAAGCAAACTAAGCCCCCGCTGTAATGAAACACCTTCTCTGGAGCCAAGT
CCAGATTTACACTGGGAGAGGTGCCAGCAACTGAATAAATACCTCTCCCA
GTGTAAATCTGGAGCCAAGTCCAGATTTACACTGGGAGAGGTGCCAGCAA
CTGAATAAATACCTCTTAGCTGAGTGG

For Granzyme B the following primers were chosen for testing:
Forward 81 ACGAGCCTGCACCAAAGTCT (SEQID 3097)
Forward 63 AAACAATGGCATGCCTCCAC (SEQID 3098)
Reverse 178 TCATTACAGCGGGGGCTTAG (SEQID 3099)
Reverse 168 GGGGGCTTAGTTTGCTTCCT (SEQID 3100)

Testing demonstrated that F81 and R178 worked well.

Using this approach, primers were designed for all the genes that were shown to have expression patterns that correlated with allograft rejection. These primer pairs are shown in Table 2, Table 8, and are added to the sequence listing. Primers can be designed from any region of a target gene using this approach.

PRIMER ENDPOINT TESTING

Primers were first tested to examine whether they would produce the correct size product without non-specific amplification. The standard real-time PCR protocol was used without the Rox and Sybr green dyes. Each primer pair was tested on cDNA made from universal mononuclear leukocyte reference RNA that was produced from 50 individuals as described in Example 3 (R50).

The PCR reaction consisted of 1X RealTime PCR Buffer (Ambion, Austin, TX), 2mM MgCl2 (Applied BioSystems, B02953), 0.2mM dATP (NEB), 0.2mM dTTP (NEB), 0.2mM dCTP (NEB), 0.2mM dGTP (NEB), .625U AmpliTaq Gold (Applied BioSystems, Foster City, CA), 0.3μM of each primer to be used (Sigma Genosys, The Woodlands, TX), 5μl of the R50 reverse-transcription reaction and water to a final volume of 19μl.

Following 40 cycles of PCR, 10 microliters of each product was combined with Sybr green at a final dilution of 1:72,000. Melt curves for each PCR product were determined on an ABI 7900 (Applied BioSystems, Foster City, CA), and primer pairs yielding a product with one clean peak were chosen for further analysis. One microliter of the product from these primer pairs was examined by agarose gel electrophoresis on an Agilent Bioanalyzer, DNA1000 chip (Palo Alto, CA). Results for 2 genes are shown in Figure 9. From the primer design and the sequence of the target gene, one can calculate the expected size of the amplified DNA product. Only primer pairs with amplification of the desired product and minimal amplification of contaminants were used for real-time PCR. Primers that produced multiple products of different sizes are likely not specific for the gene of interest and may amplify multiple genes or chromosomal loci.

PRIMER OPTIMIZATION/EFFICIENCY

Once primers passed the end-point PCR, the primers were tested to determine the efficiency of the reaction in a real-time PCR reaction. cDNA was synthesized from starting total RNA as described above. A set of 5 serial dilutions of the R50 reverse-transcribed cDNA (as described above) were made in water: 1:10, 1:20, 1:40, 1:80, and 1:160.

The Sybr Green real-time PCR reaction was performed using the Taqman PCR Reagent kit (Applied BioSystems, Foster City, CA, N808-0228). A master mix was made that consisted of all reagents except the primes and template. The final concentration of all ingredients in the reaction was 1X Taqman Buffer A (Applied BioSystems), 2mM MgCl2 (Applied BioSystems), 200μM dATP (Applied BioSystems), 200μM dCTP (Applied BioSystems), 200μM dGTP (Applied BioSystems), 400μM dUTP (Applied BioSystems), 1:400,000 diluted Sybr Green dye (Molecular Probes), 1.25U AmpliTaq Gold (Applied BioSystems). The PCR master mix was dispensed into two, light-tight tubes. Each β-Actin primer F75 and R178 (Sigma-Genosys, The Woodlands, TX), was added to one tube of PCR master mix and Each β-GUS primer F178 and R242 (Sigma-Genosys), was added to the other tube of PCR master mix to a final primer concentration of 300nM. 45μl of the β-Actin or β-GUS master mix was dispensed into wells, in a 96-well plate (Applied BioSystems). 5μl of the template dilution series was dispensed into triplicate wells for each primer. The reaction was run on an ABI 7900 Sequence Detection System (Applied BioSystems) with the following conditions: 10 min. at 95°C; 40 cycles of

95°C for 15 sec, 60°C for 1 min; followed by a disassociation curve starting at 50°C and ending at 95°C. .

The Sequence Detection System v2.0 software was used to analyze the fluorescent signal from each well. The high end of the baseline was adjusted to between 8 and 20 cycles to reduce the impact on any data curves, yet be as high as possible to reduce baseline drift. A threshold value was selected that allowed the majority of the amplification curves to cross the threshold during the linear phase of amplification. The disassociation curve for each well was compared to other wells for that marker. This comparison allowed identification of "bad" wells, those that did not amplify, that amplified the wrong size product, or that amplified multiple products. The cycle number at which each amplification curve crossed the threshold (C_T) was recorded and the file transferred to MS Excel for further analysis. The C_T values for triplicate wells were averaged. The data were plotted as a function of the $\log_{10}$ of the calculated starting concentration of RNA. The starting RNA concentration for each cDNA dilution was determined based on the original amount of RNA used in the RT reaction, the dilution of the RT reaction, and the amount used (5 µl) in the real-time PCR reaction. For each gene, a linear regression line was plotted through all of the dilutions series points. The slope of the line was used to calculate the efficiency of the reaction for each primer set using the equation:

$$E = 10^{\left(-1/\text{slope}\right)} - 1$$

Using this equation (Pfaffl 2001, Applied Biosystems User Bulletin #2), the efficiency for these β-actin primers is 1.28 and the efficiency for these β-GUS primers is 1.14 (Figure 10). This efficiency was used when comparing the expression levels among multiple genes and multiple samples. This same method was used to calculate reaction efficiency for primer pairs for each gene studied. A primer pair was considered successful if the efficiency was reproducibly determined to be between 0.7 and 2.4.

SYBR-GREEN ASSAYS

Once markers passed the Primer Efficiency QPCR (as stated above), they were used in real-time PCR assays. Patient RNA samples were reverse-transcribed to cDNA (as described above) and 1:10 dilutions made in water. In addition to the patient samples, a no template control (NTC) and a pooled reference RNA (see example 3) described in were included on every plate.

The Sybr Green real-time PCR reaction was performed using the Taqman Core PCR Reagent kit (Applied BioSystems, Foster City, CA, N808-0228). A master mix was made that consisted of all reagents except the primers and template. The final concentration of all ingredients in the reaction was 1X Taqman Buffer A (Applied BioSystems), 2mM MgCl2 (Applied BioSystems), 200µM dATP (Applied BioSystems), 200µM dCTP (Applied BioSystems), 200µM dGTP (Applied BioSystems), 400µM dUTP (Applied BioSystems), 1:400,000 diluted Sybr Green dye (Molecular Probes), 1.25U AmpliTaq Gold (Applied BioSystems). The PCR master mix was aliquotted into eight light-tight tubes, one for each marker to be examined across a set of samples. The optimized primer pair for each marker was then added to the PCR master mix to a final primer concentration of 300nM. 18µl of the each marker master mix was dispensed into wells in a 384well plate (Applied BioSystems). 2µl of the

1:10 diluted control or patient cDNA sample was dispensed into triplicate wells for each primer pair. The reaction was run on an ABI 7900 Sequence Detection System (Applied BioSystems) using the cycling conditions described above.

The Sequence Detection System v2.0 software (Applied BioSystems) was used to analyze the fluorescent signal from each well. The high end of the baseline was adjusted to between 8 and 20 cycles to reduce the impact on any data curves, yet be as high as possible to reduce baseline drift. A threshold value was selected that allowed the majority of the amplification curves to cross the threshold during the linear phase of amplification. The disassociation curve for each well was compared to other wells for that marker. This comparison allowed identification of "bad" wells, those that did not amplify, that amplified the wrong size product, or that amplified multiple products. The cycle number at which each amplification curve crossed the threshold (C_T) was recorded and the file transferred to MS Excel for further analysis. The C_T value representing any well identified as bad by analysis of disassociation curves was deleted. The C_T values for triplicate wells were averaged. A standard deviation (Stdev) and a coefficient of variation (CV) were calculated for the triplicate wells. If the CV was greater than 2, an outlier among the three wells was identified and deleted. Then the average was re-calculated. In each plate, ΔC_T was calculated for each marker-control combination by subtracting the average C_T of the target marker from the average C_T of the control (β-Actin or β-GUS). The expression relative to the control marker was calculated by taking two to the power of the ΔC_T of the target marker. For example, expression relative to β-Actin was calculated by the equation:

$$ErA = 2^{(C_{T,Actin} - C_{T,Target})}$$

All plates were run in duplicate and analyzed in the same manner. The percent variation was determined for each sample-marker combination (relative expression) by taking the absolute value of the value of the RE for the second plate from the RE for the first plate, and dividing that by the average. If more than 25% of the variation calculations on a plate are greater than 50%, then a third plate was run.

TAQMAN PROTOCOL

Real-time PCR assays were also done using Taqman PCR chemistry.

The Taqman real-time PCR reaction was performed using the Taqman Universal PCR Master Mix (Applied BioSystems, Foster City, CA, #4324018). The master mix was aliquoted into eight, light-tight tubes, one for each marker. The optimized primer pair for each marker was then added to the correctly labeled tube of PCR master mix. A FAM/TAMRA dual-labeled Taqman probe (Biosearch Technologies, Navoto, CA, DLO-FT-2) was then added to the correctly labeled tube of PCR master mix. Alternatively, different combinations of fluorescent reporter dyes and quenchers can be used such that the absorption wavelength for the quencher matches the emission wavelength for the reporter, as shown in Table 5. 18µl of the each marker master mix was dispensed into a 384well plate (Applied BioSystems). 2µl of the template sample was dispensed into triplicate wells for each primer pair. The final concentration of each reagent was: 1X TaqMan Universal PCR Master Mix, 300nM each primer, 0.25nM probe, 2µl 1:10 diluted template. The reaction was run on an ABI 7900 Sequence Detection

System (Applied Biosystems) using standard conditions (95°C for 10 min., 40 cycles of 95°C for 15 sec, 60°C for 1 min.).

The Sequence Detector v2.0 software (Applied BioSystems) was used to analyze the fluorescent signal from each well. The high end of the baseline was adjusted to between 8 and 20 cycles to reduce the impact on any data curves, yet be as high as possible to reduce baseline drift. A threshold value was selected that allowed most of the amplification curves to cross the threshold during the linear phase of amplification. The cycle number at which each amplification curve crossed the threshold (C_T) was recorded and the file transferred to MS Excel for further analysis. The C_T values for triplicate wells were averaged. The C_T values for triplicate wells were averaged. A standard deviation (Stdev) and a coefficient of variation (CV) were calculated for the triplicate wells. If the CV was greater than 2, an outlier among the three wells was identified and deleted. Then the average was re-calculated. In each plate, ΔC_T was calculated for each marker-control combination by subtracting the average C_T of the target marker from the average C_T of the control (β-Actin or β-GUS). The expression relative to the control marker was calculated by taking two to the power of the ΔC_T of the target marker. All plates were run in duplicate and analyzed in the same manner. The percent variation was determined for each sample-marker combination (relative expression) by taking the absolute value of the value of the RE for the second plate from the RE for the first plate, and dividing that by the average. If more than 25% of the variation calculations on a plate are greater than 50%, then a third plate was run.

BI-PLEXING

Variation of real-time PCR assays can arise from unequal amounts of RNA starting material between reactions. In some assays, to reduce variation, the control gene amplification was included in the same reaction well as the target gene. To differentiate the signal from the two genes, different fluorescent dyes were used for the control gene. β-Actin was used as the control gene and the TaqMan probe used was labeled with the fluorescent dye VIC and the quencher TAMRA (Biosearch Technologies, Navoto, CA, DLO-FT-2). Alternatively, other combinations of fluorescent reporter dyes and quenchers (Table 5) can be used as long as the emission wavelength of the reporter for the control gene is sufficiently different from the wavelength of the reporter dye used for the target. The control gene primers and probe were used at limiting concentrations in the reaction (150 nM primers and 0.125 nM probe) to ensure that there were enough reagents to amplify the target marker. The plates were run under the same protocol and the data are analyzed in the same way, but with a separate baseline and threshold for the VIC signal. Outliers were removed as above from both the FAM and VIC signal channels. The expression relative to control was calculated as above, using the VIC signal from the control gene.

ABSOLUTE QUANTITATION

Instead of calculating the expression relative to a reference marker, an absolute quantitation can be performed using real-time PCR. To determine the absolute quantity of each marker, a standard curve is constructed using serial dilutions from a known amount of template for each marker on the plate. The standard curve may be made using cloned genes purified from bacteria or using synthetic

complimentary oligonucleotides. In either case, a dilution series that covers the expected range of expression is used as template in a series of wells in the plate. From the average C_T values for these known amounts of template a standard curve can be plotted. From this curve the C_T values for the unknowns are used to identify the starting concentration of cDNA. These absolute quantities can be compared between disease classes (i.e. rejection vs. no-rejection) or can be taken as expression relative to a control gene to correct for variation among samples in sample collection, RNA purification and quantification, cDNA synthesis, and the PCR amplification.

CELL TYPE SPECIFIC EXPRESSION

Some markers are expressed only in specific types of cells. These markers may be useful markers for differentiation of rejection samples from no-rejection samples or may be used to identify differential expression of other markers in a single cell type. A specific marker for cytotoxic T-lymphocytes (such as CD8) can be used to identify differences in cell proportions in the sample. Other markers that are known to be expressed in this cell type can be compared to the level of CD8 to indicate differential gene expression within CD8 T-cells.

Control genes for PCR

As discussed above, PCR expression measurements can be made as either absolute quantification of gene expression using a standard curve or relative expression of a gene of interest compared to a control gene. In the latter case, the gene of interest and the control gene are measured in the same sample. This can be done in separate reactions or in the same reaction (biplex format, see above). In either case, the final measurement for expression of a gene is expressed as a ratio of gene expression to control gene expression. It is important for a control gene to be constitutively expressed in the target tissue of interest and have minimal variation in expression on a per cell basis between individuals or between samples derived from an individual. If the gene has this type of expression behavior, the relative expression ratio will help correct for variability in the amount of sample RNA used in an assay. In addition, an ideal control gene has a high level of expression in the sample of interest compared to the genes being assayed. This is important if the gene of interest and control gene are used in a biplex format. The assay is set up so that the control gene reaches its threshold Ct value early and its amplification is limited by primers so that it does not compete for limiting reagents with the gene of interest.

To identify an ideal control gene for an assay, a number of genes were tested for variability between samples and expression in both mononuclear RNA samples and whole blood RNA samples using the RNA procurement and preparation methods and real-time PCR assays described above. 6 whole-blood and 6 mononuclear RNA samples from transplant recipients were tested. The intensity levels and variability of each gene in duplicate experiments on both sample types are shown in Figure 11. Based on criteria of low variability and high expression across samples, β-actin, 18s, GAPDH, b2microglobulin were found to be good examples of control genes for the PAX samples. A single control gene may be incorporated as an internal biplex control is assays.

Controlling for variation in real time PCR

Due to differences in reagents, experimenters, and preparation methods, and the variability of pipetting steps, there is significant plate-to-plate variation in real-time PCR experiments. This variation can be reduced by automation (to reduce variability and error), reagent lot quality control, and optimal data handling. However, the results on replicate plates are still likely to be different since they are run in the machine at different times.

Variation can also enter in data extraction and analysis. Real-time PCR results are measured as the time (measured in PCR cycles) at which the fluorescence intensity (□Rn in Applied Biosystems SDS v2.1 software) crosses a user-determined threshold (CT). When performing relative quantification, the CT value for the target gene is subtracted from the CT value for a control gene. This difference, called ΔCT, is the value compared among experiments to determine whether there is a difference between samples. Variation in setting the threshold can introduce additional error. This is especially true in the duplexed experimental format, where both the target gene and the control gene are measured in the same reaction tube. Duplexing is performed using dyes specific to each of the two genes. Since two different fluorescent dyes are used on the plate, two different thresholds are set. Both of these thresholds contribute to each ΔCT. Slight differences in the each dye's threshold settings (relative to the other dye) from one plate to the next can have significant effects on the ΔCT.

There are several methods for setting the threshold for a PCR plate. Older versions of SDS software (Applied Biosystems) determine the average baseline fluorescence for the plate and the standard deviation of the baseline. The threshold is set to 10x the standard deviation of the baseline. In SDS 2.0 the users must set the baseline by themselves. Software from other machine manufacturers either requires the user to set the threshold themselves or uses different algorithms. The latest version of the SDS software (SDS 2.1) contains Automatic baseline and threshold setting. The software sets the baseline separately for each well on the plate using the ΔRn at cycles preceding detectable levels.

Variability among plates is dependent on reproducible threshold setting. This requires a mathematical or experimental data driven threshold setting protocol. Reproducibly setting the threshold according to a standard formula will minimize variation that might be introduced in the threshold setting process. Additionally, there may be experimental variation among plates that can be reduced by setting the threshold to a component of the data. We have developed a system that uses a set of reactions on each plate that are called the threshold calibrator (TCb). The TCb wells are used to set the threshold on all plates.

1. The TCb wells contain a template, primers, and probes that are common among all plates within an experiment.
2. The threshold is set within the minimum threshold and maximum threshold determined above.
3. The threshold is set to a value in this range that results in the average CT value for the TCb wells to be the same on all plates.

These methods were used to derive the primers depicted in Table 2C.

Example 13: Real-time PCR expression markers of acute allograft rejection

In examples 14 and 16, genes were identified as useful markers of cardiac and renal allograft rejection using microarrays. Some genes identified through these studies are listed in Table 2. In order to validate these findings, obtain a more precise measurement of expression levels and develop PCR reagents for diagnostic testing, real-time PCR assays were performed on samples from allograft recipients using primers to the identified genes. Some gene specific PCR primers were developed and tested for all genes in Table 2A as described in example 12. Some primers are listed in Table 2C and the sequence listing. These primers were used to measure expression of the genes relative to β-actin or β-gus in 69 mononuclear RNA samples obtained from cardiac allograft recipients using Sybr green real-time PCR assays as described in example 12. Each sample was associated with an ISHLT cardiac rejection biopsy grade. The samples were tested in 2 phases. In phase I, 14 Grade 0, 1 Grade 1A, 3 Grade 2 and 9 Grade 3A samples were tested. In phase II, 19 Grade 2, 4 Grade 1B, 4 Grade 2 and 15 Grade 3A samples were tested. Data was analyzed for each phase individually and for the combined phase I + II sample set. These data are summarized in Table 6.

The average fold change in expression between rejection (3A) and no rejection (0) samples was calculated. A t-test was done to determine the significance with which each gene was differentially expressed between rejection and no rejection and a p-value was calculated. Genes with high average fold changes and low p-values are considered best candidates for further development as rejection markers. However, it is important to note that a gene with a low average fold change and a high p-value may still be a useful marker for rejection in some patients and may work as part of a gene expression panel to diagnose rejection. These same PCR data were used to create PCR gene expression panels for diagnosis of acute rejection as discussed in example 17.

Non-parametric tests such as the Fisher Exact Test and Mann-Whitney U test are useful for choosing useful markers. They assess the ability of markers to discrininate between different classes as well as their significance. For example, one could use the median of all samples (including both non-rejector and rejector samples) as a threshold and apply the Fisher Exact test to the numbers of rejectors and non-rejectors above and below the threshold.

These methods were used to generate the data in Table 2D.

Example 14: Identification of diagnostic nucleotide sets for diagnosis of Cardiac Allograft Rejection using microarrays

Genes were identified which have expression patterns useful for the diagnosis and monitoring of acute cardiac allograft rejection. Further, sets of genes that work together in a diagnostic algorithm for allograft rejection were identified. Acute allograft rejection is a process that occurs in all solid organ transplantation including, heart, lung, liver, kidney, pancreas, pancreatic islet cell, intestine and others. Gene expression markers of acute cardiac rejection may be useful for diagnosis and monitoring of all

allograft recipients. Patients, patient clinical data and patient samples used in the discovery of markers below were derived from a clinical study described in example 5.

The collected clinical data was used to define patient or sample groups for correlation of expression data. Patient groups were identified for comparison. For example, a patient group that possesses a useful or interesting clinical distinction, verses a patient group that does not possess the distinction. Measures of cardiac allograft rejection were derived from the clinical data to divide patients (and patient samples) into groups with higher and lower rejection activity over some period of time or at any one point in time. Such data were rejection grades as determined from histological reading of the cardiac biopsy specimens by a pathologist and data measuring progression of end-organ damage, including depressed left ventricular dysfunction (decreased cardiac output, decreased ejection fraction, clinical signs of low cardiac output) and usage of inotropic agents (Kobashigawa 1998).

Mononuclear RNA samples were collected and prepared from patients who had recently undergone a cardiac allograft transplantation using the protocol described in example 2. The allograft rejection status at the time of sample collection was determined by examination of cardiac biopsies as described in example 5 and as summarized here.

300 patient samples were included in the analysis. Each patient sample was associated with a biopsy and other clinical data collected at the time of the sample. The cardiac biopsies were graded by a pathologist at the local center and by three centralized pathologists who read the biopsy slides from all four local centers in a blinded manner. Biopsy grades included 0, 1A, 1B, 2, 3A, and 3B. No grade 4 rejection was identified. Dependent variables were developed based on these grades using the local center pathology reading, the reading of a centralized and blinded pathologist, the highest of the readings, local or centralized and a consensus grade derived from all pathological readings. Samples were classified as no rejection or rejection in the following ways: Grade 0 vs. Grades 1-4, Grades 0 and 1A vs. Grades 1B-4, Grade 0 vs. Grade 3A, Grade 0 vs. Grades 1B-4, and Grade 0 vs. Grades 1B and 3A-4. Grade 0 samples were selected such that they were not immediately followed by an episode of acute rejection in the same patient. Comparing Grade 0 samples to Grade 3A samples gives the greatest difference between the rejection and no rejection groups on average.

Taking the highest of all pathologist readings has the effect of removing any sample from the no rejection class that was not a unanimous Grade 0. It also results in an increase in the number of rejection samples used in an analysis with the assumption that if a pathologist saw features of rejection, the call was likely correct and the other pathologists may have missed the finding. Many leading cardiac pathologists and clinicians believe that ISHLT grade 2 rejection does not represent significant acute rejection. Thus, for correlation analysis, exclusion of Grade 2 samples may be warranted.

Clinical data were also used to determine criteria for including samples in the analysis. For example, a patient with an active infection or in the early post-transplant period (ongoing surgical inflammation) might have immune activation unrelated to rejection and thus be difficult to identify as patients without rejection. The strictest inclusion criteria required that samples be from patients who did not have a bacterial or viral infection, were at least two weeks post cardiac transplant, were asymptomatic and were not currently admitted to the hospital.

After preparation of RNA (example 2), amplification, labeling, hybridization, scanning, feature extraction and data processing were done as described in Example 11, using the oligonucleotide microarrays described in Example 9. The resulting log ratio of expression of Cy3 (patient sample)/ Cy5 (R50 reference RNA) was used for analysis.

Significance analysis for microarrays (SAM, Tusher 2001, Example 15) was used to discover genes that were differentially expressed between the rejection and no-rejection groups. Many different combinations of dependent variables, inclusion criteria, static/referenced, and data subsets were used in SAM analysis to develop the primary lists of genes significantly differentially expressed between rejection and no-rejection. As described in example 15, SAM assigns a false detection rate to each gene identified as differentially expressed. The most significant of these genes were identified.

An exemplary analysis was the comparison of Grade 0 samples to Grade 3A-4 samples using SAM. Data from the all the pathological readings was used to identify consensus Grade 0 samples and samples with at least one reading of Grade 3A or above. Using this definition of rejection and no rejection, expression profiles from rejection samples were compared to no rejection samples using SAM. The analysis identified 7 genes with a FDR of 1%, 15 genes @ 1.4%, 35 genes @ 3.9%. Many more genes were identified at higher FDR levels.

In Table 7, a number of SAM analyses are summarized. In each case the highest grade from the 3 pathologists was taken for analysis. No rejection and rejection classes are defined. Samples are either used regardless of redundancy with respect to patients or a requirement is made that only one sample is used per patient or per patient per class. The number of samples used in the analysis is given and the lowest FDR achieved is noted.

Some of the genes identified by SAM as candidate rejection markers are noted in Table 2A and B. SAM chooses genes as significantly different based on the magnitude of the difference between the groups and the variation among the samples within each group. It is important to note that a gene which is not identified by SAM as differentially expressed between rejection and no rejection may still be a useful rejection marker because: 1. The microarray technology is not adequately sensitive to detect all genes expressed at low levels. 2. A gene might be a useful member of a gene expression panel in that it is a useful rejection marker only in a subset of patients. This gene may not be significantly differentially expressed between all rejection and no rejection samples.

For the purposes of cross-validation of the results, the datasets were also divided into subsets to compare analysis between two subsets of roughly half of the data. The types of subsets constructed were as follows. First half/second half subsets were the first half of the samples and the second half of the samples from a dataset ordered by sample number. Odd/even subsets used the same source, a dataset ordered by sample number, but the odd subset consisted of every 2nd sample starting with the first and the even subset consisted of every 2nd sample starting with the second sample, Center 14/other subsets were the same datasets, divided by transplant hospital. The center 14 subset consisted of all samples from patients at center 14, while the other subset consisted of all samples from the other three centers (12,13, and 15). When a gene was found to be significantly differentially expressed in both sets of data, a higher priority was put on that gene for development of a diagnostic test. This was reflected

in a "Array Score" value (Table 2B) that also considered the false detection rate for the gene and the importance of the gene in classification models (see example 17).

Alternatively one can divide samples into 10 equal parts and do 10-fold cross validation of the results of SAM.

Microarray data was also used to generate classification models for diagnosis of rejection as described in example 17. Genes identified through classification models as useful in the diagnosis of rejection are noted in in Table 2B in the column "models".

As genes were identified as useful rejection markers by microarray significance analysis, classification models, PCR analysis, or through searching the prior art, a variety of approaches were employed to discover genes that had similar expression behavior (coexpression) to the gene of interest. If a gene is a useful rejection marker, then a gene that is identified as having similar expression behavior is also likely to be a useful rejection marker. Hierarchical clustering (Eisen et al. 1998, see example 15) was used to identify co-expressed genes for established rejection markers. Genes were identified from the nearest branches of the clustering dendrogram. Gene expression profiles generated from 240 samples derived from transplant recipients were generated as described above. Hierarchical clustering was performed and co-expressed genes of rejection markers were identified. An example is shown in Figure 12. SEQ ID NO:85 was shown to be significantly differentially expressed between rejection and no rejection using both microarrays and PCR. Gene SEQ ID NO:3020 was identified by hierarchical clustering as closely co-expressed with SEQ ID NO:85. In table 2B, genes identified as co-expressed with established markers are identified as such by listing the SEQ ID that they are co-expressed with in the column labeled "clusters".

Some of the primers for real-time PCR validation were designed for each of the marker genes as described in Example 12 and are listed in Table 2C and the sequence listing. PCR expression measurements using these primers were used to validate array findings, more accurately measure differential gene expression and create PCR gene expression panels for diagnosis of rejection as described in example 17.

Alternative methods of analyzing the data may involve 1) using the sample channel without normalization by the reference channel, 2) using an intensity-dependent normalization based on the reference which provides a greater correction when the signal in the reference channel is large, 3) using the data without background subtraction or subtracting an empirically derived function of the background intensity rather than the background itself.

These methods were used to identify genes listed in Table 2B.

Example 15: Correlation and Classification Analysis

After generation and processing of expression data sets from microarrays as described in Example 11, a log ratio value is used for most subsequent analysis. This is the logarithm of the expression ratio for each gene between sample and universal reference. The processing algorithm assigns a number of flags to data that are of low signal to noise, saturated signal or are in some other way of low or uncertain quality. Correlation analysis can proceed with all the data (including the flagged data) or can be done on filtered data sets where the flagged data is removed from the set. Filtered data should have

less variability and noise and may result in more significant or predictive results. Flagged data contains all information available and may allow discovery of genes that are missed with the filtered data set. After filtering the data for quality as described above and in example 11, missing data are common in microarray data sets. Some algorithms don't require complete data sets and can thus tolerate missing values. Other algorithms are optimal with or require imputed values for missing data. Analysis of data sets with missing values can proceed by filtering all genes from the analysis that have more than 5%, 10%, 20%, 40%, 50%, 60% or other % of values missing across all samples in the analysis. Imputation of data for missing values can be done by a variety of methods such as using the row mean, the column mean, the nearest neighbor or some other calculated number. Except when noted, default settings for filtering and imputation were used to prepare the data for all analytical software packages.

In addition to expression data, clinical data are included in the analysis. Continuous variables, such as the ejection fraction of the heart measured by echocardiography or the white blood cell count can be used for correlation analysis. Any piece of clinical data collected on study subjects can be used in a correlation or classification analysis. In some cases, it may be desirable to take the logarithm of the values before analysis. These variables can be included in an analysis along with gene expression values, in which case they are treated as another "gene". Sets of markers can be discovered that work to diagnose a patient condition and these can include both genes and clinical parameters. Categorical variables such as male or female can also be used as variables for correlation analysis. For example, the sex of a patient may be an important splitter for a classification tree.

Clinical data are used as supervising vectors (dependent variables) for the significance or classification analysis of expression data. In this case, clinical data associated with the samples are used to divide samples in to clinically meaningful diagnostic categories for correlation or classification analysis. For example, pathologic specimens from kidney biopsies can be used to divide lupus patients into groups with and without kidney disease. A third or more categories can also be included (for example "unknown" or "not reported"). After generation of expression data and definition of supervising vectors, correlation, significance and classification analysis are used to determine which set of genes and set of genes are most appropriate for diagnosis and classification of patients and patient samples. Two main types of expression data analyses are commonly performed on the expression data with differing results and purposes. The first is significance analyses or analyses of difference. In this case, the goal of the analysis is to identify genes that are differentially expressed between sample groups and to assign a statistical confidence to those genes that are identified. These genes may be markers of the disease process in question and are further studied and developed as diagnostic tools for the indication. The second major type of analysis is classification analysis. While significance analysis identifies individual genes that are differentially expressed between sample groups, classification analysis identifies gene sets and an algorithm for their gene expression values that best distinguish sample (patient) groups. The resulting gene expression panel and algorithm can be used to create and implement a diagnostic test. The set of genes and the algorithm for their use as a diagnostic tool are often referred to herein as a "model". Individual markers can also be used to create a gene expression diagnostic model. However, multiple genes (or gene sets) are often more useful and accurate diagnostic tools.

Significance analysis for microarrays (SAM)

Significance analysis for microarrays (SAM) (Tusher 2001) is a method through which genes with a correlation between their expression values and the response vector are statistically discovered and assigned a statistical significance. The ratio of false significant to significant genes is the False Discovery Rate (FDR). This means that for each threshold there are some number of genes that are called significant, and the FDR gives a confidence level for this claim. If a gene is called differentially expressed between two classes by SAM, with a FDR of 5%, there is a 95% chance that the gene is actually differentially expressed between the classes. SAM will identify genes that are differentially expressed between the classes. The algorithm selects genes with low variance within a class and large variance between classes. The algorithm may not identify genes that are useful in classification, but are not differentially expressed in many of the samples. For example, a gene that is a useful marker for disease in women and not men, may not be a highly significant marker in a SAM analysis, but may be useful as part of a gene set for diagnosis of a multi-gene algorithm.

After generation of data from patient samples and definition of categories using clinical data as supervising vectors, SAM is used to detect genes that are likely to be differentially expressed between the groupings. Those genes with the highest significance can be validated by real-time PCR (Example 13) or can be used to build a classification algorithm as described here.

Classification

Classification algorithms are used to identify sets of genes and formulas for the expression levels of those genes that can be applied as diagnostic and disease monitoring tests. The same classification algorithms can be applied to all types of expression and proteomic data, including microarray and PCR based expression data. Examples of classification models are given in example 17. The discussion below describes the algorithms that were used and how they were used.

Classification and Regression Trees (CART) is a decision tree classification algorithm (Breiman 1984). From gene expression and or other data, CART can develop a decision tree for the classification of samples. Each node on the decision tree involves a query about the expression level of one or more genes or variables. Samples that are above the threshold go down one branch of the decision tree and samples that are not go down the other branch. Genes from expression data sets can be selected for classification building with CART by significant differential expression in SAM analysis (or other significance test), identification by supervised tree-harvesting analysis, high fold change between sample groups, or known relevance to classification of the target diseases. In addition, clinical data can be used as independent variables for CART that are of known importance to the clinical question or are found to be significant predictors by multivariate analysis or some other technique. CART identifies predictive variables and their associated decision rules for classification (diagnosis). CART also identifies surrogates for each splitter (genes that are the next best substitute for a useful gene in classification). Analysis is performed in CART by weighting misclassification costs to optimize desired performance of the assay. For example, it may be most important that the sensitivity of a test

for a given diagnosis be > 90%. CART models can be built and tested using 10 fold cross-validation or v-fold cross validation (see below). CART works best with a smaller number of variables (5-50). Multiple Additive Regression Trees (Friedman, JH 1999, MART) is similar to CART in that it is a classification algorithm that builds decision trees to distinguish groups. MART builds numerous trees for any classification problem and the resulting model involves a combination of the multiple trees. MART can select variables as it build models and thus can be used on large data sets, such as those derived from an 8000 gene microarray. Because MART uses a combination of many trees and does not take too much information from any one tree, it resists over training. MART identifies a set of genes and an algorithm for their use as a classifier.

A Nearest Shrunken Centroids Classifier can be applied to microarray or other data sets by the methods described by Tibshirani et al. 2002. This algorithms also identified gene sets for classification and determines their 10 fold cross validation error rates for each class of samples. The algorithm determines the error rates for models of any size, from one gene to all genes in the set. The error rates for either or both sample classes can are minimized when a particular number of genes are used. When this gene number is determined, the algorithm associated with the selected genes can be identified and employed as a classifier on prospective sample.

For each classification algorithm and for significance analysis, gene sets and diagnostic algorithms that are built are tested by cross validation and prospective validation. Validation of the algorithm by these means yields an estimate of the predictive value of the algorithm on the target population. There are many approaches, including a 10 fold cross validation analysis in which 10% of the training samples are left out of the analysis and the classification algorithm is built with the remaining 90%. The 10% are then used as a test set for the algorithm. The process is repeated 10 times with 10% of the samples being left out as a test set each time. Through this analysis, one can derive a cross validation error which helps estimate the robustness of the algorithm for use on prospective (test) samples. Any % of the samples can be left out for cross validation (v-fold cross validation, LOOCV). When a gene set is established for a diagnosis with an acceptable cross validation error, this set of genes is tested using samples that were not included in the initial analysis (test samples). These samples may be taken from archives generated during the clinical study. Alternatively, a new prospective clinical study can be initiated, where samples are obtained and the gene set is used to predict patient diagnoses.

Example 16: Acute allograft rejection: biopsy tissue gene expression profiling

Acute allograft rejection involves activation of recipient leukocytes and infiltration into the rejecting organ. For example, CD8 T-cells are activated by CD4 T-cells and enter the allograft where they destroy graft tissue. These activated, graft-associated leukocytes may reside in the graft, die or exit the graft. Upon exiting, the cells can find their way into the urine or blood (in the case of renal allografts), bile or blood (liver allografts) or blood (cardiac allografts). These activated cells have specific gene expression patterns that can be measured using microarrays, PCR or other methods. These gene expression patterns can be measured in the graft tissue (graft associated leukocytes), blood leukocytes, urine leukocytes or stool/biliary leukocytes. Thus graft associated leukocyte gene expression patterns are used to discover markers of activated leukocytes that can be measured outside the graft for diagnostic testing.

Renal biopsy and cardiac biopsy tissue specimens were obtained for gene expression profiling. The specimens were obtained at the time of allograft biopsy and were preserved by flash freezing in liquid nitrogen using standard approaches or immersion in an RNA stablization reagent as per the manufacturers recommendation (RNAlater, Qiagen, Valencia, CA). Biopsy allograft pathological evaluation was also obtained and samples were classified as having a particular ISHLT rejection grade (for cardiac) or acute rejection, chronic rejection, acute tubular necrosis or no disease (for renal).

28 renal biopsy tissue samples were transferred to RLT buffer, homogenized and RNA was prepared using RNeasy preparation kits (Qiagen, Valencia, CA). Average total RNA yield was 1.3 ug. Samples were subjected to on column DNAse digestion. 18 samples were derived from patients with ongoing acute allograft rejection and 10 were from controls with chronic rejection or acute renal failure.

RNA from the samples was used for amplification, labeling and hybridization to leukocyte arrays (example 11). Significance analysis for microarrays (SAM, Tusher 2001, Example 15) was used to identify genes that were differentially expressed between the acute rejection samples and controls. Leukocyte markers of acute rejection that are associated with the graft should be genes that are expressed at some level in activated leukocytes. Since leukocytes appear in graft tissue with some frequency with acute rejection, leukocyte genes associate with rejection are identified by SAM as upregulated in acute rejection in this experiment. 35 genes were identified as upregulated in acute rejection by SAM with less than a 5% false detection rate and 139 were detected with < 10.0% FDR. Results of this analysis are shown in Table 8.

For each of these genes, to 50mer oligonucleotide sequence was used to search NCBI databases including Unigene and OMIM. Genes were identified by sequence analysis to be either known leukocyte specific markers, known leukocyte expressed markers, known not to be leukocyte expressed or expression unknown. This information helped selected candidate leukocyte markers from all upregulated genes. This is necessary because some of the upregulated genes may have been expressed by renal tissue. Those genes that are leukocyte specific or leukocyte expressed were selected for evaluation by PCR in urine and blood samples from patients with and without acute allograft rejection (cardiac and renal). These genes are useful expression markers of acute rejection in allograft tissue specimens and may also be useful gene expression markers for the process in circulating leukocytes, or urine leukocytes. Genes with known leukocyte expression are noted in Table 8. In addition, some of the leukocyte expressed genes from this analysis were selected for PCR validation and development for diagnosis of acute cardiac rejection and are noted in Table 2.

Five cardiac rejection markers in the peripheral blood were assayed using real-time PCR in renal biopsy specimens. The average fold change for these genes between acute rejection (n = 6) and controls (n = 6) is given below. Work is ongoing to increase the number of samples tested and the significance of the results.

PCR assays of cardiac rejection peripheral blood markers in renal allograft tissue. R = rejection, NR = No rejection.

Gene	Fold change (R/NR)
Granzyme B	2.16
CD20	1.42
NK cell receptor	1.72
T-box 21	1.74
IL4	1.3

Markers of renal rejection that are secreted from cells may be measured in the urine or serum of patients as a diagnostic or screening assay for rejection. Genes with lower molecular weight are most likely to be filtered into the urine to be measured in this way. Standard immunoassays may be used to measure these proteins. In table 8, genes that are known to be secreted are noted.

Example 17: Microarray and PCR gene expression panels for diagnosis and monitoring of acute allograft rejection

Array panels / classification models

Using the methods of the invention, gene expression panels were discovered for screening and diagnosis of acute allograft rejection. Gene expression panels can be implemented for diagnostic testing using any one of a variety of technologies, including, but not limited to, microarrays and real-time PCR.

Using peripheral blood mononuclear cell RNA that was collected and prepared from cardiac allograft recipients as described in examples 2 and 5, leukocyte gene expression profiles were generated and analyzed using microarrays as described in examples 11, 13, and 15. 300 samples were analyzed. ISHLT rejection grades were used to divide patients into classes of rejection and no rejection. Multiple Additive Regression Trees (MART, Friedman, JH 1999, example 15) was used to build a gene expression panel and algorithm for the diagnosis of rejection with high sensitivity. Default settings for the implementaion of MART called TreeNet 1.0 (Salford Systems, San Diego, CA) were used except where noted.

82 Grade 0 (rejection) samples and 76 Grade 1B-4 (no rejection) samples were divided into training (80% of each class) and testing (20% of each class) sets. A MART algorithm was then developed on the training set to distinguish rejection from no rejection samples using a cost of 1.02:1 for misclassification of rejection as no rejection. The resulting algorithm was then used to classify the test samples. The algorithm correctly classified 51 of 66 (77%) no rejection samples in the training set and 9 of 16 (56%) no rejection samples in the test set. For rejection samples 64 of 64 (100%) were correctly classified in the training set and 12 of 12 were correctly classified in the test set. The algorithm used 37 genes. MART ranks genes by order of importance to the model. In order, the 37 genes were: SEQ IDs: 3058, 3030, 3034, 3069, 3081, 3072, 3041, 3052, 3048, 3045, 3059, 3075, 3024, 279, 3023, 3053, 3022, 3067, 3020, 3047, 3033, 3068, 3060, 3063, 3028, 3032, 3025, 3046, 3065, 3080, 3039, 3055, 49, 3080, 3038, 3071.

Another MART model was built by excluding samples derived from patients in the first month post transplant and from patients with known CMV infection. 20 Grade 0 (rejection) samples and 25 Grade 1B-4 (no rejection) samples were divided into training (80% of each class) and testing (20% of each class) sets. A MART algorithm was then developed on the training set to distinguish rejection from no rejection samples using default settings. The resulting algorithm was then used to classify the test samples. The algorithm correctly classified 100% of samples of both classes in the training and testing sets. However, this model required 169 genes. The sample analysis was done a second time with the only difference being requirement that all decision trees in the algorithm be composed of two nodes (single decision, "stump model"). In this case 15/16 no rejection samples were correctly identified in the training set and 4/4 no rejection samples were correctly identified in the test set. For the rejection samples, 17/19 were correctly identified in the training set and 5/6 were correctly classified in the test set. This model required 23 genes. In order of importance, they were: SEQ IDs: 3042, 2783, 3076, 3029, 3026, 2751, 3036, 3073, 3035, 3050, 3051, 3027, 3074, 3062, 3044, 3077, 2772, 3049, 3043, 3079, 3070, 3057, 3078.

Real-time PCR panels / classification models

PCR primers were developed for top rejection markers and used in real-time PCR assays on transplant patient samples as described in examples 12 and 13. This data was used to build PCR gene expression panels for diagnosis of rejection. Using MART (example 15) a 10-fold cross validated model was created to diagnose rejection using 12 no rejection samples (grade 0) and 10 rejection samples (grade 3A). Default settings were used with the exception of assigning a 1.02:1 cost for misclassification of rejection as no rejection and requirement that all decision trees be limited to 2 nodes ("stump model"). 20 genes were used in the model, including: SEQ IDs:101, 3021, 102, 2781, 78, 87, 86, 36, 77, 2766, 3018, 80, 3019, 2752, 79, 99, 3016, 2790, 3020, 3056, 88. The 10-fold cross-validated sensitivity for rejection was 100% and the specificity was 85%. Some PCR primers for the genes are listed in Table 2C and the sequence listing.

A different analysis of the PCR data was performed using the nearest shrunken centroids classifier (Tibshirani et al. 2002; PAM version 1.01, see example 15). A 10-fold cross validated model was created to diagnose rejection using 13 no rejection samples (grade 0) and 10 rejection samples (grade 3A). Default settings were used with the exception of using a prior probability setting of (0.5, 0.5). The algorithm derives algorithms using any number of the genes. A 3-gene model was highly accurate with a 10 fold cross-validated sensitivity for rejection of 90%, and a specificity of 85%.

The 3 genes used in this model were: SEQ IDs 2784, 79, and 2794. Some of the PCR primers used are given in Table 2C and the sequence listing. An ROC curve was plotted for the 3-gene model and is shown in Figure 13.

Example 18: Assay sample preparation

In order to show that XDx's leukocyte-specific markers can be detected in whole blood, we collected whole blood RNA using the PAXgene whole blood collection, stabilization, and RNA isolation kit (PreAnalytix). Varying amounts of the whole blood RNA were used in the initial RT reaction (1, 2, 4, and 8ug), and varying dilutions of the different RT reactions were tested (1:5, 1:10,

1:20, 1:40, 1:80, 1:160). We did real-time PCR assays with primers specific to XDx's markers and showed that we can reliably detect these markers in whole blood.

Total RNA was prepared from 14 mononuclear samples (CPT, BD) paired with 14 whole blood samples (PAXgene, PreAnalytix) from transplant recipients. cDNA was prepared from each sample using 2ug total RNA as starting material. Resulting cDNA was diluted 1:10 and Sybr green real-time PCR assays were performed.

For real-time PCR assays, Ct values of 15-30 are desired for each gene. If a gene's Ct value is much above 30, the result may be variable and non-linear. For PAX sample, target RNA will be more dilute than in CPT samples. cDNA dilutions must be appropriate to bring Ct values to less than 30. Ct values for the first 5 genes tested in this way are shown in the table below for both whole blood RNA (PAX) and mononuclear RNA (CPT).

Gene	Ct PAX	Ct CPT
CD20	27.41512	26.70474
4761	28.45656	26.52635
3096	29.09821	27.83281
GranzymeB	31.18779	30.56954
IL4	33.11774	34.8002
Actin	19.17622	18.32966
B-GUS	26.89142	26.92735

With one exception, the genes have higher Ct values in whole blood. Using this protocol, all genes can be detected with Cts <35. For genes found to have Ct values above 30 in target samples, less diluted cDNA may be needed.

Example 19: Allograft rejection diagnostic gene sequence analysis

Gene products that are secreted from cells or expressed as surface proteins have special diagnostic utility in that an assay may be developed to detect relative quantities of proteins in blood plasma or serum. Secreted proteins may also be detectable in urine, which may be a useful sample for the detection of rejection in renal allograft recipients. Cell surface markers may be detected using antigen specific antibodies in ELISA assays or using flow srting techniques such as FACS.

Each gene that is found to be differentially regulated in one population of patients has several potential applications. It may be a target for new pharmaceuticals, a diagnostic marker for a condition, a benchmark for titrating drug delivery and clearance, or used in screening small molecules for new therapeutics. Any of these applications may be improved by an understanding of the physiologic function and localization of the gene product in vivo and by relating those functions to known diseases and disorders. Identifying the basic function of each candidate gene helps identify the signaling or metabolic pathways the gene is a part of, leading us to investigate other members of those pathways as potential diagnostic markers or targets of interest to drug developers.

For each of the markers in table 2, we attempted to identify the basic function and subcellular localization of the gene. These results are summarized in Table 9. In addition to initial DNA sequencing and processing, sequence analysis, and analysis of novel clones, information was obtained from the following public resources: Online Mendelian Inheritance in Man at the NCBI, LocusLink at the NCBI, the SWISS-PROT database, and Protein Reviews on the Web. For each marker represented by a curated reference mRNA from the RefSeq project, the corresponding reference protein accession number is listed. Curated sequences are those that have been manually processed by NCBI staff to represent the best estimate of the mRNA sequence as it is transcribed, based on alignments of draft DNA sequence, predicted initiation, termination and splice sites, and submissions of EST and full-length mRNA sequences from the scientific community.

These methods were used to derive the data in Table 2E.

Example 20: Detection of proteins expressed by diagnostic gene sequences

One of ordinary skill in the art is aware of many possible methods of protein detection. The following example illustrates one possible method.

The designated coding region of the sequence is amplified by PCR with adapter sequences at either end for subcloning. An epitope or other affinity "tag" such as a "His-tag" may be added to facilitate purification and/or detection of the protein. The amplified sequence is inserted into an appropriate expression vector, most typically a shuttle vector which can replicate in either bacteria, most typically E. coli, and the organism/cell of choice for expression such as a yeast or mammalian cell. Such shuttle vectors typically contain origins of replication for bacteria and an antibiotic resistance marker for selection in bacteria, as well as the relevant replication and selection sequences for transformation/transfection into the ultimate expression cell type. In addition, the sequence of interest is inserted into the vector so that the signals necessary for transcription (a promoter) and translation operably linked to the coding region. Said expression could be accomplished in bacteria, fungi, or mammalian cells, or by in vitro translation.

The expression vector would then typically be used to transform bacteria and clones analyzed to ensure that the proper sequence had been inserted into the expression vector in the productive orientation for expression. Said verified expression vector is then transfected into a host cell and transformants selected by a variety of methods including antibiotic resistance or nutritional complementation of an auxotrophic marker. Said transformed cells are then grown under conditions conducive to expression of the protein of interest, the cells and conditioned media harvested, and the protein of interest isolated from the most enriched source, either the cell pellet or media.

The protein is then be isolated by standard of chromatographic or other methods, including immunoaffinity chromatography using the affinity "tag" sequence or other methods, including cell fractionation, ion exchange, size exclusion chromatography, or selective precipitation. The isolated and purified protein is then be used as an antigen to generate specific antibodies. This is accomplished by standard methods including injection into heterologous species with an adjuvant, isolation of monoclonal antibodies from mice, or in vitro selection of antibodies from bacteriophage display antibody libraries. These antibodies are then used to detect the presence of the indicated protein of interest in a complex bodily fluid using standard methods such as ELISA or RIA.

Example 21: Detecting changes in the rate of hematopoiesis

Gene expression profiling of blood cells from cardiac allograft recipients was done using microarrays and real-time PCR as described in other examples herein.

Two of the genes in that were most correlated with cardiac transplant acute rejection with both microarrays and PCR were hemoglobin Beta and 2,3 DPGM. These genes are well know to be specific markers of erythrocyte lineages. This correlation was found using both purified peripheral mononuclear cells and whole blood RNA preparations.

Analysis of the five genes from the PCR data most strongly correlated with rejection showed that their expression levels were extremely highly correlated within each other (R2 > 0.85).

Gene	Hs	Acc	SEQ ID No
hemoglobin, beta (HBB)	Hs.155376	NM_000518	86
2,3-bisphosphoglycerate mutase (BPG	Hs.198365	X04327	87
cDNA FLJ20347	Hs.102669	AK000354	94
602620663F1cDNA	Hs.34549	AI123826	107
HA1247 cDNA	Hs.33757	AI114652	91

This suggested that they were all elevated as part of a single response or process. When the microarray data was used to cluster these genes with each other and the other genes on the microarray, we found that these five genes clustered reasonably near each and of the other array genes which clustered tightly with them, four of the top 40 or so were platelet related genes. In addition, these a number of these genes clustered closely with CD34. CD34 is a marker of hematopoietic stem cells and is seen in the peripheral blood with increased hematopoisis.

CD34, platelet RNA and erythrocyte RNA all mark immature or progenitor blood cells and it is clear that theses marker of acute rejection are part of a coordinated hematopoietic response. A small increase in the rate of production of RBCs and platelets may result in large fold changes in RNA levels. Immune activation from acute rejection may lead to increased hamatopoiesis in the bone marrow and non-marrow sites. This leads to an increase in many lineages because of the lack of complete specificity of the marrow response. Alternatively, increased hematopoiesis may occur in a transplant recipient due to an infection (viral or other), allergy or other stimulus to the system. This results in production of cells or a critical mass of immune cells that can cause rejection. In this scenario, monitoring for markers of immune activation would provide an opportunity for early diagnosis.

Table 1

Disease Classification	Disease/Patient Group
Cardiovascular Disease	Atherosclerosis
	Unstable angina
	Myocardial Infarction
	Restenosis after angioplasty
	Congestive Heart Failure
	Myocarditis
	Endocarditis
	Endothelial Dysfunction
	Cardiomyopathy
	Cardiovascular drug use
Infectious Disease	Hepatitis A, B, C, D, E, G
	Malaria
	Tuberculosis
	HIV
	Pneumocystis Carinii
	Giardia
	Toxoplasmosis
	Lyme Disease
	Rocky Mountain Spotted Fever
	Cytomegalovirus
	Epstein Barr Virus
	Herpes Simplex Virus
	Clostridium Dificile Colitis
	Meningitis (all organisms)
	Pneumonia (all organisms)
	Urinary Tract Infection (all organisms)
	Infectious Diarrhea (all organisms)
	Anti-infectious drug use
Angiogenesis	Pathologic angiogenesis
	Physiologic angiogenesis
	Treatment induced angiogenesis
	Pro or anti-angiogenic drug use
Transplant Rejection	Heart
	Lung
	Liver
	Pancreas
	Bowel
	Bone Marrow
	Stem Cell
	Graft versus host disease
	Transplant vasculopathy
	Skin
	Cornea
	Islet Cells
	Kidney
	Xenotransplants
	Mechanical Organ
	Immunosupressive drug use
Hematological Disorders	Anemia – Iron Deficiency
	Anemia – B12, Folate deficiency
	Anemia – Aplastic
	Anemia – hemolytic
	Anemia – Renal failure
	Anemia – Chronic disease
	Polycythemia rubra vera
	Pernicious anemia
	Idiophic Thrombocytopenic purpura
	Thrombotic Thrombocytopenic purpura
	Essential thrombocytosis
	Leukemia
	Cytopenias due to immunosupression
	Cytopenias due to Chemotherapy
	Myelodyspiasia

Table 2A.

Gene	Gene Name	SEQ ID 50mer	HS	ACC	SEQ ID RNA/cDNA
HSRRN18S	18S ribosomal RNA	1	NA	X03205	333
ACTB	Actin, beta	2	Hs.288061	NM_001101	334
GUSB	Glucuronidase, beta	3	Hs.183868	NM_000181	335
B2M	beta 2 microglobulin	4	Hs.75415	NM_004048	336
TSN	Translin	5	Hs.75066	NM_004622	337
CCR7	1707	6	Hs.1652	NM_001838	338
IL1R2	4685-IL1R	7	Hs.25333	NM_004633	339
AIF-1	Allograft inflammatory factor 1, all variants	8	Hs.76364	NM_004847	340
ALAS2	ALAS2	9	Hs.323383	NM_000032.1	341
APELIN	APELIN	10	Hs.303084	NM_017413	342
CD80	B7-1, CD80	11	Hs.838	NM_005191	343
EPB41	Band 4.1	12	Hs.37427	NM_004437	344
CBLB	c-cbl-B	13	Hs.3144	NM_004351	345
CCR5	CCR5	14	Hs.54443	NM_000579	346
MME	CD10	15	Hs.1298	NM_000902	347
KLRC1	CD159a	16	Hs.74082	NM_002259	348
FCGR3A	CD16	17	Hs.176663	NM_000569	349
FCGR3B	CD16b	18	Hs.372679	NM_000570	350
LAG3	CD223	19	Hs.74011	NM_002286	351
PECAM1	CD31	20	Hs.78146	NM_000442	352
CD34	CD34	21	Hs.374990	NM_001773	353
FCGR1A	CD64	22	Hs.77424	NM_000566	354
TFRC	CD71 = T9, transferrin receptor	23	Hs.77356	NM_003234	355
CMA1	chymase	24	Hs.135626	NM_001836	356
KIT	c-Kit	25	Hs.81665	NM_000222	357
MPL	c-mpl	26	Hs.84171	NM_005373	358
EphB6	EphB6	27	Hs.3796	NM_004445	359
EPOR	EPO-R	28	Hs.127826	NM_000121.2	360
Foxp3	Foxp3	29	Hs.247700	NM_014009	361
GATA1	GATA1	30	Hs.765	NM_002049	362
ITGA2B	GP IIb	31	NM_000419.2	NM_000419	363
GNLY	granulysin	32	Hs.105806	NM_006433	364
GZMA	GZMA	33	Hs.90708	NM_006144	365
HBA	hemoglobin, alpha 1	34	Hs.398636	NM_000558.3	366
HBZ	hemoglobin, zeta	35	Hs.272003	NM_005332.2	367
HBB	hemoglobin, beta	36	Hs.155376	NM_000518.4	368
HBD	hemoglobin, delta	37	Hs.36977	NM_000519.2	369
HBE	hemoglobin, epsilon 1	38	Hs.117848	NM_005330	370
HBG	hemoglobin, gamma A	39	Hs.283108	NM_000559.2	371
HBQ	hemoglobin, theta 1	40	Hs.247921	NM_005331	372
HLA-DP	MH/c, class II, DP alpha 1	41	Hs.198253	NM_033554	373
HLA-DQ	MHC, class II, DQ alpha 1	42	Hs.198253	NM_002122	374
HLA-DRB	MHC, class II, DR beta 1	43	Hs.375570	NM_002124.1	375
ICOS	ICOS	44	Hs.56247	NM_012092	376
IL18	IL18	45	Hs.83077	NM_001562	377
IL3	interleukin 3 (colony-stimulating factor, multiple)	46	Hs.694	NM_000588	378
ITGA4	Integrin, alpha 4 (antigen CD49D, alpha 4 subunit of VLA-4 receptor)	47	Hs.40034	NM_000885	379

Gene	Gene Name	SEQ ID 50mer	HS	ACC	SEQ ID RNA/cDNA
ITGAM	integrin, alpha M (complement component receptor 3, alpha; also known as CD11b (p170), macrophage antigen alpha polypeptide)	48	Hs.172631	NM_000632	380
ITGB7	integrin, beta 7	49	Hs.1741	NM_000889	381
CEBPB	LAP, CCAAT/enhancer binding protein (C/EBP), beta	50	Hs.99029	NM_005194	382
NF-E2	NF-E2	51	Hs.75643	NM_006163	383
PDCD1	programmed cell death 1, PD-1	52	Hs.158297	NM_005018	384
PF4	platelet factor 4 (chemokine (C-X-C motif) ligand 4)	53	Hs.81564	NM_002619	385
PRKCQ	protein kinase C, theta	54	Hs.211593	NM_006257.1	386
PPARGC1	PPARgamma	55	Hs.198468	NM_013261	387
RAG1	recombination activating gene 1	56	Hs.73958	NM_000448	388
RAG2	recombination activating gene 2	57	Na	NM_000536	389
CXCL12	chemokine (C-X-C motif) ligand 12 (stromal cell-derived factor 1) (SDF-1)	58	Hs.237356	NM_000609	390
TNFRSF4	tumor necrosis factor receptor superfamily, member 4	59	Hs.129780	NM_003327	391
TNFSF4	tumor necrosis factor (ligand) superfamily, member 4 (tax-transcriptionally activated glycoprotein 1, 34kDa)	60	Hs.181097	NM_003326	392
TPS1	tryptase, alpha	61	Hs.334455	NM_003293	393
ADA	ADA adenosine deaminase	62	Hs.1217	NM_000022	394
CPM	Carboxypeptidase M	63	Hs.334873	NM_001874.1	395
CSF2	colony stimulating factor, GM-CSF	64	Hs.1349	NM_000758.2	396
CSF3	colony stimulating factor 3, G-CSF	65	Hs.2233	NM_172219	397
CRP	C-reactive protein, pentraxin-related (CRP),	66	Hs.76452	NM_000567.1	398
FLT3	FMS-Related Tyrosine Kinase 3	67	Hs.385	NM_004119	399
GATA3	GATA binding protein 3	68	Hs.169946	NM_002051.1	400
IL7R	Interleukin 7 receptor	69	Hs.362807	NM_002185.1	401
KLF1	Kruppel-like factor 1 (erythroid), EKLF	70	Hs.37860	NM_006563.1	402
LCK	lymphocyte-specific protein tyrosine kinase	71	Hs.1765	NM_005356.2	403
LEF1	lymphoid enhancer-binding factor 1	72	Hs.44865	NM_016269.2	404
PLAUR	Urokinase-type Plasminogen Activator Receptor, CD87, uPAR	73	Hs.179657	NM_002659.1	405
TNFSF13B	Tumor necrosis factor (ligand) superfamily, member 13b, BlyS/TALL-1/BAFF	74	Hs.270737	NM_006573.3	406
IL8	Interleukin 8	75	Hs.624	NM_000584	407
GZMB	Granzyme B (granzyme 2, cytotoxic T-lymphocyte-associated serine esterase 1)	76	Hs.1051	NM_004131	408
TNFSF6	Tumor necrosis factor (ligand) superfamily, member 6	77	Hs.2007	NM_000639	409

Gene	Gene Name	SEQ ID 50mer	HS	ACC	SEQ ID RNA/cDNA
TCIRG1	T-cell, immune regulator 1, ATPase, H+ transporting, lysosomal V0 protein a isoform 3	78	Hs.46465	NM_006019	410
PRF1	Perforin 1 (pore forming protein)	79	Hs.2200	NM_005041	411
IL4	Interleukin 4	80	Hs.73917	NM_000589	412
IL13	Interleukin 13	81	Hs.845	NM_002188	413
CTLA4	Cytotoxic T-lymphocyte-associated protein 4	82	Hs.247824	NM_005214	414
CD8A	CD8 antigen, alpha polypeptide (p32)	83	Hs.85258	NM_001768	415
BY55	Natural killer cell receptor, immunoglobulin superfamily member	84	Hs.81743	NM_007053	416
OID_4460	EST	85	Hs.205159	AF150295	417
HBB	Hemoglobin, beta	86	Hs.155376	NM_000518	418
BPGM	2,3-bisphosphoglycerate mutase	87	Hs.198365	NM_001724	419
MTHFD2	Methylene tetrahydrofolate dehydrogenase (NAD+ dependent), methenyltetrahydrofolate cyclohydrolase	88	Hs.154672	NM_006636	420
TAP1	Transporter 1, ATP-binding cassette, sub-family B (MDR1/TAP)	89	Hs.352018	NM_000593	421
KPNA6	Karyopherin alpha 6 (importin alpha 7)	90	Hs.301553	AW021037	422
OID_4365	Mitochondrial solute carrier	91	Hs.300496	AI114652	423
IGHM	Immunoglobulin heavy constant mu	92	Hs.300697	BC032249	424
OID_573	KIAA1486 protein	93	Hs.210958	AB040919	425
OID_873	KIAA1892 protein	94	Hs.102669	AK000354	426
OID_3	EST	95	Hs.104157	AW968823	427
CXCR4	Chemokine (C-X-C motif) receptor 4	96	Hs.89414	NM_003467	428
CD69	CD69 antigen (p60, early T-cell activation antigen)	97	Hs.82401	NM_001781	429
CCL5	Chemokine (C-C motif) ligand 5 (RANTES, SCYA5)	98	Hs.241392	NM_002985	430
IL6	Interleukin 6	99	Hs.93913	NM_000600	431
IL2	Interleukin 2	100	Hs.89679	NM_000586	432
KLRF1	Killer cell lectin-like receptor subfamily F, member 1	101	Hs.183125	NM_016523	433
LYN	v-yes-1 Yamaguchi sarcoma viral related oncogene homolog	102	Hs.80887	NM_002350	434
IL2RA	Interleukin 2 receptor, alpha	103	Hs.1724	NM_000417	435
CCL4	Chemokine (C-C motif) ligand 4, SCYA4	104	Hs.75703	NM_002984	436
OID_6207	EST	105	Hs.92440	D20522	437
ChGn	Chondroitin beta 1,4 N-acetylgalactosaminyltransferase	106	Hs.11260	NM_018371	438
OID_4281	EST	107	Hs.34549	AA053887	439
CXCL9	Chemokine (C-X-C motif) ligand 9 (MIG)	108	Hs.77367	NM_002416	440
CXCL10	Chemokine (C-X-C motif) ligand 10, SCYB10	109	Hs.2248	NM_001565	441

Gene	Gene Name	SEQ ID 50mer	HS	ACC	SEQ ID RNA/cDNA
IL17	Interleukin 17 (cytotoxic T-lymphocyte-associated serine esterase 8)	110	Hs.41724	NM_002190	442
IL15	Interleukin 15	111	Hs.168132	NM_000585	443
IL10	Interleukin 10	112	Hs.193717	NM_000572	444
IFNG	Interferon, gamma	113	Hs.856	NM_000619	445
HLA-DRB1	Major histocompatibility complex, class II, DR beta 1	114	Hs.308026	NM_002124	446
CD8B1	CD8 antigen, beta polypeptide 1 (p37)	115	Hs.2299	NM_004931	447
CD4	CD4 antigen (p55)	116	Hs.17483	NM_000616	448
CXCR3	Chemokine (C-X-C motif) receptor 3, GPR9	117	Hs.198252	NM_001504	449
OID_7094	XDx EST 479G12	118	NA	NA	450
OID_7605	EST	119	Hs.109302	AA808018	451
CXCL1	Chemokine (C-X-C motif) ligand 1 (melanoma growth stimulating activity, alpha)	120	Hs.789	NM_001511	452
OID_253	EST	121	Hs.83086	AK091125	453
GPI	Glucose phosphate isomerase	122	Hs.409162	NM_000175	454
CD47	CD47 antigen (Rh-related antigen, integrin-associated signal transducer)	123	Hs.82685	NM_001777	455
HLA-F	Major histocompatibility complex, class I, F	124	Hs.377850	NM_018950	456
OID_5350	EST	125	Hs.4283	AK055687	457
TCRGC2	T cell receptor gamma constant 2	126	Hs.112259	M17323	458
OID_7016	EST	127	NA	BI018696	459
PTGS2	Prostaglandin-endoperoxide synthase 2 (prostaglandin G/H synthase and cyclooxygenase)	128	Hs.196384	NM_000963	460
OID_5847	Hypothetical protein FLJ32919	129	Hs.293224	NM_144588	461
PRDM1	PR domain containing 1, with ZNF domain	130	Hs.388346	NM_001198	462
CKB	Creatine kinase, Brain	131	Hs.173724	NM_001823	463
TNNI3	Troponin I, cardiac	132	Hs.351382	NM_000363	464
TNNT2	Troponin T2, cardiac	133	Hs.296865	NM_000364	465
MB	Myoglobin	134	Hs.118836	NM_005368	466
SLC7A11	Solute carrier family 7, (cationic amino acid transporter, y+ system) member 11	135	Hs.6682	NM_014331	467
TNFRSF5	tumor necrosis factor receptor superfamily, member 5; CD40	136	Hs.25648	NM_001250	468
TNFRSF7	tumor necrosis factor receptor superfamily, member 7; CD27	137	Hs.355307	NM_001242	469
CD86	CD86 antigen (CD28 antigen ligand 2, B7-2 antigen)	138	Hs.27954	NM_175862	470
AIF1v2	Allograft inflammatory factor 1, splice variant 2	139	Hs.76364	NM_004847	471
EBV BCLF-1	BCLF-1 major capsid	140	NA	AJ507799	472
EBV EBV	EBNA repetitive sequence	141	NA	AJ507799	473
CMV p67	pp67	142	NA	X17403	474
CMV TRL7	c6843-6595	143	NA	X17403	475
CMV IE1e3	IE1 exon 3	144	NA	X17403	476

Gene	Gene Name	SEQ ID 50mer	HS	ACC	SEQ ID RNA/cDNA
CMV IE1e4	IE1 exon 4 (40 variants)	145	NA	X17403	477
EBV EBNA-1	EBNA-1 coding region	146	NA	AJ507799	478
EBV BZLF-1	Zebra gene	147	NA	AJ507799	479
EBV EBN	EBNA repetitive sequence	148	NA	AJ507799	480
EBV EBNA-LP	Short EBNA leader peptide exon	149	NA	AJ507799	481
CMV IE1	IE1S	150	NA	X17403	482
CMV IE1	IE1-MC (exon 3)	151	NA	X17403	483
CLC	Charot-Leyden crystal protein	152	Hs.889	NM_001828	484
TERF2IP	telomeric repeat binding factor 2, interacting protein	153	Hs.274428	NM_018975	485
HLA-A	Major histocompatibility complex, class I, A	154	Hs.181244	NM_002116	486
OID_5891	EST 3' end	155	None	AW297949	487
MSCP	mitochondrial solute carrier protein	156	Hs.283716	NM_018579	488
DUSP5	dual specificity phosphatase 5	157	Hs.2128	NM_004419	489
PRO1853	Hypothetical protein PRO1853	158	Hs.433466	NM_018607	490
OID_6420	73A7, FLJ00290 protein	159	Hs.98531	AK090404	491
CDSN	Corneodesmosin	160	Hs.507	NM_001264	492
OID_4269	EST	161	Hs.44628	BM727677	493
RPS25	Ribosomal protein S25	162	Hs.409158	NM_001028	494
GAPD	Glyceraldehyde-3-phosphate dehydrogenase	163	Hs.169476	NM_002046	495
RPLP1	Ribosomal protein, large, P1	164	Hs.424299	NM_001003	496
OID_5115	qz23b07.x1 cDNA, 3' end /clone=IMAGE:2027701	165	NA	AI364926	497
SLC9A8	Solute carrier family 9 (sodium/hydrogen exchanger), isoform 8	166	Hs.380978	AB023156	498
OID_1512	IMAGE:3865861 5 clone 5'	167	Hs.381302	BE618004	499
POLR2D	Polymerase (RNA) II (DNA directed) polypeptide D	168	Hs.194638	NM_004805	500
ARPC3	Actin related protein 2/3 complex, subunit 3, 21kDa	169	Hs.293750	NM_005719	501
OID_6282	EST 3' end	170	Hs.17132	BC041913	502
PRO1073	PRO1073 protein	171	Hs.356442	AF001542	503
OID_7222	EST, weakly similar to A43932 mucin 2 precursor, intestinal	172	Hs.28310	BG260891	504
FPRL1	Formyl peptide receptor-like 1	173	Hs.99855	NM_001462	505
FKBPL	FK506 binding protein like	174	Hs.99134	NM_022110	506
PREB	Prolactin regulatory element binding	175	Hs.279784	NM_013388	507
OID_1551	Hypothetical protein LOC200227	176	Hs.250824	BE887646	508
OID_7595	DKFZP566F0546 protein	177	Hs.144505	NM_015653	509
RNF19	Ring finger protein 19	178	Hs.48320	NM_015435	510
SMCY	SMC (mouse) homolog, Y chromosome (SMCY)	179	Hs.80358	NM_004653	511
OID_4184	CMV HCMVUL109	180	NA	X17403	512
OID_7504	Hypothetical protein FLJ35207	181	Hs.86543	NM_152312	513
DNAJC3	DnaJ (Hsp40) homolog, subfamily C, member 3	182	Hs.9683	NM_006260	514
ARHU	Ras homolog gene family, member U	183	Hs.20252	NM_021205	515
OID_7200	Hypothetical protein FLJ22059	184	Hs.13323	NM_022752	516

Gene	Gene Name	SEQ ID 50mer	HS	ACC	SEQ ID RNA/cDNA
SERPINB2	Serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 2	185	Hs.75716	NM_002575	517
ENO1	Enolase 1, alpha	186	Hs.254105	NM_001428	518
OID_7696	EST 3' end	187	Hs.438092	AW297325	519
OID_4173	CMV HCMVTRL2 (IRL2)	188	NA	X17403	520
CSF2RB	Upstream variant mRNA of colony stimulating factor 2 receptor, beta, low-affinity (granulocyte-macrophage)	189	Hs.285401	AL540399	521
OID_7410	CM2-LT0042-281299-062-e11 LT0042 cDNA, mRNA sequence	190	Hs.375145	AW837717	522
OID_4180	CMV HCMVUS28	191	NA	X17403	523
OID_5101	EST	192	Hs.144814	BG461987	524
MOP3	MOP-3	193	Hs.380419	NM_018183	525
RPL18A	Ribosomal protein L18a	194	Hs.337766	NM_000980	526
INPP5A	Inositol polyphosphate-5-phosphatase, 40kDa	195	Hs.124029	NM_005539	527
hIAN7	Immune associated nucleotide	196	Hs.124675	BG772661	528
RPS29	Ribosomal protein S29	197	Hs.539	NM_001032	529
OID_6008	EST 3' end	198	Hs.352323	AW592876	530
OID_4186	CMV HCMVUL122	199	NA	X17403	531
VNN2	vanin 2	200	Hs.121102	NM_004665	532
OID_7703	KIAA0907 protein	201	Hs.24656	NM_014949	533
OID_7057	480F8	202	NA	480F8	534
OID_4291	EST	203	Hs.355841	BC038439	535
OID_1366	EST	204	Hs.165695	AW850041	536
EEF1A1	Eukaryotic translation elongation factor 1 alpha 1	205	Hs.422118	NM_001402	537
PA2G4	Proliferation-associated 2G4, 38kDa	206	Hs.374491	NM_006191	538
GAPD	Glyceraldehyde-3-phosphate dehydrogenase	207	Hs.169476	NM_002046	539
CHD4	Chromodomain helicase DNA binding protein 4	208	Hs.74441	NM_001273	540
OID_7951	E2F-like protein (LOC51270)	209	Hs.142908	NM_016521	541
DAB1	Disabled homolog 1 (Drosophila)	210	Hs.344127	NM_021080	542
OID_3406	Hypothetical protein FLJ20356	211	Hs.61053	NM_018986	543
OID_6986	462H9 EST	212	Hs.434526	AK093608	544
OID_5962	EST 3' end	213	Hs.372917	AW452467	545
OID_5152	EST 3' end	214	Hs.368921	AI392805	546
S100A8	S100 calcium-binding protein A8 (calgranulin A)	215	Hs.416073	NM_002964	547
HNRPU	HNRPU Heterogeneous nuclear ribonucleoprotein U (scaffold attachment factor A)	216	Hs.103804	BM467823	548
ERCC5	Excision repair cross-complementing rodent repair deficiency, complementation group 5 (xeroderma pigmentosum, complementation group G (Cockayne syndrome))	217	Hs.48576	NM_000123	549
RPS27	Ribosomal protein S27 (metallopanstimulin 1)	218	Hs.195453	NM_001030	550
ACRC	acidic repeat containing (ACRC),	219	Hs.135167	NM_052957	551

Gene	Gene Name	SEQ ID 50mer	HS	ACC	SEQ ID RNA/cDNA
PSMD11	Proteasome (prosome, macropain) 26S subunit, non-ATPase, 11	220	Hs.90744	AI684022	552
OID_1016	FLJ00048 protein	221	Hs.289034	AK024456	553
OID_1309	AV706481 cDNA	222	None	AV706481	554
OID_7582	Weakly similar to ZINC FINGER PROTEIN 142	223	Hs.16493	AK027866	555
OID_4317	ta73c09.x1 3' end /clone=IMAGE:2049712 Ribosomal Protein S15	224	Hs.387179	AI318342	556
OID_5889	3' end /clone=IMAGE:3083913	225	Hs.255698	AW297843	557
UBL1	Ubiquitin-like 1 (sentrin)	226	Hs.81424	NM_003352	558
OID_3687	EST	227	None	W03955	559
OID_7371	EST 5'	228	Hs.290874	BE730505	560
SH3BGRL3	SH3 domain binding glutamic acid-rich protein like 3	229	Hs.109051	NM_031286	561
SEMA7A	Sema domain, immunoglobulin domain (Ig), and GPI membrane anchor, (semaphorin) 7A	230	Hs.24640	NM_003612	562
OID_5708	EST 3' end	231	Hs.246494	AW081540	563
OID_5992	EST 3' end	232	Hs.257709	AW467992	564
IL21	Interleukin 21	233	Hs.302014	NM_021803	565
HERC3	Hect domain and RLD 3 (HERC3)	234	Hs.35804	NM_014606	566
OID_7799	AluJo/FLAM SINE/Alu	235		AW837717	567
P11	26 serine protease	236	Hs.997	NM_006025	568
OID_7766	EST 3' end	237	Hs.437931	AW294711	569
TIMM10	translocase of inner mitochondrial membrane 10 (yeast) homolog (TIMM10)	238	Hs.235750	NM_012456	570
EGLN1	Egl nine homolog 1 (C. elegans)	239	Hs.6523	AJ310543	571
TBCC	Tubulin-specific chaperone c	240	Hs.75064	NM_003192	572
RNF3	Ring finger protein 3	241	Hs.8834	NM_006315	573
OID_6451	170F9, hypothetical protein FLJ21439	242	Hs.288872	AL834168	574
CCNDBP1	cyclin D-type binding-protein 1 (CCNDBP1)	243	Hs.36794	NM_012142	575
OID_8063	MUC18 gene exons 1&2	244	NA	X68264	576
SUV39H1	Suppressor of variegation 3-9 homolog 1 (Drosophila)	245	Hs.37936	NM_003173	577
HSPC048	HSPC048 protein	246	Hs.278944	NM_014148	578
OID_5625	EST 3' end from T cells	247	Hs.279121	AW063780	579
WARS	Tryptophanyl-tRNA synthetase	248	Hs.82030	NM_004184	580
OID_6823	107H8	249	Hs.169610	AL832642	581
OID_7073	119F12	250	Hs.13264	AL705961	582
OID_5339	EST 3' end	251	Hs.436022	AI625119	583
OID_4263	fetal retina 937202 cDNA clone IMAGE:565899	252	Hs.70877	AA136584	584
MGC26766	Hypothetical protein MGC26766	253	Hs.288156	AK025472	585
SERPINB11	Serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 11	254	Hs.350958	NM_080475	586
OID_6711	58G4, IMAGE:4359351 5'	255	none	BF968628	587
RNF10	Ring finger protein 10	256	Hs.5094	NM_014868	588
MKRN1	Makorin, ring finger protein, 1	257	Hs.7838	NM_013446	589
RPS16	ribosomal protein S16	258	Hs.397609	NM_001020	590

Gene	Gene Name	SEQ ID 50mer	HS	ACC	SEQ ID RNA/cDNA
BAZ1A	Bromodomain adjacent to zinc finger domain, 1A	259	Hs.8858	NM_013448	591
OID_5998	EST 3' end	260	Hs.330268	AW468459	592
ATP5L	ATP synthase, H+ transporting, mitochondrial F0 complex, subunit g	261	Hs.107476	NM_006476	593
OID_6393	52B9	262	NA	52B9	594
RoXaN	Ubiquitous tetratricopeptide containing protein RoXaN	263	Hs.25347	BC004857	595
NCBP2	Nuclear cap binding protein subunit 2, 20kDa	264	Hs.240770	NM_007362	596
OID_6273	EST 3' end	265	Hs.158976	AW294774	597
HZF12	zinc finger protein 12	266	Hs.164284	NM_033204	598
CCL3	Chemokine (C-C motif) ligand 3	267	Hs.73817	D90144	599
OID_4323	IMAGE:1283731 3'	268	Hs.370770	AA744774	600
OID_5181	tg93h12.x1 NCI_CGAP_CLL1 cDNA clone IMAGE:2116391 3' similar to contains TAR1.t1 MER22	269	NA	AI400725	601
PRDX4	Peroxiredoxin 4	270	Hs.83383	NM_006406	602
BTK	Bruton agammaglobulinemia tyrosine kinase	271	Hs.159494	NM_000061	603
OID_6298	Importin beta subunit mRNA	272	Hs.180446	AI948513	604
PGK1	Phosphoglycerate kinase 1	273	Hs.78771	NM_000291	605
TNFRSF10A	Tumor necrosis factor receptor superfamily, member 10a	274	Hs.249190	NM_003844	606
ADM	adrenomedullin	275	Hs.394	NM_001124	607
OID_357	138G5	276	NA	138G5	608
C20orf6	461A4 chromosome 20 open reading frame 6	277	Hs.88820	NM_016649	609
OID_3226	DKFZP564O0823 protein	278	Hs.105460	NM_015393	610
ASAH1	N-acylsphingosine amidohydrolase (acid ceramidase) 1	279	Hs.75811	NM_004315	611
ATF5	Activating transcription factor 5	280	Hs.9754	NM_012068	612
OID_4887	hypothetical protein MGC14376	281	Hs.417157	NM_032895	613
OID_4239	EST	282	Hs.177376	BQ022840	614
MDM2	Mouse double minute 2, homolog of; p53-binding protein (MDM2), transcript variant MDM2,	283	Hs.170027	NM_002392	615
XRN2	5'-3' exoribonuclease 2	284	Hs.268555	AF064257	616
OID_6039	Endothelial differentiation, lysophosphatidic acid G-protein-coupled receptor, 4 (EDG4)	285	Hs.122575	BE502246	617
OID_4210	IMAGE:4540096	286	Hs.374836	AI300700	618
OID_7698	EST 3' end	287	Hs.118899	AA243283	619
PRKRA	Protein kinase, interferon-inducible double stranded RNA dependent activator	288	Hs.18571	NM_003690	620
OID_4288	IMAGE:2091815	289	Hs.309108	AI378046	621
OID_5620	EST 3' end from T cells	290	Hs.279116	AW063678	622
OID_7384	EST 5'	291	Hs.445429	BF475239	623
OID_1209	EST Weakly similar to hypothetical protein FLJ20378	292	Hs.439346	C14379	624
CDKN1B	Cyclin-dependent kinase inhibitor 1B (p27, Kip1)	293	Hs.238990	NM_004064	625

Gene	Gene Name	SEQ ID 50mer	HS	ACC	SEQ ID RNA/cDNA
PLOD	Procollagen-lysine, 2-oxoglutarate 5-dioxygenase (lysine hydroxylase, Ehlers-Danlos syndrome type VI)	294	Hs.75093	NM_000302	626
OID_5128	EST	295	Hs.283438	AK097845	627
OID_5877	EST 3' end	296	Hs.438118	AW297664	628
FZD4	Frizzled (Drosophila) homolog 4	297	Hs.19545	NM_012193	629
HLA-B	Major histocompatibility complex, class I, B	298	Hs.77961	NM_005514	630
OID_5624	EST 3' end from T cells	299	Hs.279120	AW063921	631
FPR1	Formyl peptide receptor 1	300	Hs.753	NM_002029	632
ODF2	Outer dense fiber of sperm tails 2	301	Hs.129055	NM_153437	633
OID_5150	tg04g01.x1 cDNA, 3' end /clone=IMAGE:2107824	302	Hs.160981	AI392793	634
OID_5639	EST 3' end from T cells	303	Hs.279139	AW064243	635
OID_6619	469A10	304	NA	469A10	636
OID_6933	463C7, 4 EST hits. Aligned	305	Hs.86650	AI089520	637
OID_7049	480E2	306	NA	480E2	638
IL17C	Interleukin 17C	307	Hs.278911	NM_013278	639
OID_5866	EST 3' end	308	Hs.255649	BM684739	640
CD44	CD44	309	Hs.169610	AA916990	641
VPS45A	Vacuolar protein sorting 45A (yeast)	310	Hs.6650	NM_007259	642
OID_4932	aa92c03.r1 Stratagene fetal retina 937202 cDNA clone IMAGE:838756	311	NA	AA457757	643
OID_7821	EST	312	NA	AA743221	644
OID_4916	zr76a03.r1 Soares_NhHMPu_S1 cDNA clone IMAGE:669292	313	NA	AA252909	645
OID_4891	Hypothetical protein LOC255488	314	Hs.294092	AL832329	646
HADHB	Hydroxyacyl-Coenzyme A dehydrogenase/3-ketoacyl-Coenzyme A thiolase/enoyl-Coenzyme A hydratase (trifunctional protein), beta subunit	315	Hs.146812	NM_000183	647
FLJ22757	Hypothetical protein FLJ22757	316	Hs.236449	NM_024898	648
RAC1	Ras-related C3 botulinum toxin substrate 1 (rho family, small GTP binding protein Rac1)	317	Hs.173737	AK054993	649
OID_6415	72D4, FLJ00290 protein	318	Hs.98531	CA407201	650
NMES1	Normal mucosa of esophagus specific 1	319	Hs.112242	NM_032413	651
DMBT1	Deleted in malignant brain tumors 1, transcript variant 2	320	Hs.279611	NM_007329	652
RPS23	ribosomal protein S23	321	Hs.3463	NM_001025	653
ZF	HCF-binding transcription factor Zhangfei	322	Hs.29417	NM_021212	654
NFE2L3	Nuclear factor (erythroid-derived 2)-like 3	323	Hs.22900	NM_004289	655
RAD9	RAD9 homolog (S. pombe)	324	Hs.240457	NM_004584	656
OID_6295	EST 3' end	325	Hs.389327	AI880607	657
DEFCAP	Death effector filament-forming Ced-4-like apoptosis protein, transcript variant B	326	Hs.104305	NM_014922	658
RPL27A	Ribosomal protein L27a	327	Hs.76064	BF214146	659
IL22	Interleukin 22 (IL22)	328	Hs.287369	NM_020525	660

Gene	Gene Name	SEQ ID 50mer	HS	ACC	SEQ ID RNA/cDNA
PSMA4	Proteasome (prosome, macropain) subunit, alpha type, 4, (PSMA4)	329	Hs.251531	NM_002789	661
CCNI	cyclin I (CCNI)	330	Hs.79933	NM_006835	662
THBD	Thrombomodulin	331	Hs.2030	NM_000361	663
CGR19	Cell growth regulatory with ring finger domain	332	Hs.59106	NM_006568	664

SEQ ID 50mer	Gene	Gene Name	ACC	SEQ ID RNA/cDNA	Non-Para Score	Median Rank in NR	Down Regulated
152	CLC	Charcot-Leyden crystal protein	NM_001828	484	779	4342	
153	TERF2IP	telomeric repeat binding factor 2, interacting protein	NM_018975	485	744	1775	
154	HLA-A	Major histocompatibility complex, class I, A	NM_002116	486	735	125	1
155	OID_5891	EST 3' end	AW297949	487	730	7044.5	1
156	MSCP	mitochondrial solute carrier protein	NM_018579	488	730	3465.5	
157	DUSP5	dual specificity phosphatase 5	NM_004419	489	726	3122.5	
158	PRO1853	Hypothetical protein PRO1853	NM_018607	490	725	4153	
159	OID_6420	73A7, FLJ00290 protein	AK090404	491	725	7000.5	
160	CDSN	Corneodesmosin	NM_001264	492	722	2732	
161	OID_4269	EST	BM727677	493	715	5598.5	
162	RPS25	Ribosomal protein S25	NM_001028	494	710	164.5	
163	GAPD	Glyceraldehyde-3-phosphate dehydrogenase	NM_002046	495	707	215.5	
164	RPLP1	Ribosomal protein, large, P1	NM_001003	496	703	157	
165	OID_5115	qz23b07.x1 cDNA, 3' end /clone=IMAGE:2027701	AI364926	497	703	6629	1
166	SLC9A8	Solute carrier family 9 (sodium/hydrogen exchanger), isoform 8	AB023156	498	702	2538.5	
167	OID_1512	IMAGE:3865861 5 clone 5'	BE618004	499	700	4008	1
168	POLR2D	Polymerase (RNA) II (DNA directed) polypeptide D	NM_004805	500	700	4190.5	
169	ARPC3	Actin related protein 2/3 complex, subunit 3, 21kDa	NM_005719	501	698	470.5	
170	OID_6282	EST 3' end	BC041913	502	697	4371.5	
171	PRO1073	PRO1073 protein	AF001542	503	697	6754	
172	OID_7222	EST, weakly similar to A43932 mucin 2 precursor, intestinal	BG260891	504	695	6759	
173	FPRL1	Formyl peptide receptor-like 1	NM_001462	505	692	4084.5	
174	FKBPL	FK506 binding protein like	NM_022110	506	691	1780.5	
175	PREB	Prolactin regulatory element binding	NM_013388	507	690	3568	
176	OID_1551	Hypothetical protein LOC200227	BE887646	508	689	6423	1
177	OID_7595	DKFZP566F0546 protein	NM_015653	509	689	3882.5	
178	RNF19	Ring finger protein 19	NM_015435	510	689	7700.5	
179	SMCY	SMC (mouse) homolog, Y chromosome (SMCY)	NM_004653	511	687	6074.5	
180	OID_4184	CMV HCMVUL109	X17403	512	687	6810.5	
181	OID_7504	Hypothetical protein FLJ35207	NM_152312	513	686	6939	
182	DNAJC3	DnaJ (Hsp40) homolog, subfamily C, member 3	NM_006260	514	686	3932.5	
183	ARHU	Ras homolog gene family, member U	NM_021205	515	686	7584	
184	OID_7200	Hypothetical protein FLJ22059	NM_022752	516	685	2804.5	
185	SERPINB2	Serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 2	NM_002575	517	684	4690.5	
186	ENO1	Enolase 1, alpha	NM_001428	518	684	327	
187	OID_7696	EST 3' end	AW297325	519	683	4875.5	

SEQ ID 50mer	Gene	Gene Name	ACC	SEQ ID RNA/cDNA	Non-Para Score	Median Rank in NR	Down Regulated
188	OID_4173	CMV HCMVTRL2 (IRL2)	X17403	520	683	4010.5	
189	CSF2RB	Upstream variant mRNA of colony stimulating factor 2 receptor, beta, low-affinity (granulocyte-macrophage)	AL540399	521	683	3753	
190	OID_7410	CM2-LT0042-281299-062-e11 LT0042 cDNA, mRNA sequence	AW837717	522	682	7445	
191	OID_4180	CMV HCMVUS28	X17403	523	681	4359	
192	OID_5101	EST	BG461987	524	681	7272	
193	MOP3	MOP-3	NM_018183	525	681	4085.5	1
194	RPL18A	Ribosomal protein L18a	NM_000980	526	680	238	
195	INPP5A	Inositol polyphosphate-5-phosphatase, 40kDa	NM_005539	527	680	4838.5	1
196	hIAN7	Immune associated nucleotide	BG772661	528	680	4718	
197	RPS29	Ribosomal protein S29	NM_001032	529	680	107.5	
198	OID_6008	EST 3' end	AW592876	530	679	6560.5	
199	OID_4186	CMV HCMVUL122	X17403	531	677	4788.5	
200	VNN2	vanin 2	NM_004665	532	677	2620.5	
201	OID_7703	KIAA0907 protein	NM_014949	533	676	6104.5	
202	OID_7057	480F8	480F8	534	675	6862	
203	OID_4291	EST	BC038439	535	674	5618.5	
204	OID_1366	EST	AW850041	536	674	5590.5	1
205	EEF1A1	Eukaryotic translation elongation factor 1 alpha 1	NM_001402	537	672	232	
206	PA2G4	Proliferation-associated 2G4, 38kDa	NM_006191	538	672	4402	
207	GAPD	Glyceraldehyde-3-phosphate dehydrogenase	NM_002046	539	671	194.5	
208	CHD4	Chromodomain helicase DNA binding protein 4	NM_001273	540	671	2578.5	
209	OID_7951	E2F-like protein (LOC51270)	NM_016521	541	671	4467	
210	DAB1	Disabled homolog 1 (Drosophila)	NM_021080	542	670	6357.5	
211	OID_3406	Hypothetical protein FLJ20356	NM_018986	543	669	2087	
212	OID_6986	462H9 EST	AK093608	544	669	4454	1
213	OID_5962	EST 3' end	AW452467	545	668	5870.5	1
214	OID_5152	EST 3' end	AI392805	546	668	6354.5	
215	S100A8	S100 calcium-binding protein A8 (calgranulin A)	NM_002964	547	668	134	
216	HNRPU	HNRPU Heterogeneous nuclear ribonucleoprotein U (scaffold attachment factor A)	BM467823	548	668	4108	
217	ERCC5	Excision repair cross-complementing rodent repair deficiency, complementation group 5 (xeroderma pigmentosum, complementation group G (Cockayne syndrome))	NM_000123	549	668	6430.5	
218	RPS27	Ribosomal protein S27 (metallopanstimulin 1)	NM_001030	550	668	160	

SEQ ID 50mer	Gene	Gene Name	ACC	SEQ ID RNA/cDNA	Non-Para Score	Median Rank in NR	Down Regulated
219	ACRC	acidic repeat containing (ACRC),	NM_052957	551	668	4871.5	1
220	PSMD11	Proteasome (prosome, macropain) 26S subunit, non-ATPase, 11	AI684022	552	668	4138	
221	OID_1016	FLJ00048 protein	AK024456	553	667	5199	
222	OID_1309	AV706481 cDNA	AV706481	554	667	7279.5	
223	OID_7582	Weakly similar to ZINC FINGER PROTEIN 142	AK027866	555	667	5003.5	1
224	OID_4317	ta73c09.x1 3' end /clone=IMAGE:2049712 Ribosomal Protein S15	AI318342	556	667	6499	
225	OID_5889	3' end /clone=IMAGE:3083913	AW297843	557	666	6837	1
226	UBL1	Ubiquitin-like 1 (sentrin)	NM_003352	558	666	1978.5	
227	OID_3687	EST	W03955	559	666	5519.5	
228	OID_7371	EST 5'	BE730505	560	665	7751.5	
229	SH3BGRL3	SH3 domain binding glutamic acid-rich protein like 3	NM_031286	561	665	310	
230	SEMA7A	Sema domain, immunoglobulin domain (Ig), and GPI membrane anchor, (semaphorin) 7A	NM_003612	562	665	3505.5	
231	OID_5708	EST 3' end	AW081540	563	665	6224.5	
232	OID_5992	EST 3' end	AW467992	564	665	5648	
233	IL21	Interleukin 21	NM_021803	565	664	5036.5	
234	HERC3	Hect domain and RLD 3 (HERC3)	NM_014606	566	664	3056.5	1
235	OID_7799	AluJo/FLAM SINE/Alu	AW837717	567	664	3544	
236	P11	26 serine protease	NM_006025	568	664	7173	
237	OID_7766	EST 3' end	AW294711	569	663	7270.5	
238	TIMM10	translocase of inner mitochondrial membrane 10 (yeast) homolog (TIMM10)	NM_012456	570	663	4779.5	
239	EGLN1	Egl nine homolog 1 (C. elegans)	AJ310543	571	662	7172.5	
240	TBCC	Tubulin-specific chaperone c	NM_003192	572	662	3384	
241	RNF3	Ring finger protein 3	NM_006315	573	661	4062	
242	OID_6451	170F9, hypothetical protein FLJ21439	AL834168	574	661	7126	1
243	CCNDBP1	cyclin D-type binding-protein 1 (CCNDBP1)	NM_012142	575	661	1919	
244	OID_8063	MUC18 gene exons 1&2	X68264	576	661	4692.5	
245	SUV39H1	Suppressor of variegation 3-9 homolog 1 (Drosophila)	NM_003173	577	661	5103	1
246	HSPC048	HSPC048 protein	NM_014148	578	660	5981.5	
247	OID_5625	EST 3' end from T cells	AW063780	579	660	4437	1
248	WARS	Tryptophanyl-tRNA synthetase	NM_004184	580	660	905.5	
249	OID_6823	107H8	AL832642	581	659	2619	
250	OID_7073	119F12	AL705961	582	659	6837.5	
251	OID_5339	EST 3' end	AI625119	583	658	4414.5	1
252	OID_4263	fetal retina 937202 cDNA clone IMAGE:565899	AA136584	584	658	5870	
253	MGC26766	Hypothetical protein MGC26766	AK025472	585	658	1892.5	

SEQ ID 50mer	Gene	Gene Name	ACC	SEQ ID RNA/cDNA	Non-Para Score	Median Rank in NR	Down Regulated
254	SERPINB11	Serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 11	NM_080475	586	658	7535.5	1
255	OID_6711	58G4, IMAGE:4359351 5'	BF968628	587	658	7264	
256	RNF10	Ring finger protein 10	NM_014868	588	658	3127.5	
257	MKRN1	Makorin, ring finger protein, 1	NM_013446	589	658	2228.5	
258	RPS16	ribosomal protein S16	NM_001020	590	657	165.5	
259	BAZ1A	Bromodomain adjacent to zinc finger domain, 1A	NM_013448	591	657	2533	
260	OID_5998	EST 3' end	AW468459	592	657	6339.5	
261	ATP5L	ATP synthase, H+ transporting, mitochondrial F0 complex, subunit g	NM_006476	593	657	1155	
262	OID_6393	52B9	52B9	594	657	7420.5	
263	RoXaN	Ubiquitous tetratricopeptide containing protein RoXaN	BC004857	595	656	7378	
264	NCBP2	Nuclear cap binding protein subunit 2, 20kDa	NM_007362	596	656	4666.5	
265	OID_6273	EST 3' end	AW294774	597	656	5498.5	
266	HZF12	zinc finger protein 12	NM_033204	598	656	4715.5	
267	CCL3	Chemokine (C-C motif) ligand 3	D90144	599	656	4910	1
268	OID_4323	IMAGE:1283731 3'	AA744774	600	655	6406.5	1
269	OID_5181	tg93h12.x1 NCI_CGAP_CLL1 cDNA clone IMAGE:2116391 3' similar to contains TAR1.t1 MER22	AI400725	601	655	4838	1
270	PRDX4	Peroxiredoxin 4	NM_006406	602	655	3397.5	
271	BTK	Bruton agammaglobulinemia tyrosine kinase	NM_000061	603	655	2358	
272	OID_6298	Importin beta subunit mRNA	AI948513	604	655	2433.5	
273	PGK1	Phosphoglycerate kinase 1	NM_000291	605	655	2059.5	
274	TNFRSF10A	Tumor necrosis factor receptor superfamily, member 10a	NM_003844	606	654	4897.5	1
275	ADM	adrenomedullin	NM_001124	607	654	4235	
276	OID_357	138G5	138G5	608	654	5427.5	1
277	C20orf6	461A4 chromosome 20 open reading frame 6	NM_016649	609	654	6343	1
278	OID_3226	DKFZP564O0823 protein	NM_015393	610	653	6187.5	
279	ASAH1	N-acylsphingosine amidohydrolase (acid ceramidase) 1	NM_004315	611	653	1003	
280	ATF5	Activating transcription factor 5	NM_012068	612	653	4545.5	
281	OID_4887	hypothetical protein MGC14376	NM_032895	613	653	2310	1
282	OID_4239	EST	BQ022840	614	652	2774.5	
283	MDM2	Mouse double minute 2, homolog of; p53-binding protein (MDM2), transcript variant MDM2,	NM_002392	615	652	4342	
284	XRN2	5'-3' exoribonuclease 2	AF064257	616	652	6896.5	

SEQ ID 50mer	Gene	Gene Name	ACC	SEQ ID RNA/cDNA	Non-Para Score	Median Rank in NR	Down Regulated
285	OID_6039	Endothelial differentiation, lysophosphatidic acid G-protein-coupled receptor, 4 (EDG4)	BE502246	617	652	5147	
286	OID_4210	IMAGE:4540096	AI300700	618	652	1330.5	
287	OID_7698	EST 3' end	AA243283	619	652	7432.5	1
288	PRKRA	Protein kinase, interferon-inducible double stranded RNA dependent activator	NM_003690	620	652	3512.5	
289	OID_4288	IMAGE:2091815	AI378046	621	651	6401.5	
290	OID_5620	EST 3' end from T cells	AW063678	622	651	6400	
291	OID_7384	EST 5'	BF475239	623	651	6875	
292	OID_1209	EST Weakly similar to hypothetical protein FLJ20378	C14379	624	651	1356.5	1
293	CDKN1B	Cyclin-dependent kinase inhibitor 1B (p27, Kip1)	NM_004064	625	650	4272.5	
294	PLOD	Procollagen-lysine, 2-oxoglutarate 5-dioxygenase (lysine hydroxylase, Ehlers-Danlos syndrome type VI)	NM_000302	626	650	3101	
295	OID_5128	EST	AK097845	627	650	6476	
296	OID_5877	EST 3' end	AW297664	628	650	6864.5	1
297	FZD4	Frizzled (Drosophila) homolog 4	NM_012193	629	650	5816	
298	HLA-B	Major histocompatibility complex, class I, B	NM_005514	630	650	229	
299	OID_5624	EST 3' end from T cells	AW063921	631	649	7812.5	
300	FPR1	Formyl peptide receptor 1	NM_002029	632	649	1156.5	
301	ODF2	Outer dense fiber of sperm tails 2	NM_153437	633	649	4982.5	
302	OID_5150	tg04g01.x1 cDNA, 3' end /clone=IMAGE:2107824	AI392793	634	649	7638	
303	OID_5639	EST 3' end from T cells	AW064243	635	648	6805	1
304	OID_6619	469A10	469A10	636	647	7110	1
305	OID_6933	463C7, 4 EST hits. Aligned	AI089520	637	647	6880.5	1
306	OID_7049	480E2	480E2	638	647	7128.5	
307	IL17C	Interleukin 17C	NM_013278	639	647	6411.5	
308	OID_5866	EST 3' end	BM684739	640	647	6532	1
309	CD44	CD44	AA916990	641	646	4758	
310	VPS45A	Vacuolar protein sorting 45A (yeast)	NM_007259	642	646	3371	
311	OID_4932	aa92c03.r1 Stratagene fetal retina 937202 cDNA clone IMAGE:838756	AA457757	643	646	6057	1
312	OID_7821	EST	AA743221	644	645	7507	
313	OID_4916	zr76a03.r1 Soares_NhHMPu_S1 cDNA clone IMAGE:669292	AA252909	645	645	6962.5	1
314	OID_4891	Hypothetical protein LOC255488	AL832329	646	645	6148.5	

SEQ ID 50mer	Gene	Gene Name	ACC	SEQ ID RNA/cDNA	Non-Para Score	Median Rank in NR	Down Regulated
315	HADHB	Hydroxyacyl-Coenzyme A dehydrogenase/3-ketoacyl-Coenzyme A thiolase/enoyl-Coenzyme A hydratase (trifunctional protein), beta subunit	NM_000183	647	645	3212.5	
316	FLJ22757	Hypothetical protein FLJ22757	NM_024898	648	644	1965.5	1
317	RAC1	Ras-related C3 botulinum toxin substrate 1 (rho family, small GTP binding protein Rac1)	AK054993	649	644	1533	
318	OID_6415	72D4, FLJ00290 protein	CA407201	650	644	4881	
319	NMES1	Normal mucosa of esophagus specific 1	NM_032413	651	644	6217	1
320	DMBT1	Deleted in malignant brain tumors 1, transcript variant 2	NM_007329	652	644	7284	
321	RPS23	ribosomal protein S23	NM_001025	653	643	219.5	
322	ZF	HCF-binding transcription factor Zhangfei	NM_021212	654	643	4069	
323	NFE2L3	Nuclear factor (erythroid-derived 2)-like 3	NM_004289	655	643	3378	
324	RAD9	RAD9 homolog (S. pombe)	NM_004584	656	643	6453	
325	OID_6295	EST 3' end	AI880607	657	643	7493.5	
326	DEFCAP	Death effector filament-forming Ced-4-like apoptosis protein, transcript variant B	NM_014922	658	643	3059	
327	RPL27A	Ribosomal protein L27a	BF214146	659	642	6571	1
328	IL22	Interleukin 22 (IL22)	NM_020525	660	642	3891	1
329	PSMA4	Proteasome (prosome, macropain) subunit, alpha type, 4, (PSMA4)	NM_002789	661	641	1934.5	
330	CCNI	cyclin I (CCNI)	NM_006835	662	641	980.5	
331	THBD	Thrombomodulin	NM_000361	663	640	4732.5	
332	CGR19	Cell growth regulatory with ring finger domain	NM_006568	664	640	5510	

Gene	SEQ ID 50mer	SEQ ID RNA/cDNA	PCR Forward Primer 1 SEQ ID	PCR Reverse Primer 1 SEQ ID	PCR Probe 1 SEQ ID	PCR Forward Primer 2 SEQ ID	PCR Reverse Primer 2 SEQ ID	PCR Probe 2 SEQ ID
HSRRN18S	1	333	665	996	1327			
ACTB	2	334	666	997	1328			
GUSB	3	335	667	998	1329	1656	1904	2152
B2M	4	336	668	999	1330			
TSN	5	337	669	1000	1331	1657	1905	2153
CCR7	6	338	670	1001	1332			
IL1R2	7	339	671	1002	1333	1658	1906	2154
AIF-1	8	340	672	1003	1334			
ALAS2	9	341	673	1004	1335			
APELIN	10	342	674	1005	1336			
CD80	11	343	675	1006	1337	1659	1907	2145
EPB41	12	344	676	1007	1338			
CBLB	13	345	677	1008	1339	1660	1908	2156
CCR5	14	346	678	1009	1340	1661	1909	2157
MME	15	347	679	1010	1341	1662	1910	2158
KLRC1	16	348	680	1011	1342	1663	1911	2159
FCGR3A	17	349	681	1012	1343			
FCGR3B	18	350	682	1013	1344	1664	1912	2160
LAG3	19	351	683	1014	1345	1665	1913	2161
PECAM1	20	352	684	1015	1346	1666	1914	2162
CD34	21	353	685	1016	1347	1667	1915	2163
FCGR1A	22	354	686	1017	1348	1668	1916	2164
TFRC	23	355	687	1018	1349			
CMA1	24	356	688	1019	1350	1669	1917	2165
KIT	25	357	689	1020	1351			
MPL	26	358	690	1021	1352	1670	1918	2166
EphB6	27	359	691	1022	1353			
EPO-R	28	360	692	1023	1354			
Foxp3	29	361	693	1024	1355	1671	1919	2167
GATA-1	30	362	694	1025	1356			
ITGA2B	31	363	695	1026	1357	1672	1920	2168
GNLY	32	364	696	1027	1358	1673	1921	2169
GZMA	33	365	697	1028	1359	1674	1922	2170
HBA	34	366	698	1029	1360	1675	1923	2171
HBZ	35	367	699	1030	1361	1676	1924	2172
HBB	36	368	700	1031	1362	1677	1925	2173
HBD	37	369	701	1032	1363	1678	1926	2174
HBE	38	370	702	1033	1364	1679	1927	2175
HBG	39	371	703	1034	1365	1680	1928	2176
HBQ	40	372	704	1035	1366	1681	1929	2177
HLA-DP	41	373	705	1036	1367	1682	1930	2178
HLA-DQ	42	374	706	1037	1368	1683	1931	2179
HLA-DRB	43	375	707	1038	1369	1684	1932	2180
ICOS	44	376	708	1039	1370	1685	1933	2181
IL18	45	377	709	1040	1371	1686	1934	2182
IL3	46	378	710	1041	1372	1687	1935	2183
ITGA4	47	379	711	1042	1373			
ITGAM	48	380	712	1043	1374	1688	1936	2184
ITGB7	49	381	713	1044	1375			
CEBPB	50	382	714	1045	1376	1689	1937	2185
NF-E2	51	383	715	1046	1377			
PDCD1	52	384	716	1047	1378	1690	1938	2186
PF4	53	385	717	1048	1379	1691	1939	2187
PRKCQ	54	386	718	1049	1380	1692	1940	2188
PPARGC1	55	387	719	1050	1381			

Gene	SEQ ID 50mer	SEQ ID RNA/cDNA	PCR Forward Primer 1 SEQ ID	PCR Reverse Primer 1 SEQ ID	PCR Probe 1 SEQ ID	PCR Forward Primer 2 SEQ ID	PCR Reverse Primer 2 SEQ ID	PCR Probe 2 SEQ ID
RAG1	56	388	720	1051	1382	1693	1941	2189
RAG2	57	389	721	1052	1383	1694	1942	2190
CXCL12	58	390	722	1053	1384	1695	1943	2191
TNFRSF4	59	391	723	1054	1385	1696	1944	2192
TNFSF4	60	392	724	1055	1386	1697	1945	2193
TPS1	61	393	725	1056	1387	1698	1946	2194
ADA	62	394	726	1057	1388	1699	1947	2195
CPM	63	395	727	1058	1389	1700	1948	2196
CSF2	64	396	728	1059	1390	1701	1949	2197
CSF3	65	397	729	1060	1391	1702	1950	2198
CRP	66	398	730	1061	1392	1703	1951	2199
FLT3	67	399	731	1062	1393	1704	1952	2200
GATA3	68	400	732	1063	1394	1705	1953	2201
IL7R	69	401	733	1064	1395	1706	1954	2202
KLF1	70	402	734	1065	1396	1707	1955	2203
LCK	71	403	735	1066	1397	1708	1956	2204
LEF1	72	404	736	1067	1398	1709	1957	2205
PLAUR	73	405	737	1068	1399	1710	1958	2206
TNFSF13B	74	406	738	1069	1400	1711	1959	2207
IL8	75	407	739	1070	1401			
GZMB	76	408	740	1071	1402			
TNFSF6	77	409	741	1072	1403			
TCIRG1	78	410	742	1073	1404			
PRF1	79	411	743	1074	1405			
IL4	80	412	744	1075	1406			
IL13	81	413	745	1076	1407			
CTLA4	82	414	746	1077	1408			
CD8A	83	415	747	1078	1409			
BY55	84	416	748	1079	1410			
OID_4460	85	417	749	1080	1411			
HBB	86	418	750	1081	1412			
BPGM	87	419	751	1082	1413			
MTHFD2	88	420	752	1083	1414			
TAP1	89	421	753	1084	1415			
KPNA6	90	422	754	1085	1416			
OID_4365	91	423	755	1086	1417			
IGHM	92	424	756	1087	1418			
OID_573	93	425	757	1088	1419	1712	1960	2208
OID_873	94	426	758	1089	1420			
OID_3	95	427	759	1090	1421			
CXCR4	96	428	760	1091	1422			
CD69	97	429	761	1092	1423			
CCL5	98	430	762	1093	1424			
IL6	99	431	763	1094	1425			
IL2	100	432	764	1095	1426			
KLRF1	101	433	765	1096	1427			
LYN	102	434	766	1097	1428			
IL2RA	103	435	767	1098	1429			
CCL4	104	436	768	1099	1430			
OID_6207	105	437	769	1100	1431			
ChGn	106	438	770	1101	1432			
OID_4281	107	439	771	1102	1433			
CXCL9	108	440	772	1103	1434			
CXCL10	109	441	773	1104	1435			
IL17	110	442	774	1105	1436			

Gene	SEQ ID 50mer	SEQ ID RNA/cDNA	PCR Forward Primer 1 SEQ ID	PCR Reverse Primer 1 SEQ ID	PCR Probe 1 SEQ ID	PCR Forward Primer 2 SEQ ID	PCR Reverse Primer 2 SEQ ID	PCR Probe 2 SEQ ID
IL15	111	443	775	1106	1437			
IL10	112	444	776	1107	1438			
IFNG	113	445	777	1108	1439	1713	1961	2209
HLA-DRB1	114	446	778	1109	1440	1714	1962	2210
CD8B1	115	447	779	1110	1441			
CD4	116	448	780	1111	1442			
CXCR3	117	449	781	1112	1443			
OID_7094	118	450	782	1113	1444			
OID_7605	119	451	783	1114	1445			
CXCL1	120	452	784	1115	1446			
OID_253	121	453	785	1116	1447			
GPI	122	454	786	1117	1448			
CD47	123	455	787	1118	1449			
HLA-F	124	456	788	1119	1450			
OID_5350	125	457	789	1120	1451			
TCRGC2	126	458	790	1121	1452			
OID_7016	127	459	791	1122				
PTGS2	128	460	792	1123	1454			
OID_5847	129	461	793	1124	1455			
PRDM1	130	462	794	1125	1456			
CKB	131	463	795	1126	1457			
TNNI3	132	464	796	1127	1458			
TNNT2	133	465	797	1128	1459			
MB	134	466	798	1129	1460			
SLC7A11	135	467	799	1130	1461			
TNFRSF5	136	468	800	1131	1462	1715	1963	2211
TNFRSF7	137	469	801	1132	1463			
CD86	138	470	802	1133	1464			
AIF1v2	139	471	803	1134	1465			
EV BCLF-1	140	472	804	1135	1466	1716	1964	2212
EV EBV	141	473	805	1136	1467	1717	1965	2213
CMV p67	142	474	806	1137	1468	1718	1966	2214
CMV TRL7	143	475	807	1138	1469	1719	1967	2215
CMV IE1e3	144	476	808	1139	1470	1720	1968	2216
CMV IE1e4	145	477	809	1140	1471	1721	1969	2217
EV EBNA-1	146	478	810	1141	1472	1722	1970	2218
EV BZLF-1	147	479	811	1142	1473	1723	1971	2219
EV EBN	148	480	812	1143	1474	1724	1972	2220
EV EBNA-L	149	481	813	1144	1475			
CMV IE1	150	482	814	1145	1476	1725	1973	2221
CMV IE1	151	483	815	1146	1477			
CLC	152	484	816	1147	1478	1726	1974	2222
TERF2IP	153	485	817	1148	1479	1727	1975	2223
HLA-A	154	486	818	1149	1480	1728	1976	2224
OID_5891	155	487	819	1150	1481	1729	1977	2225
MSCP	156	488	820	1151	1482	1730	1978	2226
DUSP5	157	489	821	1152	1483	1731	1979	2227
PRO1853	158	490	822	1153	1484	1732	1980	2228
OID_6420	159	491	823	1154	1485	1733	1981	2229
CDSN	160	492	824	1155	1486	1734	1982	2230
OID_4269	161	493	825	1156	1487	1735	1983	2231
RPS25	162	494	826	1157	1488	1736	1984	2232
GAPD	163	495	827	1158	1489	1737	1985	2233
RPLP1	164	496	828	1159	1490	1738	1986	2234
OID_5115	165	497	829	1160	1491	1739	1987	2235

Gene	SEQ ID 50mer	SEQ ID RNA/cDNA	PCR Forward Primer 1 SEQ ID	PCR Reverse Primer 1 SEQ ID	PCR Probe 1 SEQ ID	PCR Forward Primer 2 SEQ ID	PCR Reverse Primer 2 SEQ ID	PCR Probe 2 SEQ ID
SLC9A8	166	498	830	1161	1492	1740	1988	2236
OID_1512	167	499	831	1162	1493	1741	1989	2237
POLR2D	168	500	832	1163	1494	1742	1990	2238
ARPC3	169	501	833	1164	1495	1743	1991	2239
OID_6282	170	502	834	1165	1496	1744	1992	2240
PRO1073	171	503	835	1166	1497	1745	1993	2241
OID_7222	172	504	836	1167	1498	1746	1994	2242
FPRL1	173	505	837	1168	1499	1747	1995	2243
FKBPL	174	506	838	1169	1500	1748	1996	2244
PREB	175	507	839	1170	1501	1749	1997	2245
OID_1551	176	508	840	1171	1502	1750	1998	2246
OID_7595	177	509	841	1172	1503	1751	1999	2247
RNF19	178	510	842	1173	1504	1752	2000	2248
SMCY	179	511	843	1174	1505	1753	2001	2249
OID_4184	180	512	844	1175	1506	1754	2002	2250
OID_7504	181	513	845	1176	1507	1755	2003	2251
DNAJC3	182	514	846	1177	1508	1756	2004	2252
ARHU	183	515	847	1178	1509	1757	2005	2253
OID_7200	184	516	848	1179	1510	1758	2006	2254
SERPINB2	185	517	849	1180	1511			
ENO1	186	518	850	1181	1512	1759	2007	2255
OID_7696	187	519	851	1182	1513	1760	2008	2256
OID_4173	188	520	852	1183	1514	1761	2009	2257
CSF2RB	189	521	853	1184	1515	1762	2010	2258
OID_7410	190	522	854	1185	1516	1763	2011	2259
OID_4180	191	523	855	1186	1517	1764	2012	2260
OID_5101	192	524	856	1187	1518	1765	2013	2261
MOP3	193	525	857	1188	1519	1766	2014	2262
RPL18A	194	526	858	1189	1520	1767	2015	2263
INPP5A	195	527	859	1190	1521	1768	2016	2264
hIAN7	196	528	860	1191	1522	1769	2017	2265
RPS29	197	529	861	1192	1523	1770	2018	2266
OID_6008	198	530	862	1193	1524	1771	2019	2267
OID_4186	199	531	863	1194	1525	1772	2020	2268
VNN2	200	532	864	1195	1526	1773	2021	2269
OID_7703	201	533	865	1196	1527	1774	2022	2270
OID_7057	202	534	866	1197	1528	1775	2023	2271
OID_4291	203	535	867	1198	1529	1776	2024	2272
OID_1366	204	536	868	1199	1530	1777	2025	2273
EEF1A1	205	537	869	1200	1531	1778	2026	2274
PA2G4	206	538	870	1201	1532	1779	2027	2275
GAPD	207	539	871	1202	1533	1780	2028	2276
CHD4	208	540	872	1203	1534	1781	2029	2277
OID_7951	209	541	873	1204	1535	1782	2030	2278
DAB1	210	542	874	1205	1536	1783	2031	2279
OID_3406	211	543	875	1206	1537	1784	2032	2280
OID_6986	212	544	876	1207	1538	1785	2033	2281
OID_5962	213	545	877	1208	1539	1786	2034	2282
OID_5152	214	546	878	1209	1540	1787	2035	2283
S100A8	215	547	879	1210	1541	1788	2036	2284
HNRPU	216	548	880	1211	1542	1789	2037	2285
ERCC5	217	549	881	1212	1543	1790	2038	2286
RPS27	218	550	882	1213	1544	1791	2039	2287
ACRC	219	551	883	1214	1545	1792	2040	2288
PSMD11	220	552	884	1215	1546	1793	2041	2289

Gene	SEQ ID 50mer	SEQ ID RNA/cDNA	PCR Forward Primer 1 SEQ ID	PCR Reverse Primer 1 SEQ ID	PCR Probe 1 SEQ ID	PCR Forward Primer 2 SEQ ID	PCR Reverse Primer 2 SEQ ID	PCR Probe 2 SEQ ID
OID_1016	221	553	885	1216	1547	1794	2042	2290
OID_1309	222	554	886	1217	1548	1795	2043	2291
OID_7582	223	555	887	1218	1549	1796	2044	2292
OID_4317	224	556	888	1219	1550	1797	2045	2293
OID_5889	225	557	889	1220	1551	1798	2046	2294
UBL1	226	558	890	1221	1552	1799	2047	2295
OID_3687	227	559	891	1222	1553	1800	2048	2296
OID_7371	228	560	892	1223	1554	1801	2049	2297
SH3BGRL3	229	561	893	1224	1555	1802	2050	2298
SEMA7A	230	562	894	1225	1556	1803	2051	2299
OID_5708	231	563	895	1226	1557	1804	2052	2300
OID_5992	232	564	896	1227	1558	1805	2053	2301
IL21	233	565	897	1228	1559	1806	2054	2302
HERC3	234	566	898	1229	1560	1807	2055	2303
OID_7799	235	567	899	1230	1561	1808	2056	2304
P11	236	568	900	1231	1562	1809	2057	2305
OID_7766	237	569	901	1232	1563	1810	2058	2306
TIMM10	238	570	902	1233	1564	1811	2059	2307
EGLN1	239	571	903	1234	1565	1812	2060	2308
TBCC	240	572	904	1235	1566	1813	2061	2309
RNF3	241	573	905	1236	1567	1814	2062	2310
OID_6451	242	574	906	1237	1568	1815	2063	2311
CCNDBP1	243	575	907	1238	1569	1816	2064	2312
OID_8063	244	576	908	1239	1570	1817	2065	2313
SUV39H1	245	577	909	1240	1571	1818	2066	2314
HSPC048	246	578	910	1241	1572	1819	2067	2315
OID_5625	247	579	911	1242	1573	1820	2068	2316
WARS	248	580	912	1243	1574	1821	2069	2317
OID_6823	249	581	913	1244	1575	1822	2070	2318
OID_7073	250	582	914	1245	1576	1823	2071	2319
OID_5339	251	583	915	1246	1577	1824	2072	2320
OID_4263	252	584	916	1247	1578	1825	2073	2321
MGC26766	253	585	917	1248	1579	1826	2074	2322
SERPINB11	254	586	918	1249	1580	1827	2075	2323
OID_6711	255	587	919	1250	1581	1828	2076	2324
RNF10	256	588	920	1251	1582	1829	2077	2325
MKRN1	257	589	921	1252	1583	1830	2078	2326
RPS16	258	590	922	1253	1584	1831	2079	2327
BAZ1A	259	591	923	1254	1585	1832	2080	2328
OID_5998	260	592	924	1255	1586	1833	2081	2329
ATP5L	261	593	925	1256	1587	1834	2082	2330
OID_6393	262	594	926	1257	1588			
RoXaN	263	595	927	1258	1589	1835	2083	2331
NCBP2	264	596	928	1259	1590	1836	2084	2332
OID_6273	265	597	929	1260	1591	1837	2085	2333
HZF12	266	598	930	1261	1592	1838	2086	2334
CCL3	267	599	931	1262	1593	1839	2087	2335
OID_4323	268	600	932	1263	1594	1840	2088	2336
OID_5181	269	601						
PRDX4	270	602	933	1264	1595	1841	2089	2337
BTK	271	603	934	1265	1596	1842	2090	2338
OID_6298	272	604	935	1266	1597	1843	2091	2339
PGK1	273	605	936	1267	1598	1844	2092	2340
TNFRSF10A	274	606	937	1268	1599	1845	2093	2341
ADM	275	607	938	1269	1600	1846	2094	2342

Gene	SEQ ID 50mer	SEQ ID RNA/cDNA	PCR Forward Primer 1 SEQ ID	PCR Reverse Primer 1 SEQ ID	PCR Probe 1 SEQ ID	PCR Forward Primer 2 SEQ ID	PCR Reverse Primer 2 SEQ ID	PCR Probe 2 SEQ ID
OID_357	276	608	939	1270	1601	1847	2095	2343
C20orf6	277	609	940	1271	1602	1848	2096	2344
OID_3226	278	610	941	1272	1603	1849	2097	2345
ASAH1	279	611	942	1273	1604	1850	2098	2346
ATF5	280	612	943	1274	1605	1851	2099	2347
OID_4887	281	613	944	1275	1606	1852	2100	2348
OID_4239	282	614	945	1276	1607	1853	2101	2349
MDM2	283	615	946	1277	1608	1854	2102	2350
XRN2	284	616	947	1278	1609	1855	2103	2351
OID_6039	285	617	948	1279	1610	1856	2104	2352
OID_4210	286	618	949	1280	1611	1857	2105	2353
OID_7698	287	619	950	1281	1612	1858	2106	2354
PRKRA	288	620	951	1282	1613	1859	2107	2355
OID_4288	289	621	952	1283	1614	1860	2108	2356
OID_5620	290	622	953	1284	1615	1861	2109	2357
OID_7384	291	623	954	1285	1616	1862	2110	2358
OID_1209	292	624	955	1286	1617	1863	2111	2359
CDKN1B	293	625	956	1287	1618	1864	2112	2360
PLOD	294	626	957	1288	1619	1865	2113	2361
OID_5128	295	627	958	1289	1620	1866	2114	2362
OID_5877	296	628	959	1290	1621	1867	2115	2363
FZD4	297	629	960	1291	1622	1868	2116	2364
HLA-B	298	630	961	1292	1623	1869	2117	2365
OID_5624	299	631	962	1293	1624	1870	2118	2366
FPR1	300	632	963	1294	1625	1871	2119	2367
ODF2	301	633	964	1295	1626	1872	2120	2368
OID_5150	302	634	965	1296	1627	1873	2121	2369
OID_5639	303	635	966	1297	1628	1874	2122	2370
OID_6619	304	636	967	1298	1629	1875	2123	2371
OID_6933	305	637	968	1299	1630	1876	2124	2372
OID_7049	306	638	969	1300	1631	1877	2125	2373
IL17C	307	639	970	1301	1632	1878	2126	2374
OID_5866	308	640	971	1302	1633	1879	2127	2375
CD44	309	641	972	1303	1634	1880	2128	2376
VPS45A	310	642	973	1304	1635	1881	2129	2377
OID_4932	311	643	974	1305	1636	1882	2130	2378
OID_7821	312	644	975	1306	1637	1883	2131	2379
OID_4916	313	645	976	1307	1638	1884	2132	2380
OID_4891	314	646	977	1308	1639	1885	2133	2381
HADHB	315	647	978	1309	1640	1886	2134	2382
FLJ22757	316	648	979	1310	1641	1887	2135	2383
RAC1	317	649	980	1311	1642	1888	2136	2384
OID_6415	318	650	981	1312	1643	1889	2137	2385
NMES1	319	651	982	1313	1644	1890	2138	2386
DMBT1	320	652	983	1314	1645	1891	2139	2387
RPS23	321	653	984	1315	1646	1892	2140	2388
ZF	322	654	985	1316	1647	1893	2141	2389
NFE2L3	323	655	986	1317	1648	1894	2142	2390
RAD9	324	656	987	1318	1649	1895	2143	2391
OID_6295	325	657	988	1319	1650	1896	2144	2392
DEFCAP	326	658	989	1320	1651	1897	2145	2393
RPL27A	327	659	990	1321	1652	1898	2146	2394
IL22	328	660	991	1322	1653	1899	2147	2395
PSMA4	329	661	992	1323	1654	1900	2148	2396
CCNI	330	662	993	1324	1655	1901	2149	2397

Gene	SEQ ID 50mer	SEQ ID RNA/cDNA	PCR Forward Primer 1 SEQ ID	PCR Reverse Primer 1 SEQ ID	PCR Probe 1 SEQ ID	PCR Forward Primer 2 SEQ ID	PCR Reverse Primer 2 SEQ ID	PCR Probe 2 SEQ ID
THBD	331	663	994	1325	1656	1902	2150	2398
CGR19	332	664	995	1326	1657	1903	2151	2399

Gene	Gene Name	SEQ ID 50mer	SEQ ID RNA/cDNA	n	Non-parametric Odds ratio	Fisher p-value	t-test p-value
HBB	Hemoglobin, beta	86	418	55	8.33	0.00	0.00
OID_4365	Mitochondrial solute carrier	91	423	53	6.16	0.00	0.00
OID_873	KIAA1892 protein	94	426	55	5.09	0.01	0.01
IL4	Interleukin 4	80	412	46	4.90	0.02	0.01
OID_4281	EST	107	439	56	5.19	0.01	0.01
IGHM	Immunoglobulin heavy constant mu	92	424	52	2.89	0.09	0.01
BPGM	2,3-bisphosphoglycerate mutase	87	419	43	7.31	0.01	0.01
CTLA4	Cytotoxic T-lymphocyte-associated protein 4	82	414	52	1.84		0.02
SLC7A11	Solute carrier family 7, (cationic amino acid transporter, y+ system) member 11	135	467	48	2.50	0.15	0.03
IL13	Interleukin 13	81	413	29	4.95	0.07	0.04
OID_6207	EST	105	437	37	3.58	0.10	0.04
PRDM1	PR domain containing 1, with ZNF domain	130	462	57	1.44		0.07
LYN	v-yes-1 Yamaguchi sarcoma viral related oncogene homolog	102	434	55	1.08		0.08
KPNA6	Karyopherin alpha 6 (importin alpha 7)	90	422	51	1.50		0.09
OID_7094	XDx EST 479G12	118	450	35	1.13		0.09
IL15	Interleukin 15	111	443	51	3.78	0.05	0.09
OID_4460	EST	85	417	47	2.73	0.14	0.10
OID_7016	EST	127	459	53	2.14	0.27	0.10
MTHFD2	Methylene tetrahydrofolate dehydrogenase (NAD+ dependent), methenyltetrahydrofolate cyclohydrolase	88	420	43	3.50	0.07	0.11
TCIRG1	T-cell, immune regulator 1, ATPase, H+ transporting, lysosomal V0 protein a isoform 3	78	410	57	1.08		0.11
OID_5847	Hypothetical protein FLJ32919	129	461	45	1.08		0.12
CXCR4	Chemokine (C-X-C motif	96	428	56	1.29		0.12
CXCR3	Chemokine (C-X-C motif	117	449	54	2.10	0.27	0.12
GPI	Glucose phosphate isome	122	454	57	1.44	0.60	0.12
KLRF1	Killer cell lectin-like rece	101	433	50	1.68		0.13
CCL5	Chemokine (C-C motif) l	98	430	34	1.96		0.13
CD47	CD47 antigen (Rh-related	123	455	55	1.45		0.13
IL10	Interleukin 10	112	444	33	1.43		0.13
OID_253	EST	121	453	26	1.93		0.15
CXCL10	Chemokine (C-X-C motif	109	441	53	1.75		0.16

Gene	Gene Name	SEQ ID 50mer	SEQ ID RNA/cDNA	n	Non-parametric Odds ratio	Fisher p-value	t-test p-value
IFNG	Interferon, gamma	113	445	41	1.33		0.16
PRF1	Perforin 1 (pore forming	79	411	48	1.20		0.17
IL2	Interleukin 2	100	432	33	2.00		0.17
HLA-DRB1	Major histocompatibility	114	446	42	1.50		0.18
IL6	Interleukin 6	99	431	49	1.33		0.18
IL2RA	Interleukin 2 receptor, alpha	103	435	39	2.03	0.34	0.19
OID_573	KIAA1486 protein	93	425	8	3.00		0.19
CXCL9	Chemokine (C-X-C motif) ligand 9 (MIG)	108	440	46	1.71		0.20
OID_3	EST	95	427	49	2.19		0.20
CD8B1	CD8 antigen, beta polypeptide 1 (p37)	115	447	55	1.21		0.22
CD69	CD69 antigen (p60, early T-cell activation antigen)	97	429	30	1.71		0.23
OID_7605	EST	119	451	47	3.11	0.08	0.24
TNFSF6	Tumor necrosis factor (ligand) superfamily, member 6	77	409	54	1.36		0.25
CXCL1	Chemokine (C-X-C motif) ligand 1 (melanoma growth stimulating activity, alpha)	120	452	20	2.00		0.26
OID_5350	EST	125	457	49	2.08	0.26	0.28
CD8A	CD8 antigen, alpha polypeptide (p32)	83	415	57	1.39		0.28
CD4	CD4 antigen (p55)	116	448	55	1.64		0.28
PTGS2	Prostaglandin-endoperoxide synthase 2 (prostaglandin G/H synthase and cyclooxygenase)	128	460	46	2.05	0.37	0.29
GZMB	Granzyme B (granzyme 2, cytotoxic T-lymphocyte-associated serine esterase 1)	76	408	40	1.81		0.33
CCL4	Chemokine (C-C motif) ligand 4, SCYA4	104	436	53	2.25		0.35
ChGn	Chondroitin beta 1,4 N-acetylgalactosaminyltransferase	106	438	31	2.57		0.36
TCRGC2	T cell receptor gamma constant 2	126	458	52	1.33		0.39
HLA-F	Major histocompatibility complex, class I, F	124	456	54	2.36	0.17	0.40
TAP1	Transporter 1, ATP-binding cassette, sub-family B (MDR1/TAP)	89	421	36	1.93		0.45

Gene	Gene Name	SEQ ID 50mer	SEQ ID RNA/cDNA	n	Non-parametric Odds ratio	Fisher p-value	t-test p-value
BY55	Natural killer cell receptor, immunoglobulin superfamily member	84	416	52	2.49	0.16	0.48
IL8	Interleukin 8	75	407	49	2.10	0.26	0.49

Gene	ACC	SEQ ID 50mer	SEQ ID RNA/cDNA	RefSeq Peptide Accession #	SEQ ID Protein
ACTB	NM_001101	2	334	NP_001092	2400
GUSB	NM_000181	3	335	NP_000172	2401
B2M	NM_004048	4	336	NP_004039	2402
TSN	NM_004622	5	337	NP_004613	2403
CCR7	NM_001838	6	338	NP_001829	2404
IL1R2	NM_004633	7	339	NP_004624	2405
AIF-1	NM_004847	8	340	NP_004838	2406
ALAS2	NM_000032.1	9	341	NP_000023	2407
APELIN	NM_017413	10	342	NP_059109	2408
CD80	NM_005191	11	343	NP_005182	2409
EPB41	NM_004437	12	344	NP_004428	2410
CBLB	NM_004351	13	345	NP_733762	2411
CCR5	NM_000579	14	346	NP_000570	2412
MME	NM_000902	15	347	NP_000893	2413
KLRC1	NM_002259	16	348	NP_002250	2414
FCGR3A	NM_000569	17	349	NP_000560	2415
FCGR3B	NM_000570	18	350	NP_000561	2416
LAG3	NM_002286	19	351	NP_002277	2417
PECAM1	NM_000442	20	352	NP_000433	2418
CD34	NM_001773	21	353	NP_001764	2419
FCGR1A	NM_000566	22	354	NP_000557	2420
TFRC	NM_003234	23	355	NP_003225	2421
CMA1	NM_001836	24	356	NP_001827	2422
KIT	NM_000222	25	357	NP_000213	2423
MPL	NM_005373	26	358	NP_005364	2424
EphB6	NM_004445	27	359	NP_004436	2425
EPO-R	NM_000121.2	28	360	NP_000112	2426
Foxp3	NM_014009	29	361	NP_054728	2427
GATA-1	NM_002049	30	362	NP_002040	2428
ITGA2B	NM_000419	31	363	NP_000410	2429
GNLY	NM_006433	32	364	NP_006424	2430
GZMA	NM_006144	33	365	NP_006135	2431
HBA	NM_000558.3	34	366	NP_000549	2432
HBZ	NM_005332.2	35	367	NP_005323	2433
HBD	NM_000519.2	37	369	NP_000510	2434
HBE	NM_005330	38	370	NP_005321	2435
HBG	NM_000559.2	39	371	NP_000550	2436
HBQ	NM_005331	40	372	NP_005322	2437
HLA-DP	NM_033554	41	373	NP_291032	2438
HLA-DQ	NM_002122	42	374	NP_002113	2439
ICOS	NM_012092	44	376	NP_036224	2440
IL18	NM_001562	45	377	NP_001553	2441
IL3	NM_000588	46	378	NP_000579	2442
ITGA4	NM_000885	47	379	NP_000876	2443
ITGAM	NM_000632	48	380	NP_000623	2444
ITGB7	NM_000889	49	381	NP_000880	2445
CEBPB	NM_005194	50	382	NP_005185	2446
NF-E2	NM_006163	51	383	NP_006154	2447
PDCD1	NM_005018	52	384	NP_005009	2448
PF4	NM_002619	53	385	NP_002610	2449
PRKCQ	NM_006257.1	54	386	NP_006248	2450
PPARGC1	NM_013261	55	387	NP_037393	2451
RAG1	NM_000448	56	388	NP_000439	2452
RAG2	NM_000536	57	389	NP_000527	2453
CXCL12	NM_000609	58	390	NP_000600	2454
TNFRSF4	NM_003327	59	391	NP_003318	2455

Gene	ACC	SEQ ID 50mer	SEQ ID RNA/cDNA	RefSeq Peptide Accession #	SEQ ID Protein
TNFSF4	NM_003326	60	392	NP_003317	2456
TPS1	NM_003293	61	393	NP_003284	2457
ADA	NM_000022	62	394	NP_000013	2458
CPM	NM_001874.1	63	395	NP_001865	2459
CSF2	NM_000758.2	64	396	NP_000749	2460
CSF3	NM_172219	65	397	NP_757373	2461
CRP	NM_000567.1	66	398	NP_000558	2462
FLT3	NM_004119	67	399	NP_004110	2463
GATA3	NM_002051.1	68	400	NP_002042	2464
IL7R	NM_002185.1	69	401	NP_002176	2465
KLF1	NM_006563.1	70	402	NP_006554	2466
LCK	NM_005356.2	71	403	NP_005347	2467
LEF1	NM_016269.2	72	404	NP_057353	2468
PLAUR	NM_002659.1	73	405	NP_002650	2469
TNFSF13B	NM_006573.3	74	406	NP_006564	2470
IL8	NM_000584	75	407	NP_000575	2471
GZMB	NM_004131	76	408	NP_004122	2472
TNFSF6	NM_000639	77	409	NP_000630	2473
TCIRG1	NM_006019	78	410	NP_006010	2474
PRF1	NM_005041	79	411	NP_005032	2475
IL4	NM_000589	80	412	NP_000580	2476
IL13	NM_002188	81	413	NP_002179	2477
CTLA4	NM_005214	82	414	NP_005205	2478
CD8A	NM_001768	83	415	NP_001759	2479
BY55	NM_007053	84	416	NP_008984	2480
HBB	NM_000518	86	418	NP_000509	2481
BPGM	NM_001724	87	419	NP_001715	2482
MTHFD2	NM_006636	88	420	NP_006627	2483
TAP1	NM_000593	89	421	NP_000584	2484
OID_873	AK000354	94	426	NP_056212	2485
CXCR4	NM_003467	96	428	NP_003458	2486
CD69	NM_001781	97	429	NP_001772	2487
CCL5	NM_002985	98	430	NP_002976	2488
IL6	NM_000600	99	431	NP_000591	2489
IL2	NM_000586	100	432	NP_000577	2490
KLRF1	NM_016523	101	433	NP_057607	2491
LYN	NM_002350	102	434	NP_002341	2492
IL2RA	NM_000417	103	435	NP_000408	2493
CCL4	NM_002984	104	436	NP_002975	2494
ChGn	NM_018371	106	438	NP_060841	2495
CXCL9	NM_002416	108	440	NP_002407	2496
CXCL10	NM_001565	109	441	NP_001556	2497
IL17	NM_002190	110	442	NP_002181	2498
IL15	NM_000585	111	443	NP_000576	2499
IL10	NM_000572	112	444	NP_000563	2500
IFNG	NM_000619	113	445	NP_000610	2501
HLA-DRB1	NM_002124	114	446	NP_002115	2502
CD8B1	NM_004931	115	447	NP_004922	2503
CD4	NM_000616	116	448	NP_000607	2504
CXCR3	NM_001504	117	449	NP_001495	2505
CXCL1	NM_001511	120	452	NP_001502	2506
GPI	NM_000175	122	454	NP_000166	2507
CD47	NM_001777	123	455	NP_001768	2508
HLA-F	NM_018950	124	456	NP_061823	2509
PTGS2	NM_000963	128	460	NP_000954	2510
OID_5847	NM_144588	129	461	NP_653189	2511

Gene	ACC	SEQ ID 50mer	SEQ ID RNA/cDNA	RefSeq Peptide Accession #	SEQ ID Protein
PRDM1	NM_001198	130	462	NP_001189	2512
CKB	NM_001823	131	463	NP_001814	2513
TNNI3	NM_000363	132	464	NP_000354	2514
TNNT2	NM_000364	133	465	NP_000355	2515
MB	NM_005368	134	466	NP_005359	2516
SLC7A11	NM_014331	135	467	NP_055146	2517
TNFRSF5	NM_001250	136	468	NP_001241	2518
TNFRSF7	NM_001242	137	469	NP_001233	2519
CD86	NM_175862	138	470	NP_787058	2520
AIF1v2	NM_004847	139	471	NP_004838	2521
CMV IE1e3	NC_001347, compl	144	476	NP_040060	2522
CMV IE1e4	NC_001347, compl	145	477	NP_040060	2523
EV EBNA-1	NC_001345, 10795	146	478	NP_039875	2524
EV BZLF-1	NC_001345, compl	147	479	NP_039871	2525
CMV IE1	NC_001347, compl	150	482	NP_040060	2526
CMV IE1	NC_001347, compl	151	483	NP_040060	2527
CLC	NM_001828	152	484	NP_001819	2528
TERF2IP	NM_018975	153	485	NP_061848	2529
HLA-A	NM_002116	154	486	NP_002107	2530
MSCP	NM_018579	156	488	NP_061049	2531
DUSP5	NM_004419	157	489	NP_004410	2532
PRO1853	NM_018607	158	490	NP_061077	2533
CDSN	NM_001264	160	492	NP_001255	2534
RPS25	NM_001028	162	494	NP_001019	2535
GAPD	NM_002046	163	495	NP_002037	2536
RPLP1	NM_001003	164	496	NP_000994	2537
POLR2D	NM_004805	168	500	NP_004796	2538
ARPC3	NM_005719	169	501	NP_005710	2539
FPRL1	NM_001462	173	505	NP_001453	2540
FKBPL	NM_022110	174	506	NP_071393	2541
PREB	NM_013388	175	507	NP_037520	2542
OID_7595	NM_015653	177	509	NP_056468	2543
RNF19	NM_015435	178	510	NP_056250	2544
SMCY	NM_004653	179	511	NP_004644	2545
OID_7504	NM_152312	181	513	NP_689525	2546
DNAJC3	NM_006260	182	514	NP_006251	2547
ARHU	NM_021205	183	515	NP_067028	2548
OID_7200	NM_022752	184	516	NP_073589	2549
SERPINB2	NM_002575	185	517	NP_002566	2550
ENO1	NM_001428	186	518	NP_001419	2551
MOP3	NM_018183	193	525	NP_060653	2552
RPL18A	NM_000980	194	526	NP_000971	2553
INPP5A	NM_005539	195	527	NP_005530	2554
RPS29	NM_001032	197	529	NP_001023	2555
VNN2	NM_004665	200	532	NP_004656	2556
OID_7703	NM_014949	201	533	NP_055764	2557
EEF1A1	NM_001402	205	537	NP_001393	2558
PA2G4	NM_006191	206	538	NP_006182	2559
GAPD	NM_002046	207	539	NP_002037	2560
CHD4	NM_001273	208	540	NP_001264	2561
OID_7951	NM_016521	209	541	NP_057605	2562
DAB1	NM_021080	210	542	NP_066566	2563
OID_3406	NM_018986	211	543	NP_061859	2564
S100A8	NM_002964	215	547	NP_002955	2565
ERCC5	NM_000123	217	549	NP_000114	2566
RPS27	NM_001030	218	550	NP_001021	2567

Gene	ACC	SEQ ID 50mer	SEQ ID RNA/cDNA	RefSeq Peptide Accession #	SEQ ID Protein
ACRC	NM_052957	219	551	NP_443189	2568
UBL1	NM_003352	226	558	NP_003343	2569
SH3BGRL3	NM_031286	229	561	NP_112576	2570
SEMA7A	NM_003612	230	562	NP_003603	2571
IL21	NM_021803	233	565	NP_068575	2572
HERC3	NM_014606	234	566	NP_055421	2573
P11	NM_006025	236	568	NP_006016	2574
TIMM10	NM_012456	238	570	NP_036588	2575
EGLN1	AJ310543	239	571	NP_071334	2576
TBCC	NM_003192	240	572	NP_003183	2577
RNF3	NM_006315	241	573	NP_006306	2578
CCNDBP1	NM_012142	243	575	NP_036274	2579
SUV39H1	NM_003173	245	577	NP_003164	2580
HSPC048	NM_014148	246	578	NP_054867	2581
WARS	NM_004184	248	580	NP_004175	2582
SERPINB11	NM_080475	254	586	NP_536723	2583
RNF10	NM_014868	256	588	NP_055683	2584
MKRN1	NM_013446	257	589	NP_038474	2585
RPS16	NM_001020	258	590	NP_001011	2586
BAZ1A	NM_013448	259	591	NP_038476	2587
ATP5L	NM_006476	261	593	NP_006467	2588
NCBP2	NM_007362	264	596	NP_031388	2589
HZF12	NM_033204	266	598	NP_149981	2590
CCL3	D90144	267	599	NP_002974	2591
PRDX4	NM_006406	270	602	NP_006397	2592
BTK	NM_000061	271	603	NP_000052	2593
PGK1	NM_000291	273	605	NP_000282	2594
TNFRSF10A	NM_003844	274	606	NP_003835	2595
ADM	NM_001124	275	607	NP_001115	2596
C20orf6	NM_016649	277	609	NP_057733	2597
OID_3226	NM_015393	278	610	NP_056208	2598
ASAH1	NM_004315	279	611	NP_004306	2599
ATF5	NM_012068	280	612	NP_036200	2600
OID_4887	NM_032895	281	613	NP_116284	2601
MDM2	NM_002392	283	615	NP_002383	2602
XRN2	AF064257	284	616	NP_036387	2603
PRKRA	NM_003690	288	620	NP_003681	2604
CDKN1B	NM_004064	293	625	NP_004055	2605
PLOD	NM_000302	294	626	NP_000293	2606
FZD4	NM_012193	297	629	NP_036325	2607
HLA-B	NM_005514	298	630	NP_005505	2608
FPR1	NM_002029	300	632	NP_002020	2609
ODF2	NM_153437	301	633	NP_702915	2610
IL17C	NM_013278	307	639	NP_037410	2611
VPS45A	NM_007259	310	642	NP_009190	2612
HADHB	NM_000183	315	647	NP_000174	2613
FLJ22757	NM_024898	316	648	NP_079174	2614
NMES1	NM_032413	319	651	NP_115789	2615
DMBT1	NM_007329	320	652	NP_015568	2616
RPS23	NM_001025	321	653	NP_001016	2617
ZF	NM_021212	322	654	NP_067035	2618
NFE2L3	NM_004289	323	655	NP_004280	2619
RAD9	NM_004584	324	656	NP_004575	2620
DEFCAP	NM_014922	326	658	NP_055737	2621
IL22	NM_020525	328	660	NP_065386	2622
PSMA4	NM_002789	329	661	NP_002780	2623

Gene	ACC	SEQ ID 50mer	SEQ ID RNA/cDNA	RefSeq Peptide Accession #	SEQ ID Protein
CCNI	NM_006835	330	662	NP_006826	2624
THBD	NM_000361	331	663	NP_000352	2625
CGR19	NM_006568	332	664	NP_006559	2626
HSRRN18S	X03205	1	333		
HBB	NG_000007	36	368		
HLA-DRB		43	375		
OID_4460	AF150295	85	417		
KPNA6	AW021037	90	422		
OID_4365	AI114652	91	423		
IGHM	BC032249	92	424		
OID_573	AB040919	93	425		
OID_3	AW968823	95	427		
OID_6207	D20522	105	437		
OID_4281	AA053887	107	439		
OID_7094		118	450		
OID_7605	AA808018	119	451		
OID_253	AK091125	121	453		
OID_5350	AK055687	125	457		
TCRGC2	M17323	126	458		
OID_7016	BI018696	127	459		
EV EBV		141	473		
CMV p67	NC_001347	142	474		
CMV TRL7		143	475		
EV EBN		148	480		
EV EBNA-LP		149	481		
OID_5891	AW297949	155	487		
OID_6420	AK090404	159	491		
OID_4269	BM727677	161	493		
OID_5115	AI364926	165	497		
SLC9A8	AB023156	166	498		
OID_1512	BE618004	167	499		
OID_6282	BC041913	170	502		
PRO1073	AF001542	171	503		
OID_7222	BG260891	172	504		
OID_1551	BE887646	176	508		
OID_4184	X17403	180	512		
OID_7696	AW297325	187	519		
OID_4173	X17403	188	520		
CSF2RB	AL540399	189	521		
OID_7410	AW837717	190	522		
OID_4180	X17403	191	523		
OID_5101	BG461987	192	524		
hIAN7	BG772661	196	528		
OID_6008	AW592876	198	530		
OID_4186	X17403	199	531		
OID_7057	480F8	202	534		
OID_4291	BC038439	203	535		
OID_1366	AW850041	204	536		
OID_6986	AK093608	212	544		
OID_5962	AW452467	213	545		
OID_5152	AI392805	214	546		
HNRPU	BM467823	216	548		
PSMD11	AI684022	220	552		
OID_1016	AK024456	221	553		
OID_1309	AV706481	222	554		
OID_7582	AK027866	223	555		

Gene	ACC	SEQ ID 50mer	SEQ ID RNA/cDNA	RefSeq Peptide Accession #	SEQ ID Protein
OID_4317	AI318342	224	556		
OID_5889	AW297843	225	557		
OID_3687	W03955	227	559		
OID_7371	BE730505	228	560		
OID_5708	AW081540	231	563		
OID_5992	AW467992	232	564		
OID_7799	AW837717	235	567		
OID_7766	AW294711	237	569		
OID_6451	AL834168	242	574		
OID_8063	X68264	244	576		
OID_5625	AW063780	247	579		
OID_6823	AL832642	249	581		
OID_7073	AL705961	250	582		
OID_5339	AI625119	251	583		
OID_4263	AA136584	252	584		
MGC26766	AK025472	253	585		
OID_6711	BF968628	255	587		
OID_5998	AW468459	260	592		
OID_6393	52B9	262	594		
RoXaN	BC004857	263	595		
OID_6273	AW294774	265	597		
OID_4323	AA744774	268	600		
OID_5181	AI400725	269	601		
OID_6298	AI948513	272	604		
OID_357	138G5	276	608		
OID_4239	BQ022840	282	614		
OID_6039	BE502246	285	617		
OID_4210	AI300700	286	618		
OID_7698	AA243283	287	619		
OID_4288	AI378046	289	621		
OID_5620	AW063678	290	622		
OID_7384	BF475239	291	623		
OID_1209	C14379	292	624		
OID_5128	AK097845	295	627		
OID_5877	AW297664	296	628		
OID_5624	AW063921	299	631		
OID_5150	AI392793	302	634		
OID_5639	AW064243	303	635		
OID_6619	469A10	304	636		
OID_6933	AI089520	305	637		
OID_7049	480E2	306	638		
OID_5866	BM684739	308	640		
CD44	AA916990	309	641		
OID_4932	AA457757	311	643		
OID_7821	AA743221	312	644		
OID_4916	AA252909	313	645		
OID_4891	AL832329	314	646		
RAC1	AK054993	317	649		
OID_6415	CA407201	318	650		
OID_6295	AI880607	325	657		
RPL27A	BF214146	327	659		

Table 3: Viral genomes were used to design oligonucleotides for the microarrays. The accession numbers for the viral genomes used are given, along with the gene name and location of the region used for oligonucleotide design.

Virus	Gene Name	Genome Location
Adenovirus, type 2 Accession #J01917	E1a	1226..1542
	E1b_1	3270...3503
	E2a_2	complement(24089..25885)
	E3-1	27609..29792
	E4 (last exon at 3'-end)	complement(33193..32802)
	IX	3576..4034
	Iva2	complement(4081..5417)
	DNA Polymerase	complement(5187..5418)
Cytomegalovirus (CMV) Accession #X17403	HCMVTRL2 (IRL2)	1893..2240
	HCMVTRL7 (IRL7)	complement(6595..6843)
	HCMVUL21	complement(26497..27024)
	HCMVUL27	complement(32831..34657)
	HCMVUL33	43251..44423
	HCMVUL54	complement(76903..80631)
	HCMVUL75	complement(107901..110132)
	HCMVUL83	complement(119352..121037)
	HCMVUL106	complement(154947..155324)
	HCMVUL109	complement(157514..157810)
	HCMVUL113	161503..162800
	HCMVUL122	complement(169364..170599)
	HCMVUL123 (last exon at 3'-end)	complement(171006..172225)
	HCMVUS28	219200..220171
Epstein-Barr virus (EBV) Accession # NC_001345	Exon in EBNA-1 RNA	67477..67649
	Exon in EBNA-1 RNA	98364..98730
	BRLF1	complement(103366..105183)
	BZLF1 (first of 3 exons)	complement(102655..103155)
	BMLF1	complement(82743..84059)
	BALF2	complement(161384..164770)
Human Herpesvirus 6 (HHV6) Accession #NC_001664	U16/U17	complement(26259..27349)
	U89	complement(133091..135610)
	U90	complement(135664..135948)
	U86	complement(125989..128136)
	U83	123528..123821
	U22	complement(33739..34347)
	DR2 (DR2L)	791..2653
	DR7 (DR7L)	5629..6720
	U95	142941..146306
	U94	complement(141394..142866)
	U39	complement(59588..62080)
	U42	complement(69054..70598)
	U81	complement(121810..122577)
	U91	136485..136829

Table 4: Dependent variables for discovery of gene expression markers of cardiac allograft rejection.

Dependent Variable	Description	Number of Rejection Samples	Number of No-Rejection Samples
0 vs 1-4 Bx	Grade 0 vs. Grades 1-4, local biopsy reading	65	114
s0 vs 1B-4 HG	Stable Grade 0 vs Grades 1B-4, highest grade, Grade 1A not included	41	57
0-1A vs 1B-4 HG	Grades 0 and 1A vs Grades 1B-4, highest grade.	121	58
0 vs 3A HG	Grade 0 vs Grade 3A, highest grade. Grades 1A-2 and Grade 3B were not included.	56	29
0 vs 1B-4	Grade 0 vs Grades 1B-4, highest grade. Grade 1A was not included.	57	57
0 vs 1A-4	Grade 0 vs. Grades 1-4, highest grade	56	123

Table 5: Real-time PCR assay chemistries. Various combinations of reporter and quencher dyes are useful for real-time PCR assays.

Reporter	Quencher
FAM	TAMRA
	BHQ1
TET	TAMRA
	BHQ1
JOE	TAMRA
	BHQ1
HEX	TAMRA
	BHQ1
VIC	TAMRA
	BHQ1
ROX	BHQ2
TAMRA	BHQ2

Table 6: Real-time PCR results for rejection markers

Gene Array Probe SEQ ID	Phase 1				Phase 2				All Data			
	Fold	t-Test	NR	R	Fold	t-Test	NR	R	Fold	t-Test	NR	R
95	1.093	0.36084	10	8					0.935	0.31648	21	13
111	1.415	0.0095	12	10					1.415	0.0095	12	10
79	1.822	0.01146	6	7	0.63	0.04185	19	15	0.72	0.05632	35	26
3016	1.045	0.41017	12	10					1.001	0.49647	16	15
75	0.84	0.36674	11	8	0.595	0.15788	16	13	0.628	0.08402	34	26
2765	1.653	0.01508	10	10	0.776	0.11082	19	14	0.956	0.37421	38	29
97					0.75	0.26201	8	8	0.543	0.11489	17	12
2635	1.553	0.00533	13	10	0.834	0.16853	18	15	0.988	0.46191	36	27
96	1.495	0.06288	13	9	1.157	0.27601	18	15	1.155	0.21096	33	25
100	1.43	0.166	10	5					1.408	0.14418	12	8
2766	0.956	0.43918	12	10	0.989	0.48275	19	14	0.978	0.45101	31	24
2726	1.037	0.38205	11	9					1.037	0.38205	11	9
2768	1.211	0.02386	9	9					1.211	0.02386	9	9
94	1.601	0.02418	11	10					1.831	0.00094	17	15
2769	1.133	0.23094	12	9	1.081	0.19632	19	15	1.101	0.15032	31	24
2770	1.734	0.00017	13	10					1.381	0.01323	20	15
2647	1.557	0.04502	10	8					1.557	0.04502	10	8
2771	1.99	0.05574	13	9					1.52	0.11108	17	13
82	2.029	0.00022	8	5	1.287	0.13022	18	14	1.256	0.05356	33	23
83	1.546	0.05865	13	10	0.577	0.03934	18	14	0.795	0.11993	39	26
98					0.716	0.13	19	15	0.577	0.03352	19	14
36	1.605	0.09781	12	8	2.618	0.01227	18	11	2.808	0.00015	38	23
80	5.395	0.00049	9	6	4.404	0.05464	10	10	2.33	0.02369	29	18
89									0.295	0.02856	6	6
77	1.894	0.01602	10	10	0.537	0.01516	19	15	0.863	0.21987	35	29
2772	1.583	0.06276	10	6	0.714	0.13019	13	10	1.136	0.28841	28	17
2773	1.391	0.09236	11	6					1.391	0.09236	11	6
2774	1.59	0.00022	13	10					1.59	0.00022	13	10
102	1.245	0.05079	11	10	1.018	0.42702	17	15	1.117	0.08232	32	28
2775	0.719	0.16243	11	9					0.719	0.16243	11	9
2776	1.257	0.0516	12	9					1.257	0.0516	12	9
2667	1.343	0.03806	13	9					1.13	0.15962	20	12
115	1.199	0.26299	11	9					1.199	0.26299	11	9
2669	2.146	0.00813	12	10					1.296	0.14285	18	12
2777	1.142	0.20245	13	10					1.142	0.20245	13	10
78	1.324	0.01985	12	9	0.967	0.33851	18	14	1.007	0.46864	38	24
2670	1.388	0.11209	13	9					1.388	0.11209	13	9
88	1.282	0.14267	7	7	0.995	0.48504	17	14	1.008	0.47383	30	23
2778	1.128	0.19528	13	9					1.128	0.19528	13	9
2779	1.991	0.02513	9	5	0.642	0.05002	18	14	0.868	0.26275	32	21
2780	1.597	0.00355	13	10	0.802	0.11649	17	14	1.013	0.45521	38	26
2781					0.492	0.01344	12	12	0.819	0.25555	17	15

Table 6: Real-time PCR results for rejection markers

Gene Array Probe SEQ ID	Phase 1				Phase 2				All Data			
	Fold	t-Test	NR	R	Fold	t-Test	NR	R	Fold	t-Test	NR	R
101					0.652	0.04317	19	15	0.773	0.09274	29	22
106	1.234	0.19141	13	8					1.234	0.19141	13	8
2683	1.598	0.03723	8	8	0.633	0.03893	14	10	0.86	0.18731	28	22
2782	1.213	0.03305	12	10	0.912	0.07465	19	15	0.969	0.31955	39	27
87					4.947	0.02192	18	15	3.857	0.00389	30	23
99	0.639	0.06613	7	5	0.839	0.30304	16	8	0.694	0.04347	27	15
2692	0.801	0.21236	12	8	0.893	0.33801	18	15	0.782	0.06938	38	25
104	2.292	0.0024	11	8	0.621	0.05152	19	15	0.913	0.34506	30	23
76	1.809	0.00893	9	8	0.693	0.13027	13	8	1.274	0.11887	28	19
91	1.969	0.07789	11	8	4.047	0.00812	19	13	3.535	0.00033	37	23
92	2.859	0.05985	11	8	9.783	0.03047	18	14	8.588	0.00192	37	24
85	0.95	0.43363	12	8	0.699	0.0787	13	13	0.633	0.01486	33	24
126	1.76	0.02199	11	10					1.76	0.02199	11	10
2783	0.945	0.46023	10	5	0.852	0.26701	17	10	0.986	0.48609	29	17
2707	1.055	0.31435	13	10					1.055	0.31435	13	10
123	1.154	0.11677	11	10					1.154	0.11677	11	10
84	1.786	0.00255	9	6	0.523	0.04965	18	14	0.785	0.14976	34	22
2784	2.12	0.00022	12	10	0.498	0.01324	18	13	0.935	0.37356	37	25
2785	1.181	0.1377	10	10					1.181	0.1377	10	10
124	1.353	0.08122	11	9					1.353	0.08122	11	9
90	1.355	0.02288	13	10	0.973	0.39248	15	13	1.125	0.08671	28	23
2786	1.306	0.0773	12	10					1.306	0.0773	12	10
2787	1.086	0.32378	12	10					1.086	0.32378	12	10
3018	1.523	0.1487	12	10	0.84	0.27108	18	13	1.101	0.33276	36	26
125	1.252	0.05782	11	10					1.252	0.05782	11	10
2788	1.255	0.1221	11	10					1.255	0.1221	11	10
2789	1.152	0.31252	9	6					1.152	0.31252	9	6
3019	1.268	0.21268	6	7	0.981	0.45897	16	10	1.012	0.46612	29	19
2790	0.881	0.17766	11	8	1.22	0.04253	18	10	0.966	0.33826	40	23
2791	1.837	0.00553	13	10					1.837	0.00553	13	10
3020	1.271	0.10162	12	10	0.853	0.10567	19	13	0.965	0.36499	36	25
2792	1.504	0.05096	12	10	0.713	0.02979	19	15	0.846	0.16914	31	25
2793	1.335	0.03133	12	10	0.883	0.18577	19	15	0.916	0.23865	36	27
2794	1.936	0.00176	13	9	0.717	0.09799	19	14	0.877	0.22295	40	25
2752	1.499	0.03077	12	8	0.808	0.15363	17	13	1.004	0.48903	36	23
2795	0.815	0.24734	8	5	0.965	0.41772	19	15	0.938	0.3265	32	22
119	1.272	0.20279	10	10					1.272	0.20279	10	10

Table 7: Significance analysis for microarrays for identification of markers of acute rejection. In each case the highest grade from the 3 pathologists was taken for analysis. No rejection and rejection classes are defined. Samples are either used regardless of redundancy with respect to patients or a requirement is made that only one sample is used per patient or per patient per class. The number of samples used in the analysis is given and the lowest FDR achieved is noted.

No Rejection	Rejection	# Samples	Low FDR
All Samples			
Grade 0	Grade 3A-4	148	1
Grade 0	Grade 1B, 3A-4	158	1.5
Non-redundant within class			
Grade 0	Grade 3A-4	86	7
Grade 0	Grade 1B, 3A-4	93	16
Non-redundant (1 sample/patient)			
Grade 0	Grade 3A-4	73	11

Table 8: Renal rejection tissue gene expression SAM analysis

Array probe ID	Gene	FDR	Protein SEQ ID	Leukocyte expression	Secreted
2697	CD69 antigen (p60, early T-cell activat	1.5625	2925	+	
2645	Ras association (RalGDS/AF-6)	1.5625	2926		
2707	CD33 antigen (gp67) (CD33), mRNA	1.5625	2927	+	
2679	Ras association (RalGDS/AF-6) domain fa	1.5625	2928		
2717	EST, 5 end	1.5625			
2646	mRNA for KIAA0209 gene, partial cds /cd	1.5625	2929		
2667	leupaxin (LPXN), mRNA /cds=(93,1253)	1.5625	2930	+	
2706	c- EST 3 end /clone=IMAGE:	2.1111			
2740	c- insulin induced gene 1 (INSIG1), mRNA	2.2			
117	**chemokine (C-X-C motif) receptor 3**	2.8125	2931		
2669	IL2-inducible T-cell kinase (ITK), mRNA	2.8125	2932	+	
2674	glioma pathogenesis-related protein (RT	2.8125	2933		
2743	c- nuclear receptor subfamily 1, group I	2.8125			
326	death effector filament-forming Ced-4-l	2.8125	2934		
2716	EST cDNA, 3 end	2.8125			
2727	c- chemokine (C-X-C motif), receptor 4	3.1316	2935	+	
2721	c- EST 3 end /clone=IMAGE:	3.1316			
2641	hypothetical protein FLJ20647 (FLJ20647	3.1316	2936		
2671	tumor necrosis factor, alpha-induced pr	3.525	2937		
2752	protein tyrosine phosphatase, receptor	3.8077	2938	+	
2737	7f37g03.x1 cDNA, 3 end /clone=IMAGE:	3.8077			
2719	c- EST372075 cDNA	3.8077			
2684	molecule possessing ankyrin repeats ind	3.8077	2939		
76	granzyme B (granzyme 2, cytotoxic T-lym	3.8077	2940	+	+
2677	lectin-like NK cell receptor (LLT1), mR	3.8077	2941	+	
2748	c-107G11	3.9			
2703	c- EST, 5 end /clone=IMAGE	3.9			
2711	SAM domain, SH3 domain and nuclear	3.9	2942		
2663	phosphodiesterase 4B, cAMP-specific	3.9	2943		+
98	small inducible cytokine A5 (RANTES)	4.5645	2944	+	+
2657	tumor necrosis factor receptor superfam	4.8286	2945		
2683	B-cell lymphoma/leukaemia 11B (BCL11B)	4.8286	2946	+	
2686	phospholipase A2, group VII (platelet-a	4.8286	2947		+
2687	phosphatidylinositol 3-kinase catalytic	4.8286	2948		
2644	AV659177 cDNA, 3 end	4.9028			
2664	regulator of G-protein signalling 10 (R	5.0238	2949		
2747	c- integral membrane protein 2A (ITM2A),	5.0238	2950		
2744	c- interferon consensus sequence binding	5.0238			
2678	HSPC022 protein (HSPC022), mRNA	5.0238	2951		
2731	c- xj98c03.x1 NCI_CGAP_Co18 cDNA	5.0238			
2713	caspase recruitment domain protein 9 (L	5.0238	2952		
2736	c- small inducible cytokine A4 (homologo	5.1395	2953	+	+
2708	major histocompatibility complex, class	5.15	2954		
249	c-107H8	5.15			
2670	CD72 antigen (CD72), mRNA	5.15	2955	+	
2661	heat shock 70kD protein 6 (HSP70B)	5.15	2956		
2680	bridging integrator 2 (BIN2), mRNA /cds	5.15	2957		
2754	UI-H-BW0-aiy-b-10-0-UI.s1 cDNA, 3 end	5.15			
2728	c- EST380762 cDNA	5.15			
174	FKBPL	5.15	2958		
2742	c- chromobox homolog 3 (DM)	5.15			
2668	basement membrane-induced gene(ICB-1)	5.15	2959		
2750	Lysosomal-assoc. multispanning memb	5.15	2960		

Table 8: Renal rejection tissue gene expression SAM analysis

Array probe ID	Gene	FDR	Protein SEQ ID	Leukocyte expression	Secreted
2746	174D1	5.15			
2738	c- AV716627 cDNA, 5 end	5.15			
2627	solute carrier family 17 (sodium phosph	5.15	2961		
2739	c- asparaginyl-tRNA synthetase (NARS)	5.15			
124	major histocompatibility complex, class	5.15	2962		
2647	mRNA for T-cell specific protein /cds	5.15	2963	+	
2628	c-EST, 3 end	5.2295			
2638	Express cDNA library cDNA 5	5.2903			
2725	c- 601571679F1 cDNA, 5 end	5.3385	2964		
2714	qg78c05.x1 cDNA, 3 end /clone	5.3385	2965		
2635	interleukin 2 receptor gamma chain	5.3385	2966	+	
2751	7264, lectin, galactoside-binding, soluble	5.4167	2967		+
2629	8, cDNA: FLJ21559 fis, clone COL06406	5.5299	2968		
2695	mRNA; cDNA DKFZp434E0516	5.5588	2969		
2741	c- hexokinase 2 (HK2), mRNA	5.5986			
41	Similar to major histocompatibility antigen	5.5986	2970		
2691	CD5 antigen (p56-62) (CD5)	5.5986	2971		
2726	c- 602650370T1 cDNA, 3	5.6014			
2722	c- EST cDNA clone	5.6014			
2689	interleukin-2 receptor	5.6014	2972		
2734	c- nuclear receptor subfamily 1, group I	5.6667			
2631	pre-B-cell colony-enhancing factor	5.7566	2973		+
2656	postmeiotic segregation increased	5.7756	2974		
2696	protein tyrosine phosphatase, receptor	5.7756	2975		
2676	butyrophilin, subfamily 3, member A2	5.8165	2976		
2701	c- EST 3 end	5.9048			
2730	EST 3 end /clone=IMAGE	5.9048			
2710	high affin. immunoglobulin epsilon recept.	5.9048	2977		
2632	encoding major histocompatibility comple	5.9048	2978		
2724	c- EST 3 end	5.9048			
2698	EST	6.0353			
2662	interferon regulatory factor 1 (IRF1),	6.0988	2979		
139	allograft inflammatory factor 1 (AIF1),	6.1379	2980		
2753	platelet activating receptor homolog (H	6.3182	2981		
2704	c- EST 3 end /clone=IMAGE:	7.0337			
2675	pim-2 oncogene (PIM2), mRNA	7.1222	2982		+
2700	proteoglycan 1, secretory granule (PRG1	7.375	2983		+
2640	mRNA for KIAA0870 protein, partial cds	7.375	2984		
2723	c- EST, 5 end /clone=IMAGE	7.375			
2658	FYN-binding protein (FYB-120/130) (FYB)	7.375	2985		
2688	major histocompatibility complex, class	7.375	2986		
2735	c- EST, 3 end /clone=IMAGE:	7.375			
2702	c- hypothetical protein MGC4707	7.634			
2681	hypothetical protein FLJ10652	8.1117	2987		
2755	EST, 3 end	8.1117			
2715	hypothetical protein FLJ10842	8.1117			
2732	c- EST cDNA, 3 end	8.1117			
2652	hexokinase 2 (HK2), mRNA	8.1117			
2651	colony stimulating factor 3 receptor	8.1117	2988		
2718	RNA binding motif protein, X chrom	8.2788			
2673	Src-like-adapter (SLA), mRNA	8.3048	2989		
2733	c- major histocompatibility complex	8.467			
2712	histamine receptor H2 (HRH2)	8.8583	2990		

Table 8: Renal rejection tissue gene expression SAM analysis

Array probe ID	Gene	FDR	Protein SEQ ID	Leukocyte expression	Secreted
2659	hemopoietic cell kinase (HCK)	8.8583	2991		
2654	xanthene dehydrogenase (XDH)	8.8583	2992		
2636	Arabidopsis root cap 1	8.8583	2993		
2639	fatty acid binding protein 1, liver	8.8583			
2690	adenosine deaminase (ADA)	8.8583	2994		
2705	c- EST, 3 end	8.8583	2995		
2685	hypothetical protein MGC10823	8.8583	2996		
2692	membrane-spanning 4-domains,	8.8583	2997		
2693	rearranged immunoglobulin mRNA for mu	8.8583			+
2648	protein tyrosine kinase related mRNA	8.8583			
2650	major histocompatibility complex, class	8.8583	2998		
2720	c- EST 3 end /clone=IMAGE:	8.8583			
2660	major histocompatibility complex, class	8.8583	2999		
2666	BCL2-related protein A1 (BCL2A1), mRNA	9.1446	3000		
2699	c-EST	9.4767			
2633	interleukin 4 receptor	9.4767	3001		
74	tumor necrosis factor (ligand) superfam	9.4767	3002		
2672	interferon-induced, hepatitis C-assoc.	9.4767	3003		
2642	cDNA FLJ20673 fis, clone KAIA4464	9.4767	3004		
2682	VNN3 protein (HSA238982), mRNA	9.4767	3005		
2655	cathepsin K (pycnodysostosis) (CTSK)	9.4767	3006		
2630	Integrin, alpha L (CD11A (p180), lymphoc	9.4767	3007		
2745	EST, 5 end	9.4885	3008		
2643	nuclear receptor subfamily 1, group I,	9.625			
2694	CDW52 antigen (CAMPATH-1)	9.625	3009		
2749	6977, c-178F5	9.6903	3010		
2665	small inducible cytokine subfamily A	9.6903	3011		
2649	signal transducer and activator	9.7878	3012		
2637	324,	9.7878			
2634	70 activation (Act-2) mRNA	9.7878	3013		
2709	coagulation factor VII	9.7878	3014		
2653	integrin, beta 2 (antigen CD18 (p95)	9.7878	3015		
2729	EST 3' end	9.8321			

Table 9

Array Probe SEQ ID	Gene	Gene Name	mRNA Accession #	RefSeq Peptide Accession #	Current UniGene Cluster (Build 156)	Localization	Function
111	IL15	Interleukin 15	NM_000585	NP_000576	Hs.168132	Secreted	T-cell activation and proliferation
79	PRF1	Perforin 1 (pore forming protein)	NM_005041	NP_005032	Hs.2200	Secreted	CD8, CTL effector; channel-forming protein capable of lysing non-specifically a variety of target cells; clearance of virally infected host cells and tumor cells; .
110	IL17	Interleukin 17 (cytotoxic T-lymphocyte-associated serine esterase 8)	NM_002190	NP_002181	Hs.41724	Secreted	Induces stromal cells to produce proinflammatory and hematopoietic cytokines; enhances IL6, IL8 and ICAM-1 expression in fibroblasts; osteoclastic bone resorption in RA; expressed in only in activated CD4+T cells
75	IL8	Interleukin 8	NM_000584	NP_000575	Hs.624	Secreted	Proinflammatory cytokine
120	CXCL1	Chemokine (C-X-C motif) ligand 1 (melanoma growth stimulating activity, alpha)	NM_001511	NP_001502	Hs.789	Secreted	Neurogenesis, immune system development, signaling
113	IFNG	Interferon, gamma	NM_000619	NP_000610	Hs.856	Secreted	Antiviral defense and immune activation
100	IL2	Interleukin 2	NM_000586	NP_000577	Hs.89679	Secreted	Promotes growth of B and T cells
4	B2M	beta 2 microglobulin	NM_004048	NP_004039	Hs.75415	Secreted	
98	CCL5	Chemokine (C-C motif) ligand 5 (RANTES, SCYA5)	NM_002985	NP_002976	Hs.241392	Secreted	Chemoattractant for monocytes, memory T helper cells and eosinophils; causes release of histamine from basophils and activates eosinophils; One of the major HIV-suppressive factors produced by CD8+ cells
112	IL10	Interleukin 10	NM_000572	NP_000563	Hs.193717	Secreted	Chemotactic factor for CD8+T cells; down-regulates expression of Th1 cytokines, MHC class II Ags, and costimulatory molecules on macrophages; enhances B cell survival, proliferation, and antibody production; blocks NF kappa B, JAK-STAT regulation;
80	IL4	Interleukin 4	NM_000589	NP_000580	Hs.73917	Secreted	TH2, cytokine, stimulates CTL
2773	IL7	Interleukin 7	NM_000880	NP_000871	Hs.72927	Secreted	Proliferation of lymphoid progenitors

Table 9

Array Probe SEQ ID	Gene	Gene Name	mRNA Accession #	RefSeq Peptide Accession #	Current UniGene Cluster (Build 156)	Localization	Function
109	CXCL10	Chemokine (C-X-C motif) ligand 10, SCYB10	NM_001565	NP_001556	Hs.2248	Secreted	Stimulation of monocytes; NK and T cell migration, modulation of adhesion molecule expression
2665	CCL17	Chemokine (C-C motif) ligand 17	NM_002987	NP_002978	Hs.66742	Secreted	T cell development, trafficking and activation
101	KLRF1	Killer cell lectin-like receptor subfamily F, member 1	NM_016523	NP_057607	Hs.183125	Secreted	Induction of IgE, IgG4, CD23, CD72, surface IgM, and class II MHC antigen in B cells
99	IL6	Interleukin 6	NM_000600	NP_000591	Hs.93913	Secreted	B cell maturation
104	CCL4	Chemokine (C-C motif) ligand 4	NM_002984	NP_002975	Hs.75703	Secreted	Inflammatory and chemokinetic properties; one of the major HIV-suppressive factors produced by CD8+ T cells
76	GZMB	Granzyme B (granzyme 2, cytotoxic T-lymphocyte-associated serine esterase 1)	NM_004131	NP_004122	Hs.1051	Secreted	Apoptosis; CD8, CTL effector
2785	OID_4789	KIAA0963 protein	NM_014963	NP_055778	Hs.7724	Secreted	Proinflammatory; chemoattraction and activation of neutrophils
2791	XCL1	Chemokine (C motif) ligand 1 (SCYC2)	NM_002995	NP_002986	Hs.3195	Secreted	Chemotactic factor for lymphocytes but not monocytes or neutrophils
130	PRDM1	PR domain containing 1, with ZNF domain	NM_001198	NP_001189	Hs.388346	Nuclear	Transcription factor; promotes B cell maturation, represses human beta-IFN gene expression
2781	TBX21	T-box 21	NM_013351	NP_037483	Hs.272409	Nuclear	TH1 differentiation, transcription factor
88	MTHFD2	Methylene tetrahydrofolate dehydrogenase (NAD+ dependent), methenyltetrahydrofolate cyclohydrolase	NM_006636	NP_006627	Hs.154672	Mitochondrial	Folate metabolism
103	IL2RA	Interleukin 2 receptor, alpha	NM_000417	NP_000408	Hs.1724	Membrane-bound and soluble forms	T cell mediated immune response
77	TNFSF6	Tumor necrosis factor (ligand) superfamily, member 6	NM_000639	NP_000630	Hs.2007	Membrane-bound and soluble forms	CD8, CTL effector; proapoptotic
115	CD8B1	CD8 antigen, beta polypeptide 1 (p37)	NM_004931	NP_004922	Hs.2299	Membrane-bound and soluble forms	CTL mediated killing
128	PTGS2	Prostaglandin-endoperoxide synthase 2 (prostaglandin G/H synthase and cyclooxygenase)	NM_000963	NP_000954	Hs.196384	Membrane-associated	Angiogenesis, cell migration, synthesis of inflammatory prostaglandins

Table 9

Array Probe SEQ ID	Gene	Gene Name	mRNA Accession #	RefSeq Peptide Accession #	Current UniGene Cluster (Build 156)	Localization	Function
89	TAP1	Transporter 1, ATP-binding cassette, sub-family B (MDR1/TAP)	NM_000593	NP_000584	Hs.352018	ER membrane	Transports antigens into ER for association with MHC class I molecules
92	IGHM	Immunoglobulin heavy constant mu	BC032249		Hs.300697	Cytoplasmic and secreted forms	Antibody subunit
122	GPI	Glucose phosphate isomerase	NM_000175	NP_000166	Hs.409162	Cytoplasmic and secreted forms	Glycolysis and gluconeogenesis (cytoplasmic); neurotrophic factor (secreted)
2783	GSN	Gelsolin (amyloidosis, Finnish type)	NM_000177	NP_000168	Hs.290070	Cytoplasmic and secreted forms	Controls actin filament assembly/disassembly
2780	STK39	Serine threonine kinase 39 (STE20/SPS1 homolog, yeast)	NM_013233	NP_037365	Hs.199263	Cytoplasmic and nuclear	Mediator of stress-activated signals; Serine/Thr Kinase, activated p38
2770	PSMB8	Proteasome (prosome, macropain) subunit, beta type, 8 (large multifunctional protease 7)	AK092738		Hs.180062	Cytoplasmic	Processing of MHC class I antigens
2667	LPXN	Leupaxin	NM_004811	NP_004802	Hs.49587	Cytoplasmic	Signal transduction
2669	ITK	IL2-inducible T-cell kinase	L10717		Hs.211576	Cytoplasmic	Intracellular kinase, T-cell proliferation and differentiation
90	KPNA6	Karyopherin alpha 6 (importin alpha 7)	AW021037		Hs.301553	Cytoplasmic	Nucleocytoplasmic transport
2794	SH2D2A	SH2 domain protein 2A	NM_003975	NP_003966	Hs.103527	Cytoplasmic	CD8 T activation, signal transduction
2765	TNFSF5	Tumor necrosis factor (ligand) superfamily, member 5 (hyper-IgM syndrome)	NM_000074	NP_000065	Hs.652	Cellular membrane	B-cell proliferation, IgE production, immunoglobulin class switching; expressed on CD4+ and CD8+ T cells
97	CD69	CD69 antigen (p60, early T-cell activation antigen)	NM_001781	NP_001772	Hs.82401	Cellular membrane	Activation of lymphocytes, monocytes, and platelets
2635	IL2RG	Interleukin 2 receptor, gamma (severe combined immunodeficiency)	NM_000206	NP_000197	Hs.84	Cellular membrane	Signalling component of many interleukin receptors (IL2,IL4,IL7,IL9, and IL15),
96	CXCR4	Chemokine (C-X-C motif) receptor 4	NM_003467	NP_003458	Hs.89414	Cellular membrane	B-cell lymphopoiesis, leukocyte migration, angiogenesis; mediates intracellular calcium flux
2766	CD19	CD19 antigen	NM_001770	NP_001761	Hs.96023	Cellular membrane	Signal transduction; B lymphocyte development, activation, and differentiation

Table 9

Array Probe SEQ ID	Gene	Gene Name	mRNA Accession #	RefSeq Peptide Accession #	Current UniGene Cluster (Build 156)	Localization	Function
2769	ITGB1	Integrin, beta 1 (fibronectin receptor, beta polypeptide, antigen CD29 includes MDF2, MSK12)	NM_002211	NP_002202	Hs.287797	Cellular membrane	Cell-cell and cell-matrix interactions
2647	TRB	T cell receptor beta, constant region	K02885		Hs.300697	Cellular membrane	Antigen recognition
82	CTLA4	Cytotoxic T-lymphocyte-associated protein 4	NM_005214	NP_005205	Hs.247824	Cellular membrane	Negative regulation of T cell activation, expressed by activated T cells
83	CD8A	CD8 antigen, alpha polypeptide (p32)	NM_001768	NP_001759	Hs.85258	Cellular membrane	CD8 T-cell specific marker and class I MHC receptor
114	HLA-DRB1	Major histocompatibility complex, class II, DR beta 1	NM_002124	NP_002115	Hs.308026	Cellular membrane	Antigen presentation
2772	CD3Z	CD3Z antigen, zeta polypeptide (TiT3 complex)	NM_000734	NP_000725	Hs.97087	Cellular membrane	T-cell marker; couples antigen recognition to several intracellular signal-transduction pathways
2	ACTB	Actin, beta	NM_001101	NP_001092	Hs.288061	Cellular membrane	Cell adhesion and recognition
2774	ITGAL	Integrin, alpha L (antigen CD11A (p180), lymphocyte function-associated antigen 1; alpha polypeptide)	NM_002209	NP_002200	Hs.174103	Cellular membrane	All leukocytes; cell-cell adhesion, signaling
78	TCIRG1	T-cell, immune regulator 1, ATPase, H+ transporting, lysosomal V0 protein a isoform 3	NM_006019	NP_006010	Hs.46465	Cellular membrane	T cell activation
2670	CD72	CD72 antigen	NM_001782	NP_001773	Hs.116481	Cellular membrane	B cell proliferation
2779	D12S2489E	DNA segment on chromosome 12 (unique) 2489 expressed sequence	NM_007360	NP_031386	Hs.74085	Cellular membrane	NK cells marker
2692	MS4A1	Membrane-spanning 4-domains, subfamily A, member 1, CD20	NM_152866	NP_690605	Hs.89751	Cellular membrane	B-cell activation, plasma cell development
126	TCRGC2	T cell receptor gamma constant 2	M17323		Hs.112259	Cellular membrane	
116	CD4	CD4 antigen (p55)	NM_000616	NP_000607	Hs.17483	Cellular membrane	T cell activation, signal transduction, T-B cell adhesion

Table 9

Array Probe SEQ ID	Gene	Gene Name	mRNA Accession #	RefSeq Peptide Accession #	Current UniGene Cluster (Build 156)	Localization	Function
117	CXCR3	Chemokine (C-X-C motif) receptor 3, GPR9	NM_001504	NP_001495	Hs.198252	Cellular membrane	Integrin activation, cytoskeletal changes and chemotactic migration of leukocytes
2707	CD33	CD33 antigen (gp67)	NM_001772	NP_001763	Hs.83731	Cellular membrane	Cell adhesion; receptor that inhibits the proliferation of normal and leukemic myeloid cells
123	CD47	CD47 antigen (Rh-related antigen, integrin-associated signal transducer)	NM_001777	NP_001768	Hs.82685	Cellular membrane	Cell adhesion, membrane transport, signaling transduction, permeability
84	BY55	Natural killer cell receptor, immunoglobulin superfamily member	NM_007053	NP_008984	Hs.81743	Cellular membrane	NK cells and CTLs, costim with MHC I
2784	KLRD1	Killer cell lectin-like receptor subfamily D, member 1	NM_002262	NP_002253	Hs.41682	Cellular membrane	NK cell regulation
124	HLA-F	Major histocompatibility complex, class I, F	NM_018950	NP_061823	Hs.377850	Cellular membrane	Antigen presentation
2752	PTPRCAP	Protein tyrosine phosphatase, receptor type, C-associated protein	NM_005608	NP_005599	Hs.155975	Cellular membrane	T cell activation

Table 12: Markers for CMV Infection

New SEQID	Source	Unigene	Acc	GI	Name	Strand	Probe Sequence	SAM FDR
408	cDNA	Hs.1051	NM_004131	7262379	granzyme B	1	GGAGCCAAGTCCAGATT TACACTGGGAGAGGTGC CAGCAACTGAATAAAT	0%
3108	db mining	Hs.169824	NM_002258	4504878	killer cell lectin-like receptor	1	TGGATCTGCCAAAAAGA ACTAACACCTGTGAGAA ATAAAGTGTATCCTGA	0%
3109	cDNA	Hs.170019	NM_004350	4757917	runt-related transcription factor 3	1	GCTGGGTGGAAACTGCT TTGCACTATCGTTTGCT TGGTGTTTGTTTTTAA	0%
433	cDNA	Hs.183125	NM_016523	7705573	killer cell lectin-like receptor F	1	TTCCAGGCTTTTGCTAC TCTTCACTCAGCTACAA TAAACATCCTGAATGT	0%
3110	db mining	Hs.2014	X06557	37003	T-cell receptor-delta	1	GGGGTTTATGTCCTAAC TGCTTTGTATGCTGTTT TATAAAGGGATAGAAG	0.10%
3111	cDNA	Hs.211535	AI823649	5444320	EST IMAGE:2400148	-1	GAAGCCTTTTCTTTTCT GTTCACCCTCACCAAGA GCACAACTTAAATAGG	0.10%
3112	cDNA	**Hs.301704**	AW002985	5849991	eomesodermin (Xenopus laevis)	-1	AACAAGCCATGTTTGCC CTAGTCCAGGATTGCCT CACTTGAGACTTGCTA	0%
3112	Table 3B	**Hs.301704**	AW002985	5849991	eomesodermin (Xenopus laevis)	-1	AACAAGCCATGTTTGCC CTAGTCCAGGATTGCCT CACTTGAGACTTGCTA	0%
3113	cDNA	Hs.318885	NM_000636	10835186	superoxide dismutase 2	1	TACTTTGGGGACTTGTA GGGATGCCTTTCTAGTC CTATTCTATTGCAGTT	0.10%
3114	literature	Hs.41682	NM_007334	7669498	killer cell lectin-like receptor D	1	GGGCAGAGAAGGTGGAG AGTAAAGACCCAACATT ACTAACAATGATACAG	0%
3115	cDNA	Hs.71245	AI954499	5746809	EST IMAGE:502221	-1	TGGTAATAGTGTTTGAC TCCAGGGAAGAACAGAT GGGTGCCAGAGTGAAA	0%
3116	cDNA	Hs.75596	NM_000878	4504664	interleukin 2 receptor, beta	1	ATGGAAATTGTATTTGC CTTCTCCACTTTGGGAG GCTCCCACTTCTTGGG	0%
436	cDNA	**Hs.75703**	NM_002984	4506844	small inducible cytokine A4	1	CCACTGTCACTGTTTCT CTGCTGTTGCAAATACA TGGATAACACATTTGA	0%
436	cDNA	**Hs.75703**	NM_002984	4506844	small inducible cytokine A4	1	CCACTGTCACTGTTTCT CTGCTGTTGCAAATACA TGGATAACACATTTGA	0.10%
436	cDNA	**Hs.75703**	NM_002984	4506844	small inducible cytokine A4	1	GTCCACTGTCACTGTTT CTCTGCTGTTGCAAATA CATGGATAACACATTT	0%
436	cDNA	**Hs.75703**	NM_002984	4506844	small inducible cytokine A4	-1	TGGTCCACTGTCACTGT TTCTCTGCTGTTGCAAA TACATGGATAACACAT	0.10%
415	cDNA	Hs.85258	BC025715	19344021	CD8 antigen	1	CTGAGAGCCCAAACTGC TGTCCCAAACATGCACT TCCTTGCTTAAGGTAT	0.10%
3117	cDNA	**Hs.111554**	AA806222	2874972	cDNA 196D7	-1	TGATTTCTGTAATGTTT GACCTAATAATAGCCCT TTTCGTCTCTGACCCA	0%
WBC	N/A	N/A	N/A	N/A		N/A	N/A	0.10%
WPT	N/A	N/A	N/A	N/A		N/A	N/A	0%

1. An *in-vitro* method for assessing the immune status of an individual comprising

(a) selecting one or more nucleic acids having an expression level that correlates with the rate of hematopoiesis or the distribution of hematopoietic cells along their maturation pathway in said individual and also correlates with the immune status of said individual; and

(b) detecting the expression level of said nucleic acid to assess the immune status of said individual.

2. The method of claim 1 wherein said one or more nucleic acids comprise a nucleotide sequence chosen from SEQ ID NO: 52, SEQ ID NO: 67, SEQ ID NO: 19, SEQ ID NO: 39, SEQ ID NO: 63, SEQ ID NO: 26, SEQ ID NO: 68, SEQ ID NO: 13, SEQ ID NO: 200 and SEQ ID NO: 36.

3. The method claim 1 wherein said expression level is detected by measuring the RNA level expressed by said one or more nucleic acids.

4. The method of claim 3, wherein said RNA is isolated from said individual prior to detecting said RNA level expressed by said one or more nucleic acids.

5. The method of claim 3 wherein said RNA level is detected by PCR.

6. The method of claim 3 wherein said RNA level is detected by hybridization.

7. The method of claim 3 wherein said RNA level is detected by hybridization to an oligonucleotide.

8. The method of claim 7 wherein said oligonucleotide comprises DNA, RNA, cDNA, PNA, genomic DNA, or synthetic oligonucleotides.

9. The method of claim 1, wherein said immune status is capable of indicating whether said individual is experiencing organ transplant rejection.

10. The method of claim 9, wherein said organ transplant is selected from the group consisting of: cardiac allograft, kidney allograft, liver allograft, bone marrow allograft, xenograft, and artificial organ transplant.

11. The method of claim 9, wherein said immune status is capable of indicating whether said individual is experiencing cardiac allograft rejection.

SEQUENCE LISTING

<110> EXPRESSION DIAGNOSTICS, INC.
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Fry, Kirk
Woodward, Robert
Ly, Ngoc
Prentice, James
Morris, MacDonald
Rosenberg, Steven

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cttgtattaa agacagaggc agaaaaaaaa aaaaaaa 1177

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<212> DNA
<213> Homo sapiens

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agggaaagct gtgctgccag atgtgtgagc caggaacatt cctcgtgaag gactgtgacc 360

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aaa 1323

<210> 470
<211> 2781
<212> DNA
<213> Homo sapiens

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gtgctgctcc tctgaagatt caagcttatt tcaatgagac tgcagacctg ccatgccaat 240

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gcatccacca gatgaattct gaactgtcag tgcttgctaa cttcagtcaa cctgaaatag 540

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aaaaaaaaaa aaaaaaaaaa a 2781

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<212> DNA
<213> Homo sapiens

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gcttcaaagg tgaggggggaa actgtaggcg gtggagacag ggctgggggt aggagggtta 180

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gatgggattg aaggggcttc taatgaccca gatatggaaa cagaagacaa aattgtaagc 1320

cagagtcaac aaattaaata aattaccccc tcctccagat caa 1363

<210> 472
<211> 1080
<212> DNA
<213> Homo sapiens

<400> 472
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aaagctgttc acaaaggcaa gcctccctga ccgttcccag taggtgttga tgcacaggga 180

caccaaaggc acgttcatga caaacttttc ctcaaacccg tggatcatag cctcgactac 240

gtagaagaag gctggatagg cagtgtcata ggcagtatcc tgcacagtct caataacggc 300

ctgatccacc acgtgggcca gagatgtggc ggtctcaaac tgctgccccc gggcctcttg 360

gaatgcagct ggggccaggg gagtcggcag gttacccacc attagccggt gcacagccct 420

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<211> 195
<212> DNA
<213> Homo sapiens

<400> 473
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<211> 223
<212> DNA
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gcggtggtgg tcaacatata tctccagata caggagatga ggaaaaaaaa ggaggacaag 120

tctaacggaa taatatccga tcatatatat ggagggatat caggtcatca ttgtgtatca 180

aaagatgatt tgtacaacag ggaaggatac ggttttaaag gtt 223

<210> 475
<211> 249
<212> DNA
<213> Homo sapiens

<400> 475
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gttgacttgc tggttcctaa aagttcgcaa aaacgattgt gtgaagattt tatgacgttg 120

gttgactagt tcatgagatt ctgctgtacg tgtgatggtt attcgctggt tcgttctaag 180

atgagtatcg tactgtgtct gcgatggtcg tctcttactg gcattctctc ggctgcctct 240

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<210> 476
<211> 185
<212> DNA
<213> Homo sapiens

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<223> n is a, c, g, t or u

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cgggc 185

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<211> 300
<212> DNA
<213> Homo sapiens

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<223> n is a, c, g, t or u

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<223> n is a, c, g, t or u

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<223> n is a, c, g, t or u

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<222> (197)..(197)
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<222> (204)..(204)
<223> n is a, c, g, t or u

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<221> misc_feature
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<223> n is a, c, g, t or u

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anatcatctt tctnntaagt tcatccttnt tngcacggnc cttagcctnc antgcacccc 180

cnaacttgtt agcggcnccc ttgntcacat catgcagctc cttaatacaa gccatccaca 240

tctcccgctt atcctcnggt acaatgtagt tctcatacat gctctgcata gttagcccaa 300

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<211> 363
<212> DNA

<213> Homo sapiens

<400> 478
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ggt 363

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<211> 600
<212> DNA
<213> Homo sapiens

<400> 479
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aacatccagg cttgggcaca tctgcttcaa caggaggcgc agcctgtcat tttcagatga 120

tttggcagca gccacctcac ggtagtgctg cagcagttgc ttaaacttgg cccggcattt 180

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<210> 480
<211> 146
<212> DNA
<213> Homo sapiens

<400> 480
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tccgagggga ccctctggcc cgatac 146

<210> 481
<211> 66
<212> DNA

<213> Homo sapiens

<400> 481
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ccagag 66

<210> 482
<211> 176
<212> DNA
<213> Homo sapiens

<400> 482
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acatgctgaa aaaatatacc cagacggaag agaaattcac tggcgccttt aatatgatgg 120

gaggatgttt gcagaatgcc ttagatatct tagataaggt tcatgagcct ttcgag 176

<210> 483
<211> 185
<212> DNA
<213> Homo sapiens

<220>
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tgttaacctc cttcctnaac atagtctgca ggaacgtcgt ggccttggtc acgggtgtct 180

cgggc 185

<210> 484
<211> 641
<212> DNA
<213> Homo sapiens

<400> 484
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ccagaaggag acaacaatgt ccctgctacc cgtgccatac acagaggctg cctctttgtc 120

tactggttct actgtgacaa tcaaagggcg accacttgcc tgtttcttga atgaaccata 180

tctgcaggtg gatttccaca ctgagatgaa ggaggaatca gacattgtct tccatttcca 240

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gctgccagat aagtaccagg taatggtcaa tggccaatcc tcttacacct ttgaccatag 420

aatcaagcct gaggctgtga agatggtgca agtgtggaga gatatctccc tgaccaaatt 480

taatgtcagc tatttaaaga gataaccaga cttcatgttg ccaaggaatc cctgtctcta 540

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tcctgctcat taaaacttaa tcaaacttca aaaaaaaaaa a 641

<210> 485
<211> 2165
<212> DNA
<213> Homo sapiens

<400> 485
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tagtgctcgg cgtcagacat ggcggaggcg atggatttgg gcaaagaccc caacgggccc 180

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cacaaaaaag gacccgccaa aaccaaatta tagcggcaaa tttttttttgg ccataaatag 240

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<400> 2365
agcgaccaca gctccgatga cca 23

<210> 2366
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<213> Homo sapiens

<400> 2366
ccgagggcgt tccacccgtt 20

<210> 2367
<211> 24

<212> DNA
<213> Homo sapiens

<400> 2367
tcccccagct ccctcctcac tttg 24

<210> 2368
<211> 20
<212> DNA
<213> Homo sapiens

<400> 2368
acccggctgc gcaggtctga 20

<210> 2369
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<212> DNA
<213> Homo sapiens

<400> 2369
tgagccactg gcccacaagg g 21

<210> 2370
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<213> Homo sapiens

<400> 2370
tccgtgacct cgggctcccc 20

<210> 2371
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<212> DNA
<213> Homo sapiens

<400> 2371
ccccgcgttg aaggcgttga 20

<210> 2372
<211> 24
<212> DNA
<213> Homo sapiens

<400> 2372
tgggcatggg ttatcctctg ctgg 24

<210> 2373
<211> 30
<212> DNA
<213> Homo sapiens

<400> 2373
tgtcgtggag taaagaggga aacatgacca 30

<210> 2374
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<212> DNA
<213> Homo sapiens

<400> 2374
cgggagcagg acagggagcc a 21

<210> 2375
<211> 30
<212> DNA
<213> Homo sapiens

<400> 2375
tggctcagta gcaacttggg gacttgtttt 30

<210> 2376
<211> 32
<212> DNA
<213> Homo sapiens

<400> 2376
tgtttttgga aatcactaat agggccagcc tc 32

<210> 2377
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<212> DNA
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<400> 2377
tgggagtctt gtgtctgtgc caacca 26

<210> 2378
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<212> DNA
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<400> 2378
aggggaggt ggcagtggct g 21

<210> 2379
<211> 20
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<400> 2379
acgcacaggg atggacgcgg 20

<210> 2380
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<212> DNA
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<400> 2380
cctctgtgac atggtggtaa cagcacaga 29

<210> 2381
<211> 27
<212> DNA
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<400> 2381
cccatggcat gaacaaatag gatgcct 27

<210> 2382
<211> 34
<212> DNA
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<400> 2382
tcccaactgc aaaccctcat ttagtcttta gtga 34

<210> 2383
<211> 22
<212> DNA
<213> Homo sapiens

<400> 2383
tggagggaca gaggtgggtg gg 22

<210> 2384
<211> 33
<212> DNA
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<400> 2384
cgccagtgag ttaagttgta cagaacatcg tca 33

<210> 2385
<211> 25
<212> DNA
<213> Homo sapiens

<400> 2385
gggaagacag acagcagcag accca 25

<210> 2386
<211> 31
<212> DNA
<213> Homo sapiens

<400> 2386
caccctttgg acattttgca actcttcaat g 31

<210> 2387
<211> 21
<212> DNA
<213> Homo sapiens

<400> 2387
tgggacccag gacgacgtcc a 21

<210> 2388
<211> 24
<212> DNA
<213> Homo sapiens

<400> 2388
tgccacttct ggtctcgtcg gtga 24

<210> 2389
<211> 28
<212> DNA
<213> Homo sapiens

<400> 2389
ctccccagcc cacaatttca aataatgc 28

<210> 2390
<211> 34
<212> DNA
<213> Homo sapiens

<400> 2390
accaacttac tcttaaaaag gatggctgcc aaga 34

<210> 2391
<211> 21
<212> DNA
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<400> 2391
tgtcagctcc acgggggtcc c 21

<210> 2392
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<212> DNA
<213> Homo sapiens

<400> 2392
gagtccagaa agaaatgcct ggggca 26

<210> 2393
<211> 25
<212> DNA
<213> Homo sapiens

<400> 2393
cccaaagaag ggtcagccaa agcca 25

<210> 2394
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<212> DNA

<213> Homo sapiens

<400> 2394
ggcctggtgt ctgctctgcg g 21

<210> 2395
<211> 27
<212> DNA
<213> Homo sapiens

<400> 2395
tcagccaagc tagcctcctt agccagc 27

<210> 2396
<211> 34
<212> DNA
<213> Homo sapiens

<400> 2396
tcagtatgta atgtcctatt ttcccactgc acca 34

<210> 2397
<211> 30
<212> DNA
<213> Homo sapiens

<400> 2397
ttcctgattt tgcatgttct cattcccaaa 30

<210> 2398
<211> 29
<212> DNA
<213> Homo sapiens

<400> 2398
tccagaaaat tggaagcagt ctggaatgg 29

<210> 2399
<211> 25
<212> DNA
<213> Homo sapiens

<400> 2399
cccagttcac agtcccattc tggca 25

<210> 2400
<211> 375
<212> PRT
<213> Homo sapiens

<400> 2400

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

```
Cys Lys Ala Gly Phe Ala Gly Asp Asp Ala Pro Arg Ala Val Phe Pro
            20                  25                  30

Ser Ile Val Gly Arg Pro Arg His Gln Gly Val Met Val Gly Met Gly
        35                  40                  45

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

Leu Thr Leu Lys Tyr Pro Ile Glu His Gly Ile Val Thr Asn Trp Asp
65                  70                  75                  80

Asp Met Glu Lys Ile Trp His His Thr Phe Tyr Asn Glu Leu Arg Val
                85                  90                  95

Ala Pro Glu Glu His Pro Val Leu Leu Thr Glu Ala Pro Leu Asn Pro
            100                 105                 110

Lys Ala Asn Arg Glu Lys Met Thr Gln Ile Met Phe Glu Thr Phe Asn
        115                 120                 125

Thr Pro Ala Met Tyr Val Ala Ile Gln Ala Val Leu Ser Leu Tyr Ala
    130                 135                 140

Ser Gly Arg Thr Thr Gly Ile Val Met Asp Ser Gly Asp Gly Val Thr
145                 150                 155                 160

His Thr Val Pro Ile Tyr Glu Gly Tyr Ala Leu Pro His Ala Ile Leu
                165                 170                 175

Arg Leu Asp Leu Ala Gly Arg Asp Leu Thr Asp Tyr Leu Met Lys Ile
            180                 185                 190

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

Val Arg Asp Ile Lys Glu Lys Leu Cys Tyr Val Ala Leu Asp Phe Glu
    210                 215                 220

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

Glu Leu Pro Asp Gly Gln Val Ile Thr Ile Gly Asn Glu Arg Phe Arg
                245                 250                 255
```

```
Cys Pro Glu Ala Leu Phe Gln Pro Ser Phe Leu Gly Met Glu Ser Cys
            260                 265                 270

Gly Ile His Glu Thr Thr Phe Asn Ser Ile Met Lys Cys Asp Val Asp
        275                 280                 285

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

Met Tyr Pro Gly Ile Ala Asp Arg Met Gln Lys Glu Ile Thr Ala Leu
305                 310                 315                 320

Ala Pro Ser Thr Met Lys Ile Lys Ile Ile Ala Pro Pro Glu Arg Lys
                325                 330                 335

Tyr Ser Val Trp Ile Gly Gly Ser Ile Leu Ala Ser Leu Ser Thr Phe
            340                 345                 350

Gln Gln Met Trp Ile Ser Lys Gln Glu Tyr Asp Glu Ser Gly Pro Ser
        355                 360                 365

Ile Val His Arg Lys Cys Phe
    370                 375
```

<210> 2401
<211> 651
<212> PRT
<213> Homo sapiens

<400> 2401

```
Met Ala Arg Gly Ser Ala Val Ala Trp Ala Ala Leu Gly Pro Leu Leu
1               5                   10                  15

Trp Gly Cys Ala Leu Gly Leu Gln Gly Gly Met Leu Tyr Pro Gln Glu
            20                  25                  30

Ser Pro Ser Arg Glu Cys Lys Glu Leu Asp Gly Leu Trp Ser Phe Arg
        35                  40                  45

Ala Asp Phe Ser Asp Asn Arg Arg Arg Gly Phe Glu Glu Gln Trp Tyr
    50                  55                  60

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

Ser Ser Phe Asn Asp Ile Ser Gln Asp Trp Arg Leu Arg His Phe Val
                85                  90                  95
```

```
Gly Trp Val Trp Tyr Glu Arg Glu Val Ile Leu Pro Glu Arg Trp Thr
            100                 105                 110

Gln Asp Leu Arg Thr Arg Val Val Leu Arg Ile Gly Ser Ala His Ser
        115                 120                 125

Tyr Ala Ile Val Trp Val Asn Gly Val Asp Thr Leu Glu His Glu Gly
    130                 135                 140

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

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

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

Ser Lys Tyr Pro Lys Gly Tyr Phe Val Gln Asn Thr Tyr Phe Asp Phe
        195                 200                 205

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

Thr Thr Tyr Ile Asp Asp Ile Thr Val Thr Thr Ser Val Glu Gln Asp
225                 230                 235                 240

Ser Gly Leu Val Asn Tyr Gln Ile Ser Val Lys Gly Ser Asn Leu Phe
                245                 250                 255

Lys Leu Glu Val Arg Leu Leu Asp Ala Glu Asn Lys Val Val Ala Asn
            260                 265                 270

Gly Thr Gly Thr Gln Gly Gln Leu Lys Val Pro Gly Val Ser Leu Trp
        275                 280                 285

Trp Pro Tyr Leu Met His Glu Arg Pro Ala Tyr Leu Tyr Ser Leu Glu
    290                 295                 300

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

Thr Leu Pro Val Gly Ile Arg Thr Val Ala Val Thr Lys Ser Gln Phe
                325                 330                 335
```

```
Leu Ile Asn Gly Lys Pro Phe Tyr Phe His Gly Val Asn Lys His Glu
            340                 345                 350

Asp Ala Asp Ile Arg Gly Lys Gly Phe Asp Trp Pro Leu Leu Val Lys
        355                 360                 365

Asp Phe Asn Leu Leu Arg Trp Leu Gly Ala Asn Ala Phe Arg Thr Ser
    370                 375                 380

His Tyr Pro Tyr Ala Glu Glu Val Met Gln Met Cys Asp Arg Tyr Gly
385                 390                 395                 400

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

Phe Phe Asn Asn Val Ser Leu His His His Met Gln Val Met Glu Glu
            420                 425                 430

Val Val Arg Arg Asp Lys Asn His Pro Ala Val Val Met Trp Ser Val
        435                 440                 445

Ala Asn Glu Pro Ala Ser His Leu Glu Ser Ala Gly Tyr Tyr Leu Lys
    450                 455                 460

Met Val Ile Ala His Thr Lys Ser Leu Asp Pro Ser Arg Pro Val Thr
465                 470                 475                 480

Phe Val Ser Asn Ser Asn Tyr Ala Ala Asp Lys Gly Ala Pro Tyr Val
                485                 490                 495

Asp Val Ile Cys Leu Asn Ser Tyr Tyr Ser Trp Tyr His Asp Tyr Gly
            500                 505                 510

His Leu Glu Leu Ile Gln Leu Gln Leu Ala Thr Gln Phe Glu Asn Trp
        515                 520                 525

Tyr Lys Lys Tyr Gln Lys Pro Ile Ile Gln Ser Glu Tyr Gly Ala Glu
    530                 535                 540

Thr Ile Ala Gly Phe His Gln Asp Pro Pro Leu Met Phe Thr Glu Glu
545                 550                 555                 560

Tyr Gln Lys Ser Leu Leu Glu Gln Tyr His Leu Gly Leu Asp Gln Lys
                565                 570                 575
```

```
Arg Arg Lys Tyr Val Val Gly Glu Leu Ile Trp Asn Phe Ala Asp Phe
            580                 585                 590

Met Thr Glu Gln Ser Pro Thr Arg Val Leu Gly Asn Lys Lys Gly Ile
        595                 600                 605

Phe Thr Arg Gln Arg Gln Pro Lys Ser Ala Ala Phe Leu Leu Arg Glu
    610                 615                 620

Arg Tyr Trp Lys Ile Ala Asn Glu Thr Arg Tyr Pro His Ser Val Ala
625                 630                 635                 640

Lys Ser Gln Cys Leu Glu Asn Ser Pro Phe Thr
                645                 650
```

<210> 2402
<211> 119
<212> PRT
<213> Homo sapiens

<400> 2402

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

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

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

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

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

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

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

Val Lys Trp Asp Arg Asp Met
        115
```

<210> 2403
<211> 228

<212> PRT
<213> Homo sapiens

<400> 2403

Met Ser Val Ser Glu Ile Phe Val Glu Leu Gln Gly Phe Leu Ala Ala
1 5 10 15

Glu Gln Asp Ile Arg Glu Glu Ile Arg Lys Val Val Gln Ser Leu Glu
20 25 30

Gln Thr Ala Arg Glu Ile Leu Thr Leu Leu Gln Gly Val His Gln Gly
35 40 45

Ala Gly Phe Gln Asp Ile Pro Lys Arg Cys Leu Lys Ala Arg Glu His
50 55 60

Phe Gly Thr Val Lys Thr His Leu Thr Ser Leu Lys Thr Lys Phe Pro
65 70 75 80

Ala Glu Gln Tyr Tyr Arg Phe His Glu His Trp Arg Phe Val Leu Gln
85 90 95

Arg Leu Val Phe Leu Ala Ala Phe Val Val Tyr Leu Glu Thr Glu Thr
100 105 110

Leu Val Thr Arg Glu Ala Val Thr Glu Ile Leu Gly Ile Glu Pro Asp
115 120 125

Arg Glu Lys Gly Phe His Leu Asp Val Glu Asp Tyr Leu Ser Gly Val
130 135 140

Leu Ile Leu Ala Ser Glu Leu Ser Arg Leu Ser Val Asn Ser Val Thr
145 150 155 160

Ala Gly Asp Tyr Ser Arg Pro Leu His Ile Ser Thr Phe Ile Asn Glu
165 170 175

Leu Asp Ser Gly Phe Arg Leu Leu Asn Leu Lys Asn Asp Ser Leu Arg
180 185 190

Lys Arg Tyr Asp Gly Leu Lys Tyr Asp Val Lys Lys Val Glu Glu Val
195 200 205

Val Tyr Asp Leu Ser Ile Arg Gly Phe Asn Lys Glu Thr Ala Ala Ala
210 215 220

Cys Val Glu Lys
225

<210> 2404
<211> 378
<212> PRT
<213> Homo sapiens

<400> 2404

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

Val Ile Phe Gln Val Cys Leu Cys Gln Asp Glu Val Thr Asp Asp Tyr
20 25 30

Ile Gly Asp Asn Thr Thr Val Asp Tyr Thr Leu Phe Glu Ser Leu Cys
35 40 45

Ser Lys Lys Asp Val Arg Asn Phe Lys Ala Trp Phe Leu Pro Ile Met
50 55 60

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

Leu Thr Tyr Ile Tyr Phe Lys Arg Leu Lys Thr Met Thr Asp Thr Tyr
85 90 95

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

Phe Trp Ala Tyr Ser Ala Ala Lys Ser Trp Val Phe Gly Val His Phe
115 120 125

Cys Lys Leu Ile Phe Ala Ile Tyr Lys Met Ser Phe Phe Ser Gly Met
130 135 140

Leu Leu Leu Leu Cys Ile Ser Ile Asp Arg Tyr Val Ala Ile Val Gln
145 150 155 160

Ala Val Ser Ala His Arg His Arg Ala Arg Val Leu Leu Ile Ser Lys
165 170 175

Leu Ser Cys Val Gly Ile Trp Ile Leu Ala Thr Val Leu Ser Ile Pro
180 185 190

Glu Leu Leu Tyr Ser Asp Leu Gln Arg Ser Ser Ser Glu Gln Ala Met
195 200 205

Arg Cys Ser Leu Ile Thr Glu His Val Glu Ala Phe Ile Thr Ile Gln
210 215 220

Val Ala Gln Met Val Ile Gly Phe Leu Val Pro Leu Leu Ala Met Ser
225 230 235 240

Phe Cys Tyr Leu Val Ile Ile Arg Thr Leu Leu Gln Ala Arg Asn Phe
245 250 255

Glu Arg Asn Lys Ala Ile Lys Val Ile Ile Ala Val Val Val Val Phe
260 265 270

Ile Val Phe Gln Leu Pro Tyr Asn Gly Val Val Leu Ala Gln Thr Val
275 280 285

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

Asn Ile Ala Tyr Asp Val Thr Tyr Ser Leu Ala Cys Val Arg Cys Cys
305 310 315 320

Val Asn Pro Phe Leu Tyr Ala Phe Ile Gly Val Lys Phe Arg Asn Asp
325 330 335

Leu Phe Lys Leu Phe Lys Asp Leu Gly Cys Leu Ser Gln Glu Gln Leu
340 345 350

Arg Gln Trp Ser Ser Cys Arg His Ile Arg Arg Ser Ser Met Ser Val
355 360 365

Glu Ala Glu Thr Thr Thr Thr Phe Ser Pro
370 375

<210> 2405
<211> 398
<212> PRT
<213> Homo sapiens

<400> 2405

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

Gln Pro Ala Ala His Thr Gly Ala Ala Arg Ser Cys Arg Phe Arg Gly
20 25 30

```
Arg His Tyr Lys Arg Glu Phe Arg Leu Glu Gly Glu Pro Val Ala Leu
        35                  40                  45

Arg Cys Pro Gln Val Pro Tyr Trp Leu Trp Ala Ser Val Ser Pro Arg
    50                  55                  60

Ile Asn Leu Thr Trp His Lys Asn Asp Ser Ala Arg Thr Val Pro Gly
65                  70                  75                  80

Glu Glu Glu Thr Arg Met Trp Ala Gln Asp Gly Ala Leu Trp Leu Leu
                85                  90                  95

Pro Ala Leu Gln Glu Asp Ser Gly Thr Tyr Val Cys Thr Thr Arg Asn
            100                 105                 110

Ala Ser Tyr Cys Asp Lys Met Ser Ile Glu Leu Arg Val Phe Glu Asn
        115                 120                 125

Thr Asp Ala Phe Leu Pro Phe Ile Ser Tyr Pro Gln Ile Leu Thr Leu
    130                 135                 140

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

Asp Lys Thr Asp Val Lys Ile Gln Trp Tyr Lys Asp Ser Leu Leu Leu
                165                 170                 175

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

Leu Val His Asp Val Ala Leu Glu Asp Ala Gly Tyr Tyr Arg Cys Val
        195                 200                 205

Leu Thr Phe Ala His Glu Gly Gln Gln Tyr Asn Ile Thr Arg Ser Ile
    210                 215                 220

Glu Leu Arg Ile Lys Lys Lys Lys Glu Glu Thr Ile Pro Val Ile Ile
225                 230                 235                 240

Ser Pro Leu Lys Thr Ile Ser Ala Ser Leu Gly Ser Arg Leu Thr Ile
                245                 250                 255

Pro Cys Lys Val Phe Leu Gly Thr Gly Thr Pro Leu Thr Thr Met Leu
            260                 265                 270

Trp Trp Thr Ala Asn Asp Thr His Ile Glu Ser Ala Tyr Pro Gly Gly
```

275 280 285

Arg Val Thr Glu Gly Pro Arg Gln Glu Tyr Ser Glu Asn Asn Glu Asn
290 295 300

Tyr Ile Glu Val Pro Leu Ile Phe Asp Pro Val Thr Arg Glu Asp Leu
305 310 315 320

His Met Asp Phe Lys Cys Val Val His Asn Thr Leu Ser Phe Gln Thr
325 330 335

Leu Arg Thr Thr Val Lys Glu Ala Ser Ser Thr Phe Ser Trp Gly Ile
340 345 350

Val Leu Ala Pro Leu Ser Leu Ala Phe Leu Val Leu Gly Gly Ile Trp
355 360 365

Met His Arg Arg Cys Lys His Arg Thr Gly Lys Ala Asp Gly Leu Thr
370 375 380

Val Leu Trp Pro His His Gln Asp Phe Gln Ser Tyr Pro Lys
385 390 395

<210> 2406
<211> 132
<212> PRT
<213> Homo sapiens

<400> 2406

Met Glu Phe Asp Leu Asn Gly Asn Gly Asp Ile Gly Glu Lys Arg Val
1 5 10 15

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

Pro Thr Cys Ser Ile Pro His Asp Leu Gly Gly Gly Pro Pro Thr Thr
35 40 45

Val Gly Gly Arg Arg Met Gly Met Arg Lys Trp Glu Arg Arg Glu Arg
50 55 60

Val Ser Pro Pro Ser Pro His Pro His Pro Leu Pro Pro Asp Ile Met
65 70 75 80

Ser Leu Lys Arg Met Leu Glu Lys Leu Gly Val Pro Lys Thr His Leu
85 90 95

```
Glu Leu Lys Lys Leu Ile Gly Glu Val Ser Ser Gly Ser Gly Glu Thr
            100                 105                 110

Phe Ser Tyr Pro Asp Phe Leu Arg Met Met Leu Gly Lys Arg Ser Ala
        115                 120                 125

Ile Leu Lys Met
    130
```

<210> 2407
<211> 587
<212> PRT
<213> Homo sapiens

<400> 2407

```
Met Val Thr Ala Ala Met Leu Leu Gln Cys Cys Pro Val Leu Ala Arg
1               5                   10                  15

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

Phe Gly Ile Gly Arg Cys Pro Ile Leu Ala Thr Gln Gly Pro Asn Cys
        35                  40                  45

Ser Gln Ile His Leu Lys Ala Thr Lys Ala Gly Gly Asp Ser Pro Ser
    50                  55                  60

Trp Ala Lys Gly His Cys Pro Phe Met Leu Ser Glu Leu Gln Asp Gly
65                  70                  75                  80

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

Lys Ala Phe Lys Thr Asp Leu Pro Ser Ser Leu Val Ser Val Ser Leu
            100                 105                 110

Arg Lys Pro Phe Ser Gly Pro Gln Glu Gln Glu Gln Ile Ser Gly Lys
        115                 120                 125

Val Thr His Leu Ile Gln Asn Asn Met Pro Gly Asn Tyr Val Phe Ser
    130                 135                 140

Tyr Asp Gln Phe Phe Arg Asp Lys Ile Met Glu Lys Lys Gln Asp His
145                 150                 155                 160

Thr Tyr Arg Val Phe Lys Thr Val Asn Arg Trp Ala Asp Ala Tyr Pro
```

165 170 175

Phe Ala Gln His Phe Phe Glu Ala Ser Val Ala Ser Lys Asp Val Ser
180 185 190

Val Trp Cys Ser Asn Asp Tyr Leu Gly Met Ser Arg His Pro Gln Val
195 200 205

Leu Gln Ala Thr Gln Glu Thr Leu Gln Arg His Gly Ala Gly Ala Gly
210 215 220

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

Gln Glu Leu Ala Glu Leu His Gln Lys Asp Ser Ala Leu Leu Phe Ser
245 250 255

Ser Cys Phe Val Ala Asn Asp Ser Thr Leu Phe Thr Leu Ala Lys Ile
260 265 270

Leu Pro Gly Cys Glu Ile Tyr Ser Asp Ala Gly Asn His Ala Ser Met
275 280 285

Ile Gln Gly Ile Arg Asn Ser Gly Ala Ala Lys Phe Val Phe Arg His
290 295 300

Asn Asp Pro Asp His Leu Lys Lys Leu Leu Glu Lys Ser Asn Pro Lys
305 310 315 320

Ile Pro Lys Ile Val Ala Phe Glu Thr Val His Ser Met Asp Gly Ala
325 330 335

Ile Cys Pro Leu Glu Glu Leu Cys Asp Val Ser His Gln Tyr Gly Ala
340 345 350

Leu Thr Phe Val Asp Glu Val His Ala Val Gly Leu Tyr Gly Ser Arg
355 360 365

Gly Ala Gly Ile Gly Glu Arg Asp Gly Ile Met His Lys Ile Asp Ile
370 375 380

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

Ala Ser Thr Arg Asp Leu Val Asp Met Val Arg Ser Tyr Ala Ala Gly
405 410 415

```
Phe Ile Phe Thr Thr Ser Leu Pro Pro Met Val Leu Ser Gly Ala Leu
            420                 425                 430

Glu Ser Val Arg Leu Leu Lys Gly Glu Glu Gly Gln Ala Leu Arg Arg
        435                 440                 445

Ala His Gln Arg Asn Val Lys His Met Arg Gln Leu Leu Met Asp Arg
    450                 455                 460

Gly Leu Pro Val Ile Pro Cys Pro Ser His Ile Ile Pro Ile Arg Val
465                 470                 475                 480

Gly Asn Ala Ala Leu Asn Ser Lys Leu Cys Asp Leu Leu Leu Ser Lys
                485                 490                 495

His Gly Ile Tyr Val Gln Ala Ile Asn Tyr Pro Thr Val Pro Arg Gly
            500                 505                 510

Glu Glu Leu Leu Arg Leu Ala Pro Ser Pro His His Ser Pro Gln Met
        515                 520                 525

Met Glu Asp Phe Val Glu Lys Leu Leu Leu Ala Trp Thr Ala Val Gly
    530                 535                 540

Leu Pro Leu Gln Asp Val Ser Val Ala Ala Cys Asn Phe Cys Arg Arg
545                 550                 555                 560

Pro Val His Phe Glu Leu Met Ser Glu Trp Glu Arg Ser Tyr Phe Gly
                565                 570                 575

Asn Met Gly Pro Gln Tyr Val Thr Thr Tyr Ala
            580                 585
```

<210> 2408
<211> 122
<212> PRT
<213> Homo sapiens

<400> 2408

```
Met Ser Ala Thr Trp Cys Ser Pro Glu Gly Gln Gly Met Gly Gln Gly
1               5                   10                  15

Pro Gly Arg Glu Val Gly Gly Asn Ser Ala Ala Ser Gly Pro Ala Ser
            20                  25                  30
```

```
Pro Ile Arg Asp Pro Cys Leu Ser Glu Ala Gly Leu Lys Gly Pro Pro
        35                  40                  45

Ser Ala His Pro Arg Arg Leu Cys Leu Leu His Arg Leu Val Cys Phe
    50                  55                  60

Ser Gly Gly Leu Thr Ser Ile Gln Leu Ser Pro Arg Thr Cys Cys Ser
65                  70                  75                  80

His Gln Trp Ala Gln Leu Phe Ser Pro Ala Cys Phe Pro Gln Trp Arg
                85                  90                  95

Ala Pro Gly Cys Ser Leu Asp Asp Ser Arg Ser Leu Thr Arg Ile Arg
            100                 105                 110

Pro Val His Leu Pro Gly Pro Ser Leu Asp
        115                 120
```

<210> 2409
<211> 288
<212> PRT
<213> Homo sapiens

<400> 2409

```
Met Gly His Thr Arg Arg Gln Gly Thr Ser Pro Ser Lys Cys Pro Tyr
1               5                   10                  15

Leu Asn Phe Phe Gln Leu Leu Val Leu Ala Gly Leu Ser His Phe Cys
            20                  25                  30

Ser Gly Val Ile His Val Thr Lys Glu Val Lys Glu Val Ala Thr Leu
        35                  40                  45

Ser Cys Gly His Asn Val Ser Val Glu Glu Leu Ala Gln Thr Arg Ile
    50                  55                  60

Tyr Trp Gln Lys Glu Lys Lys Met Val Leu Thr Met Met Ser Gly Asp
65                  70                  75                  80

Met Asn Ile Trp Pro Glu Tyr Lys Asn Arg Thr Ile Phe Asp Ile Thr
                85                  90                  95

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

Thr Tyr Glu Cys Val Val Leu Lys Tyr Glu Lys Asp Ala Phe Lys Arg
        115                 120                 125
```

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

Pro Ser Ile Ser Asp Phe Glu Ile Pro Thr Ser Asn Ile Arg Arg Ile
145 150 155 160

Ile Cys Ser Thr Ser Gly Gly Phe Pro Glu Pro His Leu Ser Trp Leu
165 170 175

Glu Asn Gly Glu Glu Leu Asn Ala Ile Asn Thr Thr Val Ser Gln Asp
180 185 190

Pro Glu Thr Glu Leu Tyr Ala Val Ser Ser Lys Leu Asp Phe Asn Met
195 200 205

Thr Thr Asn His Ser Phe Met Cys Leu Ile Lys Tyr Gly His Leu Arg
210 215 220

Val Asn Gln Thr Phe Asn Trp Asn Thr Thr Lys Gln Glu His Phe Pro
225 230 235 240

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

Ile Phe Val Ile Cys Cys Leu Thr Tyr Cys Phe Ala Pro Arg Cys Arg
260 265 270

Glu Arg Arg Arg Asn Glu Arg Leu Arg Arg Glu Ser Val Arg Pro Val
275 280 285

<210> 2410
<211> 588
<212> PRT
<213> Homo sapiens

<400> 2410

Met His Cys Lys Val Ser Leu Leu Asp Asp Thr Val Tyr Glu Cys Val
1 5 10 15

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

His Leu Asn Leu Leu Glu Glu Asp Tyr Phe Gly Leu Ala Ile Trp Asp
35 40 45

```
Asn Ala Thr Ser Lys Thr Trp Leu Asp Ser Ala Lys Glu Ile Lys Lys
    50                  55                  60

Gln Val Arg Gly Val Pro Trp Asn Phe Thr Phe Asn Val Lys Phe Tyr
65                  70                  75                  80

Pro Pro Asp Pro Ala Gln Leu Thr Glu Asp Ile Thr Arg Tyr Tyr Leu
                85                  90                  95

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

Phe Ala Thr Leu Ala Leu Leu Gly Ser Tyr Thr Ile Gln Ser Glu Leu
        115                 120                 125

Gly Asp Tyr Asp Pro Glu Leu His Gly Val Asp Tyr Val Ser Asp Phe
    130                 135                 140

Lys Leu Ala Pro Asn Gln Thr Lys Glu Leu Glu Glu Lys Val Met Glu
145                 150                 155                 160

Leu His Lys Ser Tyr Arg Ser Met Thr Pro Ala Gln Ala Asp Leu Glu
                165                 170                 175

Phe Leu Glu Asn Ala Lys Lys Leu Ser Met Tyr Gly Val Asp Leu His
            180                 185                 190

Lys Ala Lys Asp Leu Glu Gly Val Asp Ile Ile Leu Gly Val Cys Ser
        195                 200                 205

Ser Gly Leu Leu Val Tyr Lys Asp Lys Leu Arg Ile Asn Arg Phe Pro
    210                 215                 220

Trp Pro Lys Val Leu Lys Ile Ser Tyr Lys Arg Ser Ser Phe Phe Ile
225                 230                 235                 240

Lys Ile Arg Pro Gly Glu Gln Glu Gln Tyr Glu Ser Thr Ile Gly Phe
                245                 250                 255

Lys Leu Pro Ser Tyr Arg Ala Ala Lys Lys Leu Trp Lys Val Cys Val
            260                 265                 270

Glu His His Thr Phe Phe Arg Leu Thr Ser Thr Asp Thr Ile Pro Lys
        275                 280                 285

Ser Lys Phe Leu Ala Leu Gly Ser Lys Phe Arg Tyr Ser Gly Arg Thr
```

290 295 300

Gln Ala Gln Thr Arg Gln Ala Ser Ala Leu Ile Asp Arg Pro Ala Pro
305 310 315 320

His Phe Glu Arg Thr Ala Ser Lys Arg Ala Ser Arg Ser Leu Asp Gly
325 330 335

Ala Ala Ala Val Asp Ser Ala Asp Arg Ser Pro Arg Pro Thr Ser Ala
340 345 350

Pro Ala Ile Thr Gln Gly Gln Val Ala Glu Gly Gly Val Leu Asp Ala
355 360 365

Ser Ala Lys Lys Thr Val Val Pro Lys Ala Gln Lys Glu Thr Val Lys
370 375 380

Ala Glu Val Lys Lys Glu Asp Glu Pro Pro Glu Gln Ala Glu Pro Glu
385 390 395 400

Pro Thr Glu Ala Trp Lys Lys Lys Arg Glu Arg Leu Asp Gly Glu Asn
405 410 415

Ile Tyr Ile Arg His Ser Asn Leu Met Leu Glu Asp Leu Asp Lys Ser
420 425 430

Gln Glu Glu Ile Lys Lys His His Ala Ser Ile Ser Glu Leu Lys Lys
435 440 445

Asn Phe Met Glu Ser Val Pro Glu Pro Arg Pro Ser Glu Trp Asp Lys
450 455 460

Arg Leu Ser Thr His Ser Pro Phe Arg Thr Leu Asn Ile Asn Gly Gln
465 470 475 480

Ile Pro Thr Gly Glu Gly Pro Pro Leu Val Lys Thr Gln Thr Val Thr
485 490 495

Ile Ser Asp Asn Ala Asn Ala Val Lys Ser Glu Ile Pro Thr Lys Asp
500 505 510

Val Pro Ile Val His Thr Glu Thr Lys Thr Ile Thr Tyr Glu Ala Ala
515 520 525

Gln Thr Val Lys Gly Gly Ile Ser Glu Thr Arg Ile Glu Lys Arg Ile
530 535 540

```
Val Ile Thr Gly Asp Ala Asp Ile Asp His Asp Gln Val Leu Val Gln
545                 550                 555                 560

Ala Ile Lys Glu Ala Lys Glu Gln His Pro Asp Met Ser Val Thr Lys
                565                 570                 575

Val Val Val His Gln Glu Thr Glu Ile Ala Asp Glu
            580                 585

<210>  2411
<211>  982
<212>  PRT
<213>  Homo sapiens

<400>  2411

Met Ala Asn Ser Met Asn Gly Arg Asn Pro Gly Gly Arg Gly Gly Asn
1               5                   10                  15

Pro Arg Lys Gly Arg Ile Leu Gly Ile Ile Asp Ala Ile Gln Asp Ala
            20                  25                  30

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

Thr Trp Lys Leu Met Asp Lys Val Val Arg Leu Cys Gln Asn Pro Lys
    50                  55                  60

Leu Gln Leu Lys Asn Ser Pro Pro Tyr Ile Leu Asp Ile Leu Pro Asp
65                  70                  75                  80

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

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

Ser Leu Met Lys Lys Ser Lys Arg Ala Ile Arg Leu Phe Lys Glu Gly
        115                 120                 125

Lys Glu Arg Met Tyr Glu Glu Gln Ser Gln Asp Arg Arg Asn Leu Thr
    130                 135                 140

Lys Leu Ser Leu Ile Phe Ser His Met Leu Ala Glu Ile Lys Ala Ile
145                 150                 155                 160
```

```
Phe Pro Asn Gly Gln Phe Gln Gly Asp Asn Phe Arg Ile Thr Lys Ala
                165                 170                 175

Asp Ala Ala Glu Phe Trp Arg Lys Phe Phe Gly Asp Lys Thr Ile Val
            180                 185                 190

Pro Trp Lys Val Phe Arg Gln Cys Leu His Glu Val His Gln Ile Ser
        195                 200                 205

Ser Gly Leu Glu Ala Met Ala Leu Lys Ser Thr Ile Asp Leu Thr Cys
    210                 215                 220

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

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

His Pro Gly Tyr Met Ala Phe Leu Thr Tyr Asp Glu Val Lys Ala Arg
            260                 265                 270

Leu Gln Lys Tyr Ser Thr Lys Pro Gly Ser Tyr Ile Phe Arg Leu Ser
        275                 280                 285

Cys Thr Arg Leu Gly Gln Trp Ala Ile Gly Tyr Val Thr Gly Asp Gly
    290                 295                 300

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

Ile Asp Gly Ser Arg Glu Gly Phe Tyr Leu Tyr Pro Asp Gly Arg Ser
                325                 330                 335

Tyr Asn Pro Asp Leu Thr Gly Leu Cys Glu Pro Thr Pro His Asp His
            340                 345                 350

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

Thr Phe Gln Leu Cys Lys Ile Cys Ala Glu Asn Asp Lys Asp Val Lys
    370                 375                 380

Ile Glu Pro Cys Gly His Leu Met Cys Thr Ser Cys Leu Thr Ala Trp
385                 390                 395                 400

Gln Glu Ser Asp Gly Gln Gly Cys Pro Phe Cys Arg Cys Glu Ile Lys
```

405 410 415

Gly Thr Glu Pro Ile Ile Val Asp Pro Phe Asp Pro Arg Asp Glu Gly
420 425 430

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

Leu Asp Asp Asp Asp Asp Arg Glu Glu Ser Leu Met Met Asn Arg Leu
450 455 460

Ala Asn Val Arg Lys Cys Thr Asp Arg Gln Asn Ser Pro Val Thr Ser
465 470 475 480

Pro Gly Ser Ser Pro Leu Ala Gln Arg Arg Lys Pro Gln Pro Asp Pro
485 490 495

Leu Gln Ile Pro His Leu Ser Leu Pro Pro Val Pro Pro Arg Leu Asp
500 505 510

Leu Ile Gln Lys Gly Ile Val Arg Ser Pro Cys Gly Ser Pro Thr Gly
515 520 525

Ser Pro Lys Ser Ser Pro Cys Met Val Arg Lys Gln Asp Lys Pro Leu
530 535 540

Pro Ala Pro Pro Pro Pro Leu Arg Asp Pro Pro Pro Pro Pro Pro Glu
545 550 555 560

Arg Pro Pro Pro Ile Pro Pro Asp Asn Arg Leu Ser Arg His Ile His
565 570 575

His Val Glu Ser Val Pro Ser Lys Asp Pro Pro Met Pro Leu Glu Ala
580 585 590

Trp Cys Pro Arg Asp Val Phe Gly Thr Asn Gln Leu Val Gly Cys Arg
595 600 605

Leu Leu Gly Glu Gly Ser Pro Lys Pro Gly Ile Thr Ala Ser Ser Asn
610 615 620

Val Asn Gly Arg His Ser Arg Val Gly Ser Asp Pro Val Leu Met Arg
625 630 635 640

Lys His Arg Arg His Asp Leu Pro Leu Glu Gly Ala Lys Val Phe Ser
645 650 655

```
Asn Gly His Leu Gly Ser Glu Glu Tyr Asp Val Pro Pro Arg Leu Ser
            660                 665                 670

Pro Pro Pro Pro Val Thr Thr Leu Leu Pro Ser Ile Lys Cys Thr Gly
        675                 680                 685

Pro Leu Ala Asn Ser Leu Ser Glu Lys Thr Arg Asp Pro Val Glu Glu
    690                 695                 700

Asp Asp Asp Glu Tyr Lys Ile Pro Ser Ser His Pro Val Ser Leu Asn
705                 710                 715                 720

Ser Gln Pro Ser His Cys His Asn Val Lys Pro Pro Val Arg Ser Cys
                725                 730                 735

Asp Asn Gly His Cys Met Leu Asn Gly Thr His Gly Pro Ser Ser Glu
            740                 745                 750

Lys Lys Ser Asn Ile Pro Asp Leu Ser Ile Tyr Leu Lys Gly Asp Val
        755                 760                 765

Phe Asp Ser Ala Ser Asp Pro Val Pro Leu Pro Pro Ala Arg Pro Pro
    770                 775                 780

Thr Arg Asp Asn Pro Lys His Gly Ser Ser Leu Asn Arg Thr Pro Ser
785                 790                 795                 800

Asp Tyr Asp Leu Leu Ile Pro Pro Leu Gly Glu Asp Ala Phe Asp Ala
                805                 810                 815

Leu Pro Pro Ser Leu Pro Pro Pro Pro Pro Pro Ala Arg His Ser Leu
            820                 825                 830

Ile Glu His Ser Lys Pro Pro Gly Ser Ser Ser Arg Pro Ser Ser Gly
        835                 840                 845

Gln Asp Leu Phe Leu Leu Pro Ser Asp Pro Phe Val Asp Leu Ala Ser
    850                 855                 860

Gly Gln Val Pro Leu Pro Pro Ala Arg Arg Leu Pro Gly Glu Asn Val
865                 870                 875                 880

Lys Thr Asn Arg Thr Ser Gln Asp Tyr Asp Gln Leu Pro Ser Cys Ser
                885                 890                 895
```

Asp Gly Ser Gln Ala Pro Ala Arg Pro Pro Lys Pro Arg Pro Arg Arg
900 905 910

Thr Ala Pro Glu Ile His His Arg Lys Pro His Gly Pro Glu Ala Ala
915 920 925

Leu Glu Asn Val Asp Ala Lys Ile Ala Lys Leu Met Gly Glu Gly Tyr
930 935 940

Ala Phe Glu Glu Val Lys Arg Ala Leu Glu Ile Ala Gln Asn Asn Val
945 950 955 960

Glu Val Ala Arg Ser Ile Leu Arg Glu Phe Ala Phe Pro Pro Pro Val
965 970 975

Ser Pro Arg Leu Asn Leu
980

<210> 2412
<211> 352
<212> PRT
<213> Homo sapiens

<400> 2412

Met Asp Tyr Gln Val Ser Ser Pro Ile Tyr Asp Ile Asn Tyr Tyr Thr
1 5 10 15

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

Leu Pro Pro Leu Tyr Ser Leu Val Phe Ile Phe Gly Phe Val Gly Asn
35 40 45

Met Leu Val Ile Leu Ile Leu Ile Asn Cys Lys Arg Leu Lys Ser Met
50 55 60

Thr Asp Ile Tyr Leu Leu Asn Leu Ala Ile Ser Asp Leu Phe Phe Leu
65 70 75 80

Leu Thr Val Pro Phe Trp Ala His Tyr Ala Ala Ala Gln Trp Asp Phe
85 90 95

Gly Asn Thr Met Cys Gln Leu Leu Thr Gly Leu Tyr Phe Ile Gly Phe
100 105 110

Phe Ser Gly Ile Phe Phe Ile Ile Leu Leu Thr Ile Asp Arg Tyr Leu

```
     115                 120                 125

Ala Val Val His Ala Val Phe Ala Leu Lys Ala Arg Thr Val Thr Phe
    130                 135                 140

Gly Val Val Thr Ser Val Ile Thr Trp Val Val Ala Val Phe Ala Ser
145                 150                 155                 160

Leu Pro Gly Ile Ile Phe Thr Arg Ser Gln Lys Glu Gly Leu His Tyr
                165                 170                 175

Thr Cys Ser Ser His Phe Pro Tyr Ser Gln Tyr Gln Phe Trp Lys Asn
            180                 185                 190

Phe Gln Thr Leu Lys Ile Val Ile Leu Gly Leu Val Leu Pro Leu Leu
        195                 200                 205

Val Met Val Ile Cys Tyr Ser Gly Ile Leu Lys Thr Leu Leu Arg Cys
    210                 215                 220

Arg Asn Glu Lys Lys Arg His Arg Ala Val Arg Leu Ile Phe Thr Ile
225                 230                 235                 240

Met Ile Val Tyr Phe Leu Phe Trp Ala Pro Tyr Asn Ile Val Leu Leu
                245                 250                 255

Leu Asn Thr Phe Gln Glu Phe Phe Gly Leu Asn Asn Cys Ser Ser Ser
            260                 265                 270

Asn Arg Leu Asp Gln Ala Met Gln Val Thr Glu Thr Leu Gly Met Thr
        275                 280                 285

His Cys Cys Ile Asn Pro Ile Ile Tyr Ala Phe Val Gly Glu Lys Phe
    290                 295                 300

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

Cys Lys Cys Cys Ser Ile Phe Gln Gln Glu Ala Pro Glu Arg Ala Ser
                325                 330                 335

Ser Val Tyr Thr Arg Ser Thr Gly Glu Gln Glu Ile Ser Val Gly Leu
            340                 345                 350
```

<210> 2413
<211> 750

<212> PRT
<213> Homo sapiens

<400> 2413

Met Gly Lys Ser Glu Ser Gln Met Asp Ile Thr Asp Ile Asn Thr Pro
1 5 10 15

Lys Pro Lys Lys Lys Gln Arg Trp Thr Arg Leu Glu Ile Ser Leu Ser
20 25 30

Val Leu Val Leu Leu Leu Thr Ile Ile Ala Val Arg Met Ile Ala Leu
35 40 45

Tyr Ala Thr Tyr Asp Asp Gly Ile Cys Lys Ser Ser Asp Cys Ile Lys
50 55 60

Ser Ala Ala Arg Leu Ile Gln Asn Met Asp Ala Thr Thr Glu Pro Cys
65 70 75 80

Arg Asp Phe Phe Lys Tyr Ala Cys Gly Gly Trp Leu Lys Arg Asn Val
85 90 95

Ile Pro Glu Thr Ser Ser Arg Tyr Gly Asn Phe Asp Ile Leu Arg Asp
100 105 110

Glu Leu Glu Val Val Leu Lys Asp Val Leu Gln Glu Pro Lys Thr Glu
115 120 125

Asp Ile Val Ala Val Gln Lys Ala Lys Ala Leu Tyr Arg Ser Cys Ile
130 135 140

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

Leu Pro Asp Ile Tyr Gly Trp Pro Val Ala Thr Glu Asn Trp Glu Gln
165 170 175

Lys Tyr Gly Ala Ser Trp Thr Ala Glu Lys Ala Ile Ala Gln Leu Asn
180 185 190

Ser Lys Tyr Gly Lys Lys Val Leu Ile Asn Leu Phe Val Gly Thr Asp
195 200 205

Asp Lys Asn Ser Val Asn His Val Ile His Ile Asp Gln Pro Arg Leu
210 215 220

Gly Leu Pro Ser Arg Asp Tyr Tyr Glu Cys Thr Gly Ile Tyr Lys Glu
225 230 235 240

Ala Cys Thr Ala Tyr Val Asp Phe Met Ile Ser Val Ala Arg Leu Ile
245 250 255

Arg Gln Glu Glu Arg Leu Pro Ile Asp Glu Asn Gln Leu Ala Leu Glu
260 265 270

Met Asn Lys Val Met Glu Leu Glu Lys Glu Ile Ala Asn Ala Thr Ala
275 280 285

Lys Pro Glu Asp Arg Asn Asp Pro Met Leu Leu Tyr Asn Lys Met Arg
290 295 300

Leu Ala Gln Ile Gln Asn Asn Phe Ser Leu Glu Ile Asn Gly Lys Pro
305 310 315 320

Phe Ser Trp Leu Asn Phe Thr Asn Glu Ile Met Ser Thr Val Asn Ile
325 330 335

Ser Ile Thr Asn Glu Glu Asp Val Val Val Tyr Ala Pro Glu Tyr Leu
340 345 350

Thr Lys Leu Lys Pro Ile Leu Thr Lys Tyr Ser Ala Arg Asp Leu Gln
355 360 365

Asn Leu Met Ser Trp Arg Phe Ile Met Asp Leu Val Ser Ser Leu Ser
370 375 380

Arg Thr Tyr Lys Glu Ser Arg Asn Ala Phe Arg Lys Ala Leu Tyr Gly
385 390 395 400

Thr Thr Ser Glu Thr Ala Thr Trp Arg Arg Cys Ala Asn Tyr Val Asn
405 410 415

Gly Asn Met Glu Asn Ala Val Gly Arg Leu Tyr Val Glu Ala Ala Phe
420 425 430

Ala Gly Glu Ser Lys His Val Val Glu Asp Leu Ile Ala Gln Ile Arg
435 440 445

Glu Val Phe Ile Gln Thr Leu Asp Asp Leu Thr Trp Met Asp Ala Glu
450 455 460

Thr Lys Lys Arg Ala Glu Glu Lys Ala Leu Ala Ile Lys Glu Arg Ile

465 470 475 480

Gly Tyr Pro Asp Asp Ile Val Ser Asn Asp Asn Lys Leu Asn Asn Glu
485 490 495

Tyr Leu Glu Leu Asn Tyr Lys Glu Asp Glu Tyr Phe Glu Asn Ile Ile
500 505 510

Gln Asn Leu Lys Phe Ser Gln Ser Lys Gln Leu Lys Lys Leu Arg Glu
515 520 525

Lys Val Asp Lys Asp Glu Trp Ile Ser Gly Ala Ala Val Val Asn Ala
530 535 540

Phe Tyr Ser Ser Gly Arg Asn Gln Ile Val Phe Pro Ala Gly Ile Leu
545 550 555 560

Gln Pro Pro Phe Phe Ser Ala Gln Gln Ser Asn Ser Leu Asn Tyr Gly
565 570 575

Gly Ile Gly Met Val Ile Gly His Glu Ile Thr His Gly Phe Asp Asp
580 585 590

Asn Gly Arg Asn Phe Asn Lys Asp Gly Asp Leu Val Asp Trp Trp Thr
595 600 605

Gln Gln Ser Ala Ser Asn Phe Lys Glu Gln Ser Gln Cys Met Val Tyr
610 615 620

Gln Tyr Gly Asn Phe Ser Trp Asp Leu Ala Gly Gly Gln His Leu Asn
625 630 635 640

Gly Ile Asn Thr Leu Gly Glu Asn Ile Ala Asp Asn Gly Gly Leu Gly
645 650 655

Gln Ala Tyr Arg Ala Tyr Gln Asn Tyr Ile Lys Lys Asn Gly Glu Glu
660 665 670

Lys Leu Leu Pro Gly Leu Asp Leu Asn His Lys Gln Leu Phe Phe Leu
675 680 685

Asn Phe Ala Gln Val Trp Cys Gly Thr Tyr Arg Pro Glu Tyr Ala Val
690 695 700

Asn Ser Ile Lys Thr Asp Val His Ser Pro Gly Asn Phe Arg Ile Ile
705 710 715 720

Gly Thr Leu Gln Asn Ser Ala Glu Phe Ser Glu Ala Phe His Cys Arg
725 730 735

Lys Asn Ser Tyr Met Asn Pro Glu Lys Lys Cys Arg Val Trp
740 745 750

<210> 2414
<211> 233
<212> PRT
<213> Homo sapiens

<400> 2414

Met Asp Asn Gln Gly Val Ile Tyr Ser Asp Leu Asn Leu Pro Pro Asn
1 5 10 15

Pro Lys Arg Gln Gln Arg Lys Pro Lys Gly Asn Lys Ser Ser Ile Leu
20 25 30

Ala Thr Glu Gln Glu Ile Thr Tyr Ala Glu Leu Asn Leu Gln Lys Ala
35 40 45

Ser Gln Asp Phe Gln Gly Asn Asp Lys Thr Tyr His Cys Lys Asp Leu
50 55 60

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

Leu Ile Leu Met Ala Ser Val Val Thr Ile Val Val Ile Pro Ser Thr
85 90 95

Leu Ile Gln Arg His Asn Asn Ser Ser Leu Asn Thr Arg Thr Gln Lys
100 105 110

Ala Arg His Cys Gly His Cys Pro Glu Glu Trp Ile Thr Tyr Ser Asn
115 120 125

Ser Cys Tyr Tyr Ile Gly Lys Glu Arg Arg Thr Trp Glu Glu Ser Leu
130 135 140

Leu Ala Cys Thr Ser Lys Asn Ser Ser Leu Leu Ser Ile Asp Asn Glu
145 150 155 160

Glu Glu Met Lys Phe Leu Ser Ile Ile Ser Pro Ser Ser Trp Ile Gly
165 170 175

```
Val Phe Arg Asn Ser Ser His His Pro Trp Val Thr Met Asn Gly Leu
            180                 185                 190

Ala Phe Lys His Glu Ile Lys Asp Ser Asp Asn Ala Glu Leu Asn Cys
        195                 200                 205

Ala Val Leu Gln Val Asn Arg Leu Lys Ser Ala Gln Cys Gly Ser Ser
    210                 215                 220

Ile Ile Tyr His Cys Lys His Lys Leu
225                 230
```

<210> 2415
<211> 290
<212> PRT
<213> Homo sapiens

<400> 2415

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

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

Gln Cys Gly Ile Met Trp Gln Leu Leu Leu Pro Thr Ala Leu Leu Leu
        35                  40                  45

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

Phe Leu Glu Pro Gln Trp Tyr Arg Val Leu Glu Lys Asp Ser Val Thr
65                  70                  75                  80

Leu Lys Cys Gln Gly Ala Tyr Ser Pro Glu Asp Asn Ser Thr Gln Trp
                85                  90                  95

Phe His Asn Glu Ser Leu Ile Ser Ser Gln Ala Ser Ser Tyr Phe Ile
            100                 105                 110

Asp Ala Ala Thr Val Asp Asp Ser Gly Glu Tyr Arg Cys Gln Thr Asn
        115                 120                 125

Leu Ser Thr Leu Ser Asp Pro Val Gln Leu Glu Val His Ile Gly Trp
    130                 135                 140

Leu Leu Leu Gln Ala Pro Arg Trp Val Phe Lys Glu Glu Asp Pro Ile
145                 150                 155                 160
```

His Leu Arg Cys His Ser Trp Lys Asn Thr Ala Leu His Lys Val Thr
165 170 175

Tyr Leu Gln Asn Gly Lys Gly Arg Lys Tyr Phe His His Asn Ser Asp
180 185 190

Phe Tyr Ile Pro Lys Ala Thr Leu Lys Asp Ser Gly Ser Tyr Phe Cys
195 200 205

Arg Gly Leu Val Gly Ser Lys Asn Val Ser Ser Glu Thr Val Asn Ile
210 215 220

Thr Ile Thr Gln Gly Leu Ala Val Ser Thr Ile Ser Ser Phe Phe Pro
225 230 235 240

Pro Gly Tyr Gln Val Ser Phe Cys Leu Val Met Val Leu Leu Phe Ala
245 250 255

Val Asp Thr Gly Leu Tyr Phe Ser Val Lys Thr Asn Ile Arg Ser Ser
260 265 270

Thr Arg Asp Trp Lys Asp His Lys Phe Lys Trp Arg Lys Asp Pro Gln
275 280 285

Asp Lys
290

<210> 2416
<211> 233
<212> PRT
<213> Homo sapiens

<400> 2416

Met Trp Gln Leu Leu Leu Pro Thr Ala Leu Leu Leu Leu Val Ser Ala
1 5 10 15

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

Gln Trp Tyr Ser Val Leu Glu Lys Asp Ser Val Thr Leu Lys Cys Gln
35 40 45

Gly Ala Tyr Ser Pro Glu Asp Asn Ser Thr Gln Trp Phe His Asn Glu
50 55 60

```
Ser Leu Ile Ser Ser Gln Ala Ser Ser Tyr Phe Ile Asp Ala Ala Thr
65                  70                  75                  80

Val Asn Asp Ser Gly Glu Tyr Arg Cys Gln Thr Asn Leu Ser Thr Leu
                85                  90                  95

Ser Asp Pro Val Gln Leu Glu Val His Ile Gly Trp Leu Leu Leu Gln
            100                 105                 110

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

His Ser Trp Lys Asn Thr Ala Leu His Lys Val Thr Tyr Leu Gln Asn
    130                 135                 140

Gly Lys Asp Arg Lys Tyr Phe His His Asn Ser Asp Phe His Ile Pro
145                 150                 155                 160

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

Gly Ser Lys Asn Val Ser Ser Glu Thr Val Asn Ile Thr Ile Thr Gln
            180                 185                 190

Gly Leu Ala Val Ser Thr Ile Ser Ser Phe Ser Pro Pro Gly Tyr Gln
        195                 200                 205

Val Ser Phe Cys Leu Val Met Val Leu Leu Phe Ala Val Asp Thr Gly
    210                 215                 220

Leu Tyr Phe Ser Val Lys Thr Asn Ile
225                 230


<210>  2417
<211>  525
<212>  PRT
<213>  Homo sapiens

<400>  2417

Met Trp Glu Ala Gln Phe Leu Gly Leu Leu Phe Leu Gln Pro Leu Trp
1               5                   10                  15

Val Ala Pro Val Lys Pro Leu Gln Pro Gly Ala Glu Val Pro Val Val
            20                  25                  30

Trp Ala Gln Glu Gly Ala Pro Ala Gln Leu Pro Cys Ser Pro Thr Ile
        35                  40                  45
```

```
Pro Leu Gln Asp Leu Ser Leu Leu Arg Arg Ala Gly Val Thr Trp Gln
    50                  55                  60

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

Ala Pro Gly Pro His Pro Ala Ala Pro Ser Ser Trp Gly Pro Arg Pro
                85                  90                  95

Arg Arg Tyr Thr Val Leu Ser Val Gly Pro Gly Gly Leu Arg Ser Gly
            100                 105                 110

Arg Leu Pro Leu Gln Pro Arg Val Gln Leu Asp Glu Arg Gly Arg Gln
        115                 120                 125

Arg Gly Asp Phe Ser Leu Trp Leu Arg Pro Ala Arg Arg Ala Asp Ala
    130                 135                 140

Gly Glu Tyr Arg Ala Ala Val His Leu Arg Asp Arg Ala Leu Ser Cys
145                 150                 155                 160

Arg Leu Arg Leu Arg Leu Gly Gln Ala Ser Met Thr Ala Ser Pro Pro
                165                 170                 175

Gly Ser Leu Arg Ala Ser Asp Trp Val Ile Leu Asn Cys Ser Phe Ser
            180                 185                 190

Arg Pro Asp Arg Pro Ala Ser Val His Trp Phe Arg Asn Arg Gly Gln
        195                 200                 205

Gly Arg Val Pro Val Arg Glu Ser Pro His His His Leu Ala Glu Ser
    210                 215                 220

Phe Leu Phe Leu Pro Gln Val Ser Pro Met Asp Ser Gly Pro Trp Gly
225                 230                 235                 240

Cys Ile Leu Thr Tyr Arg Asp Gly Phe Asn Val Ser Ile Met Tyr Asn
                245                 250                 255

Leu Thr Val Leu Gly Leu Glu Pro Pro Thr Pro Leu Thr Val Tyr Ala
            260                 265                 270

Gly Ala Gly Ser Arg Val Gly Leu Pro Cys Arg Leu Pro Ala Gly Val
        275                 280                 285
```

```
Gly Thr Arg Ser Phe Leu Thr Ala Lys Trp Thr Pro Pro Gly Gly Gly
    290                 295                 300

Pro Asp Leu Leu Val Thr Gly Asp Asn Gly Asp Phe Thr Leu Arg Leu
305                 310                 315                 320

Glu Asp Val Ser Gln Ala Gln Ala Gly Thr Tyr Thr Cys His Ile His
                325                 330                 335

Leu Gln Glu Gln Gln Leu Asn Ala Thr Val Thr Leu Ala Ile Ile Thr
            340                 345                 350

Val Thr Pro Lys Ser Phe Gly Ser Pro Gly Ser Leu Gly Lys Leu Leu
        355                 360                 365

Cys Glu Val Thr Pro Val Ser Gly Gln Glu Arg Phe Val Trp Ser Ser
    370                 375                 380

Leu Asp Thr Pro Ser Gln Arg Ser Phe Ser Gly Pro Trp Leu Glu Ala
385                 390                 395                 400

Gln Glu Ala Gln Leu Leu Ser Gln Pro Trp Gln Cys Gln Leu Tyr Gln
                405                 410                 415

Gly Glu Arg Leu Leu Gly Ala Ala Val Tyr Phe Thr Glu Leu Ser Ser
            420                 425                 430

Pro Gly Ala Gln Arg Ser Gly Arg Ala Pro Gly Ala Leu Pro Ala Gly
        435                 440                 445

His Leu Leu Leu Phe Leu Thr Leu Gly Val Leu Ser Leu Leu Leu Leu
    450                 455                 460

Val Thr Gly Ala Phe Gly Phe His Leu Trp Arg Arg Gln Trp Arg Pro
465                 470                 475                 480

Arg Arg Phe Ser Ala Leu Glu Gln Gly Ile His Pro Pro Gln Ala Gln
                485                 490                 495

Ser Lys Ile Glu Glu Leu Glu Gln Glu Pro Glu Pro Glu Pro Glu Pro
            500                 505                 510

Glu Pro Glu Pro Glu Pro Glu Pro Glu Pro Glu Gln Leu
        515                 520                 525
```

<210> 2418
<211> 738
<212> PRT
<213> Homo sapiens

<400> 2418

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

Leu Thr Leu Leu Leu Cys Ser Ser Leu Glu Gly Gln Glu Asn Ser Phe
20 25 30

Thr Ile Asn Ser Val Asp Met Lys Ser Leu Pro Asp Trp Thr Val Gln
35 40 45

Asn Gly Lys Asn Leu Thr Leu Gln Cys Phe Ala Asp Val Ser Thr Thr
50 55 60

Ser His Val Lys Pro Gln His Gln Met Leu Phe Tyr Lys Asp Asp Val
65 70 75 80

Leu Phe Tyr Asn Ile Ser Ser Met Lys Ser Thr Glu Ser Tyr Phe Ile
85 90 95

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

Val Asn Asn Lys Glu Lys Thr Thr Ala Glu Tyr Gln Val Leu Val Glu
115 120 125

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

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

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

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

Phe Pro Val Glu Glu Gln Asp Arg Val Leu Ser Phe Arg Cys Gln Ala
195 200 205

Arg Ile Ile Ser Gly Ile His Met Gln Thr Ser Glu Ser Thr Lys Ser
210 215 220

```
Glu Leu Val Thr Val Thr Glu Ser Phe Ser Thr Pro Lys Phe His Ile
225                 230                 235                 240

Ser Pro Thr Gly Met Ile Met Glu Gly Ala Gln Leu His Ile Lys Cys
                245                 250                 255

Thr Ile Gln Val Thr His Leu Ala Gln Glu Phe Pro Glu Ile Ile Ile
            260                 265                 270

Gln Lys Asp Lys Ala Ile Val Ala His Asn Arg His Gly Asn Lys Ala
        275                 280                 285

Val Tyr Ser Val Met Ala Met Val Glu His Ser Gly Asn Tyr Thr Cys
    290                 295                 300

Lys Val Glu Ser Ser Arg Ile Ser Lys Val Ser Ser Ile Val Val Asn
305                 310                 315                 320

Ile Thr Glu Leu Phe Ser Lys Pro Glu Leu Glu Ser Ser Phe Thr His
                325                 330                 335

Leu Asp Gln Gly Glu Arg Leu Asn Leu Ser Cys Ser Ile Pro Gly Ala
            340                 345                 350

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

Thr Gln Asp Phe Thr Lys Ile Ala Ser Lys Ser Asp Ser Gly Thr Tyr
    370                 375                 380

Ile Cys Thr Ala Gly Ile Asp Lys Val Val Lys Lys Ser Asn Thr Val
385                 390                 395                 400

Gln Ile Val Val Cys Glu Met Leu Ser Gln Pro Arg Ile Ser Tyr Asp
                405                 410                 415

Ala Gln Phe Glu Val Ile Lys Gly Gln Thr Ile Glu Val Arg Cys Glu
            420                 425                 430

Ser Ile Ser Gly Thr Leu Pro Ile Ser Tyr Gln Leu Leu Lys Thr Ser
        435                 440                 445

Lys Val Leu Glu Asn Ser Thr Lys Asn Ser Asn Asp Pro Ala Val Phe
    450                 455                 460
```

Lys Asp Asn Pro Thr Glu Asp Val Glu Tyr Gln Cys Val Ala Asp Asn
465 470 475 480

Cys His Ser His Ala Lys Met Leu Ser Glu Val Leu Arg Val Lys Val
485 490 495

Ile Ala Pro Val Asp Glu Val Gln Ile Ser Ile Leu Ser Ser Lys Val
500 505 510

Val Glu Ser Gly Glu Asp Ile Val Leu Gln Cys Ala Val Asn Glu Gly
515 520 525

Ser Gly Pro Ile Thr Tyr Lys Phe Tyr Arg Glu Lys Glu Gly Lys Pro
530 535 540

Phe Tyr Gln Met Thr Ser Asn Ala Thr Gln Ala Phe Trp Thr Lys Gln
545 550 555 560

Lys Ala Asn Lys Glu Gln Glu Gly Glu Tyr Tyr Cys Thr Ala Phe Asn
565 570 575

Arg Ala Asn His Ala Ser Ser Val Pro Arg Ser Lys Ile Leu Thr Val
580 585 590

Arg Val Ile Leu Ala Pro Trp Lys Lys Gly Leu Ile Ala Val Val Ile
595 600 605

Ile Gly Val Ile Ile Ala Leu Leu Ile Ile Ala Ala Lys Cys Tyr Phe
610 615 620

Leu Arg Lys Ala Lys Ala Lys Gln Met Pro Val Glu Met Ser Arg Pro
625 630 635 640

Ala Val Pro Leu Leu Asn Ser Asn Asn Glu Lys Met Ser Asp Pro Asn
645 650 655

Met Glu Ala Asn Ser His Tyr Gly His Asn Asp Asp Val Gly Asn His
660 665 670

Ala Met Lys Pro Ile Asn Asp Asn Lys Glu Pro Leu Asn Ser Asp Val
675 680 685

Gln Tyr Thr Glu Val Gln Val Ser Ser Ala Glu Ser His Lys Asp Leu
690 695 700

```
Gly Lys Lys Asp Thr Glu Thr Val Tyr Ser Glu Val Arg Lys Ala Val
705                 710                 715                 720

Pro Asp Ala Val Glu Ser Arg Tyr Ser Arg Thr Glu Gly Ser Leu Asp
                725                 730                 735

Gly Thr
```

<210> 2419
<211> 328
<212> PRT
<213> Homo sapiens

<400> 2419

```
Met Leu Val Arg Arg Gly Ala Arg Ala Gly Pro Arg Met Pro Arg Gly
1               5                   10                  15

Trp Thr Ala Leu Cys Leu Leu Ser Leu Leu Pro Ser Gly Phe Met Ser
            20                  25                  30

Leu Asp Asn Asn Gly Thr Ala Thr Pro Glu Leu Pro Thr Gln Gly Thr
        35                  40                  45

Phe Ser Asn Val Ser Thr Asn Val Ser Tyr Gln Glu Thr Thr Thr Pro
    50                  55                  60

Ser Thr Leu Gly Ser Thr Ser Leu His Pro Val Ser Gln His Gly Asn
65                  70                  75                  80

Glu Ala Thr Thr Asn Ile Thr Glu Thr Thr Val Lys Phe Thr Ser Thr
                85                  90                  95

Ser Val Ile Thr Ser Val Tyr Gly Asn Thr Asn Ser Ser Val Gln Ser
            100                 105                 110

Gln Thr Ser Val Ile Ser Thr Val Phe Thr Thr Pro Ala Asn Val Ser
        115                 120                 125

Thr Pro Glu Thr Thr Leu Lys Pro Ser Leu Ser Pro Gly Asn Val Ser
    130                 135                 140

Asp Leu Ser Thr Thr Ser Thr Ser Leu Ala Thr Ser Pro Thr Lys Pro
145                 150                 155                 160

Tyr Thr Ser Ser Ser Pro Ile Leu Ser Asp Ile Lys Ala Glu Ile Lys
                165                 170                 175
```

Cys Ser Gly Ile Arg Glu Val Lys Leu Thr Gln Gly Ile Cys Leu Glu
180 185 190

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

Gly Leu Ala Arg Val Leu Cys Gly Glu Glu Gln Ala Asp Ala Asp Ala
210 215 220

Gly Ala Gln Val Cys Ser Leu Leu Leu Ala Gln Ser Glu Val Arg Pro
225 230 235 240

Gln Cys Leu Leu Leu Val Leu Ala Asn Arg Thr Glu Ile Ser Ser Lys
245 250 255

Leu Gln Leu Met Lys Lys His Gln Ser Asp Leu Lys Lys Leu Gly Ile
260 265 270

Leu Asp Phe Thr Glu Gln Asp Val Ala Ser His Gln Ser Tyr Ser Gln
275 280 285

Lys Thr Leu Ile Ala Leu Val Thr Ser Gly Ala Leu Leu Ala Val Leu
290 295 300

Gly Ile Thr Gly Tyr Phe Leu Met Asn Arg Arg Ser Trp Ser Pro Thr
305 310 315 320

Gly Glu Arg Leu Glu Leu Glu Pro
325

<210> 2420
<211> 374
<212> PRT
<213> Homo sapiens

<400> 2420

Met Trp Phe Leu Thr Thr Leu Leu Leu Trp Val Pro Val Asp Gly Gln
1 5 10 15

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

Val Phe Gln Glu Glu Thr Val Thr Leu His Cys Glu Val Leu His Leu
35 40 45

Pro Gly Ser Ser Ser Thr Gln Trp Phe Leu Asn Gly Thr Ala Thr Gln
50 55 60

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

Gly Glu Tyr Arg Cys Gln Arg Gly Leu Ser Gly Arg Ser Asp Pro Ile
85 90 95

Gln Leu Glu Ile His Arg Gly Trp Leu Leu Leu Gln Val Ser Ser Arg
100 105 110

Val Phe Thr Glu Gly Glu Pro Leu Ala Leu Arg Cys His Ala Trp Lys
115 120 125

Asp Lys Leu Val Tyr Asn Val Leu Tyr Tyr Arg Asn Gly Lys Ala Phe
130 135 140

Lys Phe Phe His Trp Asn Ser Asn Leu Thr Ile Leu Lys Thr Asn Ile
145 150 155 160

Ser His Asn Gly Thr Tyr His Cys Ser Gly Met Gly Lys His Arg Tyr
165 170 175

Thr Ser Ala Gly Ile Ser Val Thr Val Lys Glu Leu Phe Pro Ala Pro
180 185 190

Val Leu Asn Ala Ser Val Thr Ser Pro Leu Leu Glu Gly Asn Leu Val
195 200 205

Thr Leu Ser Cys Glu Thr Lys Leu Leu Leu Gln Arg Pro Gly Leu Gln
210 215 220

Leu Tyr Phe Ser Phe Tyr Met Gly Ser Lys Thr Leu Arg Gly Arg Asn
225 230 235 240

Thr Ser Ser Glu Tyr Gln Ile Leu Thr Ala Arg Arg Glu Asp Ser Gly
245 250 255

Leu Tyr Trp Cys Glu Ala Ala Thr Glu Asp Gly Asn Val Leu Lys Arg
260 265 270

Ser Pro Glu Leu Glu Leu Gln Val Leu Gly Leu Gln Leu Pro Thr Pro
275 280 285

Val Trp Phe His Val Leu Phe Tyr Leu Ala Val Gly Ile Met Phe Leu

290 295 300

Val Asn Thr Val Leu Trp Val Thr Ile Arg Lys Glu Leu Lys Arg Lys
305 310 315 320

Lys Lys Trp Asp Leu Glu Ile Ser Leu Asp Ser Gly His Glu Lys Lys
325 330 335

Val Ile Ser Ser Leu Gln Glu Asp Arg His Leu Glu Glu Glu Leu Lys
340 345 350

Cys Gln Glu Gln Lys Glu Glu Gln Leu Gln Glu Gly Val His Arg Lys
355 360 365

Glu Pro Gln Gly Ala Thr
370

<210> 2421
<211> 760
<212> PRT
<213> Homo sapiens

<400> 2421

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

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

Asn Ser His Val Glu Met Lys Leu Ala Val Asp Glu Glu Glu Asn Ala
35 40 45

Asp Asn Asn Thr Lys Ala Asn Val Thr Lys Pro Lys Arg Cys Ser Gly
50 55 60

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

Phe Met Ile Gly Tyr Leu Gly Tyr Cys Lys Gly Val Glu Pro Lys Thr
85 90 95

Glu Cys Glu Arg Leu Ala Gly Thr Glu Ser Pro Val Arg Glu Glu Pro
100 105 110

Gly Glu Asp Phe Pro Ala Ala Arg Arg Leu Tyr Trp Asp Asp Leu Lys
115 120 125

Arg Lys Leu Ser Glu Lys Leu Asp Ser Thr Asp Phe Thr Ser Thr Ile
130 135 140

Lys Leu Leu Asn Glu Asn Ser Tyr Val Pro Arg Glu Ala Gly Ser Gln
145 150 155 160

Lys Asp Glu Asn Leu Ala Leu Tyr Val Glu Asn Gln Phe Arg Glu Phe
165 170 175

Lys Leu Ser Lys Val Trp Arg Asp Gln His Phe Val Lys Ile Gln Val
180 185 190

Lys Asp Ser Ala Gln Asn Ser Val Ile Ile Val Asp Lys Asn Gly Arg
195 200 205

Leu Val Tyr Leu Val Glu Asn Pro Gly Gly Tyr Val Ala Tyr Ser Lys
210 215 220

Ala Ala Thr Val Thr Gly Lys Leu Val His Ala Asn Phe Gly Thr Lys
225 230 235 240

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

Val Arg Ala Gly Lys Ile Thr Phe Ala Glu Lys Val Ala Asn Ala Glu
260 265 270

Ser Leu Asn Ala Ile Gly Val Leu Ile Tyr Met Asp Gln Thr Lys Phe
275 280 285

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

Thr Gly Asp Pro Tyr Thr Pro Gly Phe Pro Ser Phe Asn His Thr Gln
305 310 315 320

Phe Pro Pro Ser Arg Ser Ser Gly Leu Pro Asn Ile Pro Val Gln Thr
325 330 335

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

Cys Pro Ser Asp Trp Lys Thr Asp Ser Thr Cys Arg Met Val Thr Ser
355 360 365

Glu Ser Lys Asn Val Lys Leu Thr Val Ser Asn Val Leu Lys Glu Ile
370 375 380

Lys Ile Leu Asn Ile Phe Gly Val Ile Lys Gly Phe Val Glu Pro Asp
385 390 395 400

His Tyr Val Val Val Gly Ala Gln Arg Asp Ala Trp Gly Pro Gly Ala
405 410 415

Ala Lys Ser Gly Val Gly Thr Ala Leu Leu Leu Lys Leu Ala Gln Met
420 425 430

Phe Ser Asp Met Val Leu Lys Asp Gly Phe Gln Pro Ser Arg Ser Ile
435 440 445

Ile Phe Ala Ser Trp Ser Ala Gly Asp Phe Gly Ser Val Gly Ala Thr
450 455 460

Glu Trp Leu Glu Gly Tyr Leu Ser Ser Leu His Leu Lys Ala Phe Thr
465 470 475 480

Tyr Ile Asn Leu Asp Lys Ala Val Leu Gly Thr Ser Asn Phe Lys Val
485 490 495

Ser Ala Ser Pro Leu Leu Tyr Thr Leu Ile Glu Lys Thr Met Gln Asn
500 505 510

Val Lys His Pro Val Thr Gly Gln Phe Leu Tyr Gln Asp Ser Asn Trp
515 520 525

Ala Ser Lys Val Glu Lys Leu Thr Leu Asp Asn Ala Ala Phe Pro Phe
530 535 540

Leu Ala Tyr Ser Gly Ile Pro Ala Val Ser Phe Cys Phe Cys Glu Asp
545 550 555 560

Thr Asp Tyr Pro Tyr Leu Gly Thr Thr Met Asp Thr Tyr Lys Glu Leu
565 570 575

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

Val Ala Gly Gln Phe Val Ile Lys Leu Thr His Asp Val Glu Leu Asn
595 600 605

Leu Asp Tyr Glu Arg Tyr Asn Ser Gln Leu Leu Ser Phe Val Arg Asp

610 615 620

Leu Asn Gln Tyr Arg Ala Asp Ile Lys Glu Met Gly Leu Ser Leu Gln
625 630 635 640

Trp Leu Tyr Ser Ala Arg Gly Asp Phe Phe Arg Ala Thr Ser Arg Leu
645 650 655

Thr Thr Asp Phe Gly Asn Ala Glu Lys Thr Asp Arg Phe Val Met Lys
660 665 670

Lys Leu Asn Asp Arg Val Met Arg Val Glu Tyr His Phe Leu Ser Pro
675 680 685

Tyr Val Ser Pro Lys Glu Ser Pro Phe Arg His Val Phe Trp Gly Ser
690 695 700

Gly Ser His Thr Leu Pro Ala Leu Leu Glu Asn Leu Lys Leu Arg Lys
705 710 715 720

Gln Asn Asn Gly Ala Phe Asn Glu Thr Leu Phe Arg Asn Gln Leu Ala
725 730 735

Leu Ala Thr Trp Thr Ile Gln Gly Ala Ala Asn Ala Leu Ser Gly Asp
740 745 750

Val Trp Asp Ile Asp Asn Glu Phe
755 760

<210> 2422
<211> 247
<212> PRT
<213> Homo sapiens

<400> 2422

Met Leu Leu Leu Pro Leu Pro Leu Leu Leu Phe Leu Leu Cys Ser Arg
1 5 10 15

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

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

Lys Phe Cys Gly Gly Phe Leu Ile Arg Arg Asn Phe Val Leu Thr Ala
50 55 60

```
Ala His Cys Ala Gly Arg Ser Ile Thr Val Thr Leu Gly Ala His Asn
65                  70                  75                  80

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

Phe Arg His Pro Lys Tyr Asn Thr Ser Thr Leu His His Asp Ile Met
            100                 105                 110

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

Leu Pro Phe Pro Ser Gln Phe Asn Phe Val Pro Pro Gly Arg Met Cys
    130                 135                 140

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

Thr Leu Gln Glu Val Lys Leu Arg Leu Met Asp Pro Gln Ala Cys Ser
                165                 170                 175

His Phe Arg Asp Phe Asp His Asn Leu Gln Leu Cys Val Gly Asn Pro
            180                 185                 190

Arg Lys Thr Lys Ser Ala Phe Lys Gly Asp Ser Gly Gly Pro Leu Leu
        195                 200                 205

Cys Ala Gly Val Ala Gln Gly Ile Val Ser Tyr Gly Arg Ser Asp Ala
    210                 215                 220

Lys Pro Pro Ala Val Phe Thr Arg Ile Ser His Tyr Arg Pro Trp Ile
225                 230                 235                 240

Asn Gln Ile Leu Gln Ala Asn
                245
```

<210> 2423
<211> 976
<212> PRT
<213> Homo sapiens

<400> 2423

```
Met Arg Gly Ala Arg Gly Ala Trp Asp Phe Leu Cys Val Leu Leu Leu
1               5                   10                  15

Leu Leu Arg Val Gln Thr Gly Ser Ser Gln Pro Ser Val Ser Pro Gly
```

```
            20                  25                  30

Glu Pro Ser Pro Pro Ser Ile His Pro Gly Lys Ser Asp Leu Ile Val
        35                  40                  45

Arg Val Gly Asp Glu Ile Arg Leu Leu Cys Thr Asp Pro Gly Phe Val
    50                  55                  60

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

Glu Trp Ile Thr Glu Lys Ala Glu Ala Thr Asn Thr Gly Lys Tyr Thr
                85                  90                  95

Cys Thr Asn Lys His Gly Leu Ser Asn Ser Ile Tyr Val Phe Val Arg
            100                 105                 110

Asp Pro Ala Lys Leu Phe Leu Val Asp Arg Ser Leu Tyr Gly Lys Glu
        115                 120                 125

Asp Asn Asp Thr Leu Val Arg Cys Pro Leu Thr Asp Pro Glu Val Thr
    130                 135                 140

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

Arg Phe Ile Pro Asp Pro Lys Ala Gly Ile Met Ile Lys Ser Val Lys
                165                 170                 175

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

Lys Ser Val Leu Ser Glu Lys Phe Ile Leu Lys Val Arg Pro Ala Phe
        195                 200                 205

Lys Ala Val Pro Val Val Ser Val Ser Lys Ala Ser Tyr Leu Leu Arg
    210                 215                 220

Glu Gly Glu Glu Phe Thr Val Thr Cys Thr Ile Lys Asp Val Ser Ser
225                 230                 235                 240

Ser Val Tyr Ser Thr Trp Lys Arg Glu Asn Ser Gln Thr Lys Leu Gln
                245                 250                 255

Glu Lys Tyr Asn Ser Trp His His Gly Asp Phe Asn Tyr Glu Arg Gln
            260                 265                 270
```

```
Ala Thr Leu Thr Ile Ser Ser Ala Arg Val Asn Asp Ser Gly Val Phe
        275                 280                 285

Met Cys Tyr Ala Asn Asn Thr Phe Gly Ser Ala Asn Val Thr Thr Thr
    290                 295                 300

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

Thr Thr Val Phe Val Asn Asp Gly Glu Asn Val Asp Leu Ile Val Glu
                325                 330                 335

Tyr Glu Ala Phe Pro Lys Pro Glu His Gln Gln Trp Ile Tyr Met Asn
            340                 345                 350

Arg Thr Phe Thr Asp Lys Trp Glu Asp Tyr Pro Lys Ser Glu Asn Glu
        355                 360                 365

Ser Asn Ile Arg Tyr Val Ser Glu Leu His Leu Thr Arg Leu Lys Gly
    370                 375                 380

Thr Glu Gly Gly Thr Tyr Thr Phe Leu Val Ser Asn Ser Asp Val Asn
385                 390                 395                 400

Ala Ala Ile Ala Phe Asn Val Tyr Val Asn Thr Lys Pro Glu Ile Leu
                405                 410                 415

Thr Tyr Asp Arg Leu Val Asn Gly Met Leu Gln Cys Val Ala Ala Gly
            420                 425                 430

Phe Pro Glu Pro Thr Ile Asp Trp Tyr Phe Cys Pro Gly Thr Glu Gln
        435                 440                 445

Arg Cys Ser Ala Ser Val Leu Pro Val Asp Val Gln Thr Leu Asn Ser
    450                 455                 460

Ser Gly Pro Pro Phe Gly Lys Leu Val Val Gln Ser Ser Ile Asp Ser
465                 470                 475                 480

Ser Ala Phe Lys His Asn Gly Thr Val Glu Cys Lys Ala Tyr Asn Asp
                485                 490                 495

Val Gly Lys Thr Ser Ala Tyr Phe Asn Phe Ala Phe Lys Gly Asn Asn
            500                 505                 510
```

```
Lys Glu Gln Ile His Pro His Thr Leu Phe Thr Pro Leu Leu Ile Gly
        515                 520                 525

Phe Val Ile Val Ala Gly Met Met Cys Ile Ile Val Met Ile Leu Thr
    530                 535                 540

Tyr Lys Tyr Leu Gln Lys Pro Met Tyr Glu Val Gln Trp Lys Val Val
545                 550                 555                 560

Glu Glu Ile Asn Gly Asn Asn Tyr Val Tyr Ile Asp Pro Thr Gln Leu
                565                 570                 575

Pro Tyr Asp His Lys Trp Glu Phe Pro Arg Asn Arg Leu Ser Phe Gly
            580                 585                 590

Lys Thr Leu Gly Ala Gly Ala Phe Gly Lys Val Val Glu Ala Thr Ala
        595                 600                 605

Tyr Gly Leu Ile Lys Ser Asp Ala Ala Met Thr Val Ala Val Lys Met
    610                 615                 620

Leu Lys Pro Ser Ala His Leu Thr Glu Arg Glu Ala Leu Met Ser Glu
625                 630                 635                 640

Leu Lys Val Leu Ser Tyr Leu Gly Asn His Met Asn Ile Val Asn Leu
                645                 650                 655

Leu Gly Ala Cys Thr Ile Gly Gly Pro Thr Leu Val Ile Thr Glu Tyr
            660                 665                 670

Cys Cys Tyr Gly Asp Leu Leu Asn Phe Leu Arg Arg Lys Arg Asp Ser
        675                 680                 685

Phe Ile Cys Ser Lys Gln Glu Asp His Ala Glu Ala Ala Leu Tyr Lys
    690                 695                 700

Asn Leu Leu His Ser Lys Glu Ser Ser Cys Ser Asp Ser Thr Asn Glu
705                 710                 715                 720

Tyr Met Asp Met Lys Pro Gly Val Ser Tyr Val Val Pro Thr Lys Ala
                725                 730                 735

Asp Lys Arg Arg Ser Val Arg Ile Gly Ser Tyr Ile Glu Arg Asp Val
            740                 745                 750
```

```
Thr Pro Ala Ile Met Glu Asp Asp Glu Leu Ala Leu Asp Leu Glu Asp
        755                 760                 765

Leu Leu Ser Phe Ser Tyr Gln Val Ala Lys Gly Met Ala Phe Leu Ala
    770                 775                 780

Ser Lys Asn Cys Ile His Arg Asp Leu Ala Ala Arg Asn Ile Leu Leu
785                 790                 795                 800

Thr His Gly Arg Ile Thr Lys Ile Cys Asp Phe Gly Leu Ala Arg Asp
                805                 810                 815

Ile Lys Asn Asp Ser Asn Tyr Val Val Lys Gly Asn Ala Arg Leu Pro
            820                 825                 830

Val Lys Trp Met Ala Pro Glu Ser Ile Phe Asn Cys Val Tyr Thr Phe
        835                 840                 845

Glu Ser Asp Val Trp Ser Tyr Gly Ile Phe Leu Trp Glu Leu Phe Ser
    850                 855                 860

Leu Gly Ser Ser Pro Tyr Pro Gly Met Pro Val Asp Ser Lys Phe Tyr
865                 870                 875                 880

Lys Met Ile Lys Glu Gly Phe Arg Met Leu Ser Pro Glu His Ala Pro
                885                 890                 895

Ala Glu Met Tyr Asp Ile Met Lys Thr Cys Trp Asp Ala Asp Pro Leu
            900                 905                 910

Lys Arg Pro Thr Phe Lys Gln Ile Val Gln Leu Ile Glu Lys Gln Ile
        915                 920                 925

Ser Glu Ser Thr Asn His Ile Tyr Ser Asn Leu Ala Asn Cys Ser Pro
    930                 935                 940

Asn Arg Gln Lys Pro Val Val Asp His Ser Val Arg Ile Asn Ser Val
945                 950                 955                 960

Gly Ser Thr Ala Ser Ser Ser Gln Pro Leu Leu Val His Asp Asp Val
                965                 970                 975
```

<210> 2424
<211> 635
<212> PRT
<213> Homo sapiens

<400> 2424

```
Met Pro Ser Trp Ala Leu Phe Met Val Thr Ser Cys Leu Leu Leu Ala
1               5                  10                  15

Pro Gln Asn Leu Ala Gln Val Ser Ser Gln Asp Val Ser Leu Leu Ala
            20                  25                  30

Ser Asp Ser Glu Pro Leu Lys Cys Phe Ser Arg Thr Phe Glu Asp Leu
        35                  40                  45

Thr Cys Phe Trp Asp Glu Glu Glu Ala Ala Pro Ser Gly Thr Tyr Gln
    50                  55                  60

Leu Leu Tyr Ala Tyr Pro Arg Glu Lys Pro Arg Ala Cys Pro Leu Ser
65                  70                  75                  80

Ser Gln Ser Met Pro His Phe Gly Thr Arg Tyr Val Cys Gln Phe Pro
                85                  90                  95

Asp Gln Glu Glu Val Arg Leu Phe Phe Pro Leu His Leu Trp Val Lys
            100                 105                 110

Asn Val Phe Leu Asn Gln Thr Arg Thr Gln Arg Val Leu Phe Val Asp
        115                 120                 125

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

Ser Gln Pro Gly Glu Leu Gln Ile Ser Trp Glu Glu Pro Ala Pro Glu
145                 150                 155                 160

Ile Ser Asp Phe Leu Arg Tyr Glu Leu Arg Tyr Gly Pro Arg Asp Pro
                165                 170                 175

Lys Asn Ser Thr Gly Pro Thr Val Ile Gln Leu Ile Ala Thr Glu Thr
            180                 185                 190

Cys Cys Pro Ala Leu Gln Arg Pro His Ser Ala Ser Ala Leu Asp Gln
        195                 200                 205

Ser Pro Cys Ala Gln Pro Thr Met Pro Trp Gln Asp Gly Pro Lys Gln
    210                 215                 220

Thr Ser Pro Ser Arg Glu Ala Ser Ala Leu Thr Ala Glu Gly Gly Ser
225                 230                 235                 240
```

```
Cys Leu Ile Ser Gly Leu Gln Pro Gly Asn Ser Tyr Trp Leu Gln Leu
                245                 250                 255

Arg Ser Glu Pro Asp Gly Ile Ser Leu Gly Gly Ser Trp Gly Ser Trp
            260                 265                 270

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

Leu Gln Cys Phe Thr Leu Asp Leu Lys Asn Val Thr Cys Gln Trp Gln
    290                 295                 300

Gln Gln Asp His Ala Ser Ser Gln Gly Phe Phe Tyr His Ser Arg Ala
305                 310                 315                 320

Arg Cys Cys Pro Arg Asp Arg Tyr Pro Ile Trp Glu Asn Cys Glu Glu
                325                 330                 335

Glu Glu Lys Thr Asn Pro Gly Leu Gln Thr Pro Gln Phe Ser Arg Cys
            340                 345                 350

His Phe Lys Ser Arg Asn Asp Ser Ile Ile His Ile Leu Val Glu Val
        355                 360                 365

Thr Thr Ala Pro Gly Thr Val His Ser Tyr Leu Gly Ser Pro Phe Trp
    370                 375                 380

Ile His Gln Ala Val Arg Leu Pro Thr Pro Asn Leu His Trp Arg Glu
385                 390                 395                 400

Ile Ser Ser Gly His Leu Glu Leu Glu Trp Gln His Pro Ser Ser Trp
                405                 410                 415

Ala Ala Gln Glu Thr Cys Tyr Gln Leu Arg Tyr Thr Gly Glu Gly His
            420                 425                 430

Gln Asp Trp Lys Val Leu Glu Pro Pro Leu Gly Ala Arg Gly Gly Thr
        435                 440                 445

Leu Glu Leu Arg Pro Arg Ser Arg Tyr Arg Leu Gln Leu Arg Ala Arg
    450                 455                 460

Leu Asn Gly Pro Thr Tyr Gln Gly Pro Trp Ser Ser Trp Ser Asp Pro
465                 470                 475                 480
```

```
Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Ile Ser Leu Val Thr
                485                 490                 495

Ala Leu His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu
            500                 505                 510

Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu
        515                 520                 525

Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg
    530                 535                 540

Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys
545                 550                 555                 560

Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu
                565                 570                 575

Arg Thr Pro Leu Pro Leu Cys Ser Ser Gln Ala Gln Met Asp Tyr Arg
            580                 585                 590

Arg Leu Gln Pro Ser Cys Leu Gly Thr Met Pro Leu Ser Val Cys Pro
        595                 600                 605

Pro Met Ala Glu Ser Gly Ser Cys Cys Thr Thr His Ile Ala Asn His
    610                 615                 620

Ser Tyr Leu Pro Leu Ser Tyr Trp Gln Gln Pro
625                 630                 635
```

<210> 2425
<211> 1006
<212> PRT
<213> Homo sapiens

<400> 2425

```
Met Val Cys Ser Leu Trp Val Leu Leu Leu Val Ser Ser Val Leu Ala
1               5                   10                  15

Leu Glu Glu Val Leu Leu Asp Thr Thr Gly Glu Thr Ser Glu Ile Gly
            20                  25                  30

Trp Leu Thr Tyr Pro Pro Gly Gly Trp Asp Glu Val Ser Val Leu Asp
        35                  40                  45

Asp Gln Arg Arg Leu Thr Arg Thr Phe Glu Ala Cys His Val Ala Gly
    50                  55                  60
```

```
Ala Pro Pro Gly Thr Gly Gln Asp Asn Trp Leu Gln Thr His Phe Val
65                  70                  75                  80

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

Arg Ala Cys Ser Ser Leu Gly Val Ser Gly Gly Thr Cys Arg Glu Thr
            100                 105                 110

Phe Thr Leu Tyr Tyr Arg Gln Ala Glu Glu Pro Asp Ser Pro Asp Ser
        115                 120                 125

Val Ser Ser Trp His Leu Lys Arg Trp Thr Lys Val Asp Thr Ile Ala
    130                 135                 140

Ala Asp Glu Ser Phe Pro Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser
145                 150                 155                 160

Ser Ala Ala Trp Ala Val Gly Pro His Gly Ala Gly Gln Arg Ala Gly
                165                 170                 175

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

Gly Phe Tyr Val Ala Phe Gln Asp Thr Gly Ala Cys Leu Ala Leu Val
        195                 200                 205

Ala Val Arg Leu Phe Ser Tyr Thr Cys Pro Ala Val Leu Arg Ser Phe
    210                 215                 220

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

Val Ala Ala Val Gly Thr Cys Val Ala His Ala Glu Pro Glu Glu Asp
                245                 250                 255

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

Gly Glu Gly Lys Trp Met Val Ala Val Gly Gly Cys Arg Cys Gln Pro
        275                 280                 285

Gly Tyr Gln Pro Ala Arg Gly Asp Lys Ala Cys Gln Ala Cys Pro Arg
    290                 295                 300
```

Gly Leu Tyr Lys Ser Ser Ala Gly Asn Ala Pro Cys Ser Pro Cys Pro
305 310 315 320

Ala Arg Ser His Ala Pro Asn Pro Ala Ala Pro Val Cys Pro Cys Leu
325 330 335

Glu Gly Phe Tyr Arg Ala Ser Ser Asp Pro Pro Glu Ala Pro Cys Thr
340 345 350

Gly Pro Pro Ser Ala Pro Gln Glu Leu Trp Phe Glu Val Gln Gly Ser
355 360 365

Ala Leu Met Leu His Trp Arg Leu Pro Arg Glu Leu Gly Gly Arg Gly
370 375 380

Asp Leu Leu Phe Asn Val Val Cys Lys Glu Cys Glu Gly Arg Gln Glu
385 390 395 400

Pro Ala Ser Gly Gly Gly Gly Thr Cys His Arg Cys Arg Asp Glu Val
405 410 415

His Phe Asp Pro Arg Gln Arg Gly Leu Thr Glu Ser Arg Val Leu Val
420 425 430

Gly Gly Leu Arg Ala His Val Pro Tyr Ile Leu Glu Val Gln Ala Val
435 440 445

Asn Gly Val Ser Glu Leu Ser Pro Asp Pro Pro Gln Ala Ala Ala Ile
450 455 460

Asn Val Ser Thr Ser His Glu Val Pro Ser Ala Val Pro Val Val His
465 470 475 480

Gln Val Ser Arg Ala Ser Asn Ser Ile Thr Val Ser Trp Pro Gln Pro
485 490 495

Asp Gln Thr Asn Gly Asn Ile Leu Asp Tyr Gln Leu Arg Tyr Tyr Asp
500 505 510

Gln Ala Glu Asp Glu Ser His Ser Phe Thr Leu Thr Ser Glu Thr Asn
515 520 525

Thr Ala Thr Val Thr Gln Leu Ser Pro Gly His Ile Tyr Gly Phe Gln
530 535 540

Val Arg Ala Arg Thr Ala Ala Gly His Gly Pro Tyr Gly Gly Lys Val
545 550 555 560

Tyr Phe Gln Thr Leu Pro Gln Gly Glu Leu Ser Ser Gln Leu Pro Glu
565 570 575

Arg Leu Ser Leu Val Ile Gly Ser Ile Leu Gly Ala Leu Ala Phe Leu
580 585 590

Leu Leu Ala Ala Ile Thr Val Leu Ala Val Val Phe Gln Arg Lys Arg
595 600 605

Arg Gly Thr Gly Tyr Thr Glu Gln Leu Gln Gln Tyr Ser Ser Pro Gly
610 615 620

Leu Gly Val Lys Tyr Tyr Ile Asp Pro Ser Thr Tyr Glu Asp Pro Cys
625 630 635 640

Gln Ala Ile Arg Glu Leu Ala Arg Glu Val Asp Pro Ala Tyr Ile Lys
645 650 655

Ile Glu Glu Val Ile Gly Thr Gly Ser Phe Gly Glu Val Arg Gln Gly
660 665 670

Arg Leu Gln Pro Arg Gly Arg Arg Glu Gln Thr Val Ala Ile Gln Ala
675 680 685

Leu Trp Ala Gly Gly Ala Glu Ser Leu Gln Met Thr Phe Leu Gly Arg
690 695 700

Ala Ala Val Leu Gly Gln Phe Gln His Pro Asn Ile Leu Arg Leu Glu
705 710 715 720

Gly Val Val Thr Lys Ser Arg Pro Leu Met Val Leu Thr Glu Phe Met
725 730 735

Glu Leu Gly Pro Leu Asp Ser Phe Leu Arg Gln Arg Glu Gly Gln Phe
740 745 750

Ser Ser Leu Gln Leu Val Ala Met Gln Arg Gly Val Ala Ala Ala Met
755 760 765

Gln Tyr Leu Ser Ser Phe Ala Phe Val His Arg Ser Leu Ser Ala His
770 775 780

Ser Val Leu Val Asn Ser His Leu Val Cys Lys Val Ala Arg Leu Gly

785 790 795 800

His Ser Pro Gln Gly Pro Ser Cys Leu Leu Arg Trp Ala Ala Pro Glu
805 810 815

Val Ile Ala His Gly Lys His Thr Thr Ser Ser Asp Val Trp Ser Phe
820 825 830

Gly Ile Leu Met Trp Glu Val Met Ser Tyr Gly Glu Arg Pro Tyr Trp
835 840 845

Asp Met Ser Glu Gln Glu Val Leu Asn Ala Ile Glu Gln Glu Phe Arg
850 855 860

Leu Pro Pro Pro Pro Gly Cys Pro Pro Gly Leu His Leu Leu Met Leu
865 870 875 880

Asp Thr Trp Gln Lys Asp Arg Ala Arg Arg Pro His Phe Asp Gln Leu
885 890 895

Val Ala Ala Phe Asp Lys Met Ile Arg Lys Pro Asp Thr Leu Gln Ala
900 905 910

Gly Gly Asp Pro Gly Glu Arg Pro Ser Gln Ala Leu Leu Thr Pro Val
915 920 925

Ala Leu Asp Phe Pro Cys Leu Asp Ser Pro Gln Ala Trp Leu Ser Ala
930 935 940

Ile Gly Leu Glu Cys Tyr Gln Asp Asn Phe Ser Lys Phe Gly Leu Cys
945 950 955 960

Thr Phe Ser Asp Val Ala Gln Leu Ser Leu Glu Asp Leu Pro Ala Leu
965 970 975

Gly Ile Thr Leu Ala Gly His Gln Lys Lys Leu Leu His His Ile Gln
980 985 990

Leu Leu Gln Gln His Leu Arg Gln Gln Gly Ser Val Glu Val
995 1000 1005

<210> 2426
<211> 508
<212> PRT
<213> Homo sapiens

<400> 2426

```
Met Asp His Leu Gly Ala Ser Leu Trp Pro Gln Val Gly Ser Leu Cys
1               5                  10                  15

Leu Leu Leu Ala Gly Ala Ala Trp Ala Pro Pro Pro Asn Leu Pro Asp
            20                  25                  30

Pro Lys Phe Glu Ser Lys Ala Ala Leu Leu Ala Ala Arg Gly Pro Glu
        35                  40                  45

Glu Leu Leu Cys Phe Thr Glu Arg Leu Glu Asp Leu Val Cys Phe Trp
    50                  55                  60

Glu Glu Ala Ala Ser Ala Gly Val Gly Pro Gly Asn Tyr Ser Phe Ser
65                  70                  75                  80

Tyr Gln Leu Glu Asp Glu Pro Trp Lys Leu Cys Arg Leu His Gln Ala
                85                  90                  95

Pro Thr Ala Arg Gly Ala Val Arg Phe Trp Cys Ser Leu Pro Thr Ala
            100                 105                 110

Asp Thr Ser Ser Phe Val Pro Leu Glu Leu Arg Val Thr Ala Ala Ser
        115                 120                 125

Gly Ala Pro Arg Tyr His Arg Val Ile His Ile Asn Glu Val Val Leu
    130                 135                 140

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

His Val Val Leu Arg Trp Leu Pro Pro Pro Glu Thr Pro Met Thr Ser
                165                 170                 175

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

Val Gln Arg Val Glu Ile Leu Glu Gly Arg Thr Glu Cys Val Leu Ser
        195                 200                 205

Asn Leu Arg Gly Arg Thr Arg Tyr Thr Phe Ala Val Arg Ala Arg Met
    210                 215                 220

Ala Glu Pro Ser Phe Gly Gly Phe Trp Ser Ala Trp Ser Glu Pro Val
225                 230                 235                 240
```

Ser Leu Leu Thr Pro Ser Asp Leu Asp Pro Leu Ile Leu Thr Leu Ser
245 250 255

Leu Ile Leu Val Val Ile Leu Val Leu Leu Thr Val Leu Ala Leu Leu
260 265 270

Ser His Arg Arg Ala Leu Lys Gln Lys Ile Trp Pro Gly Ile Pro Ser
275 280 285

Pro Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe
290 295 300

Gln Leu Trp Leu Tyr Gln Asn Asp Gly Cys Leu Trp Trp Ser Pro Cys
305 310 315 320

Thr Pro Phe Thr Glu Asp Pro Pro Ala Ser Leu Glu Val Leu Ser Glu
325 330 335

Arg Cys Trp Gly Thr Met Gln Ala Val Glu Pro Gly Thr Asp Asp Glu
340 345 350

Gly Pro Leu Leu Glu Pro Val Gly Ser Glu His Ala Gln Asp Thr Tyr
355 360 365

Leu Val Leu Asp Lys Trp Leu Leu Pro Arg Asn Pro Pro Ser Glu Asp
370 375 380

Leu Pro Gly Pro Gly Gly Ser Val Asp Ile Val Ala Met Asp Glu Gly
385 390 395 400

Ser Glu Ala Ser Ser Cys Ser Ser Ala Leu Ala Ser Lys Pro Ser Pro
405 410 415

Glu Gly Ala Ser Ala Ala Ser Phe Glu Tyr Thr Ile Leu Asp Pro Ser
420 425 430

Ser Gln Leu Leu Arg Pro Trp Thr Leu Cys Pro Glu Leu Pro Pro Thr
435 440 445

Pro Pro His Leu Lys Tyr Leu Tyr Leu Val Val Ser Asp Ser Gly Ile
450 455 460

Ser Thr Asp Tyr Ser Ser Gly Asp Ser Gln Gly Ala Gln Gly Gly Leu
465 470 475 480

Ser Asp Gly Pro Tyr Ser Asn Pro Tyr Glu Asn Ser Leu Ile Pro Ala

485 490 495

Ala Glu Pro Leu Pro Pro Ser Tyr Val Ala Cys Ser
500 505

<210> 2427
<211> 441
<212> PRT
<213> Homo sapiens

<400> 2427

Met Ser Pro Ile Ser Gly Ala Ser Pro Ser Trp Arg Ala Ala Pro Lys
1 5 10 15

Ala Ser Asp Leu Leu Gly Ala Arg Gly Pro Gly Gly Thr Phe Gln Gly
20 25 30

Arg Asp Leu Arg Gly Gly Ala His Ala Ser Ser Ser Ser Leu Asn Pro
35 40 45

Met Pro Pro Ser Gln Leu Gln Leu Ser Thr Val Asp Ala His Ala Arg
50 55 60

Thr Pro Val Leu Gln Val His Pro Leu Glu Ser Pro Ala Met Ile Ser
65 70 75 80

Leu Thr Pro Pro Thr Thr Ala Thr Gly Val Phe Ser Leu Lys Ala Arg
85 90 95

Pro Gly Leu Pro Pro Gly Ile Asn Val Ala Ser Leu Glu Trp Val Ser
100 105 110

Arg Glu Pro Ala Leu Leu Cys Thr Phe Pro Asn Pro Ser Ala Pro Arg
115 120 125

Lys Asp Ser Thr Leu Ser Ala Val Pro Gln Ser Ser Tyr Pro Leu Leu
130 135 140

Ala Asn Gly Val Cys Lys Trp Pro Gly Cys Glu Lys Val Phe Glu Glu
145 150 155 160

Pro Glu Asp Phe Leu Lys His Cys Gln Ala Asp His Leu Leu Asp Glu
165 170 175

Lys Gly Arg Ala Gln Cys Leu Leu Gln Arg Glu Met Val Gln Ser Leu
180 185 190

Glu Gln Gln Leu Val Leu Glu Lys Glu Lys Leu Ser Ala Met Gln Ala
195 200 205

His Leu Ala Gly Lys Met Ala Leu Thr Lys Ala Ser Ser Val Ala Ser
210 215 220

Ser Asp Lys Gly Ser Cys Cys Ile Val Ala Ala Gly Ser Gln Gly Pro
225 230 235 240

Val Val Pro Ala Trp Ser Gly Pro Arg Glu Ala Pro Asp Ser Leu Phe
245 250 255

Ala Val Arg Arg His Leu Trp Gly Ser His Gly Asn Ser Thr Phe Pro
260 265 270

Glu Phe Leu His Asn Met Asp Tyr Phe Lys Phe His Asn Met Arg Pro
275 280 285

Pro Phe Thr Tyr Ala Thr Leu Ile Arg Trp Ala Ile Leu Glu Ala Pro
290 295 300

Glu Lys Gln Arg Thr Leu Asn Glu Ile Tyr His Trp Phe Thr Arg Met
305 310 315 320

Phe Ala Phe Phe Arg Asn His Pro Ala Thr Trp Lys Val Ser Ser Ser
325 330 335

Glu Val Ala Val Thr Gly Met Ala Ser Ser Ala Ile Ala Ala Gln Ser
340 345 350

Gly Gln Ala Trp Val Trp Ala His Arg His Ile Gly Glu Glu Arg Asp
355 360 365

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

Leu Pro Val Pro Gly Leu Pro Gln Asn Ala Ile Arg His Asn Leu Ser
385 390 395 400

Leu His Lys Cys Phe Val Arg Val Glu Ser Glu Lys Gly Ala Val Trp
405 410 415

Thr Val Asp Glu Leu Glu Phe Arg Lys Lys Arg Ser Gln Arg Pro Ser
420 425 430

Arg Cys Ser Asn Pro Thr Pro Gly Pro
435 440

<210> 2428
<211> 413
<212> PRT
<213> Homo sapiens

<400> 2428

Met Glu Phe Pro Gly Leu Gly Ser Leu Gly Thr Ser Glu Pro Leu Pro
1 5 10 15

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

Phe Phe Pro Ser Gly Pro Glu Gly Leu Asp Ala Ala Ala Ser Ser Thr
35 40 45

Ala Pro Ser Thr Ala Thr Ala Ala Ala Ala Ala Leu Ala Tyr Tyr Arg
50 55 60

Asp Ala Glu Ala Tyr Arg His Ser Pro Val Phe Gln Val Tyr Pro Leu
65 70 75 80

Leu Asn Cys Met Glu Gly Ile Pro Gly Gly Ser Pro Tyr Ala Gly Trp
85 90 95

Ala Tyr Gly Lys Thr Gly Leu Tyr Pro Ala Ser Thr Val Cys Pro Thr
100 105 110

Arg Glu Asp Ser Pro Pro Gln Ala Val Glu Asp Leu Asp Gly Lys Gly
115 120 125

Ser Thr Ser Phe Leu Glu Thr Leu Lys Thr Glu Arg Leu Ser Pro Asp
130 135 140

Leu Leu Thr Leu Gly Pro Ala Leu Pro Ser Ser Leu Pro Val Pro Asn
145 150 155 160

Ser Ala Tyr Gly Gly Pro Asp Phe Ser Ser Thr Phe Phe Ser Pro Thr
165 170 175

Gly Ser Pro Leu Asn Ser Ala Ala Tyr Ser Ser Pro Lys Leu Arg Gly
180 185 190

Thr Leu Pro Leu Pro Pro Cys Glu Ala Arg Glu Cys Val Asn Cys Gly
195 200 205

```
Ala Thr Ala Thr Pro Leu Trp Arg Arg Asp Arg Thr Gly His Tyr Leu
    210                 215                 220

Cys Asn Ala Cys Gly Leu Tyr His Lys Met Asn Gly Gln Asn Arg Pro
225                 230                 235                 240

Leu Ile Arg Pro Lys Lys Arg Leu Ile Val Ser Lys Arg Ala Gly Thr
                245                 250                 255

Gln Cys Thr Asn Cys Gln Thr Thr Thr Thr Thr Leu Trp Arg Arg Asn
            260                 265                 270

Ala Ser Gly Asp Pro Val Cys Asn Ala Cys Gly Leu Tyr Tyr Lys Leu
        275                 280                 285

His Gln Val Asn Arg Pro Leu Thr Met Arg Lys Asp Gly Ile Gln Thr
    290                 295                 300

Arg Asn Arg Lys Ala Ser Gly Lys Gly Lys Lys Lys Arg Gly Ser Ser
305                 310                 315                 320

Leu Gly Gly Thr Gly Ala Ala Glu Gly Pro Ala Gly Gly Phe Met Val
                325                 330                 335

Val Ala Gly Gly Ser Gly Ser Gly Asn Cys Gly Glu Val Ala Ser Gly
            340                 345                 350

Leu Thr Leu Gly Pro Pro Gly Thr Ala His Leu Tyr Gln Gly Leu Gly
        355                 360                 365

Pro Val Val Leu Ser Gly Pro Val Ser His Leu Met Pro Phe Pro Gly
    370                 375                 380

Pro Leu Leu Gly Ser Pro Thr Gly Ser Phe Pro Thr Gly Pro Met Pro
385                 390                 395                 400

Pro Thr Thr Ser Thr Thr Val Val Ala Pro Leu Ser Ser
                405                 410
```

<210> 2429
<211> 1039
<212> PRT
<213> Homo sapiens

<400> 2429

```
Met Ala Arg Ala Leu Cys Pro Leu Gln Ala Leu Trp Leu Leu Glu Trp
1               5                  10                  15

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

Asn Leu Asp Pro Val Gln Leu Thr Phe Tyr Ala Gly Pro Asn Gly Ser
        35                  40                  45

Gln Phe Gly Phe Ser Leu Asp Phe His Lys Asp Ser His Gly Arg Val
    50                  55                  60

Ala Ile Val Val Gly Ala Pro Arg Thr Leu Gly Pro Ser Gln Glu Glu
65                  70                  75                  80

Thr Gly Gly Val Phe Leu Cys Pro Trp Arg Ala Glu Gly Gly Gln Cys
                85                  90                  95

Pro Ser Leu Leu Phe Asp Leu Arg Asp Glu Thr Arg Asn Val Gly Ser
            100                 105                 110

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

Val Ser Trp Ser Asp Val Ile Val Ala Cys Ala Pro Trp Gln His Trp
    130                 135                 140

Asn Val Leu Glu Lys Thr Glu Glu Ala Glu Lys Thr Pro Val Gly Ser
145                 150                 155                 160

Cys Phe Leu Ala Gln Pro Glu Ser Gly Arg Arg Ala Glu Tyr Ser Pro
                165                 170                 175

Cys Arg Gly Asn Thr Leu Ser Arg Ile Tyr Val Glu Asn Asp Phe Ser
            180                 185                 190

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

Ala Gly Glu Leu Val Leu Gly Ala Pro Gly Gly Tyr Tyr Phe Leu Gly
    210                 215                 220

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

Gly Ile Leu Leu Trp His Val Ser Ser Gln Ser Leu Ser Phe Asp Ser
```

245 250 255

Ser Asn Pro Glu Tyr Phe Asp Gly Tyr Trp Gly Tyr Ser Val Ala Val
260 265 270

Gly Glu Phe Asp Gly Asp Leu Asn Thr Thr Glu Tyr Val Val Gly Ala
275 280 285

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

Tyr Gln Arg Leu His Arg Leu Arg Ala Glu Gln Met Ala Ser Tyr Phe
305 310 315 320

Gly His Ser Val Ala Val Thr Asp Val Asn Gly Asp Gly Arg His Asp
325 330 335

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

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

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

Gly Arg Phe Gly Ser Ala Ile Ala Pro Leu Gly Asp Leu Asp Arg Asp
385 390 395 400

Gly Tyr Asn Asp Ile Ala Val Ala Ala Pro Tyr Gly Gly Pro Ser Gly
405 410 415

Arg Gly Gln Val Leu Val Phe Leu Gly Gln Ser Glu Gly Leu Arg Ser
420 425 430

Arg Pro Ser Gln Val Leu Asp Ser Pro Phe Pro Thr Gly Ser Ala Phe
435 440 445

Gly Phe Ser Leu Arg Gly Ala Val Asp Ile Asp Asp Asn Gly Tyr Pro
450 455 460

Asp Leu Ile Val Gly Ala Tyr Gly Ala Asn Gln Val Ala Val Tyr Arg
465 470 475 480

Ala Gln Pro Val Val Lys Ala Ser Val Gln Leu Leu Val Gln Asp Ser
485 490 495

```
Leu Asn Pro Ala Val Lys Ser Cys Val Leu Pro Gln Thr Lys Thr Pro
            500                 505                 510

Val Ser Cys Phe Asn Ile Gln Met Cys Val Gly Ala Thr Gly His Asn
        515                 520                 525

Ile Pro Gln Lys Leu Ser Leu Asn Ala Glu Leu Gln Leu Asp Arg Gln
    530                 535                 540

Lys Pro Arg Gln Gly Arg Arg Val Leu Leu Leu Gly Ser Gln Gln Ala
545                 550                 555                 560

Gly Thr Thr Leu Asn Leu Asp Leu Gly Gly Lys His Ser Pro Ile Cys
                565                 570                 575

His Thr Thr Met Ala Phe Leu Arg Asp Glu Ala Asp Phe Arg Asp Lys
            580                 585                 590

Leu Ser Pro Ile Val Leu Ser Leu Asn Val Ser Leu Pro Pro Thr Glu
        595                 600                 605

Ala Gly Met Ala Pro Ala Val Val Leu His Gly Asp Thr His Val Gln
    610                 615                 620

Glu Gln Thr Arg Ile Val Leu Asp Ser Gly Glu Asp Asp Val Cys Val
625                 630                 635                 640

Pro Gln Leu Gln Leu Thr Ala Ser Val Thr Gly Ser Pro Leu Leu Val
                645                 650                 655

Gly Ala Asp Asn Val Leu Glu Leu Gln Met Asp Ala Ala Asn Glu Gly
            660                 665                 670

Glu Gly Ala Tyr Glu Ala Glu Leu Ala Val His Leu Pro Gln Gly Ala
        675                 680                 685

His Tyr Met Arg Ala Leu Ser Asn Val Glu Gly Phe Glu Arg Leu Ile
    690                 695                 700

Cys Asn Gln Lys Lys Glu Asn Glu Thr Arg Val Val Leu Cys Glu Leu
705                 710                 715                 720

Gly Asn Pro Met Lys Lys Asn Ala Gln Ile Gly Ile Ala Met Leu Val
                725                 730                 735
```

Ser Val Gly Asn Leu Glu Glu Ala Gly Glu Ser Val Ser Phe Gln Leu
740 745 750

Gln Ile Arg Ser Lys Asn Ser Gln Asn Pro Asn Ser Lys Ile Val Leu
755 760 765

Leu Asp Val Pro Val Arg Ala Glu Ala Gln Val Glu Leu Arg Gly Asn
770 775 780

Ser Phe Pro Ala Ser Leu Val Val Ala Ala Glu Glu Gly Glu Arg Glu
785 790 795 800

Gln Asn Ser Leu Asp Ser Trp Gly Pro Lys Val Glu His Thr Tyr Glu
805 810 815

Leu His Asn Asn Gly Pro Gly Thr Val Asn Gly Leu His Leu Ser Ile
820 825 830

His Leu Pro Gly Gln Ser Gln Pro Ser Asp Leu Leu Tyr Ile Leu Asp
835 840 845

Ile Gln Pro Gln Gly Gly Leu Gln Cys Phe Pro Gln Pro Pro Val Asn
850 855 860

Pro Leu Lys Val Asp Trp Gly Leu Pro Ile Pro Ser Pro Ser Pro Ile
865 870 875 880

His Pro Ala His His Lys Arg Asp Arg Arg Gln Ile Phe Leu Pro Glu
885 890 895

Pro Glu Gln Pro Ser Arg Leu Gln Asp Pro Val Leu Val Ser Cys Asp
900 905 910

Ser Ala Pro Cys Thr Val Val Gln Cys Asp Leu Gln Glu Met Ala Arg
915 920 925

Gly Gln Arg Ala Met Val Thr Val Leu Ala Phe Leu Trp Leu Pro Ser
930 935 940

Leu Tyr Gln Arg Pro Leu Asp Gln Phe Val Leu Gln Ser His Ala Trp
945 950 955 960

Phe Asn Val Ser Ser Leu Pro Tyr Ala Val Pro Pro Leu Ser Leu Pro
965 970 975

```
Arg Gly Glu Ala Gln Val Trp Thr Gln Leu Leu Arg Ala Leu Glu Glu
            980                 985                 990

Arg Ala Ile Pro Ile Trp Trp Val  Leu Val Gly Val Leu  Gly Gly Leu
        995                 1000                1005

Leu Leu  Leu Thr Ile Leu Val  Leu Ala Met Trp Lys  Val Gly Phe
    1010                1015                1020

Phe Lys  Arg Asn Arg Pro Pro  Leu Glu Glu Asp Asp  Glu Glu Gly
    1025                1030                1035

Glu
```

<210> 2430
<211> 145
<212> PRT
<213> Homo sapiens

<400> 2430

```
Met Ala Thr Trp Ala Leu Leu Leu Leu Ala Ala Met Leu Leu Gly Asn
1               5                   10                  15

Pro Gly Leu Val Phe Ser Arg Leu Ser Pro Glu Tyr Tyr Asp Leu Ala
            20                  25                  30

Arg Ala His Leu Arg Asp Glu Glu Lys Ser Cys Pro Cys Leu Ala Gln
        35                  40                  45

Glu Gly Pro Gln Gly Asp Leu Leu Thr Lys Thr Gln Glu Leu Gly Arg
    50                  55                  60

Asp Tyr Arg Thr Cys Leu Thr Ile Val Gln Lys Leu Lys Lys Met Val
65                  70                  75                  80

Asp Lys Pro Thr Gln Arg Ser Val Ser Asn Ala Ala Thr Arg Val Cys
                85                  90                  95

Arg Thr Gly Arg Ser Arg Trp Arg Asp Val Cys Arg Asn Phe Met Arg
            100                 105                 110

Arg Tyr Gln Ser Arg Val Thr Gln Gly Leu Val Ala Gly Glu Thr Ala
        115                 120                 125

Gln Gln Ile Cys Glu Asp Leu Arg Leu Cys Ile Pro Ser Thr Gly Pro
    130                 135                 140
```

Leu
145

<210> 2431
<211> 262
<212> PRT
<213> Homo sapiens

<400> 2431

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

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

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

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

Leu Thr Ala Ala His Cys Asn Leu Asn Lys Arg Ser Gln Val Ile Leu
65 70 75 80

Gly Ala His Ser Ile Thr Arg Glu Glu Pro Thr Lys Gln Ile Met Leu
85 90 95

Val Lys Lys Glu Phe Pro Tyr Pro Cys Tyr Asp Pro Ala Thr Arg Glu
100 105 110

Gly Asp Leu Lys Leu Leu Gln Leu Thr Glu Lys Ala Lys Ile Asn Lys
115 120 125

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

Gly Thr Met Cys Gln Val Ala Gly Trp Gly Arg Thr His Asn Ser Ala
145 150 155 160

Ser Trp Ser Asp Thr Leu Arg Glu Val Asn Ile Thr Ile Ile Asp Arg
165 170 175

Lys Val Cys Asn Asp Arg Asn His Tyr Asn Phe Asn Pro Val Ile Gly
180 185 190

Met Asn Met Val Cys Ala Gly Ser Leu Arg Gly Gly Arg Asp Ser Cys
195 200 205

Asn Gly Asp Ser Gly Ser Pro Leu Leu Cys Glu Gly Val Phe Arg Gly
210 215 220

Val Thr Ser Phe Gly Leu Glu Asn Lys Cys Gly Asp Pro Arg Gly Pro
225 230 235 240

Gly Val Tyr Ile Leu Leu Ser Lys Lys His Leu Asn Trp Ile Ile Met
245 250 255

Thr Ile Lys Gly Ala Val
260

<210> 2432
<211> 142
<212> PRT
<213> Homo sapiens

<400> 2432

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

Lys Val Gly Ala His Ala Gly Glu Tyr Gly Ala Glu Ala Leu Glu Arg
20 25 30

Met Phe Leu Ser Phe Pro Thr Thr Lys Thr Tyr Phe Pro His Phe Asp
35 40 45

Leu Ser His Gly Ser Ala Gln Val Lys Gly His Gly Lys Lys Val Ala
50 55 60

Asp Ala Leu Thr Asn Ala Val Ala His Val Asp Asp Met Pro Asn Ala
65 70 75 80

Leu Ser Ala Leu Ser Asp Leu His Ala His Lys Leu Arg Val Asp Pro
85 90 95

Val Asn Phe Lys Leu Leu Ser His Cys Leu Leu Val Thr Leu Ala Ala
100 105 110

His Leu Pro Ala Glu Phe Thr Pro Ala Val His Ala Ser Leu Asp Lys
115 120 125

Phe Leu Ala Ser Val Ser Thr Val Leu Thr Ser Lys Tyr Arg
130 135 140

<210> 2433
<211> 142
<212> PRT
<213> Homo sapiens

<400> 2433

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

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

Leu Phe Leu Ser His Pro Gln Thr Lys Thr Tyr Phe Pro His Phe Asp
35 40 45

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

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

Leu Ser Lys Leu Ser Glu Leu His Ala Tyr Ile Leu Arg Val Asp Pro
85 90 95

Val Asn Phe Lys Leu Leu Ser His Cys Leu Leu Val Thr Leu Ala Ala
100 105 110

Arg Phe Pro Ala Asp Phe Thr Ala Glu Ala His Ala Ala Trp Asp Lys
115 120 125

Phe Leu Ser Val Val Ser Ser Val Leu Thr Glu Lys Tyr Arg
130 135 140

<210> 2434
<211> 147
<212> PRT
<213> Homo sapiens

<400> 2434

Met Val His Leu Thr Pro Glu Glu Lys Thr Ala Val Asn Ala Leu Trp
1 5 10 15

Gly Lys Val Asn Val Asp Ala Val Gly Gly Glu Ala Leu Gly Arg Leu
20 25 30

Leu Val Val Tyr Pro Trp Thr Gln Arg Phe Phe Glu Ser Phe Gly Asp

```
        35                  40                  45

Leu Ser Ser Pro Asp Ala Val Met Gly Asn Pro Lys Val Lys Ala His
    50                  55                  60

Gly Lys Lys Val Leu Gly Ala Phe Ser Asp Gly Leu Ala His Leu Asp
65                  70                  75                  80

Asn Leu Lys Gly Thr Phe Ser Gln Leu Ser Glu Leu His Cys Asp Lys
                85                  90                  95

Leu His Val Asp Pro Glu Asn Phe Arg Leu Leu Gly Asn Val Leu Val
            100                 105                 110

Cys Val Leu Ala Arg Asn Phe Gly Lys Glu Phe Thr Pro Gln Met Gln
        115                 120                 125

Ala Ala Tyr Gln Lys Val Val Ala Gly Val Ala Asn Ala Leu Ala His
    130                 135                 140

Lys Tyr His
145
```

<210> 2435
<211> 147
<212> PRT
<213> Homo sapiens

<400> 2435

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

Ser Lys Met Asn Val Glu Glu Ala Gly Gly Glu Ala Leu Gly Arg Leu
            20                  25                  30

Leu Val Val Tyr Pro Trp Thr Gln Arg Phe Phe Asp Ser Phe Gly Asn
        35                  40                  45

Leu Ser Ser Pro Ser Ala Ile Leu Gly Asn Pro Lys Val Lys Ala His
    50                  55                  60

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

Asn Leu Lys Pro Ala Phe Ala Lys Leu Ser Glu Leu His Cys Asp Lys
                85                  90                  95
```

Leu His Val Asp Pro Glu Asn Phe Lys Leu Leu Gly Asn Val Met Val
100 105 110

Ile Ile Leu Ala Thr His Phe Gly Lys Glu Phe Thr Pro Glu Val Gln
115 120 125

Ala Ala Trp Gln Lys Leu Val Ser Ala Val Ala Ile Ala Leu Ala His
130 135 140

Lys Tyr His
145

<210> 2436
<211> 147
<212> PRT
<213> Homo sapiens

<400> 2436

Met Gly His Phe Thr Glu Glu Asp Lys Ala Thr Ile Thr Ser Leu Trp
1 5 10 15

Gly Lys Val Asn Val Glu Asp Ala Gly Gly Glu Thr Leu Gly Arg Leu
20 25 30

Leu Val Val Tyr Pro Trp Thr Gln Arg Phe Phe Asp Ser Phe Gly Asn
35 40 45

Leu Ser Ser Ala Ser Ala Ile Met Gly Asn Pro Lys Val Lys Ala His
50 55 60

Gly Lys Lys Val Leu Thr Ser Leu Gly Asp Ala Thr Lys His Leu Asp
65 70 75 80

Asp Leu Lys Gly Thr Phe Ala Gln Leu Ser Glu Leu His Cys Asp Lys
85 90 95

Leu His Val Asp Pro Glu Asn Phe Lys Leu Leu Gly Asn Val Leu Val
100 105 110

Thr Val Leu Ala Ile His Phe Gly Lys Glu Phe Thr Pro Glu Val Gln
115 120 125

Ala Ser Trp Gln Lys Met Val Thr Ala Val Ala Ser Ala Leu Ser Ser
130 135 140

Arg Tyr His

145

<210> 2437
<211> 142
<212> PRT
<213> Homo sapiens

<400> 2437

Met Ala Leu Ser Ala Glu Asp Arg Ala Leu Val Arg Ala Leu Trp Lys
1 5 10 15

Lys Leu Gly Ser Asn Val Gly Val Tyr Thr Thr Glu Ala Leu Glu Arg
20 25 30

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

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

Asp Ala Leu Ser Leu Ala Val Glu Arg Leu Asp Asp Leu Pro His Ala
65 70 75 80

Leu Ser Ala Leu Ser His Leu His Ala Cys Gln Leu Arg Val Asp Pro
85 90 95

Ala Ser Phe Gln Leu Leu Gly His Cys Leu Leu Val Thr Leu Ala Arg
100 105 110

His Tyr Pro Gly Asp Phe Ser Pro Ala Leu Gln Ala Ser Leu Asp Lys
115 120 125

Phe Leu Ser His Val Ile Ser Ala Leu Val Ser Glu Tyr Arg
130 135 140

<210> 2438
<211> 260
<212> PRT
<213> Homo sapiens

<400> 2438

Met Arg Pro Glu Asp Arg Met Phe His Ile Arg Ala Val Ile Leu Arg
1 5 10 15

Ala Leu Ser Leu Ala Phe Leu Leu Ser Leu Arg Gly Ala Gly Ala Ile
20 25 30

Lys Ala Asp His Val Ser Thr Tyr Ala Ala Phe Val Gln Thr His Arg
35 40 45

Pro Thr Gly Glu Phe Met Phe Glu Phe Asp Glu Asp Glu Met Phe Tyr
50 55 60

Val Asp Leu Asp Lys Lys Glu Thr Val Trp His Leu Glu Glu Phe Gly
65 70 75 80

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

Leu Asn Asn Asn Leu Asn Thr Leu Ile Gln Arg Ser Asn His Thr Gln
100 105 110

Ala Thr Asn Asp Pro Pro Glu Val Thr Val Phe Pro Lys Glu Pro Val
115 120 125

Glu Leu Gly Gln Pro Asn Thr Leu Ile Cys His Ile Asp Lys Phe Phe
130 135 140

Pro Pro Val Leu Asn Val Thr Trp Leu Cys Asn Gly Glu Leu Val Thr
145 150 155 160

Glu Gly Val Ala Glu Ser Leu Phe Leu Pro Arg Thr Asp Tyr Ser Phe
165 170 175

His Lys Phe His Tyr Leu Thr Phe Val Pro Ser Ala Glu Asp Phe Tyr
180 185 190

Asp Cys Arg Val Glu His Trp Gly Leu Asp Gln Pro Leu Leu Lys His
195 200 205

Trp Glu Ala Gln Glu Pro Ile Gln Met Pro Glu Thr Thr Glu Thr Val
210 215 220

Leu Cys Ala Leu Gly Leu Val Leu Gly Leu Val Gly Ile Ile Val Gly
225 230 235 240

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

Gln Gly Thr Leu
260

<210> 2439

<211> 255
<212> PRT
<213> Homo sapiens

<400> 2439

Met Ile Leu Asn Lys Ala Leu Leu Leu Gly Ala Leu Ala Leu Thr Thr
1 5 10 15

Val Met Ser Pro Cys Gly Gly Glu Asp Ile Val Ala Asp His Val Ala
20 25 30

Ser Cys Gly Val Asn Leu Tyr Gln Phe Tyr Gly Pro Ser Gly Gln Tyr
35 40 45

Thr His Glu Phe Asp Gly Asp Glu Gln Phe Tyr Val Asp Leu Glu Arg
50 55 60

Lys Glu Thr Ala Trp Arg Trp Pro Glu Phe Ser Lys Phe Gly Gly Phe
65 70 75 80

Asp Pro Gln Gly Ala Leu Arg Asn Met Ala Val Ala Lys His Asn Leu
85 90 95

Asn Ile Met Ile Lys Arg Tyr Asn Ser Thr Ala Ala Thr Asn Glu Val
100 105 110

Pro Glu Val Thr Val Phe Ser Lys Ser Pro Val Thr Leu Gly Gln Pro
115 120 125

Asn Thr Leu Ile Cys Leu Val Asp Asn Ile Phe Pro Pro Val Val Asn
130 135 140

Ile Thr Trp Leu Ser Asn Gly Gln Ser Val Thr Glu Gly Val Ser Glu
145 150 155 160

Thr Ser Phe Leu Ser Lys Ser Asp His Ser Phe Phe Lys Ile Ser Tyr
165 170 175

Leu Thr Phe Leu Pro Ser Ala Asp Glu Ile Tyr Asp Cys Lys Val Glu
180 185 190

His Trp Gly Leu Asp Gln Pro Leu Leu Lys His Trp Glu Pro Glu Ile
195 200 205

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

Leu Ser Val Gly Leu Met Gly Ile Val Val Gly Thr Val Phe Ile Ile
225 230 235 240

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

<210> 2440
<211> 199
<212> PRT
<213> Homo sapiens

<400> 2440

Met Lys Ser Gly Leu Trp Tyr Phe Phe Leu Phe Cys Leu Arg Ile Lys
1 5 10 15

Val Leu Thr Gly Glu Ile Asn Gly Ser Ala Asn Tyr Glu Met Phe Ile
20 25 30

Phe His Asn Gly Gly Val Gln Ile Leu Cys Lys Tyr Pro Asp Ile Val
35 40 45

Gln Gln Phe Lys Met Gln Leu Leu Lys Gly Gly Gln Ile Leu Cys Asp
50 55 60

Leu Thr Lys Thr Lys Gly Ser Gly Asn Thr Val Ser Ile Lys Ser Leu
65 70 75 80

Lys Phe Cys His Ser Gln Leu Ser Asn Asn Ser Val Ser Phe Phe Leu
85 90 95

Tyr Asn Leu Asp His Ser His Ala Asn Tyr Tyr Phe Cys Asn Leu Ser
100 105 110

Ile Phe Asp Pro Pro Pro Phe Lys Val Thr Leu Thr Gly Gly Tyr Leu
115 120 125

His Ile Tyr Glu Ser Gln Leu Cys Cys Gln Leu Lys Phe Trp Leu Pro
130 135 140

Ile Gly Cys Ala Ala Phe Val Val Val Cys Ile Leu Gly Cys Ile Leu
145 150 155 160

Ile Cys Trp Leu Thr Lys Lys Lys Tyr Ser Ser Ser Val His Asp Pro
165 170 175

Asn Gly Glu Tyr Met Phe Met Arg Ala Val Asn Thr Ala Lys Lys Ser

180 185 190

Arg Leu Thr Asp Val Thr Leu
195

<210> 2441
<211> 193
<212> PRT
<213> Homo sapiens

<400> 2441

Met Ala Ala Glu Pro Val Glu Asp Asn Cys Ile Asn Phe Val Ala Met
1 5 10 15

Lys Phe Ile Asp Asn Thr Leu Tyr Phe Ile Ala Glu Asp Asp Glu Asn
20 25 30

Leu Glu Ser Asp Tyr Phe Gly Lys Leu Glu Ser Lys Leu Ser Val Ile
35 40 45

Arg Asn Leu Asn Asp Gln Val Leu Phe Ile Asp Gln Gly Asn Arg Pro
50 55 60

Leu Phe Glu Asp Met Thr Asp Ser Asp Cys Arg Asp Asn Ala Pro Arg
65 70 75 80

Thr Ile Phe Ile Ile Ser Met Tyr Lys Asp Ser Gln Pro Arg Gly Met
85 90 95

Ala Val Thr Ile Ser Val Lys Cys Glu Lys Ile Ser Thr Leu Ser Cys
100 105 110

Glu Asn Lys Ile Ile Ser Phe Lys Glu Met Asn Pro Pro Asp Asn Ile
115 120 125

Lys Asp Thr Lys Ser Asp Ile Ile Phe Phe Gln Arg Ser Val Pro Gly
130 135 140

His Asp Asn Lys Met Gln Phe Glu Ser Ser Ser Tyr Glu Gly Tyr Phe
145 150 155 160

Leu Ala Cys Glu Lys Glu Arg Asp Leu Phe Lys Leu Ile Leu Lys Lys
165 170 175

Glu Asp Glu Leu Gly Asp Arg Ser Ile Met Phe Thr Val Gln Asn Glu
180 185 190

Asp

<210> 2442
<211> 152
<212> PRT
<213> Homo sapiens

<400> 2442

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

Gly Leu Gln Ala Pro Met Thr Gln Thr Thr Pro Leu Lys Thr Ser Trp
20 25 30

Val Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu Lys Gln
35 40 45

Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly Glu Asp Gln
50 55 60

Asp Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn Leu Glu Ala Phe
65 70 75 80

Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser Ala Ile Glu Ser Ile
85 90 95

Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu Ala Thr Ala Ala Pro Thr
100 105 110

Arg His Pro Ile His Ile Lys Asp Gly Asp Trp Asn Glu Phe Arg Arg
115 120 125

Lys Leu Thr Phe Tyr Leu Lys Thr Leu Glu Asn Ala Gln Ala Gln Gln
130 135 140

Thr Thr Leu Ser Leu Ala Ile Phe
145 150

<210> 2443
<211> 1038
<212> PRT
<213> Homo sapiens

<400> 2443

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

```
Gly Pro Glu Ala Ala Val Arg Glu Thr Val Met Leu Leu Leu Cys Leu
            20                  25                  30

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

Leu Tyr Gln Gly Pro His Asn Thr Leu Phe Gly Tyr Ser Val Val Leu
    50                  55                  60

His Ser His Gly Ala Asn Arg Trp Leu Leu Val Gly Ala Pro Thr Ala
65                  70                  75                  80

Asn Trp Leu Ala Asn Ala Ser Val Ile Asn Pro Gly Ala Ile Tyr Arg
                85                  90                  95

Cys Arg Ile Gly Lys Asn Pro Gly Gln Thr Cys Glu Gln Leu Gln Leu
            100                 105                 110

Gly Ser Pro Asn Gly Glu Pro Cys Gly Lys Thr Cys Leu Glu Glu Arg
        115                 120                 125

Asp Asn Gln Trp Leu Gly Val Thr Leu Ser Arg Gln Pro Gly Glu Asn
    130                 135                 140

Gly Ser Ile Val Thr Cys Gly His Arg Trp Lys Asn Ile Phe Tyr Ile
145                 150                 155                 160

Lys Asn Glu Asn Lys Leu Pro Thr Gly Gly Cys Tyr Gly Val Pro Pro
                165                 170                 175

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

Tyr Val Lys Lys Phe Gly Glu Asn Phe Ala Ser Cys Gln Ala Gly Ile
        195                 200                 205

Ser Ser Phe Tyr Thr Lys Asp Leu Ile Val Met Gly Ala Pro Gly Ser
    210                 215                 220

Ser Tyr Trp Thr Gly Ser Leu Phe Val Tyr Asn Ile Thr Thr Asn Lys
225                 230                 235                 240

Tyr Lys Ala Phe Leu Asp Lys Gln Asn Gln Val Lys Phe Gly Ser Tyr
                245                 250                 255
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Leu Gly Tyr Ser Val Gly Ala Gly His Phe Arg Ser Gln His Thr Thr
            260                 265                 270

Glu Val Val Gly Gly Ala Pro Gln His Glu Gln Ile Gly Lys Ala Tyr
        275                 280                 285

Ile Phe Ser Ile Asp Glu Lys Glu Leu Asn Ile Leu His Glu Met Lys
    290                 295                 300

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

Leu Asn Ala Asp Gly Phe Ser Asp Leu Leu Val Gly Ala Pro Met Gln
                325                 330                 335

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

Ser Gly Ala Val Met Asn Ala Met Glu Thr Asn Leu Val Gly Ser Asp
        355                 360                 365

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

Asp Asn Asp Gly Phe Glu Asp Val Ala Ile Gly Ala Pro Gln Glu Asp
385                 390                 395                 400

Asp Leu Gln Gly Ala Ile Tyr Ile Tyr Asn Gly Arg Ala Asp Gly Ile
                405                 410                 415

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

Leu Ser Met Phe Gly Gln Ser Ile Ser Gly Gln Ile Asp Ala Asp Asn
        435                 440                 445

Asn Gly Tyr Val Asp Val Ala Val Gly Ala Phe Arg Ser Asp Ser Ala
    450                 455                 460

Val Leu Leu Arg Thr Arg Pro Val Val Ile Val Asp Ala Ser Leu Ser
465                 470                 475                 480

His Pro Glu Ser Val Asn Arg Thr Lys Phe Asp Cys Val Glu Asn Gly
                485                 490                 495
```

Trp Pro Ser Val Cys Ile Asp Leu Thr Leu Cys Phe Ser Tyr Lys Gly
500 505 510

Lys Glu Val Pro Gly Tyr Ile Val Leu Phe Tyr Asn Met Ser Leu Asp
515 520 525

Val Asn Arg Lys Ala Glu Ser Pro Pro Arg Phe Tyr Phe Ser Ser Asn
530 535 540

Gly Thr Ser Asp Val Ile Thr Gly Ser Ile Gln Val Ser Ser Arg Glu
545 550 555 560

Ala Asn Cys Arg Thr His Gln Ala Phe Met Arg Lys Asp Val Arg Asp
565 570 575

Ile Leu Thr Pro Ile Gln Ile Glu Ala Ala Tyr His Leu Gly Pro His
580 585 590

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

Leu Gln Gln Lys Lys Glu Lys Asp Ile Met Lys Lys Thr Ile Asn Phe
610 615 620

Ala Arg Phe Cys Ala His Glu Asn Cys Ser Ala Asp Leu Gln Val Ser
625 630 635 640

Ala Lys Ile Gly Phe Leu Lys Pro His Glu Asn Lys Thr Tyr Leu Ala
645 650 655

Val Gly Ser Met Lys Thr Leu Met Leu Asn Val Ser Leu Phe Asn Ala
660 665 670

Gly Asp Asp Ala Tyr Glu Thr Thr Leu His Val Lys Leu Pro Val Gly
675 680 685

Leu Tyr Phe Ile Lys Ile Leu Glu Leu Glu Glu Lys Gln Ile Asn Cys
690 695 700

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

Tyr Ile Tyr Val Asp His Leu Ser Arg Ile Asp Ile Ser Phe Leu Leu
725 730 735

Asp Val Ser Ser Leu Ser Arg Ala Glu Glu Asp Leu Ser Ile Thr Val

740 745 750

His Ala Thr Cys Glu Asn Glu Glu Glu Met Asp Asn Leu Lys His Ser
755 760 765

Arg Val Thr Val Ala Ile Pro Leu Lys Tyr Glu Val Lys Leu Thr Val
770 775 780

His Gly Phe Val Asn Pro Thr Ser Phe Val Tyr Gly Ser Asn Asp Glu
785 790 795 800

Asn Glu Pro Glu Thr Cys Met Val Glu Lys Met Asn Leu Thr Phe His
805 810 815

Val Ile Asn Thr Gly Asn Ser Met Ala Pro Asn Val Ser Val Glu Ile
820 825 830

Met Val Pro Asn Ser Phe Ser Pro Gln Thr Asp Lys Leu Phe Asn Ile
835 840 845

Leu Asp Val Gln Thr Thr Thr Gly Glu Cys His Phe Glu Asn Tyr Gln
850 855 860

Arg Val Cys Ala Leu Glu Gln Gln Lys Ser Ala Met Gln Thr Leu Lys
865 870 875 880

Gly Ile Val Arg Phe Leu Ser Lys Thr Asp Lys Arg Leu Leu Tyr Cys
885 890 895

Ile Lys Ala Asp Pro His Cys Leu Asn Phe Leu Cys Asn Phe Gly Lys
900 905 910

Met Glu Ser Gly Lys Glu Ala Ser Val His Ile Gln Leu Glu Gly Arg
915 920 925

Pro Ser Ile Leu Glu Met Asp Glu Thr Ser Ala Leu Lys Phe Glu Ile
930 935 940

Arg Ala Thr Gly Phe Pro Glu Pro Asn Pro Arg Val Ile Glu Leu Asn
945 950 955 960

Lys Asp Glu Asn Val Ala His Val Leu Leu Glu Gly Leu His His Gln
965 970 975

Arg Pro Lys Arg Tyr Phe Thr Ile Val Ile Ile Ser Ser Ser Leu Leu
980 985 990

Leu Gly Leu Ile Val Leu Leu Leu Ile Ser Tyr Val Met Trp Lys Ala
995 1000 1005

Gly Phe Phe Lys Arg Gln Tyr Lys Ser Ile Leu Gln Glu Glu Asn
1010 1015 1020

Arg Arg Asp Ser Trp Ser Tyr Ile Asn Ser Lys Ser Asn Asp Asp
1025 1030 1035

<210> 2444
<211> 1152
<212> PRT
<213> Homo sapiens

<400> 2444

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

Phe Asn Leu Asp Thr Glu Asn Ala Met Thr Phe Gln Glu Asn Ala Arg
20 25 30

Gly Phe Gly Gln Ser Val Val Gln Leu Gln Gly Ser Arg Val Val Val
35 40 45

Gly Ala Pro Gln Glu Ile Val Ala Ala Asn Gln Arg Gly Ser Leu Tyr
50 55 60

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

Pro Val Glu Ala Val Asn Met Ser Leu Gly Leu Ser Leu Ala Ala Thr
85 90 95

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

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

Asn Leu Arg Gln Gln Pro Gln Lys Phe Pro Glu Ala Leu Arg Gly Cys
130 135 140

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

```
Ile Ile Pro His Asp Phe Arg Arg Met Lys Glu Phe Val Ser Thr Val
                165                 170                 175

Met Glu Gln Leu Lys Lys Ser Lys Thr Leu Phe Ser Leu Met Gln Tyr
            180                 185                 190

Ser Glu Glu Phe Arg Ile His Phe Thr Phe Lys Glu Phe Gln Asn Asn
        195                 200                 205

Pro Asn Pro Arg Ser Leu Val Lys Pro Ile Thr Gln Leu Leu Gly Arg
    210                 215                 220

Thr His Thr Ala Thr Gly Ile Arg Lys Val Val Arg Glu Leu Phe Asn
225                 230                 235                 240

Ile Thr Asn Gly Ala Arg Lys Asn Ala Phe Lys Ile Leu Val Val Ile
                245                 250                 255

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

Pro Glu Ala Asp Arg Glu Gly Val Ile Arg Tyr Val Ile Gly Val Gly
        275                 280                 285

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

Ser Lys Pro Pro Arg Asp His Val Phe Gln Val Asn Asn Phe Glu Ala
305                 310                 315                 320

Leu Lys Thr Ile Gln Asn Gln Leu Arg Glu Lys Ile Phe Ala Ile Glu
                325                 330                 335

Gly Thr Gln Thr Gly Ser Ser Ser Ser Phe Glu His Glu Met Ser Gln
            340                 345                 350

Glu Gly Phe Ser Ala Ala Ile Thr Ser Asn Gly Pro Leu Leu Ser Thr
        355                 360                 365

Val Gly Ser Tyr Asp Trp Ala Gly Gly Val Phe Leu Tyr Thr Ser Lys
    370                 375                 380

Glu Lys Ser Thr Phe Ile Asn Met Thr Arg Val Asp Ser Asp Met Asn
385                 390                 395                 400

Asp Ala Tyr Leu Gly Tyr Ala Ala Ala Ile Ile Leu Arg Asn Arg Val
```

405 410 415

Gln Ser Leu Val Leu Gly Ala Pro Arg Tyr Gln His Ile Gly Leu Val
420 425 430

Ala Met Phe Arg Gln Asn Thr Gly Met Trp Glu Ser Asn Ala Asn Val
435 440 445

Lys Gly Thr Gln Ile Gly Ala Tyr Phe Gly Ala Ser Leu Cys Ser Val
450 455 460

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

His Tyr Tyr Glu Gln Thr Arg Gly Gly Gln Val Ser Val Cys Pro Leu
485 490 495

Pro Arg Gly Arg Ala Arg Trp Gln Cys Asp Ala Val Leu Tyr Gly Glu
500 505 510

Gln Gly Gln Pro Trp Gly Arg Phe Gly Ala Ala Leu Thr Val Leu Gly
515 520 525

Asp Val Asn Gly Asp Lys Leu Thr Asp Val Ala Ile Gly Ala Pro Gly
530 535 540

Glu Glu Asp Asn Arg Gly Ala Val Tyr Leu Phe His Gly Thr Ser Gly
545 550 555 560

Ser Gly Ile Ser Pro Ser His Ser Gln Arg Ile Ala Gly Ser Lys Leu
565 570 575

Ser Pro Arg Leu Gln Tyr Phe Gly Gln Ser Leu Ser Gly Gly Gln Asp
580 585 590

Leu Thr Met Asp Gly Leu Val Asp Leu Thr Val Gly Ala Gln Gly His
595 600 605

Val Leu Leu Leu Arg Ser Gln Pro Val Leu Arg Val Lys Ala Ile Met
610 615 620

Glu Phe Asn Pro Arg Glu Val Ala Arg Asn Val Phe Glu Cys Asn Asp
625 630 635 640

Gln Val Val Lys Gly Lys Glu Ala Gly Glu Val Arg Val Cys Leu His
645 650 655

```
Val Gln Lys Ser Thr Arg Asp Arg Leu Arg Glu Gly Gln Ile Gln Ser
            660                 665                 670

Val Val Thr Tyr Asp Leu Ala Leu Asp Ser Gly Arg Pro His Ser Arg
        675                 680                 685

Ala Val Phe Asn Glu Thr Lys Asn Ser Thr Arg Arg Gln Thr Gln Val
    690                 695                 700

Leu Gly Leu Thr Gln Thr Cys Glu Thr Leu Lys Leu Gln Leu Pro Asn
705                 710                 715                 720

Cys Ile Glu Asp Pro Val Ser Pro Ile Val Leu Arg Leu Asn Phe Ser
                725                 730                 735

Leu Val Gly Thr Pro Leu Ser Ala Phe Gly Asn Leu Arg Pro Val Leu
            740                 745                 750

Ala Glu Asp Ala Gln Arg Leu Phe Thr Ala Leu Phe Pro Phe Glu Lys
        755                 760                 765

Asn Cys Gly Asn Asp Asn Ile Cys Gln Asp Asp Leu Ser Ile Thr Phe
    770                 775                 780

Ser Phe Met Ser Leu Asp Cys Leu Val Val Gly Gly Pro Arg Glu Phe
785                 790                 795                 800

Asn Val Thr Val Thr Val Arg Asn Asp Gly Glu Asp Ser Tyr Arg Thr
                805                 810                 815

Gln Val Thr Phe Phe Phe Pro Leu Asp Leu Ser Tyr Arg Lys Val Ser
            820                 825                 830

Thr Leu Gln Asn Gln Arg Ser Gln Arg Ser Trp Arg Leu Ala Cys Glu
        835                 840                 845

Ser Ala Ser Ser Thr Glu Val Ser Gly Ala Leu Lys Ser Thr Ser Cys
    850                 855                 860

Ser Ile Asn His Pro Ile Phe Pro Glu Asn Ser Glu Val Thr Phe Asn
865                 870                 875                 880

Ile Thr Phe Asp Val Asp Ser Lys Ala Ser Leu Gly Asn Lys Leu Leu
                885                 890                 895
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```
Leu Lys Ala Asn Val Thr Ser Glu Asn Asn Met Pro Arg Thr Asn Lys
            900                 905                 910

Thr Glu Phe Gln Leu Glu Leu Pro Val Lys Tyr Ala Val Tyr Met Val
        915                 920                 925

Val Thr Ser His Gly Val Ser Thr Lys Tyr Leu Asn Phe Thr Ala Ser
    930                 935                 940

Glu Asn Thr Ser Arg Val Met Gln His Gln Tyr Gln Val Ser Asn Leu
945                 950                 955                 960

Gly Gln Arg Ser Pro Pro Ile Ser Leu Val Phe Leu Val Pro Val Arg
                965                 970                 975

Leu Asn Gln Thr Val Ile Trp Asp Arg Pro Gln Val Thr Phe Ser Glu
            980                 985                 990

Asn Leu Ser Ser Thr Cys His Thr  Lys Glu Arg Leu Pro  Ser His Ser
        995                 1000                1005

Asp Phe  Leu Ala Glu Leu Arg  Lys Ala Pro Val Val  Asn Cys Ser
    1010                1015                1020

Ile Ala  Val Cys Gln Arg Ile  Gln Cys Asp Ile Pro  Phe Phe Gly
    1025                1030                1035

Ile Gln  Glu Glu Phe Asn Ala  Thr Leu Lys Gly Asn  Leu Ser Phe
    1040                1045                1050

Asp Trp  Tyr Ile Lys Thr Ser  His Asn His Leu Leu  Ile Val Ser
    1055                1060                1065

Thr Ala  Glu Ile Leu Phe Asn  Asp Ser Val Phe Thr  Leu Leu Pro
    1070                1075                1080

Gly Gln  Gly Ala Phe Val Arg  Ser Gln Thr Glu Thr  Lys Val Glu
    1085                1090                1095

Pro Phe  Glu Val Pro Asn Pro  Leu Pro Leu Ile Val  Gly Ser Ser
    1100                1105                1110

Val Gly  Gly Leu Leu Leu Leu  Ala Leu Ile Thr Ala  Ala Leu Tyr
    1115                1120                1125
```

```
Lys Leu  Gly Phe Phe Lys Arg  Gln Tyr Lys Asp Met  Met Ser Glu
    1130                 1135                 1140

Gly Gly  Pro Pro Gly Ala Glu  Pro Gln
    1145                 1150
```

<210> 2445
<211> 798
<212> PRT
<213> Homo sapiens

<400> 2445

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

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

Glu Trp Arg Asn Pro His Leu Ser Met Leu Gly Ser Cys Gln Pro Ala
        35                  40                  45

Pro Ser Cys Gln Lys Cys Ile Leu Ser His Pro Ser Cys Ala Trp Cys
    50                  55                  60

Lys Gln Leu Asn Phe Thr Ala Ser Gly Glu Ala Glu Ala Arg Arg Cys
65                  70                  75                  80

Ala Arg Arg Glu Glu Leu Leu Ala Arg Gly Cys Pro Leu Glu Glu Leu
                85                  90                  95

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

Gln Gly Ala Arg Gly Glu Gly Ala Thr Gln Leu Ala Pro Gln Arg Val
        115                 120                 125

Arg Val Thr Leu Arg Pro Gly Glu Pro Gln Gln Leu Gln Val Arg Phe
    130                 135                 140

Leu Arg Ala Glu Gly Tyr Pro Val Asp Leu Tyr Tyr Leu Met Asp Leu
145                 150                 155                 160

Ser Tyr Ser Met Lys Asp Asp Leu Glu Arg Val Arg Gln Leu Gly His
                165                 170                 175

Ala Leu Leu Val Arg Leu Gln Glu Val Thr His Ser Val Arg Ile Gly
            180                 185                 190
```

```
Phe Gly Ser Phe Val Asp Lys Thr Val Leu Pro Phe Val Ser Thr Val
        195                 200                 205

Pro Ser Lys Leu Arg His Pro Cys Pro Thr Arg Leu Glu Arg Cys Gln
    210                 215                 220

Ser Pro Phe Ser Phe His His Val Leu Ser Leu Thr Gly Asp Ala Gln
225                 230                 235                 240

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

Ser Pro Glu Gly Gly Phe Asp Ala Ile Leu Gln Ala Ala Leu Cys Gln
            260                 265                 270

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

Asp Asp Thr Phe His Thr Ala Gly Asp Gly Lys Leu Gly Gly Ile Phe
    290                 295                 300

Met Pro Ser Asp Gly His Cys His Leu Asp Ser Asn Gly Leu Tyr Ser
305                 310                 315                 320

Arg Ser Thr Glu Phe Asp Tyr Pro Ser Val Gly Gln Val Ala Gln Ala
                325                 330                 335

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

Leu Pro Val Tyr Gln Glu Leu Ser Lys Leu Ile Pro Lys Ser Ala Val
        355                 360                 365

Gly Glu Leu Ser Glu Asp Ser Ser Asn Val Val Gln Leu Ile Met Asp
    370                 375                 380

Ala Tyr Asn Ser Leu Ser Ser Thr Val Thr Leu Glu His Ser Ser Leu
385                 390                 395                 400

Pro Pro Gly Val His Ile Ser Tyr Glu Ser Gln Cys Glu Gly Pro Glu
                405                 410                 415

Lys Arg Glu Gly Lys Ala Glu Asp Arg Gly Gln Cys Asn His Val Arg
            420                 425                 430
```

```
Ile Asn Gln Thr Val Thr Phe Trp Val Ser Leu Gln Ala Thr His Cys
        435                 440                 445

Leu Pro Glu Pro His Leu Leu Arg Leu Arg Ala Leu Gly Phe Ser Glu
    450                 455                 460

Glu Leu Ile Val Glu Leu His Thr Leu Cys Asp Cys Asn Cys Ser Asp
465                 470                 475                 480

Thr Gln Pro Gln Ala Pro His Cys Ser Asp Gly Gln Gly His Leu Gln
                485                 490                 495

Cys Gly Val Cys Ser Cys Ala Pro Gly Arg Leu Gly Arg Leu Cys Glu
            500                 505                 510

Cys Ser Val Ala Glu Leu Ser Ser Pro Asp Leu Glu Ser Gly Cys Arg
        515                 520                 525

Ala Pro Asn Gly Thr Gly Pro Leu Cys Ser Gly Lys Gly His Cys Gln
    530                 535                 540

Cys Gly Arg Cys Ser Cys Ser Gly Gln Ser Ser Gly His Leu Cys Glu
545                 550                 555                 560

Cys Asp Asp Ala Ser Cys Glu Arg His Glu Gly Ile Leu Cys Gly Gly
                565                 570                 575

Phe Gly Arg Cys Gln Cys Gly Val Cys His Cys His Ala Asn Arg Thr
            580                 585                 590

Gly Arg Ala Cys Glu Cys Ser Gly Asp Met Asp Ser Cys Ile Ser Pro
        595                 600                 605

Glu Gly Gly Leu Cys Ser Gly His Gly Arg Cys Lys Cys Asn Arg Cys
    610                 615                 620

Gln Cys Leu Asp Gly Tyr Tyr Gly Ala Leu Cys Asp Gln Cys Pro Gly
625                 630                 635                 640

Cys Lys Thr Pro Cys Glu Arg His Arg Asp Cys Ala Glu Cys Gly Ala
                645                 650                 655

Phe Arg Thr Gly Pro Leu Ala Thr Asn Cys Ser Thr Ala Cys Ala His
            660                 665                 670
```

```
Thr Asn Val Thr Leu Ala Leu Ala Pro Ile Leu Asp Asp Gly Trp Cys
        675                 680                 685

Lys Glu Arg Thr Leu Asp Asn Gln Leu Phe Phe Phe Leu Val Glu Asp
    690                 695                 700

Asp Ala Arg Gly Thr Val Val Leu Arg Val Arg Pro Gln Glu Lys Gly
705                 710                 715                 720

Ala Asp His Thr Gln Ala Ile Val Leu Gly Cys Val Gly Gly Ile Val
                725                 730                 735

Ala Val Gly Leu Gly Leu Val Leu Ala Tyr Arg Leu Ser Val Glu Ile
            740                 745                 750

Tyr Asp Arg Arg Glu Tyr Ser Arg Phe Glu Lys Glu Gln Gln Gln Leu
        755                 760                 765

Asn Trp Lys Gln Asp Ser Asn Pro Leu Tyr Lys Ser Ala Ile Thr Thr
    770                 775                 780

Thr Ile Asn Pro Arg Phe Gln Glu Ala Asp Ser Pro Thr Leu
785                 790                 795
```

<210> 2446
<211> 345
<212> PRT
<213> Homo sapiens

<400> 2446

```
Met Gln Arg Leu Val Ala Trp Asp Pro Ala Cys Leu Pro Leu Pro Pro
1               5                   10                  15

Pro Pro Pro Ala Phe Lys Ser Met Glu Val Ala Asn Phe Tyr Tyr Glu
            20                  25                  30

Ala Asp Cys Leu Ala Ala Ala Tyr Gly Gly Lys Ala Ala Pro Ala Ala
        35                  40                  45

Pro Pro Ala Ala Arg Pro Gly Pro Arg Pro Pro Ala Gly Glu Leu Gly
    50                  55                  60

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

Pro Leu Gly Ala Pro Gln Ala Pro Ala Pro Ala Thr Ala Thr Asp Thr
                85                  90                  95
```

```
Phe Glu Ala Ala Pro Pro Ala Pro Ala Pro Ala Pro Ala Ser Ser Gly
            100                 105                 110

Gln His His Asp Phe Leu Ser Asp Leu Phe Ser Asp Asp Tyr Gly Gly
        115                 120                 125

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

Leu Gly Ala Ala Lys Gly Ala Leu His Pro Gly Cys Phe Ala Pro Leu
145                 150                 155                 160

His Pro Pro Pro Pro Pro Pro Pro Pro Pro Ala Glu Leu Lys Ala Glu
                165                 170                 175

Pro Gly Phe Glu Pro Ala Asp Cys Lys Arg Lys Glu Glu Ala Gly Ala
            180                 185                 190

Pro Gly Gly Gly Ala Gly Met Ala Ala Gly Phe Pro Tyr Ala Leu Arg
        195                 200                 205

Ala Tyr Leu Gly Tyr Gln Ala Val Pro Ser Gly Ser Ser Gly Ser Leu
    210                 215                 220

Ser Thr Ser Ser Ser Ser Ser Pro Pro Gly Thr Pro Ser Pro Ala Asp
225                 230                 235                 240

Ala Lys Ala Pro Pro Thr Ala Cys Tyr Ala Gly Ala Ala Pro Ala Pro
                245                 250                 255

Ser Gln Val Lys Ser Lys Ala Lys Lys Thr Val Asp Lys His Ser Asp
            260                 265                 270

Glu Tyr Lys Ile Arg Arg Glu Arg Asn Asn Ile Ala Val Arg Lys Ser
        275                 280                 285

Arg Asp Lys Ala Lys Met Arg Asn Leu Glu Thr Gln His Lys Val Leu
    290                 295                 300

Glu Leu Thr Ala Glu Asn Glu Arg Leu Gln Lys Lys Val Glu Gln Leu
305                 310                 315                 320

Ser Arg Glu Leu Ser Thr Leu Arg Asn Leu Phe Lys Gln Leu Pro Glu
                325                 330                 335
```

```
Pro Leu Leu Ala Ser Ser Gly His Cys
            340                 345


<210>  2447
<211>  373
<212>  PRT
<213>  Homo sapiens

<400>  2447

Met Ser Pro Cys Pro Pro Gln Gln Ser Arg Asn Arg Val Ile Gln Leu
1               5                   10                  15

Ser Thr Ser Glu Leu Gly Glu Met Glu Leu Thr Trp Gln Glu Ile Met
            20                  25                  30

Ser Ile Thr Glu Leu Gln Gly Leu Asn Ala Pro Ser Glu Pro Ser Phe
        35                  40                  45

Glu Pro Gln Ala Pro Ala Pro Tyr Leu Gly Pro Pro Pro Pro Thr Thr
    50                  55                  60

Tyr Cys Pro Cys Ser Ile His Pro Asp Ser Gly Phe Pro Leu Pro Pro
65                  70                  75                  80

Pro Pro Tyr Glu Leu Pro Ala Ser Thr Ser His Val Pro Asp Pro Pro
                85                  90                  95

Tyr Ser Tyr Gly Asn Met Ala Ile Pro Val Ser Lys Pro Leu Ser Leu
            100                 105                 110

Ser Gly Leu Leu Ser Glu Pro Leu Gln Asp Pro Leu Ala Leu Leu Asp
        115                 120                 125

Ile Gly Leu Pro Ala Gly Pro Pro Lys Pro Gln Glu Asp Pro Glu Ser
    130                 135                 140

Asp Ser Gly Leu Ser Leu Asn Tyr Ser Asp Ala Glu Ser Leu Glu Leu
145                 150                 155                 160

Glu Gly Thr Glu Ala Gly Arg Arg Arg Ser Glu Tyr Val Glu Met Tyr
                165                 170                 175

Pro Val Glu Tyr Pro Tyr Ser Leu Met Pro Asn Ser Leu Ala His Ser
            180                 185                 190

Asn Tyr Thr Leu Pro Ala Ala Glu Thr Pro Leu Ala Leu Glu Pro Ser
```

195 200 205

Ser Gly Pro Val Arg Ala Lys Pro Thr Ala Arg Gly Glu Ala Gly Ser
210 215 220

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

Lys Ile Val Asn Leu Pro Val Asp Asp Phe Asn Glu Leu Leu Ala Arg
245 250 255

Tyr Pro Leu Thr Glu Ser Gln Leu Ala Leu Val Arg Asp Ile Arg Arg
260 265 270

Arg Gly Lys Asn Lys Val Ala Ala Gln Asn Cys Arg Lys Arg Lys Leu
275 280 285

Glu Thr Ile Val Gln Leu Glu Arg Glu Leu Glu Arg Leu Thr Asn Glu
290 295 300

Arg Glu Arg Leu Leu Arg Ala Arg Gly Glu Ala Asp Arg Thr Leu Glu
305 310 315 320

Val Met Arg Gln Gln Leu Thr Glu Leu Tyr Arg Asp Ile Phe Gln His
325 330 335

Leu Arg Asp Glu Ser Gly Asn Ser Tyr Ser Pro Glu Glu Tyr Ala Leu
340 345 350

Gln Gln Ala Ala Asp Gly Thr Ile Phe Leu Val Pro Arg Gly Thr Lys
355 360 365

Met Glu Ala Thr Asp
370

<210> 2448
<211> 288
<212> PRT
<213> Homo sapiens

<400> 2448

Met Gln Ile Pro Gln Ala Pro Trp Pro Val Val Trp Ala Val Leu Gln
1 5 10 15

Leu Gly Trp Arg Pro Gly Trp Phe Leu Asp Ser Pro Asp Arg Pro Trp
20 25 30

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

Asn Ala Thr Phe Thr Cys Ser Phe Ser Asn Thr Ser Glu Ser Phe Val
    50                  55                  60

Leu Asn Trp Tyr Arg Met Ser Pro Ser Asn Gln Thr Asp Lys Leu Ala
65                  70                  75                  80

Ala Phe Pro Glu Asp Arg Ser Gln Pro Gly Gln Asp Cys Arg Phe Arg
                85                  90                  95

Val Thr Gln Leu Pro Asn Gly Arg Asp Phe His Met Ser Val Val Arg
            100                 105                 110

Ala Arg Arg Asn Asp Ser Gly Thr Tyr Leu Cys Gly Ala Ile Ser Leu
        115                 120                 125

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

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

Arg Pro Ala Gly Gln Phe Gln Thr Leu Val Val Gly Val Val Gly Gly
                165                 170                 175

Leu Leu Gly Ser Leu Val Leu Leu Val Trp Val Leu Ala Val Ile Cys
            180                 185                 190

Ser Arg Ala Ala Arg Gly Thr Ile Gly Ala Arg Arg Thr Gly Gln Pro
        195                 200                 205

Leu Lys Glu Asp Pro Ser Ala Val Pro Val Phe Ser Val Asp Tyr Gly
    210                 215                 220

Glu Leu Asp Phe Gln Trp Arg Glu Lys Thr Pro Glu Pro Pro Val Pro
225                 230                 235                 240

Cys Val Pro Glu Gln Thr Glu Tyr Ala Thr Ile Val Phe Pro Ser Gly
                245                 250                 255

Met Gly Thr Ser Ser Pro Ala Arg Arg Gly Ser Ala Asp Gly Pro Arg
            260                 265                 270
```

```
Ser Ala Gln Pro Leu Arg Pro Glu Asp Gly His Cys Ser Trp Pro Leu
        275                 280                 285


<210>  2449
<211>  101
<212>  PRT
<213>  Homo sapiens

<400>  2449

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


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


Ala Glu Glu Asp Gly Asp Leu Gln Cys Leu Cys Val Lys Thr Thr Ser
        35                  40                  45


Gln Val Arg Pro Arg His Ile Thr Ser Leu Glu Val Ile Lys Ala Gly
    50                  55                  60


Pro His Cys Pro Thr Ala Gln Leu Ile Ala Thr Leu Lys Asn Gly Arg
65                  70                  75                  80


Lys Ile Cys Leu Asp Leu Gln Ala Pro Leu Tyr Lys Lys Ile Ile Lys
                85                  90                  95


Lys Leu Leu Glu Ser
            100


<210>  2450
<211>  706
<212>  PRT
<213>  Homo sapiens

<400>  2450

Met Ser Pro Phe Leu Arg Ile Gly Leu Ser Asn Phe Asp Cys Gly Ser
1               5                   10                  15


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


Val Lys Glu Tyr Val Glu Ser Glu Asn Gly Gln Met Tyr Ile Gln Lys
        35                  40                  45


Lys Pro Thr Met Tyr Pro Pro Trp Asp Ser Thr Phe Asp Ala His Ile
    50                  55                  60
```

Asn Lys Gly Arg Val Met Gln Ile Ile Val Lys Gly Lys Asn Val Asp
65 70 75 80

Leu Ile Ser Glu Thr Thr Val Glu Leu Tyr Ser Leu Ala Glu Arg Cys
85 90 95

Arg Lys Asn Asn Gly Lys Thr Glu Ile Trp Leu Glu Leu Lys Pro Gln
100 105 110

Gly Arg Met Leu Met Asn Ala Arg Tyr Phe Leu Glu Met Ser Asp Thr
115 120 125

Lys Asp Met Asn Glu Phe Glu Thr Glu Gly Phe Phe Ala Leu His Gln
130 135 140

Arg Arg Gly Ala Ile Lys Gln Ala Lys Val His His Val Lys Cys His
145 150 155 160

Glu Phe Thr Ala Thr Phe Phe Pro Gln Pro Thr Phe Cys Ser Val Cys
165 170 175

His Glu Phe Val Trp Gly Leu Asn Lys Gln Gly Tyr Gln Cys Arg Gln
180 185 190

Cys Asn Ala Ala Ile His Lys Lys Cys Ile Asp Lys Val Ile Ala Lys
195 200 205

Cys Thr Gly Ser Ala Ile Asn Ser Arg Glu Thr Met Phe His Lys Glu
210 215 220

Arg Phe Lys Ile Asp Met Pro His Arg Phe Lys Val Tyr Asn Tyr Lys
225 230 235 240

Ser Pro Thr Phe Cys Glu His Cys Gly Thr Leu Leu Trp Gly Leu Ala
245 250 255

Arg Gln Gly Leu Lys Cys Asp Ala Cys Gly Met Asn Val His His Arg
260 265 270

Cys Gln Thr Lys Val Ala Asn Leu Cys Gly Ile Asn Gln Lys Leu Met
275 280 285

Ala Glu Ala Leu Ala Met Ile Glu Ser Thr Gln Gln Ala Arg Cys Leu
290 295 300

```
Arg Asp Thr Glu Gln Ile Phe Arg Glu Gly Pro Val Glu Ile Gly Leu
305                 310                 315                 320

Pro Cys Ser Ile Lys Asn Glu Ala Arg Pro Pro Cys Leu Pro Thr Pro
                325                 330                 335

Gly Lys Arg Glu Pro Gln Gly Ile Ser Trp Glu Ser Pro Leu Asp Glu
            340                 345                 350

Val Asp Lys Met Cys His Leu Pro Glu Pro Glu Leu Asn Lys Glu Arg
        355                 360                 365

Pro Ser Leu Gln Ile Lys Leu Lys Ile Glu Asp Phe Ile Leu His Lys
    370                 375                 380

Met Leu Gly Lys Gly Ser Phe Gly Lys Val Phe Leu Ala Glu Phe Lys
385                 390                 395                 400

Lys Thr Asn Gln Phe Phe Ala Ile Lys Ala Leu Lys Lys Asp Val Val
                405                 410                 415

Leu Met Asp Asp Asp Val Glu Cys Thr Met Val Glu Lys Arg Val Leu
            420                 425                 430

Ser Leu Ala Trp Glu His Pro Phe Leu Thr His Met Phe Cys Thr Phe
        435                 440                 445

Gln Thr Lys Glu Asn Leu Phe Phe Val Met Glu Tyr Leu Asn Gly Gly
    450                 455                 460

Asp Leu Met Tyr His Ile Gln Ser Cys His Lys Phe Asp Leu Ser Arg
465                 470                 475                 480

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

Ser Lys Gly Ile Val Tyr Arg Asp Leu Lys Leu Asp Asn Ile Leu Leu
            500                 505                 510

Asp Lys Asp Gly His Ile Lys Ile Ala Asp Phe Gly Met Cys Lys Glu
        515                 520                 525

Asn Met Leu Gly Asp Ala Lys Thr Asn Thr Phe Cys Gly Thr Pro Asp
    530                 535                 540

Tyr Ile Ala Pro Glu Ile Leu Leu Gly Gln Lys Tyr Asn His Ser Val
```

545 550 555 560

Asp Trp Trp Ser Phe Gly Val Leu Leu Tyr Glu Met Leu Ile Gly Gln
565 570 575

Ser Pro Phe His Gly Gln Asp Glu Glu Glu Leu Phe His Ser Ile Arg
580 585 590

Met Asp Asn Pro Phe Tyr Pro Arg Trp Leu Glu Lys Glu Ala Lys Asp
595 600 605

Leu Leu Val Lys Leu Phe Val Arg Glu Pro Glu Lys Arg Leu Gly Val
610 615 620

Arg Gly Asp Ile Arg Gln His Pro Leu Phe Arg Glu Ile Asn Trp Glu
625 630 635 640

Glu Leu Glu Arg Lys Glu Ile Asp Pro Pro Phe Arg Pro Lys Val Lys
645 650 655

Ser Pro Phe Asp Cys Ser Asn Phe Asp Lys Glu Phe Leu Asn Glu Lys
660 665 670

Pro Arg Leu Ser Phe Ala Asp Arg Ala Leu Ile Asn Ser Met Asp Gln
675 680 685

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

Ile Ser
705

<210> 2451
<211> 798
<212> PRT
<213> Homo sapiens

<400> 2451

Met Ala Trp Asp Met Cys Asn Gln Asp Ser Glu Ser Val Trp Ser Asp
1 5 10 15

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

Leu Pro Glu Leu Asp Leu Ser Glu Leu Asp Val Asn Asp Leu Asp Thr
35 40 45

```
Asp Ser Phe Leu Gly Gly Leu Lys Trp Cys Ser Asp Gln Ser Glu Ile
    50                  55                  60

Ile Ser Asn Gln Tyr Asn Asn Glu Pro Ser Asn Ile Phe Glu Lys Ile
65                  70                  75                  80

Asp Glu Glu Asn Glu Ala Asn Leu Leu Ala Val Leu Thr Glu Thr Leu
                85                  90                  95

Asp Ser Leu Pro Val Asp Glu Asp Gly Leu Pro Ser Phe Asp Ala Leu
            100                 105                 110

Thr Asp Gly Asp Val Thr Thr Asp Asn Glu Ala Ser Pro Ser Ser Met
        115                 120                 125

Pro Asp Gly Thr Pro Pro Pro Gln Glu Ala Glu Glu Pro Ser Leu Leu
    130                 135                 140

Lys Lys Leu Leu Leu Ala Pro Ala Asn Thr Gln Leu Ser Tyr Asn Glu
145                 150                 155                 160

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

Arg Thr Asn Pro Ala Ile Val Lys Thr Glu Asn Ser Trp Ser Asn Lys
            180                 185                 190

Ala Lys Ser Ile Cys Gln Gln Gln Lys Pro Gln Arg Arg Pro Cys Ser
        195                 200                 205

Glu Leu Leu Lys Tyr Leu Thr Thr Asn Asp Asp Pro Pro His Thr Lys
    210                 215                 220

Pro Thr Glu Asn Arg Asn Ser Ser Arg Asp Lys Cys Thr Ser Lys Lys
225                 230                 235                 240

Lys Ser His Thr Gln Ser Gln Ser Gln His Leu Gln Ala Lys Pro Thr
                245                 250                 255

Thr Leu Ser Leu Pro Leu Thr Pro Glu Ser Pro Asn Asp Pro Lys Gly
            260                 265                 270

Ser Pro Phe Glu Asn Lys Thr Ile Glu Arg Thr Leu Ser Val Glu Leu
        275                 280                 285
```

```
Ser Gly Thr Ala Gly Leu Thr Pro Pro Thr Thr Pro Pro His Lys Ala
    290                 295                 300

Asn Gln Asp Asn Pro Phe Arg Ala Ser Pro Lys Leu Lys Ser Ser Cys
305                 310                 315                 320

Lys Thr Val Val Pro Pro Pro Ser Lys Lys Pro Arg Tyr Ser Glu Ser
                325                 330                 335

Ser Gly Thr Gln Gly Asn Asn Ser Thr Lys Lys Gly Pro Glu Gln Ser
            340                 345                 350

Glu Leu Tyr Ala Gln Leu Ser Lys Ser Ser Val Leu Thr Gly Gly His
        355                 360                 365

Glu Glu Arg Lys Thr Lys Arg Pro Ser Leu Arg Leu Phe Gly Asp His
    370                 375                 380

Asp Tyr Cys Gln Ser Ile Asn Ser Lys Thr Glu Ile Leu Ile Asn Ile
385                 390                 395                 400

Ser Gln Glu Leu Gln Asp Ser Arg Gln Leu Glu Asn Lys Asp Val Ser
                405                 410                 415

Ser Asp Trp Gln Gly Gln Ile Cys Ser Ser Thr Asp Ser Asp Gln Cys
            420                 425                 430

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

Thr Arg Lys Gln Leu Gln Asp Gln Glu Ile Arg Ala Glu Leu Asn Lys
    450                 455                 460

His Phe Gly His Pro Ser Gln Ala Val Phe Asp Asp Glu Ala Asp Lys
465                 470                 475                 480

Thr Gly Glu Leu Arg Asp Ser Asp Phe Ser Asn Glu Gln Phe Ser Lys
                485                 490                 495

Leu Pro Met Phe Ile Asn Ser Gly Leu Ala Met Asp Gly Leu Phe Asp
            500                 505                 510

Asp Ser Glu Asp Glu Ser Asp Lys Leu Ser Tyr Pro Trp Asp Gly Thr
        515                 520                 525

Gln Ser Tyr Ser Leu Phe Asn Val Ser Pro Ser Cys Ser Ser Phe Asn
```

530 535 540

Ser Pro Cys Arg Asp Ser Val Ser Pro Pro Lys Ser Leu Phe Ser Gln
545 550 555 560

Arg Pro Gln Arg Met Arg Ser Arg Ser Arg Ser Phe Ser Arg His Arg
565 570 575

Ser Cys Ser Arg Ser Pro Tyr Ser Arg Ser Arg Ser Arg Ser Pro Gly
580 585 590

Ser Arg Ser Ser Ser Arg Ser Cys Tyr Tyr Tyr Glu Ser Ser His Tyr
595 600 605

Arg His Arg Thr His Arg Asn Ser Pro Leu Tyr Val Arg Ser Arg Ser
610 615 620

Arg Ser Pro Tyr Ser Arg Arg Pro Arg Tyr Asp Ser Tyr Glu Glu Tyr
625 630 635 640

Gln His Glu Arg Leu Lys Arg Glu Glu Tyr Arg Arg Glu Tyr Glu Lys
645 650 655

Arg Glu Ser Glu Arg Ala Lys Gln Arg Glu Arg Gln Arg Gln Lys Ala
660 665 670

Ile Glu Glu Arg Arg Val Ile Tyr Val Gly Lys Ile Arg Pro Asp Thr
675 680 685

Thr Arg Thr Glu Leu Arg Asp Arg Phe Glu Val Phe Gly Glu Ile Glu
690 695 700

Glu Cys Thr Val Asn Leu Arg Asp Asp Gly Asp Ser Tyr Gly Phe Ile
705 710 715 720

Thr Tyr Arg Tyr Thr Cys Asp Ala Phe Ala Ala Leu Glu Asn Gly Tyr
725 730 735

Thr Leu Arg Arg Ser Asn Glu Thr Asp Phe Glu Leu Tyr Phe Cys Gly
740 745 750

Arg Lys Gln Phe Phe Lys Ser Asn Tyr Ala Asp Leu Asp Ser Asn Ser
755 760 765

Asp Asp Phe Asp Pro Ala Ser Thr Lys Ser Lys Tyr Asp Ser Leu Asp
770 775 780

Phe Asp Ser Leu Leu Lys Glu Ala Gln Arg Ser Leu Arg Arg
785 790 795

<210> 2452
<211> 1043
<212> PRT
<213> Homo sapiens

<400> 2452

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

Glu Ile Gln His Pro His Ile Lys Phe Ser Glu Trp Lys Phe Lys Leu
20 25 30

Phe Arg Val Arg Ser Phe Glu Lys Thr Pro Glu Glu Ala Gln Lys Glu
35 40 45

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

Val Leu Asp Lys Ala Asp Gly Gln Lys Pro Val Pro Thr Gln Pro Leu
65 70 75 80

Leu Lys Ala His Pro Lys Phe Ser Lys Lys Phe His Asp Asn Glu Lys
85 90 95

Ala Arg Gly Lys Ala Ile His Gln Ala Asn Leu Arg His Leu Cys Arg
100 105 110

Ile Cys Gly Asn Ser Phe Arg Ala Asp Glu His Asn Arg Arg Tyr Pro
115 120 125

Val His Gly Pro Val Asp Gly Lys Thr Leu Gly Leu Leu Arg Lys Lys
130 135 140

Glu Lys Arg Ala Thr Ser Trp Pro Asp Leu Ile Ala Lys Val Phe Arg
145 150 155 160

Ile Asp Val Lys Ala Asp Val Asp Ser Ile His Pro Thr Glu Phe Cys
165 170 175

His Asn Cys Trp Ser Ile Met His Arg Lys Phe Ser Ser Ala Pro Cys
180 185 190

Glu Val Tyr Phe Pro Arg Asn Val Thr Met Glu Trp His Pro His Thr
195 200 205

Pro Ser Cys Asp Ile Cys Asn Thr Ala Arg Arg Gly Leu Lys Arg Lys
210 215 220

Ser Leu Gln Pro Asn Leu Gln Leu Ser Lys Lys Leu Lys Thr Val Leu
225 230 235 240

Asp Gln Ala Arg Gln Ala Arg Gln Arg Lys Arg Arg Ala Gln Ala Arg
245 250 255

Ile Ser Ser Lys Asp Val Met Lys Lys Ile Ala Asn Cys Ser Lys Ile
260 265 270

His Leu Ser Thr Lys Leu Leu Ala Val Asp Phe Pro Glu His Phe Val
275 280 285

Lys Ser Ile Ser Cys Gln Ile Cys Glu His Ile Leu Ala Asp Pro Val
290 295 300

Glu Thr Asn Cys Lys His Val Phe Cys Arg Val Cys Ile Leu Arg Cys
305 310 315 320

Leu Lys Val Met Gly Ser Tyr Cys Pro Ser Cys Arg Tyr Pro Cys Phe
325 330 335

Pro Thr Asp Leu Glu Ser Pro Val Lys Ser Phe Leu Ser Val Leu Asn
340 345 350

Ser Leu Met Val Lys Cys Pro Ala Lys Glu Cys Asn Glu Glu Val Ser
355 360 365

Leu Glu Lys Tyr Asn His His Ile Ser Ser His Lys Glu Ser Lys Glu
370 375 380

Ile Phe Val His Ile Asn Lys Gly Gly Arg Pro Arg Gln His Leu Leu
385 390 395 400

Ser Leu Thr Arg Arg Ala Gln Lys His Arg Leu Arg Glu Leu Lys Leu
405 410 415

Gln Val Lys Ala Phe Ala Asp Lys Glu Glu Gly Gly Asp Val Lys Ser
420 425 430

Val Cys Met Thr Leu Phe Leu Leu Ala Leu Arg Ala Arg Asn Glu His

435 440 445

Arg Gln Ala Asp Glu Leu Glu Ala Ile Met Gln Gly Lys Gly Ser Gly
450 455 460

Leu Gln Pro Ala Val Cys Leu Ala Ile Arg Val Asn Thr Phe Leu Ser
465 470 475 480

Cys Ser Gln Tyr His Lys Met Tyr Arg Thr Val Lys Ala Ile Thr Gly
485 490 495

Arg Gln Ile Phe Gln Pro Leu His Ala Leu Arg Asn Ala Glu Lys Val
500 505 510

Leu Leu Pro Gly Tyr His His Phe Glu Trp Gln Pro Pro Leu Lys Asn
515 520 525

Val Ser Ser Ser Thr Asp Val Gly Ile Ile Asp Gly Leu Ser Gly Leu
530 535 540

Ser Ser Ser Val Asp Asp Tyr Pro Val Asp Thr Ile Ala Lys Arg Phe
545 550 555 560

Arg Tyr Asp Ser Ala Leu Val Ser Ala Leu Met Asp Met Glu Glu Asp
565 570 575

Ile Leu Glu Gly Met Arg Ser Gln Asp Leu Asp Asp Tyr Leu Asn Gly
580 585 590

Pro Phe Thr Val Val Val Lys Glu Ser Cys Asp Gly Met Gly Asp Val
595 600 605

Ser Glu Lys His Gly Ser Gly Pro Val Val Pro Glu Lys Ala Val Arg
610 615 620

Phe Ser Phe Thr Ile Met Lys Ile Thr Ile Ala His Ser Ser Gln Asn
625 630 635 640

Val Lys Val Phe Glu Glu Ala Lys Pro Asn Ser Glu Leu Cys Cys Lys
645 650 655

Pro Leu Cys Leu Met Leu Ala Asp Glu Ser Asp His Glu Thr Leu Thr
660 665 670

Ala Ile Leu Ser Pro Leu Ile Ala Glu Arg Glu Ala Met Lys Ser Ser
675 680 685

```
Glu Leu Met Leu Glu Leu Gly Gly Ile Leu Arg Thr Phe Lys Phe Ile
    690                 695                 700

Phe Arg Gly Thr Gly Tyr Asp Glu Lys Leu Val Arg Glu Val Glu Gly
705                 710                 715                 720

Leu Glu Ala Ser Gly Ser Val Tyr Ile Cys Thr Leu Cys Asp Ala Thr
                725                 730                 735

Arg Leu Glu Ala Ser Gln Asn Leu Val Phe His Ser Ile Thr Arg Ser
            740                 745                 750

His Ala Glu Asn Leu Glu Arg Tyr Glu Val Trp Arg Ser Asn Pro Tyr
        755                 760                 765

His Glu Ser Val Glu Glu Leu Arg Asp Arg Val Lys Gly Val Ser Ala
    770                 775                 780

Lys Pro Phe Ile Glu Thr Val Pro Ser Ile Asp Ala Leu His Cys Asp
785                 790                 795                 800

Ile Gly Asn Ala Ala Glu Phe Tyr Lys Ile Phe Gln Leu Glu Ile Gly
                805                 810                 815

Glu Val Tyr Lys Asn Pro Asn Ala Ser Lys Glu Glu Arg Lys Arg Trp
            820                 825                 830

Gln Ala Thr Leu Asp Lys His Leu Arg Lys Lys Met Asn Leu Lys Pro
        835                 840                 845

Ile Met Arg Met Asn Gly Asn Phe Ala Arg Lys Leu Met Thr Lys Glu
    850                 855                 860

Thr Val Asp Ala Val Cys Glu Leu Ile Pro Ser Glu Glu Arg His Glu
865                 870                 875                 880

Ala Leu Arg Glu Leu Met Asp Leu Tyr Leu Lys Met Lys Pro Val Trp
                885                 890                 895

Arg Ser Ser Cys Pro Ala Lys Glu Cys Pro Glu Ser Leu Cys Gln Tyr
            900                 905                 910

Ser Phe Asn Ser Gln Arg Phe Ala Glu Leu Leu Ser Thr Lys Phe Lys
        915                 920                 925
```

Tyr Arg Tyr Glu Gly Lys Ile Thr Asn Tyr Phe His Lys Thr Leu Ala
930 935 940

His Val Pro Glu Ile Ile Glu Arg Asp Gly Ser Ile Gly Ala Trp Ala
945 950 955 960

Ser Glu Gly Asn Glu Ser Gly Asn Lys Leu Phe Arg Arg Phe Arg Lys
965 970 975

Met Asn Ala Arg Gln Ser Lys Cys Tyr Glu Met Glu Asp Val Leu Lys
980 985 990

His His Trp Leu Tyr Thr Ser Lys Tyr Leu Gln Lys Phe Met Asn Ala
995 1000 1005

His Asn Ala Leu Lys Thr Ser Gly Phe Thr Met Asn Pro Gln Ala
1010 1015 1020

Ser Leu Gly Asp Pro Leu Gly Ile Glu Asp Ser Leu Glu Ser Gln
1025 1030 1035

Asp Ser Met Glu Phe
1040

<210> 2453
<211> 527
<212> PRT
<213> Homo sapiens

<400> 2453

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

Pro Gly Phe Ser Leu Met Asn Phe Asp Gly Gln Val Phe Phe Phe Gly
20 25 30

Gln Lys Gly Trp Pro Lys Arg Ser Cys Pro Thr Gly Val Phe His Leu
35 40 45

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

Asp Ser Cys Tyr Leu Pro Pro Leu Arg Tyr Pro Ala Thr Cys Thr Phe
65 70 75 80

Lys Gly Ser Leu Glu Ser Glu Lys His Gln Tyr Ile Ile His Gly Gly

85 90 95

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

Val Cys Lys Asn Asn Lys Lys Val Thr Phe Arg Cys Thr Glu Lys Asp
115 120 125

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

Val Tyr Ser Arg Gly Lys Ser Met Gly Ala Leu Phe Gly Gly Arg Ser
145 150 155 160

Tyr Met Pro Ser Thr His Arg Thr Thr Glu Lys Trp Asn Ser Val Ala
165 170 175

Asp Cys Leu Pro Cys Val Phe Leu Val Asp Phe Glu Phe Gly Cys Ala
180 185 190

Thr Ser Tyr Ile Leu Pro Glu Leu Gln Asp Gly Leu Ser Phe His Val
195 200 205

Ser Ile Ala Lys Asn Asp Thr Ile Tyr Ile Leu Gly Gly His Ser Leu
210 215 220

Ala Asn Asn Ile Arg Pro Ala Asn Leu Tyr Arg Ile Arg Val Asp Leu
225 230 235 240

Pro Leu Gly Ser Pro Ala Val Asn Cys Thr Val Leu Pro Gly Gly Ile
245 250 255

Ser Val Ser Ser Ala Ile Leu Thr Gln Thr Asn Asn Asp Glu Phe Val
260 265 270

Ile Val Gly Gly Tyr Gln Leu Glu Asn Gln Lys Arg Met Ile Cys Asn
275 280 285

Ile Ile Ser Leu Glu Asp Asn Lys Ile Glu Ile Arg Glu Met Glu Thr
290 295 300

Pro Asp Trp Thr Pro Asp Ile Lys His Ser Lys Ile Trp Phe Gly Ser
305 310 315 320

Asn Thr Gly Asn Gly Thr Val Phe Leu Gly Ile Pro Gly Asp Asn Lys
325 330 335

```
Gln Val Val Ser Glu Gly Phe Tyr Phe Tyr Met Leu Lys Cys Ala Glu
            340                 345                 350

Asp Asp Thr Asn Glu Glu Gln Thr Thr Phe Thr Asn Ser Gln Thr Ser
        355                 360                 365

Thr Glu Asp Pro Gly Asp Ser Thr Pro Phe Glu Asp Ser Glu Glu Phe
    370                 375                 380

Cys Phe Ser Ala Glu Ala Asn Ser Phe Asp Gly Asp Asp Glu Phe Asp
385                 390                 395                 400

Thr Tyr Asn Glu Asp Asp Glu Glu Asp Glu Ser Glu Thr Gly Tyr Trp
                405                 410                 415

Ile Thr Cys Cys Pro Thr Cys Asp Val Asp Ile Asn Thr Trp Val Pro
            420                 425                 430

Phe Tyr Ser Thr Glu Leu Asn Lys Pro Ala Met Ile Tyr Cys Ser His
        435                 440                 445

Gly Asp Gly His Trp Val His Ala Gln Cys Met Asp Leu Ala Glu Arg
    450                 455                 460

Thr Leu Ile His Leu Ser Ala Gly Ser Asn Lys Tyr Tyr Cys Asn Glu
465                 470                 475                 480

His Val Glu Ile Ala Arg Ala Leu His Thr Pro Gln Arg Val Leu Pro
                485                 490                 495

Leu Lys Lys Pro Pro Met Lys Ser Leu Arg Lys Lys Gly Ser Gly Lys
            500                 505                 510

Ile Leu Thr Pro Ala Lys Lys Ser Phe Leu Arg Arg Leu Phe Asp
        515                 520                 525
```

<210> 2454
<211> 93
<212> PRT
<213> Homo sapiens

<400> 2454

```
Met Asn Ala Lys Val Val Val Val Leu Val Leu Val Leu Thr Ala Leu
1               5                   10                  15
```

```
Cys Leu Ser Asp Gly Lys Pro Val Ser Leu Ser Tyr Arg Cys Pro Cys
            20                  25                  30

Arg Phe Phe Glu Ser His Val Ala Arg Ala Asn Val Lys His Leu Lys
        35                  40                  45

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

Asn Asn Asn Arg Gln Val Cys Ile Asp Pro Lys Leu Lys Trp Ile Gln
65                  70                  75                  80

Glu Tyr Leu Glu Lys Ala Leu Asn Lys Arg Phe Lys Met
                85                  90
```

<210> 2455
<211> 277
<212> PRT
<213> Homo sapiens

<400> 2455

```
Met Cys Val Gly Ala Arg Arg Leu Gly Arg Gly Pro Cys Ala Ala Leu
1               5                   10                  15

Leu Leu Leu Gly Leu Gly Leu Ser Thr Val Thr Gly Leu His Cys Val
            20                  25                  30

Gly Asp Thr Tyr Pro Ser Asn Asp Arg Cys Cys His Glu Cys Arg Pro
        35                  40                  45

Gly Asn Gly Met Val Ser Arg Cys Ser Arg Ser Gln Asn Thr Val Cys
    50                  55                  60

Arg Pro Cys Gly Pro Gly Phe Tyr Asn Asp Val Val Ser Ser Lys Pro
65                  70                  75                  80

Cys Lys Pro Cys Thr Trp Cys Asn Leu Arg Ser Gly Ser Glu Arg Lys
                85                  90                  95

Gln Leu Cys Thr Ala Thr Gln Asp Thr Val Cys Arg Cys Arg Ala Gly
            100                 105                 110

Thr Gln Pro Leu Asp Ser Tyr Lys Pro Gly Val Asp Cys Ala Pro Cys
        115                 120                 125

Pro Pro Gly His Phe Ser Pro Gly Asp Asn Gln Ala Cys Lys Pro Trp
    130                 135                 140
```

```
Thr Asn Cys Thr Leu Ala Gly Lys His Thr Leu Gln Pro Ala Ser Asn
145                 150                 155                 160

Ser Ser Asp Ala Ile Cys Glu Asp Arg Asp Pro Pro Ala Thr Gln Pro
                165                 170                 175

Gln Glu Thr Gln Gly Pro Pro Ala Arg Pro Ile Thr Val Gln Pro Thr
            180                 185                 190

Glu Ala Trp Pro Arg Thr Ser Gln Gly Pro Ser Thr Arg Pro Val Glu
        195                 200                 205

Val Pro Gly Gly Arg Ala Val Ala Ala Ile Leu Gly Leu Gly Leu Val
    210                 215                 220

Leu Gly Leu Leu Gly Pro Leu Ala Ile Leu Leu Ala Leu Tyr Leu Leu
225                 230                 235                 240

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

Gly Ser Phe Arg Thr Pro Ile Gln Glu Glu Gln Ala Asp Ala His Ser
            260                 265                 270

Thr Leu Ala Lys Ile
        275
```

<210> 2456
<211> 183
<212> PRT
<213> Homo sapiens

<400> 2456

```
Met Glu Arg Val Gln Pro Leu Glu Glu Asn Val Gly Asn Ala Ala Arg
1               5                   10                  15

Pro Arg Phe Glu Arg Asn Lys Leu Leu Leu Val Ala Ser Val Ile Gln
            20                  25                  30

Gly Leu Gly Leu Leu Leu Cys Phe Thr Tyr Ile Cys Leu His Phe Ser
        35                  40                  45

Ala Leu Gln Val Ser His Arg Tyr Pro Arg Ile Gln Ser Ile Lys Val
    50                  55                  60
```

```
Gln Phe Thr Glu Tyr Lys Lys Glu Lys Gly Phe Ile Leu Thr Ser Gln
65                  70                  75                  80

Lys Glu Asp Glu Ile Met Lys Val Gln Asn Asn Ser Val Ile Ile Asn
                85                  90                  95

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

Val Asn Ile Ser Leu His Tyr Gln Lys Asp Glu Glu Pro Leu Phe Gln
        115                 120                 125

Leu Lys Lys Val Arg Ser Val Asn Ser Leu Met Val Ala Ser Leu Thr
    130                 135                 140

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

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

Pro Gly Glu Phe Cys Val Leu
            180

<210>  2457
<211>  275
<212>  PRT
<213>  Homo sapiens

<400>  2457

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

Tyr Ala Ala Pro Ala Pro Val Gln Ala Leu Gln Gln Ala Gly Ile Val
            20                  25                  30

Gly Gly Gln Glu Ala Pro Arg Ser Lys Trp Pro Trp Gln Val Ser Leu
        35                  40                  45

Arg Val Arg Asp Arg Tyr Trp Met His Phe Cys Gly Gly Ser Leu Ile
    50                  55                  60

His Pro Gln Trp Val Leu Thr Ala Ala His Cys Leu Gly Pro Asp Val
65                  70                  75                  80

Lys Asp Leu Ala Thr Leu Arg Val Gln Leu Arg Glu Gln His Leu Tyr
                85                  90                  95
```

```
Tyr Gln Asp Gln Leu Leu Pro Val Ser Arg Ile Ile Val His Pro Gln
            100                 105                 110

Phe Tyr Ile Ile Gln Thr Gly Ala Asp Ile Ala Leu Leu Glu Leu Glu
        115                 120                 125

Glu Pro Val Asn Ile Ser Ser Arg Val His Thr Val Met Leu Pro Pro
    130                 135                 140

Ala Ser Glu Thr Phe Pro Pro Gly Met Pro Cys Trp Val Thr Gly Trp
145                 150                 155                 160

Gly Asp Val Asp Asn Asp Glu Pro Leu Pro Pro Pro Phe Pro Leu Lys
                165                 170                 175

Gln Val Lys Val Pro Ile Met Glu Asn His Ile Cys Asp Ala Lys Tyr
            180                 185                 190

His Leu Gly Ala Tyr Thr Gly Asp Asp Val Arg Ile Ile Arg Asp Asp
        195                 200                 205

Met Leu Cys Ala Gly Asn Ser Gln Arg Asp Ser Cys Lys Gly Asp Ser
    210                 215                 220

Gly Gly Pro Leu Val Cys Lys Val Asn Gly Thr Trp Leu Gln Ala Gly
225                 230                 235                 240

Val Val Ser Trp Asp Glu Gly Cys Ala Gln Pro Asn Arg Pro Gly Ile
                245                 250                 255

Tyr Thr Arg Val Thr Tyr Tyr Leu Asp Trp Ile His His Tyr Val Pro
            260                 265                 270

Lys Lys Pro
        275
```

<210> 2458
<211> 363
<212> PRT
<213> Homo sapiens

<400> 2458

```
Met Ala Gln Thr Pro Ala Phe Asp Lys Pro Lys Val Glu Leu His Val
1               5                   10                  15
```

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

Arg Arg Gly Ile Ala Leu Pro Ala Asn Thr Ala Glu Gly Leu Leu Asn
        35                  40                  45

Val Ile Gly Met Asp Lys Pro Leu Thr Leu Pro Asp Phe Leu Ala Lys
    50                  55                  60

Phe Asp Tyr Tyr Met Pro Ala Ile Ala Gly Cys Arg Glu Ala Ile Lys
65                  70                  75                  80

Arg Ile Ala Tyr Glu Phe Val Glu Met Lys Ala Lys Glu Gly Val Val
                85                  90                  95

Tyr Val Glu Val Arg Tyr Ser Pro His Leu Leu Ala Asn Ser Lys Val
            100                 105                 110

Glu Pro Ile Pro Trp Asn Gln Ala Glu Gly Asp Leu Thr Pro Asp Glu
        115                 120                 125

Val Val Ala Leu Val Gly Gln Gly Leu Gln Glu Gly Glu Arg Asp Phe
    130                 135                 140

Gly Val Lys Ala Arg Ser Ile Leu Cys Cys Met Arg His Gln Pro Asn
145                 150                 155                 160

Trp Ser Pro Lys Val Val Glu Leu Cys Lys Asn Tyr Gln Gln Gln Thr
                165                 170                 175

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

Leu Leu Pro Gly His Val Gln Ala Tyr Gln Glu Ala Val Lys Ser Gly
        195                 200                 205

Ile His Arg Thr Val His Ala Gly Glu Val Gly Ser Ala Glu Val Val
    210                 215                 220

Lys Glu Ala Val Asp Ile Leu Lys Thr Glu Arg Leu Gly His Gly Tyr
225                 230                 235                 240

His Thr Leu Glu Asp Gln Ala Leu Tyr Asn Arg Leu Arg Gln Glu Asn
                245                 250                 255

Met His Phe Glu Ile Cys Pro Trp Ser Ser Tyr Leu Thr Gly Ala Trp
```

260 265 270

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

Asn Tyr Ser Leu Asn Thr Asp Asp Pro Leu Ile Phe Lys Ser Thr Leu
290 295 300

Asp Thr Asp Tyr Gln Met Thr Lys Arg Asp Met Gly Phe Thr Glu Glu
305 310 315 320

Glu Phe Lys Arg Leu Asn Ile Asn Ala Ala Lys Ser Ser Phe Leu Pro
325 330 335

Glu Asp Glu Lys Arg Glu Leu Leu Asp Leu Leu Tyr Lys Ala Tyr Gly
340 345 350

Met Pro Pro Ser Ala Ser Ala Gly Gln Asn Leu
355 360

<210> 2459
<211> 443
<212> PRT
<213> Homo sapiens

<400> 2459

Met Asp Phe Pro Cys Leu Trp Leu Gly Leu Leu Leu Pro Leu Val Ala
1 5 10 15

Ala Leu Asp Phe Asn Tyr His Arg Gln Glu Gly Met Glu Ala Phe Leu
20 25 30

Lys Thr Val Ala Gln Asn Tyr Ser Ser Val Thr His Leu His Ser Ile
35 40 45

Gly Lys Ser Val Lys Gly Arg Asn Leu Trp Val Leu Val Val Gly Arg
50 55 60

Phe Pro Lys Glu His Arg Ile Gly Ile Pro Glu Phe Lys Tyr Val Ala
65 70 75 80

Asn Met His Gly Asp Glu Thr Val Gly Arg Glu Leu Leu Leu His Leu
85 90 95

Ile Asp Tyr Leu Val Thr Ser Asp Gly Lys Asp Pro Glu Ile Thr Asn
100 105 110

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

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

Glu Asn Tyr Asn Gln Tyr Asp Leu Asn Arg Asn Phe Pro Asp Ala Phe
145                 150                 155                 160

Glu Tyr Asn Asn Val Ser Arg Gln Pro Glu Thr Val Ala Val Met Lys
                165                 170                 175

Trp Leu Lys Thr Glu Thr Phe Val Leu Ser Ala Asn Leu His Gly Gly
            180                 185                 190

Ala Leu Val Ala Ser Tyr Pro Phe Asp Asn Gly Val Gln Ala Thr Gly
        195                 200                 205

Ala Leu Tyr Ser Arg Ser Leu Thr Pro Asp Asp Asp Val Phe Gln Tyr
    210                 215                 220

Leu Ala His Thr Tyr Ala Ser Arg Asn Pro Asn Met Lys Lys Gly Asp
225                 230                 235                 240

Glu Cys Lys Asn Lys Met Asn Phe Pro Asn Gly Val Thr Asn Gly Tyr
                245                 250                 255

Ser Trp Tyr Pro Leu Gln Gly Gly Met Gln Asp Tyr Asn Tyr Ile Trp
            260                 265                 270

Ala Gln Cys Phe Glu Ile Thr Leu Glu Leu Ser Cys Cys Lys Tyr Pro
        275                 280                 285

Arg Glu Glu Lys Leu Pro Ser Phe Trp Asn Asn Asn Lys Ala Ser Leu
    290                 295                 300

Ile Glu Tyr Ile Lys Gln Val His Leu Gly Val Lys Gly Gln Val Phe
305                 310                 315                 320

Asp Gln Asn Gly Asn Pro Leu Pro Asn Val Ile Val Glu Val Gln Asp
                325                 330                 335

Arg Lys His Ile Cys Pro Tyr Arg Thr Asn Lys Tyr Gly Glu Tyr Tyr
            340                 345                 350
```

```
Leu Leu Leu Leu Pro Gly Ser Tyr Ile Ile Asn Val Thr Val Pro Gly
        355                 360                 365

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

Phe Ser Ala Leu Lys Lys Asp Ile Leu Leu Pro Phe Gln Gly Gln Leu
385                 390                 395                 400

Asp Ser Ile Pro Val Ser Asn Pro Ser Cys Pro Met Ile Pro Leu Tyr
                405                 410                 415

Arg Asn Leu Pro Asp His Ser Ala Ala Thr Lys Pro Ser Leu Phe Leu
            420                 425                 430

Phe Leu Val Ser Leu Leu His Ile Phe Phe Lys
        435                 440
```

<210> 2460
<211> 144
<212> PRT
<213> Homo sapiens

<400> 2460

```
Met Trp Leu Gln Ser Leu Leu Leu Leu Gly Thr Val Ala Cys Ser Ile
1               5                   10                  15

Ser Ala Pro Ala Arg Ser Pro Ser Pro Ser Thr Gln Pro Trp Glu His
            20                  25                  30

Val Asn Ala Ile Gln Glu Ala Arg Arg Leu Leu Asn Leu Ser Arg Asp
        35                  40                  45

Thr Ala Ala Glu Met Asn Glu Thr Val Glu Val Ile Ser Glu Met Phe
    50                  55                  60

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

Gln Gly Leu Arg Gly Ser Leu Thr Lys Leu Lys Gly Pro Leu Thr Met
                85                  90                  95

Met Ala Ser His Tyr Lys Gln His Cys Pro Pro Thr Pro Glu Thr Ser
            100                 105                 110

Cys Ala Thr Gln Ile Ile Thr Phe Glu Ser Phe Lys Glu Asn Leu Lys
        115                 120                 125
```

Asp Phe Leu Leu Val Ile Pro Phe Asp Cys Trp Glu Pro Val Gln Glu
130 135 140

<210> 2461
<211> 204
<212> PRT
<213> Homo sapiens

<400> 2461

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

Leu Leu Leu Trp His Ser Ala Leu Trp Thr Val Gln Glu Ala Thr Pro
20 25 30

Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu Lys Cys Leu
35 40 45

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

Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu Val Leu Leu
65 70 75 80

Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser Cys Pro Ser
85 90 95

Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His Ser Gly Leu
100 105 110

Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile Ser Pro Glu
115 120 125

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

Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala Pro Ala Leu
145 150 155 160

Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe Gln Arg
165 170 175

Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe Leu Glu
180 185 190

Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
195 200

<210> 2462
<211> 224
<212> PRT
<213> Homo sapiens

<400> 2462

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

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

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

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

Arg Gly Thr Val Phe Ser Arg Met Pro Pro Arg Asp Lys Thr Met Arg
65 70 75 80

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

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

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

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

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

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

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

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

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

<210> 2463
<211> 993
<212> PRT
<213> Homo sapiens

<400> 2463

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

Phe Ser Ala Met Ile Phe Gly Thr Ile Thr Asn Gln Asp Leu Pro Val
20 25 30

Ile Lys Cys Val Leu Ile Asn His Lys Asn Asn Asp Ser Ser Val Gly
35 40 45

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

Cys Ala Leu Arg Pro Gln Ser Ser Gly Thr Val Tyr Glu Ala Ala Ala
65 70 75 80

Val Glu Val Asp Val Ser Ala Ser Ile Thr Leu Gln Val Leu Val Asp
85 90 95

Ala Pro Gly Asn Ile Ser Cys Leu Trp Val Phe Lys His Ser Ser Leu
100 105 110

Asn Cys Gln Pro His Phe Asp Leu Gln Asn Arg Gly Val Val Ser Met
115 120 125

Val Ile Leu Lys Met Thr Glu Thr Gln Ala Gly Glu Tyr Leu Leu Phe
130 135 140

Ile Gln Ser Glu Ala Thr Asn Tyr Thr Ile Leu Phe Thr Val Ser Ile
145 150 155 160

Arg Asn Thr Leu Leu Tyr Thr Leu Arg Arg Pro Tyr Phe Arg Lys Met
165 170 175

Glu Asn Gln Asp Ala Leu Val Cys Ile Ser Glu Ser Val Pro Glu Pro
180 185 190

Ile Val Glu Trp Val Leu Cys Asp Ser Gln Gly Glu Ser Cys Lys Glu
195 200 205

Glu Ser Pro Ala Val Val Lys Lys Glu Glu Lys Val Leu His Glu Leu
210 215 220

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

Cys Thr Arg Leu Phe Thr Ile Asp Leu Asn Gln Thr Pro Gln Thr Thr
245 250 255

Leu Pro Gln Leu Phe Leu Lys Val Gly Glu Pro Leu Trp Ile Arg Cys
260 265 270

Lys Ala Val His Val Asn His Gly Phe Gly Leu Thr Trp Glu Leu Glu
275 280 285

Asn Lys Ala Leu Glu Glu Gly Asn Tyr Phe Glu Met Ser Thr Tyr Ser
290 295 300

Thr Asn Arg Thr Met Ile Arg Ile Leu Phe Ala Phe Val Ser Ser Val
305 310 315 320

Ala Arg Asn Asp Thr Gly Tyr Tyr Thr Cys Ser Ser Ser Lys His Pro
325 330 335

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

Thr Asn Ser Ser Glu Asp Tyr Glu Ile Asp Gln Tyr Glu Glu Phe Cys
355 360 365

Phe Ser Val Arg Phe Lys Ala Tyr Pro Gln Ile Arg Cys Thr Trp Thr
370 375 380

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

Tyr Ser Ile Ser Lys Phe Cys Asn His Lys His Gln Pro Gly Glu Tyr
405 410 415

Ile Phe His Ala Glu Asn Asp Asp Ala Gln Phe Thr Lys Met Phe Thr
420 425 430

Leu Asn Ile Arg Arg Lys Pro Gln Val Leu Ala Glu Ala Ser Ala Ser

435 440 445

Gln Ala Ser Cys Phe Ser Asp Gly Tyr Pro Leu Pro Ser Trp Thr Trp
450 455 460

Lys Lys Cys Ser Asp Lys Ser Pro Asn Cys Thr Glu Glu Ile Thr Glu
465 470 475 480

Gly Val Trp Asn Arg Lys Ala Asn Arg Lys Val Phe Gly Gln Trp Val
485 490 495

Ser Ser Ser Thr Leu Asn Met Ser Glu Ala Ile Lys Gly Phe Leu Val
500 505 510

Lys Cys Cys Ala Tyr Asn Ser Leu Gly Thr Ser Cys Glu Thr Ile Leu
515 520 525

Leu Asn Ser Pro Gly Pro Phe Pro Phe Ile Gln Asp Asn Ile Ser Phe
530 535 540

Tyr Ala Thr Ile Gly Val Cys Leu Leu Phe Ile Val Val Leu Thr Leu
545 550 555 560

Leu Ile Cys His Lys Tyr Lys Lys Gln Phe Arg Tyr Glu Ser Gln Leu
565 570 575

Gln Met Val Gln Val Thr Gly Ser Ser Asp Asn Glu Tyr Phe Tyr Val
580 585 590

Asp Phe Arg Glu Tyr Glu Tyr Asp Leu Lys Trp Glu Phe Pro Arg Glu
595 600 605

Asn Leu Glu Phe Gly Lys Val Leu Gly Ser Gly Ala Phe Gly Lys Val
610 615 620

Met Asn Ala Thr Ala Tyr Gly Ile Ser Lys Thr Gly Val Ser Ile Gln
625 630 635 640

Val Ala Val Lys Met Leu Lys Glu Lys Ala Asp Ser Ser Glu Arg Glu
645 650 655

Ala Leu Met Ser Glu Leu Lys Met Met Thr Gln Leu Gly Ser His Glu
660 665 670

Asn Ile Val Asn Leu Leu Gly Ala Cys Thr Leu Ser Gly Pro Ile Tyr
675 680 685

Leu Ile Phe Glu Tyr Cys Cys Tyr Gly Asp Leu Leu Asn Tyr Leu Arg
690 695 700

Ser Lys Arg Glu Lys Phe His Arg Thr Trp Thr Glu Ile Phe Lys Glu
705 710 715 720

His Asn Phe Ser Phe Tyr Pro Thr Phe Gln Ser His Pro Asn Ser Ser
725 730 735

Met Pro Gly Ser Arg Glu Val Gln Ile His Pro Asp Ser Asp Gln Ile
740 745 750

Ser Gly Leu His Gly Asn Ser Phe His Ser Glu Asp Glu Ile Glu Tyr
755 760 765

Glu Asn Gln Lys Arg Leu Glu Glu Glu Glu Asp Leu Asn Val Leu Thr
770 775 780

Phe Glu Asp Leu Leu Cys Phe Ala Tyr Gln Val Ala Lys Gly Met Glu
785 790 795 800

Phe Leu Glu Phe Lys Ser Cys Val His Arg Asp Leu Ala Ala Arg Asn
805 810 815

Val Leu Val Thr His Gly Lys Val Val Lys Ile Cys Asp Phe Gly Leu
820 825 830

Ala Arg Asp Ile Met Ser Asp Ser Asn Tyr Val Val Arg Gly Asn Ala
835 840 845

Arg Leu Pro Val Lys Trp Met Ala Pro Glu Ser Leu Phe Glu Gly Ile
850 855 860

Tyr Thr Ile Lys Ser Asp Val Trp Ser Tyr Gly Ile Leu Leu Trp Glu
865 870 875 880

Ile Phe Ser Leu Gly Val Asn Pro Tyr Pro Gly Ile Pro Val Asp Ala
885 890 895

Asn Phe Tyr Lys Leu Ile Gln Asn Gly Phe Lys Met Asp Gln Pro Phe
900 905 910

Tyr Ala Thr Glu Glu Ile Tyr Ile Ile Met Gln Ser Cys Trp Ala Phe
915 920 925

Asp Ser Arg Lys Arg Pro Ser Phe Pro Asn Leu Thr Ser Phe Leu Gly
930 935 940

Cys Gln Leu Ala Asp Ala Glu Glu Ala Met Tyr Gln Asn Val Asp Gly
945 950 955 960

Arg Val Ser Glu Cys Pro His Thr Tyr Gln Asn Arg Arg Pro Phe Ser
965 970 975

Arg Glu Met Asp Leu Gly Leu Leu Ser Pro Gln Ala Gln Val Glu Asp
980 985 990

Ser

<210> 2464
<211> 443
<212> PRT
<213> Homo sapiens

<400> 2464

Met Glu Val Thr Ala Asp Gln Pro Arg Trp Val Ser His His His Pro
1 5 10 15

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

His Ser Tyr Met Asp Ala Ala Gln Tyr Pro Leu Pro Glu Glu Val Asp
35 40 45

Val Leu Phe Asn Ile Asp Gly Gln Gly Asn His Val Pro Pro Tyr Tyr
50 55 60

Gly Asn Ser Val Arg Ala Thr Val Gln Arg Tyr Pro Pro Thr His His
65 70 75 80

Gly Ser Gln Val Cys Arg Pro Pro Leu Leu His Gly Ser Leu Pro Trp
85 90 95

Leu Asp Gly Gly Lys Ala Leu Gly Ser His His Thr Ala Ser Pro Trp
100 105 110

Asn Leu Ser Pro Phe Ser Lys Thr Ser Ile His His Gly Ser Pro Gly
115 120 125

Pro Leu Ser Val Tyr Pro Pro Ala Ser Ser Ser Ser Leu Ser Gly Gly

130 135 140

His Ala Ser Pro His Leu Phe Thr Phe Pro Pro Thr Pro Pro Lys Asp
145 150 155 160

Val Ser Pro Asp Pro Ser Leu Ser Thr Pro Gly Ser Ala Gly Ser Ala
165 170 175

Arg Gln Asp Glu Lys Glu Cys Leu Lys Tyr Gln Val Pro Leu Pro Asp
180 185 190

Ser Met Lys Leu Glu Ser Ser His Ser Arg Gly Ser Met Thr Ala Leu
195 200 205

Gly Gly Ala Ser Ser Ser Thr His His Pro Ile Thr Thr Tyr Pro Pro
210 215 220

Tyr Val Pro Glu Tyr Ser Ser Gly Leu Phe Pro Pro Ser Ser Leu Leu
225 230 235 240

Gly Gly Ser Pro Thr Gly Phe Gly Cys Lys Ser Arg Pro Lys Ala Arg
245 250 255

Ser Ser Thr Gly Arg Glu Cys Val Asn Cys Gly Ala Thr Ser Thr Pro
260 265 270

Leu Trp Arg Arg Asp Gly Thr Gly His Tyr Leu Cys Asn Ala Cys Gly
275 280 285

Leu Tyr His Lys Met Asn Gly Gln Asn Arg Pro Leu Ile Lys Pro Lys
290 295 300

Arg Arg Leu Ser Ala Ala Arg Arg Ala Gly Thr Ser Cys Ala Asn Cys
305 310 315 320

Gln Thr Thr Thr Thr Thr Leu Trp Arg Arg Asn Ala Asn Gly Asp Pro
325 330 335

Val Cys Asn Ala Cys Gly Leu Tyr Tyr Lys Leu His Asn Ile Asn Arg
340 345 350

Pro Leu Thr Met Lys Lys Glu Gly Ile Gln Thr Arg Asn Arg Lys Met
355 360 365

Ser Ser Lys Ser Lys Lys Cys Lys Lys Val His Asp Ser Leu Glu Asp
370 375 380

```
Phe Pro Lys Asn Ser Ser Phe Asn Pro Ala Ala Leu Ser Arg His Met
385                 390                 395                 400

Ser Ser Leu Ser His Ile Ser Pro Phe Ser His Ser Ser His Met Leu
                405                 410                 415

Thr Thr Pro Thr Pro Met His Pro Pro Ser Ser Leu Ser Phe Gly Pro
            420                 425                 430

His His Pro Ser Ser Met Val Thr Ala Met Gly
        435                 440

<210>  2465
<211>  459
<212>  PRT
<213>  Homo sapiens

<400>  2465

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

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

Ala Glu Leu Asp Asp Tyr Ser Phe Ser Cys Tyr Ser Gln Leu Glu Val
        35                  40                  45

Asn Gly Ser Gln His Ser Leu Thr Cys Ala Phe Glu Asp Pro Asp Val
    50                  55                  60

Asn Ile Thr Asn Leu Glu Phe Glu Ile Cys Gly Ala Leu Val Glu Val
65                  70                  75                  80

Lys Cys Leu Asn Phe Arg Lys Leu Gln Glu Ile Tyr Phe Ile Glu Thr
                85                  90                  95

Lys Lys Phe Leu Leu Ile Gly Lys Ser Asn Ile Cys Val Lys Val Gly
            100                 105                 110

Glu Lys Ser Leu Thr Cys Lys Lys Ile Asp Leu Thr Thr Ile Val Lys
        115                 120                 125

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

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

Lys Val Leu Met His Asp Val Ala Tyr Arg Gln Glu Lys Asp Glu Asn
165 170 175

Lys Trp Thr His Val Asn Leu Ser Ser Thr Lys Leu Thr Leu Leu Gln
180 185 190

Arg Lys Leu Gln Pro Ala Ala Met Tyr Glu Ile Lys Val Arg Ser Ile
195 200 205

Pro Asp His Tyr Phe Lys Gly Phe Trp Ser Glu Trp Ser Pro Ser Tyr
210 215 220

Tyr Phe Arg Thr Pro Glu Ile Asn Asn Ser Ser Gly Glu Met Asp Pro
225 230 235 240

Ile Leu Leu Thr Ile Ser Ile Leu Ser Phe Phe Ser Val Ala Leu Leu
245 250 255

Val Ile Leu Ala Cys Val Leu Trp Lys Lys Arg Ile Lys Pro Ile Val
260 265 270

Trp Pro Ser Leu Pro Asp His Lys Lys Thr Leu Glu His Leu Cys Lys
275 280 285

Lys Pro Arg Lys Asn Leu Asn Val Ser Phe Asn Pro Glu Ser Phe Leu
290 295 300

Asp Cys Gln Ile His Arg Val Asp Asp Ile Gln Ala Arg Asp Glu Val
305 310 315 320

Glu Gly Phe Leu Gln Asp Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu
325 330 335

Lys Gln Arg Leu Gly Gly Asp Val Gln Ser Pro Asn Cys Pro Ser Glu
340 345 350

Asp Val Val Ile Thr Pro Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr
355 360 365

Cys Leu Ala Gly Asn Val Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser
370 375 380

Ser Arg Ser Leu Asp Cys Arg Glu Ser Gly Lys Asn Gly Pro His Val

385 390 395 400

Tyr Gln Asp Leu Leu Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro
405 410 415

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

Gln Gly Gln Pro Ile Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala
435 440 445

Tyr Val Thr Met Ser Ser Phe Tyr Gln Asn Gln
450 455

<210> 2466
<211> 362
<212> PRT
<213> Homo sapiens

<400> 2466

Met Ala Thr Ala Glu Thr Ala Leu Pro Ser Ile Ser Thr Leu Thr Ala
1 5 10 15

Leu Gly Pro Phe Pro Asp Thr Gln Asp Asp Phe Leu Lys Trp Trp Arg
20 25 30

Ser Glu Glu Ala Gln Asp Met Gly Pro Gly Pro Pro Asp Pro Thr Glu
35 40 45

Pro Pro Leu His Val Lys Ser Glu Asp Gln Pro Gly Glu Glu Glu Asp
50 55 60

Asp Glu Arg Gly Ala Asp Ala Thr Trp Asp Leu Asp Leu Leu Leu Thr
65 70 75 80

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

Ala Pro Ser Glu Ala Ser Gly Ala Gln Tyr Pro Pro Pro Pro Glu Thr
100 105 110

Leu Gly Ala Tyr Ala Gly Gly Pro Gly Leu Val Ala Gly Leu Leu Gly
115 120 125

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

```
Pro Asp Ala Phe Val Gly Pro Ala Leu Ala Pro Ala Pro Ala Pro Glu
145                 150                 155                 160

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

Ser Ser Gly Gly Tyr Phe Pro Arg Thr Gly Leu Ser Val Pro Ala Ala
            180                 185                 190

Ser Gly Ala Pro Tyr Gly Leu Leu Ser Gly Tyr Pro Ala Met Tyr Pro
        195                 200                 205

Ala Pro Gln Tyr Gln Gly His Phe Gln Leu Phe Arg Gly Leu Gln Gly
    210                 215                 220

Pro Ala Pro Gly Pro Ala Thr Ser Pro Ser Phe Leu Ser Cys Leu Gly
225                 230                 235                 240

Pro Gly Thr Val Gly Thr Gly Leu Gly Gly Thr Ala Glu Asp Pro Gly
                245                 250                 255

Val Ile Ala Glu Thr Ala Pro Ser Lys Arg Gly Arg Arg Ser Trp Ala
            260                 265                 270

Arg Lys Arg Gln Ala Ala His Thr Cys Ala His Pro Gly Cys Gly Lys
        275                 280                 285

Ser Tyr Thr Lys Ser Ser His Leu Lys Ala His Leu Arg Thr His Thr
    290                 295                 300

Gly Glu Lys Pro Tyr Ala Cys Thr Trp Glu Gly Cys Gly Trp Arg Phe
305                 310                 315                 320

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

Arg Pro Phe Arg Cys Gln Leu Cys Pro Arg Ala Phe Ser Arg Ser Asp
            340                 345                 350

His Leu Ala Leu His Met Lys Arg His Leu
        355                 360
```

<210> 2467
<211> 509
<212> PRT
<213> Homo sapiens

<400> 2467

```
Met Gly Cys Gly Cys Ser Ser His Pro Glu Asp Asp Trp Met Glu Asn
1               5                  10                  15

Ile Asp Val Cys Glu Asn Cys His Tyr Pro Ile Val Pro Leu Asp Gly
            20                  25                  30

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

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

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

Gly Phe Glu Lys Gly Glu Pro Leu Arg Ile Leu Glu Gln Ser Gly Glu
                85                  90                  95

Trp Trp Lys Ala Gln Ser Leu Thr Thr Gly Gln Glu Gly Phe Ile Pro
            100                 105                 110

Phe Asn Phe Val Ala Lys Ala Asn Ser Leu Glu Pro Glu Pro Trp Phe
        115                 120                 125

Phe Lys Asn Leu Ser Arg Lys Asp Ala Glu Arg Gln Leu Leu Ala Pro
    130                 135                 140

Gly Asn Thr His Gly Ser Phe Leu Ile Arg Glu Ser Glu Ser Thr Ala
145                 150                 155                 160

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

Val Val Lys His Tyr Lys Ile Arg Asn Leu Asp Asn Gly Gly Phe Tyr
            180                 185                 190

Ile Ser Pro Arg Ile Thr Phe Pro Gly Leu His Glu Leu Val Arg His
        195                 200                 205

Tyr Thr Asn Ala Ser Asp Gly Leu Cys Thr Arg Leu Ser Arg Pro Cys
    210                 215                 220

Gln Thr Gln Lys Pro Gln Lys Pro Trp Trp Glu Asp Glu Trp Glu Val
225                 230                 235                 240
```

Pro Arg Glu Thr Leu Lys Leu Val Glu Arg Leu Gly Ala Gly Gln Phe
245 250 255

Gly Glu Val Trp Met Gly Tyr Tyr Asn Gly His Thr Lys Val Ala Val
260 265 270

Lys Ser Leu Lys Gln Gly Ser Met Ser Pro Asp Ala Phe Leu Ala Glu
275 280 285

Ala Asn Leu Met Lys Gln Leu Gln His Gln Arg Leu Val Arg Leu Tyr
290 295 300

Ala Val Val Thr Gln Glu Pro Ile Tyr Ile Ile Thr Glu Tyr Met Glu
305 310 315 320

Asn Gly Ser Leu Val Asp Phe Leu Lys Thr Pro Ser Gly Ile Lys Leu
325 330 335

Thr Ile Asn Lys Leu Leu Asp Met Ala Ala Gln Ile Ala Glu Gly Met
340 345 350

Ala Phe Ile Glu Glu Arg Asn Tyr Ile His Arg Asp Leu Arg Ala Ala
355 360 365

Asn Ile Leu Val Ser Asp Thr Leu Ser Cys Lys Ile Ala Asp Phe Gly
370 375 380

Leu Ala Arg Leu Ile Glu Asp Asn Glu Tyr Thr Ala Arg Glu Gly Ala
385 390 395 400

Lys Phe Pro Ile Lys Trp Thr Ala Pro Glu Ala Ile Asn Tyr Gly Thr
405 410 415

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

Ile Val Thr His Gly Arg Ile Pro Tyr Pro Gly Met Thr Asn Pro Glu
435 440 445

Val Ile Gln Asn Leu Glu Arg Gly Tyr Arg Met Val Arg Pro Asp Asn
450 455 460

Cys Pro Glu Glu Leu Tyr Gln Leu Met Arg Leu Cys Trp Lys Glu Arg
465 470 475 480

Pro Glu Asp Arg Pro Thr Phe Asp Tyr Leu Arg Ser Val Leu Glu Asp
485 490 495

Phe Phe Thr Ala Thr Glu Gly Gln Tyr Gln Pro Gln Pro
500 505

<210> 2468
<211> 399
<212> PRT
<213> Homo sapiens

<400> 2468

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

Leu Cys Ala Thr Asp Glu Met Ile Pro Phe Lys Asp Glu Gly Asp Pro
20 25 30

Gln Lys Glu Lys Ile Phe Ala Glu Ile Ser His Pro Glu Glu Glu Gly
35 40 45

Asp Leu Ala Asp Ile Lys Ser Ser Leu Val Asn Glu Ser Glu Ile Ile
50 55 60

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

Glu Pro Tyr His Asp Lys Ala Arg Glu His Pro Asp Asp Gly Lys His
85 90 95

Pro Asp Gly Gly Leu Tyr Asn Lys Gly Pro Ser Tyr Ser Ser Tyr Ser
100 105 110

Gly Tyr Ile Met Met Pro Asn Met Asn Asn Asp Pro Tyr Met Ser Asn
115 120 125

Gly Ser Leu Ser Pro Pro Ile Pro Arg Thr Ser Asn Lys Val Pro Val
130 135 140

Val Gln Pro Ser His Ala Val His Pro Leu Thr Pro Leu Ile Thr Tyr
145 150 155 160

Ser Asp Glu His Phe Ser Pro Gly Ser His Pro Ser His Ile Pro Ser
165 170 175

Asp Val Asn Ser Lys Gln Gly Met Ser Arg His Pro Pro Ala Pro Asp

180 185 190

Ile Pro Thr Phe Tyr Pro Leu Ser Pro Gly Gly Val Gly Gln Ile Thr
195 200 205

Pro Pro Leu Gly Trp Gln Gly Gln Pro Val Tyr Pro Ile Thr Gly Gly
210 215 220

Phe Arg Gln Pro Tyr Pro Ser Ser Leu Ser Val Asp Thr Ser Met Ser
225 230 235 240

Arg Phe Ser His His Met Ile Pro Gly Pro Pro Gly Pro His Thr Thr
245 250 255

Gly Ile Pro His Pro Ala Ile Val Thr Pro Gln Val Lys Gln Glu His
260 265 270

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

Arg Lys Glu Gln Glu Pro Lys Arg Pro His Ile Lys Lys Pro Leu Asn
290 295 300

Ala Phe Met Leu Tyr Met Lys Glu Met Arg Ala Asn Val Val Ala Glu
305 310 315 320

Cys Thr Leu Lys Glu Ser Ala Ala Ile Asn Gln Ile Leu Gly Arg Arg
325 330 335

Trp His Ala Leu Ser Arg Glu Glu Gln Ala Lys Tyr Tyr Glu Leu Ala
340 345 350

Arg Lys Glu Arg Gln Leu His Met Gln Leu Tyr Pro Gly Trp Ser Ala
355 360 365

Arg Asp Asn Tyr Gly Lys Lys Lys Lys Arg Lys Arg Glu Lys Leu Gln
370 375 380

Glu Ser Ala Ser Gly Thr Gly Pro Arg Met Thr Ala Ala Tyr Ile
385 390 395

<210> 2469
<211> 335
<212> PRT
<213> Homo sapiens

<400> 2469

```
Met Gly His Pro Pro Leu Leu Pro Leu Leu Leu Leu Leu His Thr Cys
1               5                  10                  15

Val Pro Ala Ser Trp Gly Leu Arg Cys Met Gln Cys Lys Thr Asn Gly
            20                  25                  30

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

Thr Ile Val Arg Leu Trp Glu Glu Gly Glu Glu Leu Glu Leu Val Glu
    50                  55                  60

Lys Ser Cys Thr His Ser Glu Lys Thr Asn Arg Thr Leu Ser Tyr Arg
65                  70                  75                  80

Thr Gly Leu Lys Ile Thr Ser Leu Thr Glu Val Val Cys Gly Leu Asp
                85                  90                  95

Leu Cys Asn Gln Gly Asn Ser Gly Arg Ala Val Thr Tyr Ser Arg Ser
            100                 105                 110

Arg Tyr Leu Glu Cys Ile Ser Cys Gly Ser Ser Asp Met Ser Cys Glu
        115                 120                 125

Arg Gly Arg His Gln Ser Leu Gln Cys Arg Ser Pro Glu Glu Gln Cys
    130                 135                 140

Leu Asp Val Val Thr His Trp Ile Gln Glu Gly Glu Glu Gly Arg Pro
145                 150                 155                 160

Lys Asp Asp Arg His Leu Arg Gly Cys Gly Tyr Leu Pro Gly Cys Pro
                165                 170                 175

Gly Ser Asn Gly Phe His Asn Asn Asp Thr Phe His Phe Leu Lys Cys
            180                 185                 190

Cys Asn Thr Thr Lys Cys Asn Glu Gly Pro Ile Leu Glu Leu Glu Asn
        195                 200                 205

Leu Pro Gln Asn Gly Arg Gln Cys Tyr Ser Cys Lys Gly Asn Ser Thr
    210                 215                 220

His Gly Cys Ser Ser Glu Glu Thr Phe Leu Ile Asp Cys Arg Gly Pro
225                 230                 235                 240
```

Met Asn Gln Cys Leu Val Ala Thr Gly Thr His Glu Pro Lys Asn Gln
245 250 255

Ser Tyr Met Val Arg Gly Cys Ala Thr Ala Ser Met Cys Gln His Ala
260 265 270

His Leu Gly Asp Ala Phe Ser Met Asn His Ile Asp Val Ser Cys Cys
275 280 285

Thr Lys Ser Gly Cys Asn His Pro Asp Leu Asp Val Gln Tyr Arg Ser
290 295 300

Gly Ala Ala Pro Gln Pro Gly Pro Ala His Leu Ser Leu Thr Ile Thr
305 310 315 320

Leu Leu Met Thr Ala Arg Leu Trp Gly Gly Thr Leu Leu Trp Thr
325 330 335

<210> 2470
<211> 285
<212> PRT
<213> Homo sapiens

<400> 2470

Met Asp Asp Ser Thr Glu Arg Glu Gln Ser Arg Leu Thr Ser Cys Leu
1 5 10 15

Lys Lys Arg Glu Glu Met Lys Leu Lys Glu Cys Val Ser Ile Leu Pro
20 25 30

Arg Lys Glu Ser Pro Ser Val Arg Ser Ser Lys Asp Gly Lys Leu Leu
35 40 45

Ala Ala Thr Leu Leu Leu Ala Leu Leu Ser Cys Cys Leu Thr Val Val
50 55 60

Ser Phe Tyr Gln Val Ala Ala Leu Gln Gly Asp Leu Ala Ser Leu Arg
65 70 75 80

Ala Glu Leu Gln Gly His His Ala Glu Lys Leu Pro Ala Gly Ala Gly
85 90 95

Ala Pro Lys Ala Gly Leu Glu Glu Ala Pro Ala Val Thr Ala Gly Leu
100 105 110

Lys Ile Phe Glu Pro Pro Ala Pro Gly Glu Gly Asn Ser Ser Gln Asn
115 120 125

```
Ser Arg Asn Lys Arg Ala Val Gln Gly Pro Glu Glu Thr Val Thr Gln
    130                 135                 140

Asp Cys Leu Gln Leu Ile Ala Asp Ser Glu Thr Pro Thr Ile Gln Lys
145                 150                 155                 160

Gly Ser Tyr Thr Phe Val Pro Trp Leu Leu Ser Phe Lys Arg Gly Ser
                165                 170                 175

Ala Leu Glu Glu Lys Glu Asn Lys Ile Leu Val Lys Glu Thr Gly Tyr
            180                 185                 190

Phe Phe Ile Tyr Gly Gln Val Leu Tyr Thr Asp Lys Thr Tyr Ala Met
        195                 200                 205

Gly His Leu Ile Gln Arg Lys Lys Val His Val Phe Gly Asp Glu Leu
    210                 215                 220

Ser Leu Val Thr Leu Phe Arg Cys Ile Gln Asn Met Pro Glu Thr Leu
225                 230                 235                 240

Pro Asn Asn Ser Cys Tyr Ser Ala Gly Ile Ala Lys Leu Glu Glu Gly
                245                 250                 255

Asp Glu Leu Gln Leu Ala Ile Pro Arg Glu Asn Ala Gln Ile Ser Leu
            260                 265                 270

Asp Gly Asp Val Thr Phe Phe Gly Ala Leu Lys Leu Leu
        275                 280                 285


<210>  2471
<211>  99
<212>  PRT
<213>  Homo sapiens

<400>  2471

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

Ala Ala Leu Cys Glu Gly Ala Val Leu Pro Arg Ser Ala Lys Glu Leu
            20                  25                  30

Arg Cys Gln Cys Ile Lys Thr Tyr Ser Lys Pro Phe His Pro Lys Phe
        35                  40                  45
```

```
Ile Lys Glu Leu Arg Val Ile Glu Ser Gly Pro His Cys Ala Asn Thr
    50                  55                  60

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

Lys Glu Asn Trp Val Gln Arg Val Val Glu Lys Phe Leu Lys Arg Ala
                85                  90                  95

Glu Asn Ser
```

<210> 2472
<211> 247
<212> PRT
<213> Homo sapiens

<400> 2472

```
Met Gln Pro Ile Leu Leu Leu Leu Ala Phe Leu Leu Leu Pro Arg Ala
1               5                   10                  15

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

Pro Tyr Met Ala Tyr Leu Met Ile Trp Asp Gln Lys Ser Leu Lys Arg
        35                  40                  45

Cys Gly Gly Phe Leu Ile Gln Asp Asp Phe Val Leu Thr Ala Ala His
    50                  55                  60

Cys Trp Gly Ser Ser Ile Asn Val Thr Leu Gly Ala His Asn Ile Lys
65                  70                  75                  80

Glu Gln Glu Pro Thr Gln Gln Phe Ile Pro Val Lys Arg Pro Ile Pro
                85                  90                  95

His Pro Ala Tyr Asn Pro Lys Asn Phe Ser Asn Asp Ile Met Leu Leu
            100                 105                 110

Gln Leu Glu Arg Lys Ala Lys Arg Thr Arg Ala Val Gln Pro Leu Arg
        115                 120                 125

Leu Pro Ser Asn Lys Ala Gln Val Lys Pro Gly Gln Thr Cys Ser Val
    130                 135                 140

Ala Gly Trp Gly Gln Thr Ala Pro Leu Gly Lys His Ser His Thr Leu
145                 150                 155                 160
```

```
Gln Glu Val Lys Met Thr Val Gln Glu Asp Arg Lys Cys Glu Ser Asp
                165                 170                 175

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

Glu Ile Lys Lys Thr Ser Phe Lys Gly Asp Ser Gly Gly Pro Leu Val
        195                 200                 205

Cys Asn Lys Val Ala Gln Gly Ile Val Ser Tyr Gly Arg Asn Asn Gly
    210                 215                 220

Met Pro Pro Arg Ala Cys Thr Lys Val Ser Ser Phe Val His Trp Ile
225                 230                 235                 240

Lys Lys Thr Met Lys Arg Tyr
                245
```

<210> 2473
<211> 281
<212> PRT
<213> Homo sapiens

<400> 2473

```
Met Gln Gln Pro Phe Asn Tyr Pro Tyr Pro Gln Ile Tyr Trp Val Asp
1               5                   10                  15

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

Pro Thr Ser Val Pro Arg Arg Pro Gly Gln Arg Arg Pro Pro Pro Pro
        35                  40                  45

Pro Pro Pro Pro Pro Leu Pro Pro Pro Pro Pro Pro Pro Pro Leu Pro
    50                  55                  60

Pro Leu Pro Leu Pro Pro Leu Lys Lys Arg Gly Asn His Ser Thr Gly
65                  70                  75                  80

Leu Cys Leu Leu Val Met Phe Phe Met Val Leu Val Ala Leu Val Gly
                85                  90                  95

Leu Gly Leu Gly Met Phe Gln Leu Phe His Leu Gln Lys Glu Leu Ala
            100                 105                 110
```

```
Glu Leu Arg Glu Ser Thr Ser Gln Met His Thr Ala Ser Ser Leu Glu
        115                 120                 125

Lys Gln Ile Gly His Pro Ser Pro Pro Pro Glu Lys Lys Glu Leu Arg
    130                 135                 140

Lys Val Ala His Leu Thr Gly Lys Ser Asn Ser Arg Ser Met Pro Leu
145                 150                 155                 160

Glu Trp Glu Asp Thr Tyr Gly Ile Val Leu Leu Ser Gly Val Lys Tyr
                165                 170                 175

Lys Lys Gly Gly Leu Val Ile Asn Glu Thr Gly Leu Tyr Phe Val Tyr
            180                 185                 190

Ser Lys Val Tyr Phe Arg Gly Gln Ser Cys Asn Asn Leu Pro Leu Ser
        195                 200                 205

His Lys Val Tyr Met Arg Asn Ser Lys Tyr Pro Gln Asp Leu Val Met
    210                 215                 220

Met Glu Gly Lys Met Met Ser Tyr Cys Thr Thr Gly Gln Met Trp Ala
225                 230                 235                 240

Arg Ser Ser Tyr Leu Gly Ala Val Phe Asn Leu Thr Ser Ala Asp His
                245                 250                 255

Leu Tyr Val Asn Val Ser Glu Leu Ser Leu Val Asn Phe Glu Glu Ser
            260                 265                 270

Gln Thr Phe Phe Gly Leu Tyr Lys Leu
        275                 280


<210>  2474
<211>  830
<212>  PRT
<213>  Homo sapiens

<400>  2474

Met Gly Ser Met Phe Arg Ser Glu Glu Val Ala Leu Val Gln Leu Phe
1               5                   10                  15

Leu Pro Thr Ala Ala Ala Tyr Thr Cys Val Ser Arg Leu Gly Glu Leu
            20                  25                  30

Gly Leu Val Glu Phe Arg Asp Leu Asn Ala Ser Val Ser Ala Phe Gln
        35                  40                  45
```

```
Arg Arg Phe Val Val Asp Val Arg Arg Cys Glu Glu Leu Glu Lys Thr
    50                  55                  60

Phe Thr Phe Leu Gln Glu Glu Val Arg Arg Ala Gly Leu Val Leu Pro
65                  70                  75                  80

Pro Pro Lys Gly Arg Leu Pro Ala Pro Pro Pro Arg Asp Leu Leu Arg
                85                  90                  95

Ile Gln Glu Glu Thr Glu Arg Leu Ala Gln Glu Leu Arg Asp Val Arg
            100                 105                 110

Gly Asn Gln Gln Ala Leu Arg Ala Gln Leu His Gln Leu Gln Leu His
        115                 120                 125

Ala Ala Val Leu Arg Gln Gly His Glu Pro Gln Leu Ala Ala Ala His
    130                 135                 140

Thr Asp Gly Ala Ser Glu Arg Thr Pro Leu Leu Gln Ala Pro Gly Gly
145                 150                 155                 160

Pro His Gln Asp Leu Arg Val Asn Phe Val Ala Gly Ala Val Glu Pro
                165                 170                 175

His Lys Ala Pro Ala Leu Glu Arg Leu Leu Trp Arg Ala Cys Arg Gly
            180                 185                 190

Phe Leu Ile Ala Ser Phe Arg Glu Leu Glu Gln Pro Leu Glu His Pro
        195                 200                 205

Val Thr Gly Glu Pro Ala Thr Trp Met Thr Phe Leu Ile Ser Tyr Trp
    210                 215                 220

Gly Glu Gln Ile Gly Gln Lys Ile Arg Lys Ile Thr Asp Cys Phe His
225                 230                 235                 240

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

Leu Gln Gln Leu Gln Gln Gln Ser Gln Glu Leu Gln Glu Val Leu Gly
            260                 265                 270

Glu Thr Glu Arg Phe Leu Ser Gln Val Leu Gly Arg Val Leu Gln Leu
        275                 280                 285
```

```
Leu Pro Pro Gly Gln Val Gln Val His Lys Met Lys Ala Val Tyr Leu
    290                 295                 300

Ala Leu Asn Gln Cys Ser Val Ser Thr Thr His Lys Cys Leu Ile Ala
305                 310                 315                 320

Glu Ala Trp Cys Ser Val Arg Asp Leu Pro Ala Leu Gln Glu Ala Leu
                325                 330                 335

Arg Asp Ser Ser Met Glu Glu Gly Val Ser Ala Val Ala His Arg Ile
            340                 345                 350

Pro Cys Arg Asp Met Pro Pro Thr Leu Ile Arg Thr Asn Arg Phe Thr
        355                 360                 365

Ala Ser Phe Gln Gly Ile Val Asp Ala Tyr Gly Val Gly Arg Tyr Gln
    370                 375                 380

Glu Val Asn Pro Ala Pro Tyr Thr Ile Ile Thr Phe Pro Phe Leu Phe
385                 390                 395                 400

Ala Val Met Phe Gly Asp Val Gly His Gly Leu Leu Met Phe Leu Phe
                405                 410                 415

Ala Leu Ala Met Val Leu Ala Glu Asn Arg Pro Ala Val Lys Ala Ala
            420                 425                 430

Gln Asn Glu Ile Trp Gln Thr Phe Phe Arg Gly Arg Tyr Leu Leu Leu
        435                 440                 445

Leu Met Gly Leu Phe Ser Ile Tyr Thr Gly Phe Ile Tyr Asn Glu Cys
    450                 455                 460

Phe Ser Arg Ala Thr Ser Ile Phe Pro Ser Gly Trp Ser Val Ala Ala
465                 470                 475                 480

Met Ala Asn Gln Ser Gly Trp Ser Asp Ala Phe Leu Ala Gln His Thr
                485                 490                 495

Met Leu Thr Leu Asp Pro Asn Val Thr Gly Val Phe Leu Gly Pro Tyr
            500                 505                 510

Pro Phe Gly Ile Asp Pro Ile Trp Ser Leu Ala Ala Asn His Leu Ser
        515                 520                 525
```

```
Phe Leu Asn Ser Phe Lys Met Lys Met Ser Val Ile Leu Gly Val Val
    530                 535                 540

His Met Ala Phe Gly Val Val Leu Gly Val Phe Asn His Val His Phe
545                 550                 555                 560

Gly Gln Arg His Arg Leu Leu Leu Glu Thr Leu Pro Glu Leu Thr Phe
                565                 570                 575

Leu Leu Gly Leu Phe Gly Tyr Leu Val Phe Leu Val Ile Tyr Lys Trp
            580                 585                 590

Leu Cys Val Trp Ala Ala Arg Ala Ala Ser Ala Pro Ser Ile Leu Ile
        595                 600                 605

His Phe Ile Asn Met Phe Leu Phe Ser His Ser Pro Ser Asn Arg Leu
    610                 615                 620

Leu Tyr Pro Arg Gln Glu Val Val Gln Ala Thr Leu Val Val Leu Ala
625                 630                 635                 640

Leu Ala Met Val Pro Ile Leu Leu Leu Gly Thr Pro Leu His Leu Leu
                645                 650                 655

His Arg His Arg Arg Arg Leu Arg Arg Arg Pro Ala Asp Arg Gln Glu
            660                 665                 670

Glu Asn Lys Ala Gly Leu Leu Asp Leu Pro Asp Ala Ser Val Asn Gly
        675                 680                 685

Trp Ser Ser Asp Glu Glu Lys Ala Gly Gly Leu Asp Asp Glu Glu Glu
    690                 695                 700

Ala Glu Leu Val Pro Ser Glu Val Leu Met His Gln Ala Ile His Thr
705                 710                 715                 720

Ile Glu Phe Cys Leu Gly Cys Val Ser Asn Thr Ala Ser Tyr Leu Arg
                725                 730                 735

Leu Trp Ala Leu Ser Leu Ala His Ala Gln Leu Ser Glu Val Leu Trp
            740                 745                 750

Ala Met Val Met Arg Ile Gly Leu Gly Leu Gly Arg Glu Val Gly Val
        755                 760                 765

Ala Ala Val Val Leu Val Pro Ile Phe Ala Ala Phe Ala Val Met Thr
```

770 775 780

Val Ala Ile Leu Leu Val Met Glu Gly Leu Ser Ala Phe Leu His Ala
785 790 795 800

Leu Arg Leu His Trp Val Glu Phe Gln Asn Lys Phe Tyr Ser Gly Thr
805 810 815

Gly Tyr Lys Leu Ser Pro Phe Thr Phe Ala Ala Thr Asp Asp
820 825 830

<210> 2475
<211> 555
<212> PRT
<213> Homo sapiens

<400> 2475

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

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

Arg Ser His Lys Phe Val Pro Gly Ala Trp Leu Ala Gly Glu Gly Val
35 40 45

Asp Val Thr Ser Leu Arg Arg Ser Gly Ser Phe Pro Val Asp Thr Gln
50 55 60

Arg Phe Leu Arg Pro Asp Gly Thr Cys Thr Leu Cys Glu Asn Ala Leu
65 70 75 80

Gln Glu Gly Thr Leu Gln Arg Leu Pro Leu Ala Leu Thr Asn Trp Arg
85 90 95

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

Ser Thr Glu Ala Val Ala Arg Asp Ala Ala Arg Ser Ile Arg Asn Asp
115 120 125

Trp Lys Val Gly Leu Asp Val Thr Pro Lys Pro Thr Ser Asn Val His
130 135 140

Val Ser Val Ala Gly Ser His Ser Gln Ala Ala Asn Phe Ala Ala Gln
145 150 155 160

Lys Thr His Gln Asp Gln Tyr Ser Phe Ser Thr Asp Thr Val Glu Cys
165 170 175

Arg Phe Tyr Ser Phe His Val Val His Thr Pro Pro Leu His Pro Asp
180 185 190

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

Gln Pro Ala Tyr Leu Arg Leu Ile Ser Asn Tyr Gly Thr His Phe Ile
210 215 220

Arg Ala Val Glu Leu Gly Gly Arg Ile Ser Ala Leu Thr Ala Leu Arg
225 230 235 240

Thr Cys Glu Leu Ala Leu Glu Gly Leu Thr Asp Asn Glu Val Glu Asp
245 250 255

Cys Leu Thr Val Glu Ala Gln Val Asn Ile Gly Ile His Gly Ser Ile
260 265 270

Ser Ala Glu Ala Lys Ala Cys Glu Glu Lys Lys Lys Lys His Lys Met
275 280 285

Thr Ala Ser Phe His Gln Thr Tyr Arg Glu Arg His Ser Glu Val Val
290 295 300

Gly Gly His His Thr Ser Ile Asn Asp Leu Leu Phe Gly Ile Gln Ala
305 310 315 320

Gly Pro Glu Gln Tyr Ser Ala Trp Val Asn Ser Val Pro Gly Ser Pro
325 330 335

Gly Leu Val Asp Tyr Thr Leu Glu Pro Leu His Val Leu Leu Asp Ser
340 345 350

Gln Asp Pro Arg Arg Glu Ala Leu Arg Arg Ala Leu Ser Gln Tyr Leu
355 360 365

Thr Asp Arg Ala Arg Trp Arg Asp Cys Ser Arg Pro Cys Pro Pro Gly
370 375 380

Arg Gln Lys Ser Pro Arg Asp Pro Cys Gln Cys Val Cys His Gly Ser
385 390 395 400

Ala Val Thr Thr Gln Asp Cys Cys Pro Arg Gln Arg Gly Leu Ala Gln
405 410 415

Leu Glu Val Thr Phe Ile Gln Ala Trp Ser Leu Trp Gly Asp Trp Phe
420 425 430

Thr Ala Thr Asp Ala Tyr Val Lys Leu Phe Phe Gly Gly Gln Glu Leu
435 440 445

Arg Thr Ser Thr Val Trp Asp Asn Asn Asn Pro Ile Trp Ser Val Arg
450 455 460

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

Gln Val Trp Asp Gln Asp Ser Gly Arg Asp Asp Asp Leu Leu Gly Thr
485 490 495

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

Asn His Gly His Leu Lys Phe Arg Tyr His Ala Arg Cys Leu Pro His
515 520 525

Leu Gly Gly Gly Thr Cys Leu Asp Tyr Val Pro Gln Met Leu Leu Gly
530 535 540

Glu Pro Pro Gly Asn Arg Ser Gly Ala Val Trp
545 550 555

<210> 2476
<211> 153
<212> PRT
<213> Homo sapiens

<400> 2476

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

Cys Ala Gly Asn Phe Val His Gly His Lys Cys Asp Ile Thr Leu Gln
20 25 30

Glu Ile Ile Lys Thr Leu Asn Ser Leu Thr Glu Gln Lys Thr Leu Cys
35 40 45

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

Glu Lys Glu Thr Phe Cys Arg Ala Ala Thr Val Leu Arg Gln Phe Tyr
65 70 75 80

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

Phe His Arg His Lys Gln Leu Ile Arg Phe Leu Lys Arg Leu Asp Arg
100 105 110

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

Asn Gln Ser Thr Leu Glu Asn Phe Leu Glu Arg Leu Lys Thr Ile Met
130 135 140

Arg Glu Lys Tyr Ser Lys Cys Ser Ser
145 150

<210> 2477
<211> 146
<212> PRT
<213> Homo sapiens

<400> 2477

Met His Pro Leu Leu Asn Pro Leu Leu Leu Ala Leu Gly Leu Met Ala
1 5 10 15

Leu Leu Leu Thr Thr Val Ile Ala Leu Thr Cys Leu Gly Gly Phe Ala
20 25 30

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

Glu Leu Val Asn Ile Thr Gln Asn Gln Lys Ala Pro Leu Cys Asn Gly
50 55 60

Ser Met Val Trp Ser Ile Asn Leu Thr Ala Gly Met Tyr Cys Ala Ala
65 70 75 80

Leu Glu Ser Leu Ile Asn Val Ser Gly Cys Ser Ala Ile Glu Lys Thr
85 90 95

Gln Arg Met Leu Ser Gly Phe Cys Pro His Lys Val Ser Ala Gly Gln
100 105 110

Phe Ser Ser Leu His Val Arg Asp Thr Lys Ile Glu Val Ala Gln Phe
115 120 125

Val Lys Asp Leu Leu Leu His Leu Lys Lys Leu Phe Arg Glu Gly Gln
130 135 140

Phe Asn
145

<210> 2478
<211> 223
<212> PRT
<213> Homo sapiens

<400> 2478

Met Ala Cys Leu Gly Phe Gln Arg His Lys Ala Gln Leu Asn Leu Ala
1 5 10 15

Thr Arg Thr Trp Pro Cys Thr Leu Leu Phe Phe Leu Leu Phe Ile Pro
20 25 30

Val Phe Cys Lys Ala Met His Val Ala Gln Pro Ala Val Val Leu Ala
35 40 45

Ser Ser Arg Gly Ile Ala Ser Phe Val Cys Glu Tyr Ala Ser Pro Gly
50 55 60

Lys Ala Thr Glu Val Arg Val Thr Val Leu Arg Gln Ala Asp Ser Gln
65 70 75 80

Val Thr Glu Val Cys Ala Ala Thr Tyr Met Met Gly Asn Glu Leu Thr
85 90 95

Phe Leu Asp Asp Ser Ile Cys Thr Gly Thr Ser Ser Gly Asn Gln Val
100 105 110

Asn Leu Thr Ile Gln Gly Leu Arg Ala Met Asp Thr Gly Leu Tyr Ile
115 120 125

Cys Lys Val Glu Leu Met Tyr Pro Pro Pro Tyr Tyr Leu Gly Ile Gly
130 135 140

Asn Gly Thr Gln Ile Tyr Val Ile Asp Pro Glu Pro Cys Pro Asp Ser
145 150 155 160

Asp Phe Leu Leu Trp Ile Leu Ala Ala Val Ser Ser Gly Leu Phe Phe
165 170 175

Tyr Ser Phe Leu Leu Thr Ala Val Ser Leu Ser Lys Met Leu Lys Lys
180 185 190

Arg Ser Pro Leu Thr Thr Gly Val Tyr Val Lys Met Pro Pro Thr Glu
195 200 205

Pro Glu Cys Glu Lys Gln Phe Gln Pro Tyr Phe Ile Pro Ile Asn
210 215 220

<210> 2479
<211> 235
<212> PRT
<213> Homo sapiens

<400> 2479

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

His Ala Ala Arg Pro Ser Gln Phe Arg Val Ser Pro Leu Asp Arg Thr
20 25 30

Trp Asn Leu Gly Glu Thr Val Glu Leu Lys Cys Gln Val Leu Leu Ser
35 40 45

Asn Pro Thr Ser Gly Cys Ser Trp Leu Phe Gln Pro Arg Gly Ala Ala
50 55 60

Ala Ser Pro Thr Phe Leu Leu Tyr Leu Ser Gln Asn Lys Pro Lys Ala
65 70 75 80

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

Thr Phe Val Leu Thr Leu Ser Asp Phe Arg Arg Glu Asn Glu Gly Tyr
100 105 110

Tyr Phe Cys Ser Ala Leu Ser Asn Ser Ile Met Tyr Phe Ser His Phe
115 120 125

Val Pro Val Phe Leu Pro Ala Lys Pro Thr Thr Thr Pro Ala Pro Arg
130 135 140

Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg
145 150 155 160

Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly
165 170 175

Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr
180 185 190

Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Asn His
195 200 205

Arg Asn Arg Arg Arg Val Cys Lys Cys Pro Arg Pro Val Val Lys Ser
210 215 220

Gly Asp Lys Pro Ser Leu Ser Ala Arg Tyr Val
225 230 235

<210> 2480
<211> 181
<212> PRT
<213> Homo sapiens

<400> 2480

Met Leu Leu Glu Pro Gly Arg Gly Cys Cys Ala Leu Ala Ile Leu Leu
1 5 10 15

Ala Ile Val Asp Ile Gln Ser Gly Gly Cys Ile Asn Ile Thr Ser Ser
20 25 30

Ala Ser Gln Glu Gly Thr Arg Leu Asn Leu Ile Cys Thr Val Trp His
35 40 45

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

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

Arg Asp Pro Gly Ile Asp Gly Val Gly Glu Ile Ser Ser Gln Leu Met
85 90 95

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

Cys Ala Arg Ser Gln Lys Ser Gly Ile Arg Leu Gln Gly His Phe Phe
115 120 125

Ser Ile Leu Phe Thr Glu Thr Gly Asn Tyr Thr Val Thr Gly Leu Lys
130 135 140

Gln Arg Gln His Leu Glu Phe Ser His Asn Glu Gly Thr Leu Ser Ser
145 150 155 160

Gly Phe Leu Gln Glu Lys Val Trp Val Met Leu Val Thr Ser Leu Val
165 170 175

Ala Leu Gln Ala Leu
180

<210> 2481
<211> 147
<212> PRT
<213> Homo sapiens

<400> 2481

Met Val His Leu Thr Pro Glu Glu Lys Ser Ala Val Thr Ala Leu Trp
1 5 10 15

Gly Lys Val Asn Val Asp Glu Val Gly Gly Glu Ala Leu Gly Arg Leu
20 25 30

Leu Val Val Tyr Pro Trp Thr Gln Arg Phe Phe Glu Ser Phe Gly Asp
35 40 45

Leu Ser Thr Pro Asp Ala Val Met Gly Asn Pro Lys Val Lys Ala His
50 55 60

Gly Lys Lys Val Leu Gly Ala Phe Ser Asp Gly Leu Ala His Leu Asp
65 70 75 80

Asn Leu Lys Gly Thr Phe Ala Thr Leu Ser Glu Leu His Cys Asp Lys
85 90 95

Leu His Val Asp Pro Glu Asn Phe Arg Leu Leu Gly Asn Val Leu Val
100 105 110

Cys Val Leu Ala His His Phe Gly Lys Glu Phe Thr Pro Pro Val Gln
115 120 125

Ala Ala Tyr Gln Lys Val Val Ala Gly Val Ala Asn Ala Leu Ala His
130 135 140

Lys Tyr His
145

<210> 2482
<211> 259
<212> PRT
<213> Homo sapiens

<400> 2482

Met Ser Lys Tyr Lys Leu Ile Met Leu Arg His Gly Glu Gly Ala Trp
1 5 10 15

Asn Lys Glu Asn Arg Phe Cys Ser Trp Val Asp Gln Lys Leu Asn Ser
20 25 30

Glu Gly Met Glu Glu Ala Arg Asn Cys Gly Lys Gln Leu Lys Ala Leu
35 40 45

Asn Phe Glu Phe Asp Leu Val Phe Thr Ser Val Leu Asn Arg Ser Ile
50 55 60

His Thr Ala Trp Leu Ile Leu Glu Glu Leu Gly Gln Glu Trp Val Pro
65 70 75 80

Val Glu Ser Ser Trp Arg Leu Asn Glu Arg His Tyr Gly Ala Leu Ile
85 90 95

Gly Leu Asn Arg Glu Gln Met Ala Leu Asn His Gly Glu Glu Gln Val
100 105 110

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

Ser His Pro Tyr Tyr Gln Glu Ile Tyr Asn Asp Arg Arg Tyr Lys Val
130 135 140

Cys Asp Val Pro Leu Asp Gln Leu Pro Arg Ser Glu Ser Leu Lys Asp
145 150 155 160

Val Leu Glu Arg Leu Leu Pro Tyr Trp Asn Glu Arg Ile Ala Pro Glu
165 170 175

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

Arg Ala Leu Leu Lys His Leu Glu Gly Ile Ser Asp Glu Asp Ile Ile
195 200 205

Asn Ile Thr Leu Pro Thr Gly Val Pro Ile Leu Leu Glu Leu Asp Glu
210 215 220

```
Asn Leu Arg Ala Val Gly Pro His Gln Phe Leu Gly Asp Gln Glu Ala
225                 230                 235                 240

Ile Gln Ala Ala Ile Lys Lys Val Glu Asp Gln Gly Lys Val Lys Gln
                245                 250                 255

Ala Lys Lys
```

<210> 2483
<211> 344
<212> PRT
<213> Homo sapiens

<400> 2483

```
Met Ser Ala Leu Ala Ala Arg Leu Leu Gln Pro Ala His Ser Cys Ser
1               5                   10                  15

Leu Arg Leu Arg Pro Phe His Leu Ala Ala Val Arg Asn Glu Ala Val
            20                  25                  30

Val Ile Ser Gly Arg Lys Leu Ala Gln Gln Ile Lys Gln Glu Val Arg
        35                  40                  45

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

Ser Val Ile Leu Val Gly Glu Asn Pro Ala Ser His Ser Tyr Val Leu
65                  70                  75                  80

Asn Lys Thr Arg Ala Ala Ala Val Val Gly Ile Asn Ser Glu Thr Ile
                85                  90                  95

Met Lys Pro Ala Ser Ile Ser Glu Glu Glu Leu Leu Asn Leu Ile Asn
            100                 105                 110

Lys Leu Asn Asn Asp Asp Asn Val Asp Gly Leu Leu Val Gln Leu Pro
        115                 120                 125

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

Asp Lys Asp Val Asp Gly Phe His Val Ile Asn Val Gly Arg Met Cys
145                 150                 155                 160
```

Leu Asp Gln Tyr Ser Met Leu Pro Ala Thr Pro Trp Gly Val Trp Glu
165 170 175

Ile Ile Lys Arg Thr Gly Ile Pro Thr Leu Gly Lys Asn Val Val Val
180 185 190

Ala Gly Arg Ser Lys Asn Val Gly Met Pro Ile Ala Met Leu Leu His
195 200 205

Thr Asp Gly Ala His Glu Arg Pro Gly Gly Asp Ala Thr Val Thr Ile
210 215 220

Ser His Arg Tyr Thr Pro Lys Glu Gln Leu Lys Lys His Thr Ile Leu
225 230 235 240

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

Asp Met Ile Lys Glu Gly Ala Ala Val Ile Asp Val Gly Ile Asn Arg
260 265 270

Val His Asp Pro Val Thr Ala Lys Pro Lys Leu Val Gly Asp Val Asp
275 280 285

Phe Glu Gly Val Arg Gln Lys Ala Gly Tyr Ile Thr Pro Val Pro Gly
290 295 300

Gly Val Gly Pro Met Thr Val Ala Met Leu Met Lys Asn Thr Ile Ile
305 310 315 320

Ala Ala Lys Lys Val Leu Arg Leu Glu Glu Arg Glu Val Leu Lys Ser
325 330 335

Lys Glu Leu Gly Val Ala Thr Asn
340

<210> 2484
<211> 808
<212> PRT
<213> Homo sapiens

<400> 2484

Met Ala Glu Leu Leu Ala Ser Ala Gly Ser Ala Cys Ser Trp Asp Phe
1 5 10 15

Pro Arg Ala Pro Pro Ser Phe Pro Pro Pro Ala Ala Ser Arg Gly Gly
20 25 30

```
Leu Gly Gly Thr Arg Ser Phe Arg Pro His Arg Gly Ala Glu Ser Pro
        35                  40                  45

Arg Pro Gly Arg Asp Arg Asp Gly Val Arg Val Pro Met Ala Ser Ser
    50                  55                  60

Arg Cys Pro Ala Pro Arg Gly Cys Arg Cys Leu Pro Gly Ala Ser Leu
65                  70                  75                  80

Ala Trp Leu Gly Thr Val Leu Leu Leu Leu Ala Asp Trp Val Leu Leu
                85                  90                  95

Arg Thr Ala Leu Pro Arg Ile Phe Ser Leu Leu Val Pro Thr Ala Leu
            100                 105                 110

Pro Leu Leu Arg Val Trp Ala Val Gly Leu Ser Arg Trp Ala Val Leu
        115                 120                 125

Trp Leu Gly Ala Cys Gly Val Leu Arg Ala Thr Val Gly Ser Lys Ser
    130                 135                 140

Glu Asn Ala Gly Ala Gln Gly Trp Leu Ala Ala Leu Lys Pro Leu Ala
145                 150                 155                 160

Ala Ala Leu Gly Leu Ala Leu Pro Gly Leu Ala Leu Phe Arg Glu Leu
                165                 170                 175

Ile Ser Trp Gly Ala Pro Gly Ser Ala Asp Ser Thr Arg Leu Leu His
            180                 185                 190

Trp Gly Ser His Pro Thr Ala Phe Val Val Ser Tyr Ala Ala Ala Leu
        195                 200                 205

Pro Ala Ala Ala Leu Trp His Lys Leu Gly Ser Leu Trp Val Pro Gly
    210                 215                 220

Gly Gln Gly Gly Ser Gly Asn Pro Val Arg Arg Leu Leu Gly Cys Leu
225                 230                 235                 240

Gly Ser Glu Thr Arg Arg Leu Ser Leu Phe Leu Val Leu Val Val Leu
                245                 250                 255

Ser Ser Leu Gly Glu Met Ala Ile Pro Phe Phe Thr Gly Arg Leu Thr
            260                 265                 270
```

```
Asp Trp Ile Leu Gln Asp Gly Ser Ala Asp Thr Phe Thr Arg Asn Leu
        275                 280                 285

Thr Leu Met Ser Ile Leu Thr Ile Ala Ser Ala Val Leu Glu Phe Val
    290                 295                 300

Gly Asp Gly Ile Tyr Asn Asn Thr Met Gly His Val His Ser His Leu
305                 310                 315                 320

Gln Gly Glu Val Phe Gly Ala Val Leu Arg Gln Glu Thr Glu Phe Phe
                325                 330                 335

Gln Gln Asn Gln Thr Gly Asn Ile Met Ser Arg Val Thr Glu Asp Thr
            340                 345                 350

Ser Thr Leu Ser Asp Ser Leu Ser Glu Asn Leu Ser Leu Phe Leu Trp
        355                 360                 365

Tyr Leu Val Arg Gly Leu Cys Leu Leu Gly Ile Met Leu Trp Gly Ser
    370                 375                 380

Val Ser Leu Thr Met Val Thr Leu Ile Thr Leu Pro Leu Leu Phe Leu
385                 390                 395                 400

Leu Pro Lys Lys Val Gly Lys Trp Tyr Gln Leu Leu Glu Val Gln Val
                405                 410                 415

Arg Glu Ser Leu Ala Lys Ser Ser Gln Val Ala Ile Glu Ala Leu Ser
            420                 425                 430

Ala Met Pro Thr Val Arg Ser Phe Ala Asn Glu Glu Gly Glu Ala Gln
        435                 440                 445

Lys Phe Arg Glu Lys Leu Gln Glu Ile Lys Thr Leu Asn Gln Lys Glu
    450                 455                 460

Ala Val Ala Tyr Ala Val Asn Ser Trp Thr Thr Ser Ile Ser Gly Met
465                 470                 475                 480

Leu Leu Lys Val Gly Ile Leu Tyr Ile Gly Gly Gln Leu Val Thr Ser
                485                 490                 495

Gly Ala Val Ser Ser Gly Asn Leu Val Thr Phe Val Leu Tyr Gln Met
            500                 505                 510
```

Gln Phe Thr Gln Ala Val Glu Val Leu Leu Ser Ile Tyr Pro Arg Val
515 520 525

Gln Lys Ala Val Gly Ser Ser Glu Lys Ile Phe Glu Tyr Leu Asp Arg
530 535 540

Thr Pro Arg Cys Pro Pro Ser Gly Leu Leu Thr Pro Leu His Leu Glu
545 550 555 560

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

Asp Val Leu Val Leu Gln Gly Leu Thr Phe Thr Leu Arg Pro Gly Glu
580 585 590

Val Thr Ala Leu Val Gly Pro Asn Gly Ser Gly Lys Ser Thr Val Ala
595 600 605

Ala Leu Leu Gln Asn Leu Tyr Gln Pro Thr Gly Gly Gln Leu Leu Leu
610 615 620

Asp Gly Lys Pro Leu Pro Gln Tyr Glu His Arg Tyr Leu His Arg Gln
625 630 635 640

Val Ala Ala Val Gly Gln Glu Pro Gln Val Phe Gly Arg Ser Leu Gln
645 650 655

Glu Asn Ile Ala Tyr Gly Leu Thr Gln Lys Pro Thr Met Glu Glu Ile
660 665 670

Thr Ala Ala Ala Val Lys Ser Gly Ala His Ser Phe Ile Ser Gly Leu
675 680 685

Pro Gln Gly Tyr Asp Thr Glu Val Asp Glu Ala Gly Ser Gln Leu Ser
690 695 700

Gly Gly Gln Arg Gln Ala Val Ala Leu Ala Arg Ala Leu Ile Arg Lys
705 710 715 720

Pro Cys Val Leu Ile Leu Asp Asp Ala Thr Ser Ala Leu Asp Ala Asn
725 730 735

Ser Gln Leu Gln Val Glu Gln Leu Leu Tyr Glu Ser Pro Glu Arg Tyr
740 745 750

Ser Arg Ser Val Leu Leu Ile Thr Gln His Leu Ser Leu Val Glu Gln

755 760 765

Ala Asp His Ile Leu Phe Leu Glu Gly Gly Ala Ile Arg Glu Gly Gly
770 775 780

Thr His Gln Gln Leu Met Glu Lys Lys Gly Cys Tyr Trp Ala Met Val
785 790 795 800

Gln Ala Pro Ala Asp Ala Pro Glu
805

<210> 2485
<211> 453
<212> PRT
<213> Homo sapiens

<400> 2485

Met Ala Arg Lys Val Val Ser Arg Lys Arg Lys Ala Pro Ala Ser Pro
1 5 10 15

Gly Ala Gly Ser Asp Ala Gln Gly Pro Gln Phe Gly Trp Asp His Ser
20 25 30

Leu His Lys Arg Lys Arg Leu Pro Pro Val Lys Arg Ser Leu Val Tyr
35 40 45

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

Arg Val Leu His Gly Tyr Ala Ala Gln Gln Leu Pro Ser Leu Leu Lys
65 70 75 80

Glu Arg Glu Phe His Leu Gly Thr Leu Asn Lys Val Phe Ala Ser Gln
85 90 95

Trp Leu Asn His Arg Gln Val Val Cys Gly Thr Lys Cys Asn Thr Leu
100 105 110

Phe Val Val Asp Val Gln Thr Ser Gln Ile Thr Lys Ile Pro Ile Leu
115 120 125

Lys Asp Arg Glu Pro Gly Gly Val Thr Gln Gln Gly Cys Gly Ile His
130 135 140

Ala Ile Glu Leu Asn Pro Ser Arg Thr Leu Leu Ala Thr Gly Gly Asp
145 150 155 160

```
Asn Pro Asn Ser Leu Ala Ile Tyr Arg Leu Pro Thr Leu Asp Pro Val
                165                 170                 175

Cys Val Gly Asp Asp Gly His Lys Asp Trp Ile Phe Ser Ile Ala Trp
            180                 185                 190

Ile Ser Asp Thr Met Ala Val Ser Gly Ser Arg Asp Gly Ser Met Gly
        195                 200                 205

Leu Trp Glu Val Thr Asp Asp Val Leu Thr Lys Ser Asp Ala Arg His
    210                 215                 220

Asn Val Ser Arg Val Pro Val Tyr Ala His Ile Thr His Lys Ala Leu
225                 230                 235                 240

Lys Asp Ile Pro Lys Glu Asp Thr Asn Pro Asp Asn Cys Lys Val Arg
                245                 250                 255

Ala Leu Ala Phe Asn Asn Lys Asn Lys Glu Leu Gly Ala Val Ser Leu
            260                 265                 270

Asp Gly Tyr Phe His Leu Trp Lys Ala Glu Asn Thr Leu Ser Lys Leu
        275                 280                 285

Leu Ser Thr Lys Leu Pro Tyr Cys Arg Glu Asn Val Cys Leu Ala Tyr
    290                 295                 300

Gly Ser Glu Trp Ser Val Tyr Ala Val Gly Ser Gln Ala His Val Ser
305                 310                 315                 320

Phe Leu Asp Pro Arg Gln Pro Ser Tyr Asn Val Lys Ser Val Cys Ser
                325                 330                 335

Arg Glu Arg Gly Ser Gly Ile Arg Ser Val Ser Phe Tyr Glu His Ile
            340                 345                 350

Ile Thr Val Gly Thr Gly Gln Gly Ser Leu Leu Phe Tyr Asp Ile Arg
        355                 360                 365

Ala Gln Arg Phe Leu Glu Glu Arg Leu Ser Ala Cys Tyr Gly Ser Lys
    370                 375                 380

Pro Arg Leu Ala Gly Glu Asn Leu Lys Leu Thr Thr Gly Lys Gly Trp
385                 390                 395                 400
```

```
Leu Asn His Asp Glu Thr Trp Arg Asn Tyr Phe Ser Asp Ile Asp Phe
                405                 410                 415

Phe Pro Asn Ala Val Tyr Thr His Cys Tyr Asp Ser Ser Gly Thr Lys
            420                 425                 430

Leu Phe Val Ala Gly Gly Pro Leu Pro Ser Gly Leu His Gly Asn Tyr
        435                 440                 445

Ala Gly Leu Trp Ser
    450
```

<210> 2486
<211> 352
<212> PRT
<213> Homo sapiens

<400> 2486

```
Met Glu Gly Ile Ser Ile Tyr Thr Ser Asp Asn Tyr Thr Glu Glu Met
1               5                   10                  15

Gly Ser Gly Asp Tyr Asp Ser Met Lys Glu Pro Cys Phe Arg Glu Glu
            20                  25                  30

Asn Ala Asn Phe Asn Lys Ile Phe Leu Pro Thr Ile Tyr Ser Ile Ile
        35                  40                  45

Phe Leu Thr Gly Ile Val Gly Asn Gly Leu Val Ile Leu Val Met Gly
    50                  55                  60

Tyr Gln Lys Lys Leu Arg Ser Met Thr Asp Lys Tyr Arg Leu His Leu
65                  70                  75                  80

Ser Val Ala Asp Leu Leu Phe Val Ile Thr Leu Pro Phe Trp Ala Val
                85                  90                  95

Asp Ala Val Ala Asn Trp Tyr Phe Gly Asn Phe Leu Cys Lys Ala Val
            100                 105                 110

His Val Ile Tyr Thr Val Asn Leu Tyr Ser Ser Val Leu Ile Leu Ala
        115                 120                 125

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

Gln Arg Pro Arg Lys Leu Leu Ala Glu Lys Val Val Tyr Val Gly Val
145                 150                 155                 160
```

```
Trp Ile Pro Ala Leu Leu Leu Thr Ile Pro Asp Phe Ile Phe Ala Asn
                165                 170                 175

Val Ser Glu Ala Asp Asp Arg Tyr Ile Cys Asp Arg Phe Tyr Pro Asn
            180                 185                 190

Asp Leu Trp Val Val Val Phe Gln Phe Gln His Ile Met Val Gly Leu
        195                 200                 205

Ile Leu Pro Gly Ile Val Ile Leu Ser Cys Tyr Cys Ile Ile Ile Ser
    210                 215                 220

Lys Leu Ser His Ser Lys Gly His Gln Lys Arg Lys Ala Leu Lys Thr
225                 230                 235                 240

Thr Val Ile Leu Ile Leu Ala Phe Phe Ala Cys Trp Leu Pro Tyr Tyr
                245                 250                 255

Ile Gly Ile Ser Ile Asp Ser Phe Ile Leu Leu Glu Ile Ile Lys Gln
            260                 265                 270

Gly Cys Glu Phe Glu Asn Thr Val His Lys Trp Ile Ser Ile Thr Glu
        275                 280                 285

Ala Leu Ala Phe Phe His Cys Cys Leu Asn Pro Ile Leu Tyr Ala Phe
    290                 295                 300

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

Ser Arg Gly Ser Ser Leu Lys Ile Leu Ser Lys Gly Lys Arg Gly Gly
                325                 330                 335

His Ser Ser Val Ser Thr Glu Ser Glu Ser Ser Ser Phe His Ser Ser
            340                 345                 350
```

<210> 2487
<211> 199
<212> PRT
<213> Homo sapiens

<400> 2487

```
Met Ser Ser Glu Asn Cys Phe Val Ala Glu Asn Ser Ser Leu His Pro
1               5                   10                  15
```

```
Glu Ser Gly Gln Glu Asn Asp Ala Thr Ser Pro His Phe Ser Thr Arg
            20                  25                  30

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

Val Phe Ile Thr Ile Leu Ile Ile Ala Leu Ile Ala Leu Ser Val Gly
    50                  55                  60

Gln Tyr Asn Cys Pro Gly Gln Tyr Thr Phe Ser Met Pro Ser Asp Ser
65                  70                  75                  80

His Val Ser Ser Cys Ser Glu Asp Trp Val Gly Tyr Gln Arg Lys Cys
                85                  90                  95

Tyr Phe Ile Ser Thr Val Lys Arg Ser Trp Thr Ser Ala Gln Asn Ala
            100                 105                 110

Cys Ser Glu His Gly Ala Thr Leu Ala Val Ile Asp Ser Glu Lys Asp
        115                 120                 125

Met Asn Phe Leu Lys Arg Tyr Ala Gly Arg Glu Glu His Trp Val Gly
    130                 135                 140

Leu Lys Lys Glu Pro Gly His Pro Trp Lys Trp Ser Asn Gly Lys Glu
145                 150                 155                 160

Phe Asn Asn Trp Phe Asn Val Thr Gly Ser Asp Lys Cys Val Phe Leu
                165                 170                 175

Lys Asn Thr Glu Val Ser Ser Met Glu Cys Glu Lys Asn Leu Tyr Trp
            180                 185                 190

Ile Cys Asn Lys Pro Tyr Lys
        195

<210>  2488
<211>  91
<212>  PRT
<213>  Homo sapiens

<400>  2488

Met Lys Val Ser Ala Ala Ala Leu Ala Val Ile Leu Ile Ala Thr Ala
1               5                   10                  15

Leu Cys Ala Pro Ala Ser Ala Ser Pro Tyr Ser Ser Asp Thr Thr Pro
            20                  25                  30
```

Cys Cys Phe Ala Tyr Ile Ala Arg Pro Leu Pro Arg Ala His Ile Lys
35 40 45

Glu Tyr Phe Tyr Thr Ser Gly Lys Cys Ser Asn Pro Ala Val Val Phe
50 55 60

Val Thr Arg Lys Asn Arg Gln Val Cys Ala Asn Pro Glu Lys Lys Trp
65 70 75 80

Val Arg Glu Tyr Ile Asn Ser Leu Glu Met Ser
85 90

<210> 2489
<211> 212
<212> PRT
<213> Homo sapiens

<400> 2489

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

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

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

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

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

Ser Lys Glu Ala Leu Ala Glu Asn Asn Leu Asn Leu Pro Lys Met Ala
85 90 95

Glu Lys Asp Gly Cys Phe Gln Ser Gly Phe Asn Glu Glu Thr Cys Leu
100 105 110

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

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

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

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

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

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

Leu Arg Gln Met
    210
```

<210> 2490
<211> 153
<212> PRT
<213> Homo sapiens

<400> 2490

```
Met Tyr Arg Met Gln Leu Leu Ser Cys Ile Ala Leu Ser Leu Ala Leu
1               5                   10                  15

Val Thr Asn Ser Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr Gln Leu
            20                  25                  30

Gln Leu Glu His Leu Leu Leu Asp Leu Gln Met Ile Leu Asn Gly Ile
        35                  40                  45

Asn Asn Tyr Lys Asn Pro Lys Leu Thr Arg Met Leu Thr Phe Lys Phe
    50                  55                  60

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

Glu Glu Leu Lys Pro Leu Glu Glu Val Leu Asn Leu Ala Gln Ser Lys
                85                  90                  95

Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn Val Ile
            100                 105                 110

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

Asp Glu Thr Ala Thr Ile Val Glu Phe Leu Asn Arg Trp Ile Thr Phe
    130                 135                 140
```

Cys Gln Ser Ile Ile Ser Thr Leu Thr
145 150

<210> 2491
<211> 231
<212> PRT
<213> Homo sapiens

<400> 2491

Met Gln Asp Glu Glu Arg Tyr Met Thr Leu Asn Val Gln Ser Lys Lys
1 5 10 15

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

Thr Leu His Trp Tyr Lys Ile Leu Leu Gly Ile Ser Gly Thr Val Asn
35 40 45

Gly Ile Leu Thr Leu Thr Leu Ile Ser Leu Ile Leu Leu Val Ser Gln
50 55 60

Gly Val Leu Leu Lys Cys Gln Lys Gly Ser Cys Ser Asn Ala Thr Gln
65 70 75 80

Tyr Glu Asp Thr Gly Asp Leu Lys Val Asn Asn Gly Thr Arg Arg Asn
85 90 95

Ile Ser Asn Lys Asp Leu Cys Ala Ser Arg Ser Ala Asp Gln Thr Val
100 105 110

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

Ser Asn Glu Met Lys Ser Trp Ser Asp Ser Tyr Val Tyr Cys Leu Glu
130 135 140

Arg Lys Ser His Leu Leu Ile Ile His Asp Gln Leu Glu Met Ala Phe
145 150 155 160

Ile Gln Lys Asn Leu Arg Gln Leu Asn Tyr Val Trp Ile Gly Leu Asn
165 170 175

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

Asp Ser Lys Ile Phe Phe Ile Lys Gly Pro Ala Lys Glu Asn Ser Cys
195 200 205

Ala Ala Ile Lys Glu Ser Lys Ile Phe Ser Glu Thr Cys Ser Ser Val
210 215 220

Phe Lys Trp Ile Cys Gln Tyr
225 230

<210> 2492
<211> 512
<212> PRT
<213> Homo sapiens

<400> 2492

Met Gly Cys Ile Lys Ser Lys Gly Lys Asp Ser Leu Ser Asp Asp Gly
1 5 10 15

Val Asp Leu Lys Thr Gln Pro Val Arg Asn Thr Glu Arg Thr Ile Tyr
20 25 30

Val Arg Asp Pro Thr Ser Asn Lys Gln Gln Arg Pro Val Pro Glu Ser
35 40 45

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

Gly Asp Ile Val Val Ala Leu Tyr Pro Tyr Asp Gly Ile His Pro Asp
65 70 75 80

Asp Leu Ser Phe Lys Lys Gly Glu Lys Met Lys Val Leu Glu Glu His
85 90 95

Gly Glu Trp Trp Lys Ala Lys Ser Leu Leu Thr Lys Lys Glu Gly Phe
100 105 110

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

Trp Phe Phe Lys Asp Ile Thr Arg Lys Asp Ala Glu Arg Gln Leu Leu
130 135 140

Ala Pro Gly Asn Ser Ala Gly Ala Phe Leu Ile Arg Glu Ser Glu Thr
145 150 155 160

Leu Lys Gly Ser Phe Ser Leu Ser Val Arg Asp Phe Asp Pro Val His
165 170 175

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

Tyr Tyr Ile Ser Pro Arg Ile Thr Phe Pro Cys Ile Ser Asp Met Ile
195 200 205

Lys His Tyr Gln Lys Gln Ala Asp Gly Leu Cys Arg Arg Leu Glu Lys
210 215 220

Ala Cys Ile Ser Pro Lys Pro Gln Lys Pro Trp Asp Lys Asp Ala Trp
225 230 235 240

Glu Ile Pro Arg Glu Ser Ile Lys Leu Val Lys Arg Leu Gly Ala Gly
245 250 255

Gln Phe Gly Glu Val Trp Met Gly Tyr Tyr Asn Asn Ser Thr Lys Val
260 265 270

Ala Val Lys Thr Leu Lys Pro Gly Thr Met Ser Val Gln Ala Phe Leu
275 280 285

Glu Glu Ala Asn Leu Met Lys Thr Leu Gln His Asp Lys Leu Val Arg
290 295 300

Leu Tyr Ala Val Val Thr Arg Glu Glu Pro Ile Tyr Ile Ile Thr Glu
305 310 315 320

Tyr Met Ala Lys Gly Ser Leu Leu Asp Phe Leu Lys Ser Asp Glu Gly
325 330 335

Gly Lys Val Leu Leu Pro Lys Leu Ile Asp Phe Ser Ala Gln Ile Ala
340 345 350

Glu Gly Met Ala Tyr Ile Glu Arg Lys Asn Tyr Ile His Arg Asp Leu
355 360 365

Arg Ala Ala Asn Val Leu Val Ser Glu Ser Leu Met Cys Lys Ile Ala
370 375 380

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

Glu Gly Ala Lys Phe Pro Ile Lys Trp Thr Ala Pro Glu Ala Ile Asn
405 410 415

```
Phe Gly Cys Phe Thr Ile Lys Ser Asp Val Trp Ser Phe Gly Ile Leu
            420                 425                 430

Leu Tyr Glu Ile Val Thr Tyr Gly Lys Ile Pro Tyr Pro Gly Arg Thr
        435                 440                 445

Asn Ala Asp Val Met Thr Ala Leu Ser Gln Gly Tyr Arg Met Pro Arg
    450                 455                 460

Val Glu Asn Cys Pro Asp Glu Leu Tyr Asp Ile Met Lys Met Cys Trp
465                 470                 475                 480

Lys Glu Lys Ala Glu Glu Arg Pro Thr Phe Asp Tyr Leu Gln Ser Val
                485                 490                 495

Leu Asp Asp Phe Tyr Thr Ala Thr Glu Gly Gln Tyr Gln Gln Gln Pro
            500                 505                 510
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<210> 2493
<211> 272
<212> PRT
<213> Homo sapiens

<400> 2493

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

Pro Gly Cys Gln Ala Glu Leu Cys Asp Asp Asp Pro Pro Glu Ile Pro
            20                  25                  30

His Ala Thr Phe Lys Ala Met Ala Tyr Lys Glu Gly Thr Met Leu Asn
        35                  40                  45

Cys Glu Cys Lys Arg Gly Phe Arg Arg Ile Lys Ser Gly Ser Leu Tyr
    50                  55                  60

Met Leu Cys Thr Gly Asn Ser Ser His Ser Ser Trp Asp Asn Gln Cys
65                  70                  75                  80

Gln Cys Thr Ser Ser Ala Thr Arg Asn Thr Thr Lys Gln Val Thr Pro
                85                  90                  95

Gln Pro Glu Glu Gln Lys Glu Arg Lys Thr Thr Glu Met Gln Ser Pro
            100                 105                 110

Met Gln Pro Val Asp Gln Ala Ser Leu Pro Gly His Cys Arg Glu Pro
```

115 120 125

Pro Pro Trp Glu Asn Glu Ala Thr Glu Arg Ile Tyr His Phe Val Val
130 135 140

Gly Gln Met Val Tyr Tyr Gln Cys Val Gln Gly Tyr Arg Ala Leu His
145 150 155 160

Arg Gly Pro Ala Glu Ser Val Cys Lys Met Thr His Gly Lys Thr Arg
165 170 175

Trp Thr Gln Pro Gln Leu Ile Cys Thr Gly Glu Met Glu Thr Ser Gln
180 185 190

Phe Pro Gly Glu Glu Lys Pro Gln Ala Ser Pro Glu Gly Arg Pro Glu
195 200 205

Ser Glu Thr Ser Cys Leu Val Thr Thr Thr Asp Phe Gln Ile Gln Thr
210 215 220

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

Val Ala Val Ala Gly Cys Val Phe Leu Leu Ile Ser Val Leu Leu Leu
245 250 255

Ser Gly Leu Thr Trp Gln Arg Arg Gln Arg Lys Ser Arg Arg Thr Ile
260 265 270

<210> 2494
<211> 92
<212> PRT
<213> Homo sapiens

<400> 2494

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

Phe Cys Ser Pro Ala Leu Ser Ala Pro Met Gly Ser Asp Pro Pro Thr
20 25 30

Ala Cys Cys Phe Ser Tyr Thr Ala Arg Lys Leu Pro Arg Asn Phe Val
35 40 45

Val Asp Tyr Tyr Glu Thr Ser Ser Leu Cys Ser Gln Pro Ala Val Val
50 55 60

Phe Gln Thr Lys Arg Ser Lys Gln Val Cys Ala Asp Pro Ser Glu Ser
65 70 75 80

Trp Val Gln Glu Tyr Val Tyr Asp Leu Glu Leu Asn
85 90

<210> 2495
<211> 532
<212> PRT
<213> Homo sapiens

<400> 2495

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

Val Leu Leu Val Leu Leu Cys Cys Ala Ile Ser Val Leu Tyr Met Leu
20 25 30

Ala Cys Thr Pro Lys Gly Asp Glu Glu Gln Leu Ala Leu Pro Arg Ala
35 40 45

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

Glu Glu Gln His Arg Asn Tyr Val Ser Ser Leu Lys Arg Gln Ile Ala
65 70 75 80

Gln Leu Lys Glu Glu Leu Gln Glu Arg Ser Glu Gln Leu Arg Asn Gly
85 90 95

Gln Tyr Gln Ala Ser Asp Ala Ala Gly Leu Gly Leu Asp Arg Ser Pro
100 105 110

Pro Glu Lys Thr Gln Ala Asp Leu Leu Ala Phe Leu His Ser Gln Val
115 120 125

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

Ala Val Pro Phe Asp Ser Phe Thr Leu Gln Lys Val Tyr Gln Leu Glu
145 150 155 160

Thr Gly Leu Thr Arg His Pro Glu Glu Lys Pro Val Arg Lys Asp Lys
165 170 175

Arg Asp Glu Leu Val Glu Ala Ile Glu Ser Ala Leu Glu Thr Leu Asn

180 185 190

Asn Pro Ala Glu Asn Ser Pro Asn His Arg Pro Tyr Thr Ala Ser Asp
195 200 205

Phe Ile Glu Gly Ile Tyr Arg Thr Glu Arg Asp Lys Gly Thr Leu Tyr
210 215 220

Glu Leu Thr Phe Lys Gly Asp His Lys His Glu Phe Lys Arg Leu Ile
225 230 235 240

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

Asn Met Ala Asn Thr Leu Ile Asn Val Ile Val Pro Leu Ala Lys Arg
260 265 270

Val Asp Lys Phe Arg Gln Phe Met Gln Asn Phe Arg Glu Met Cys Ile
275 280 285

Glu Gln Asp Gly Arg Val His Leu Thr Val Val Tyr Phe Gly Lys Glu
290 295 300

Glu Ile Asn Glu Val Lys Gly Ile Leu Glu Asn Thr Ser Lys Ala Ala
305 310 315 320

Asn Phe Arg Asn Phe Thr Phe Ile Gln Leu Asn Gly Glu Phe Ser Arg
325 330 335

Gly Lys Gly Leu Asp Val Gly Ala Arg Phe Trp Lys Gly Ser Asn Val
340 345 350

Leu Leu Phe Phe Cys Asp Val Asp Ile Tyr Phe Thr Ser Glu Phe Leu
355 360 365

Asn Thr Cys Arg Leu Asn Thr Gln Pro Gly Lys Lys Val Phe Tyr Pro
370 375 380

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

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

Phe Trp Arg Asp Phe Gly Phe Gly Met Thr Cys Gln Tyr Arg Ser Asp
420 425 430

Phe Ile Asn Ile Gly Gly Phe Asp Leu Asp Ile Lys Gly Trp Gly Gly
435 440 445

Glu Asp Val His Leu Tyr Arg Lys Tyr Leu His Ser Asn Leu Ile Val
450 455 460

Val Arg Thr Pro Val Arg Gly Leu Phe His Leu Trp His Glu Lys Arg
465 470 475 480

Cys Met Asp Glu Leu Thr Pro Glu Gln Tyr Lys Met Cys Met Gln Ser
485 490 495

Lys Ala Met Asn Glu Ala Ser His Gly Gln Leu Gly Met Leu Val Phe
500 505 510

Arg His Glu Ile Glu Ala His Leu Arg Lys Gln Lys Gln Lys Thr Ser
515 520 525

Ser Lys Lys Thr
530

<210> 2496
<211> 125
<212> PRT
<213> Homo sapiens

<400> 2496

Met Lys Lys Ser Gly Val Leu Phe Leu Leu Gly Ile Ile Leu Leu Val
1 5 10 15

Leu Ile Gly Val Gln Gly Thr Pro Val Val Arg Lys Gly Arg Cys Ser
20 25 30

Cys Ile Ser Thr Asn Gln Gly Thr Ile His Leu Gln Ser Leu Lys Asp
35 40 45

Leu Lys Gln Phe Ala Pro Ser Pro Ser Cys Glu Lys Ile Glu Ile Ile
50 55 60

Ala Thr Leu Lys Asn Gly Val Gln Thr Cys Leu Asn Pro Asp Ser Ala
65 70 75 80

Asp Val Lys Glu Leu Ile Lys Lys Trp Glu Lys Gln Val Ser Gln Lys
85 90 95

Lys Lys Gln Lys Asn Gly Lys Lys His Gln Lys Lys Lys Val Leu Lys
100 105 110

Val Arg Lys Ser Gln Arg Ser Arg Gln Lys Lys Thr Thr
115 120 125

<210> 2497
<211> 98
<212> PRT
<213> Homo sapiens

<400> 2497

Met Asn Gln Thr Ala Ile Leu Ile Cys Cys Leu Ile Phe Leu Thr Leu
1 5 10 15

Ser Gly Ile Gln Gly Val Pro Leu Ser Arg Thr Val Arg Cys Thr Cys
20 25 30

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

Glu Ile Ile Pro Ala Ser Gln Phe Cys Pro Arg Val Glu Ile Ile Ala
50 55 60

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

Ala Ile Lys Asn Leu Leu Lys Ala Val Ser Lys Glu Met Ser Lys Arg
85 90 95

Ser Pro

<210> 2498
<211> 155
<212> PRT
<213> Homo sapiens

<400> 2498

Met Thr Pro Gly Lys Thr Ser Leu Val Ser Leu Leu Leu Leu Leu Ser
1 5 10 15

Leu Glu Ala Ile Val Lys Ala Gly Ile Thr Ile Pro Arg Asn Pro Gly
20 25 30

Cys Pro Asn Ser Glu Asp Lys Asn Phe Pro Arg Thr Val Met Val Asn
35 40 45

```
Leu Asn Ile His Asn Arg Asn Thr Asn Thr Asn Pro Lys Arg Ser Ser
    50                  55                  60

Asp Tyr Tyr Asn Arg Ser Thr Ser Pro Trp Asn Leu His Arg Asn Glu
65                  70                  75                  80

Asp Pro Glu Arg Tyr Pro Ser Val Ile Trp Glu Ala Lys Cys Arg His
                85                  90                  95

Leu Gly Cys Ile Asn Ala Asp Gly Asn Val Asp Tyr His Met Asn Ser
            100                 105                 110

Val Pro Ile Gln Gln Glu Ile Leu Val Leu Arg Arg Glu Pro Pro His
        115                 120                 125

Cys Pro Asn Ser Phe Arg Leu Glu Lys Ile Leu Val Ser Val Gly Cys
    130                 135                 140

Thr Cys Val Thr Pro Ile Val His His Val Ala
145                 150                 155

<210>  2499
<211>  162
<212>  PRT
<213>  Homo sapiens

<400>  2499

Met Arg Ile Ser Lys Pro His Leu Arg Ser Ile Ser Ile Gln Cys Tyr
1               5                   10                  15

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

Val Phe Ile Leu Gly Cys Phe Ser Ala Gly Leu Pro Lys Thr Glu Ala
        35                  40                  45

Asn Trp Val Asn Val Ile Ser Asp Leu Lys Lys Ile Glu Asp Leu Ile
    50                  55                  60

Gln Ser Met His Ile Asp Ala Thr Leu Tyr Thr Glu Ser Asp Val His
65                  70                  75                  80

Pro Ser Cys Lys Val Thr Ala Met Lys Cys Phe Leu Leu Glu Leu Gln
                85                  90                  95

Val Ile Ser Leu Glu Ser Gly Asp Ala Ser Ile His Asp Thr Val Glu
```

100 105 110

Asn Leu Ile Ile Leu Ala Asn Asn Ser Leu Ser Ser Asn Gly Asn Val
115 120 125

Thr Glu Ser Gly Cys Lys Glu Cys Glu Glu Leu Glu Glu Lys Asn Ile
130 135 140

Lys Glu Phe Leu Gln Ser Phe Val His Ile Val Gln Met Phe Ile Asn
145 150 155 160

Thr Ser

<210> 2500
<211> 178
<212> PRT
<213> Homo sapiens

<400> 2500

Met His Ser Ser Ala Leu Leu Cys Cys Leu Val Leu Leu Thr Gly Val
1 5 10 15

Arg Ala Ser Pro Gly Gln Gly Thr Gln Ser Glu Asn Ser Cys Thr His
20 25 30

Phe Pro Gly Asn Leu Pro Asn Met Leu Arg Asp Leu Arg Asp Ala Phe
35 40 45

Ser Arg Val Lys Thr Phe Phe Gln Met Lys Asp Gln Leu Asp Asn Leu
50 55 60

Leu Leu Lys Glu Ser Leu Leu Glu Asp Phe Lys Gly Tyr Leu Gly Cys
65 70 75 80

Gln Ala Leu Ser Glu Met Ile Gln Phe Tyr Leu Glu Glu Val Met Pro
85 90 95

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

Gly Glu Asn Leu Lys Thr Leu Arg Leu Arg Leu Arg Arg Cys His Arg
115 120 125

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

Ala Phe Asn Lys Leu Gln Glu Lys Gly Ile Tyr Lys Ala Met Ser Glu
145 150 155 160

Phe Asp Ile Phe Ile Asn Tyr Ile Glu Ala Tyr Met Thr Met Lys Ile
165 170 175

Arg Asn

<210> 2501
<211> 166
<212> PRT
<213> Homo sapiens

<400> 2501

Met Lys Tyr Thr Ser Tyr Ile Leu Ala Phe Gln Leu Cys Ile Val Leu
1 5 10 15

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

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

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

Arg Lys Ile Met Gln Ser Gln Ile Val Ser Phe Tyr Phe Lys Leu Phe
65 70 75 80

Lys Asn Phe Lys Asp Asp Gln Ser Ile Gln Lys Ser Val Glu Thr Ile
85 90 95

Lys Glu Asp Met Asn Val Lys Phe Phe Asn Ser Asn Lys Lys Lys Arg
100 105 110

Asp Asp Phe Glu Lys Leu Thr Asn Tyr Ser Val Thr Asp Leu Asn Val
115 120 125

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

Pro Ala Ala Lys Thr Gly Lys Arg Lys Arg Ser Gln Met Leu Phe Gln
145 150 155 160

Gly Arg Arg Ala Ser Gln

165

<210> 2502
<211> 266
<212> PRT
<213> Homo sapiens

<400> 2502

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

Val Thr Leu Met Val Leu Ser Ser Pro Leu Ala Leu Ala Gly Asp Thr
20 25 30

Arg Pro Arg Phe Leu Trp Gln Leu Lys Phe Glu Cys His Phe Phe Asn
35 40 45

Gly Thr Glu Arg Val Arg Leu Leu Glu Arg Cys Ile Tyr Asn Gln Glu
50 55 60

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

Glu Leu Gly Arg Pro Asp Ala Glu Tyr Trp Asn Ser Gln Lys Asp Leu
85 90 95

Leu Glu Gln Arg Arg Ala Ala Val Asp Thr Tyr Cys Arg His Asn Tyr
100 105 110

Gly Val Gly Glu Ser Phe Thr Val Gln Arg Arg Val Glu Pro Lys Val
115 120 125

Thr Val Tyr Pro Ser Lys Thr Gln Pro Leu Gln His His Asn Leu Leu
130 135 140

Val Cys Ser Val Ser Gly Phe Tyr Pro Gly Ser Ile Glu Val Arg Trp
145 150 155 160

Phe Arg Asn Gly Gln Glu Glu Lys Ala Gly Val Val Ser Thr Gly Leu
165 170 175

Ile Gln Asn Gly Asp Trp Thr Phe Gln Thr Leu Val Met Leu Glu Thr
180 185 190

Val Pro Arg Ser Gly Glu Val Tyr Thr Cys Gln Val Glu His Pro Ser
195 200 205

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Val Thr Ser Pro Leu Thr Val Glu Trp Arg Ala Arg Ser Glu Ser Ala
    210                 215                 220

Gln Ser Lys Met Leu Ser Gly Val Gly Gly Phe Val Leu Gly Leu Leu
225                 230                 235                 240

Phe Leu Gly Ala Gly Leu Phe Ile Tyr Phe Arg Asn Gln Lys Gly His
                245                 250                 255

Ser Gly Leu Gln Pro Thr Gly Phe Leu Ser
            260                 265


<210>  2503
<211>  210
<212>  PRT
<213>  Homo sapiens

<400>  2503

Met Arg Pro Arg Leu Trp Leu Leu Leu Ala Ala Gln Leu Thr Val Leu
1               5                   10                  15

His Gly Asn Ser Val Leu Gln Gln Thr Pro Ala Tyr Ile Lys Val Gln
            20                  25                  30

Thr Asn Lys Met Val Met Leu Ser Cys Glu Ala Lys Ile Ser Leu Ser
        35                  40                  45

Asn Met Arg Ile Tyr Trp Leu Arg Gln Arg Gln Ala Pro Ser Ser Asp
    50                  55                  60

Ser His His Glu Phe Leu Ala Leu Trp Asp Ser Ala Lys Gly Thr Ile
65                  70                  75                  80

His Gly Glu Glu Val Glu Gln Glu Lys Ile Ala Val Phe Arg Asp Ala
                85                  90                  95

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

Ile Tyr Phe Cys Met Ile Val Gly Ser Pro Glu Leu Thr Phe Gly Lys
        115                 120                 125

Gly Thr Gln Leu Ser Val Val Asp Phe Leu Pro Thr Thr Ala Gln Pro
    130                 135                 140

Thr Lys Lys Ser Thr Leu Lys Lys Arg Val Cys Arg Leu Pro Arg Pro
```

145 150 155 160

Glu Thr Gln Lys Gly Pro Leu Cys Ser Pro Ile Thr Leu Gly Leu Leu
165 170 175

Val Ala Gly Val Leu Val Leu Leu Val Ser Leu Gly Val Ala Ile His
180 185 190

Leu Cys Cys Arg Arg Arg Arg Ala Arg Leu Arg Phe Met Lys Gln Phe
195 200 205

Tyr Lys
210

<210> 2504
<211> 458
<212> PRT
<213> Homo sapiens

<400> 2504

Met Asn Arg Gly Val Pro Phe Arg His Leu Leu Leu Val Leu Gln Leu
1 5 10 15

Ala Leu Leu Pro Ala Ala Thr Gln Gly Lys Lys Val Val Leu Gly Lys
20 25 30

Lys Gly Asp Thr Val Glu Leu Thr Cys Thr Ala Ser Gln Lys Lys Ser
35 40 45

Ile Gln Phe His Trp Lys Asn Ser Asn Gln Ile Lys Ile Leu Gly Asn
50 55 60

Gln Gly Ser Phe Leu Thr Lys Gly Pro Ser Lys Leu Asn Asp Arg Ala
65 70 75 80

Asp Ser Arg Arg Ser Leu Trp Asp Gln Gly Asn Phe Pro Leu Ile Ile
85 90 95

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

Asp Gln Lys Glu Glu Val Gln Leu Leu Val Phe Gly Leu Thr Ala Asn
115 120 125

Ser Asp Thr His Leu Leu Gln Gly Gln Ser Leu Thr Leu Thr Leu Glu
130 135 140

```
Ser Pro Pro Gly Ser Ser Pro Ser Val Gln Cys Arg Ser Pro Arg Gly
145                 150                 155                 160

Lys Asn Ile Gln Gly Gly Lys Thr Leu Ser Val Ser Gln Leu Glu Leu
                165                 170                 175

Gln Asp Ser Gly Thr Trp Thr Cys Thr Val Leu Gln Asn Gln Lys Lys
            180                 185                 190

Val Glu Phe Lys Ile Asp Ile Val Val Leu Ala Phe Gln Lys Ala Ser
        195                 200                 205

Ser Ile Val Tyr Lys Lys Glu Gly Glu Gln Val Glu Phe Ser Phe Pro
    210                 215                 220

Leu Ala Phe Thr Val Glu Lys Leu Thr Gly Ser Gly Glu Leu Trp Trp
225                 230                 235                 240

Gln Ala Glu Arg Ala Ser Ser Ser Lys Ser Trp Ile Thr Phe Asp Leu
                245                 250                 255

Lys Asn Lys Glu Val Ser Val Lys Arg Val Thr Gln Asp Pro Lys Leu
            260                 265                 270

Gln Met Gly Lys Lys Leu Pro Leu His Leu Thr Leu Pro Gln Ala Leu
        275                 280                 285

Pro Gln Tyr Ala Gly Ser Gly Asn Leu Thr Leu Ala Leu Glu Ala Lys
    290                 295                 300

Thr Gly Lys Leu His Gln Glu Val Asn Leu Val Val Met Arg Ala Thr
305                 310                 315                 320

Gln Leu Gln Lys Asn Leu Thr Cys Glu Val Trp Gly Pro Thr Ser Pro
                325                 330                 335

Lys Leu Met Leu Ser Leu Lys Leu Glu Asn Lys Glu Ala Lys Val Ser
            340                 345                 350

Lys Arg Glu Lys Ala Val Trp Val Leu Asn Pro Glu Ala Gly Met Trp
        355                 360                 365

Gln Cys Leu Leu Ser Asp Ser Gly Gln Val Leu Leu Glu Ser Asn Ile
    370                 375                 380
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Lys Val Leu Pro Thr Trp Ser Thr Pro Val Gln Pro Met Ala Leu Ile
385 390 395 400

Val Leu Gly Gly Val Ala Gly Leu Leu Leu Phe Ile Gly Leu Gly Ile
405 410 415

Phe Phe Cys Val Arg Cys Arg His Arg Arg Arg Gln Ala Glu Arg Met
420 425 430

Ser Gln Ile Lys Arg Leu Leu Ser Glu Lys Lys Thr Cys Gln Cys Pro
435 440 445

His Arg Phe Gln Lys Thr Cys Ser Pro Ile
450 455

<210> 2505
<211> 368
<212> PRT
<213> Homo sapiens

<400> 2505

Met Val Leu Glu Val Ser Asp His Gln Val Leu Asn Asp Ala Glu Val
1 5 10 15

Ala Ala Leu Leu Glu Asn Phe Ser Ser Ser Tyr Asp Tyr Gly Glu Asn
20 25 30

Glu Ser Asp Ser Cys Cys Thr Ser Pro Pro Cys Pro Gln Asp Phe Ser
35 40 45

Leu Asn Phe Asp Arg Ala Phe Leu Pro Ala Leu Tyr Ser Leu Leu Phe
50 55 60

Leu Leu Gly Leu Leu Gly Asn Gly Ala Val Ala Ala Val Leu Leu Ser
65 70 75 80

Arg Arg Thr Ala Leu Ser Ser Thr Asp Thr Phe Leu Leu His Leu Ala
85 90 95

Val Ala Asp Thr Leu Leu Val Leu Thr Leu Pro Leu Trp Ala Val Asp
100 105 110

Ala Ala Val Gln Trp Val Phe Gly Ser Gly Leu Cys Lys Val Ala Gly
115 120 125

Ala Leu Phe Asn Ile Asn Phe Tyr Ala Gly Ala Leu Leu Leu Ala Cys
130 135 140

Ile Ser Phe Asp Arg Tyr Leu Asn Ile Val His Ala Thr Gln Leu Tyr
145 150 155 160

Arg Arg Gly Pro Pro Ala Arg Val Thr Leu Thr Cys Leu Ala Val Trp
165 170 175

Gly Leu Cys Leu Leu Phe Ala Leu Pro Asp Phe Ile Phe Leu Ser Ala
180 185 190

His His Asp Glu Arg Leu Asn Ala Thr His Cys Gln Tyr Asn Phe Pro
195 200 205

Gln Val Gly Arg Thr Ala Leu Arg Val Leu Gln Leu Val Ala Gly Phe
210 215 220

Leu Leu Pro Leu Leu Val Met Ala Tyr Cys Tyr Ala His Ile Leu Ala
225 230 235 240

Val Leu Leu Val Ser Arg Gly Gln Arg Arg Leu Arg Ala Met Arg Leu
245 250 255

Val Val Val Val Val Val Ala Phe Ala Leu Cys Trp Thr Pro Tyr His
260 265 270

Leu Val Val Leu Val Asp Ile Leu Met Asp Leu Gly Ala Leu Ala Arg
275 280 285

Asn Cys Gly Arg Glu Ser Arg Val Asp Val Ala Lys Ser Val Thr Ser
290 295 300

Gly Leu Gly Tyr Met His Cys Cys Leu Asn Pro Leu Leu Tyr Ala Phe
305 310 315 320

Val Gly Val Lys Phe Arg Glu Arg Met Trp Met Leu Leu Leu Arg Leu
325 330 335

Gly Cys Pro Asn Gln Arg Gly Leu Gln Arg Gln Pro Ser Ser Ser Arg
340 345 350

Arg Asp Ser Ser Trp Ser Glu Thr Ser Glu Ala Ser Tyr Ser Gly Leu
355 360 365

<210> 2506
<211> 107
<212> PRT

<213> Homo sapiens

<400> 2506

Met Ala Arg Ala Ala Leu Ser Ala Ala Pro Ser Asn Pro Arg Leu Leu
1 5 10 15

Arg Val Ala Leu Leu Leu Leu Leu Leu Val Ala Ala Gly Arg Arg Ala
20 25 30

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

Leu Gln Gly Ile His Pro Lys Asn Ile Gln Ser Val Asn Val Lys Ser
50 55 60

Pro Gly Pro His Cys Ala Gln Thr Glu Val Ile Ala Thr Leu Lys Asn
65 70 75 80

Gly Arg Lys Ala Cys Leu Asn Pro Ala Ser Pro Ile Val Lys Lys Ile
85 90 95

Ile Glu Lys Met Leu Asn Ser Asp Lys Ser Asn
100 105

<210> 2507
<211> 558
<212> PRT
<213> Homo sapiens

<400> 2507

Met Ala Ala Leu Thr Arg Asp Pro Gln Phe Gln Lys Leu Gln Gln Trp
1 5 10 15

Tyr Arg Glu His Arg Ser Glu Leu Asn Leu Arg Arg Leu Phe Asp Ala
20 25 30

Asn Lys Asp Arg Phe Asn His Phe Ser Leu Thr Leu Asn Thr Asn His
35 40 45

Gly His Ile Leu Val Asp Tyr Ser Lys Asn Leu Val Thr Glu Asp Val
50 55 60

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

Arg Glu Arg Met Phe Asn Gly Glu Lys Ile Asn Tyr Thr Glu Gly Arg
85 90 95

Ala Val Leu His Val Ala Leu Arg Asn Arg Ser Asn Thr Pro Ile Leu
100 105 110

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

Met Lys Ser Phe Cys Gln Arg Val Arg Ser Gly Asp Trp Lys Gly Tyr
130 135 140

Thr Gly Lys Thr Ile Thr Asp Val Ile Asn Ile Gly Ile Gly Gly Ser
145 150 155 160

Asp Leu Gly Pro Leu Met Val Thr Glu Ala Leu Lys Pro Tyr Ser Ser
165 170 175

Gly Gly Pro Arg Val Trp Tyr Val Ser Asn Ile Asp Gly Thr His Ile
180 185 190

Ala Lys Thr Leu Ala Gln Leu Asn Pro Glu Ser Ser Leu Phe Ile Ile
195 200 205

Ala Ser Lys Thr Phe Thr Thr Gln Glu Thr Ile Thr Asn Ala Glu Thr
210 215 220

Ala Lys Glu Trp Phe Leu Gln Ala Ala Lys Asp Pro Ser Ala Val Ala
225 230 235 240

Lys His Phe Val Ala Leu Ser Thr Asn Thr Thr Lys Val Lys Glu Phe
245 250 255

Gly Ile Asp Pro Gln Asn Met Phe Glu Phe Trp Asp Trp Val Gly Gly
260 265 270

Arg Tyr Ser Leu Trp Ser Ala Ile Gly Leu Ser Ile Ala Leu His Val
275 280 285

Gly Phe Asp Asn Phe Glu Gln Leu Leu Ser Gly Ala His Trp Met Asp
290 295 300

Gln His Phe Arg Thr Thr Pro Leu Glu Lys Asn Ala Pro Val Leu Leu
305 310 315 320

Ala Leu Leu Gly Ile Trp Tyr Ile Asn Cys Phe Gly Cys Glu Thr His
325 330 335

Ala Met Leu Pro Tyr Asp Gln Tyr Leu His Arg Phe Ala Ala Tyr Phe
340 345 350

Gln Gln Gly Asp Met Glu Ser Asn Gly Lys Tyr Ile Thr Lys Ser Gly
355 360 365

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

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

Met Ile Pro Cys Asp Phe Leu Ile Pro Val Gln Thr Gln His Pro Ile
405 410 415

Arg Lys Gly Leu His His Lys Ile Leu Leu Ala Asn Phe Leu Ala Gln
420 425 430

Thr Glu Ala Leu Met Arg Gly Lys Ser Thr Glu Glu Ala Arg Lys Glu
435 440 445

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

His Lys Val Phe Glu Gly Asn Arg Pro Thr Asn Ser Ile Val Phe Thr
465 470 475 480

Lys Leu Thr Pro Phe Met Leu Gly Ala Leu Val Ala Met Tyr Glu His
485 490 495

Lys Ile Phe Val Gln Gly Ile Ile Trp Asp Ile Asn Ser Phe Asp Gln
500 505 510

Trp Gly Val Glu Leu Gly Lys Gln Leu Ala Lys Lys Ile Glu Pro Glu
515 520 525

Leu Asp Gly Ser Ala Gln Val Thr Ser His Asp Ala Ser Thr Asn Gly
530 535 540

Leu Ile Asn Phe Ile Lys Gln Gln Arg Glu Ala Arg Val Gln
545 550 555

<210> 2508
<211> 323
<212> PRT
<213> Homo sapiens

<400> 2508

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

Ser Ala Gln Leu Leu Phe Asn Lys Thr Lys Ser Val Glu Phe Thr Phe
20 25 30

Cys Asn Asp Thr Val Val Ile Pro Cys Phe Val Thr Asn Met Glu Ala
35 40 45

Gln Asn Thr Thr Glu Val Tyr Val Lys Trp Lys Phe Lys Gly Arg Asp
50 55 60

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

Phe Ser Ser Ala Lys Ile Glu Val Ser Gln Leu Leu Lys Gly Asp Ala
85 90 95

Ser Leu Lys Met Asp Lys Ser Asp Ala Val Ser His Thr Gly Asn Tyr
100 105 110

Thr Cys Glu Val Thr Glu Leu Thr Arg Glu Gly Glu Thr Ile Ile Glu
115 120 125

Leu Lys Tyr Arg Val Val Ser Trp Phe Ser Pro Asn Glu Asn Ile Leu
130 135 140

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

Gly Ile Lys Thr Leu Lys Tyr Arg Ser Gly Gly Met Asp Glu Lys Thr
165 170 175

Ile Ala Leu Leu Val Ala Gly Leu Val Ile Thr Val Ile Val Ile Val
180 185 190

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

Gly Leu Gly Leu Ile Val Thr Ser Thr Gly Ile Leu Ile Leu Leu His
210 215 220

Tyr Tyr Val Phe Ser Thr Ala Ile Gly Leu Thr Ser Phe Val Ile Ala
225 230 235 240

Ile Leu Val Ile Gln Val Ile Ala Tyr Ile Leu Ala Val Val Gly Leu
245 250 255

Ser Leu Cys Ile Ala Ala Cys Ile Pro Met His Gly Pro Leu Leu Ile
260 265 270

Ser Gly Leu Ser Ile Leu Ala Leu Ala Gln Leu Leu Gly Leu Val Tyr
275 280 285

Met Lys Phe Val Ala Ser Asn Gln Lys Thr Ile Gln Pro Pro Arg Lys
290 295 300

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

Asn Asp Glu

<210> 2509
<211> 362
<212> PRT
<213> Homo sapiens

<400> 2509

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

Thr Asp Thr Trp Ala Gly Ser His Ser Leu Arg Tyr Phe Ser Thr Ala
20 25 30

Val Ser Arg Pro Gly Arg Gly Glu Pro Arg Tyr Ile Ala Val Glu Tyr
35 40 45

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

Arg Met Glu Pro Arg Glu Pro Trp Val Glu Gln Glu Gly Pro Gln Tyr
65 70 75 80

Trp Glu Trp Thr Thr Gly Tyr Ala Lys Ala Asn Ala Gln Thr Asp Arg
85 90 95

Val Ala Leu Arg Asn Leu Leu Arg Arg Tyr Asn Gln Ser Glu Ala Gly
100 105 110

Ser His Thr Leu Gln Gly Met Asn Gly Cys Asp Met Gly Pro Asp Gly
115 120 125

Arg Leu Leu Arg Gly Tyr His Gln His Ala Tyr Asp Gly Lys Asp Tyr
130 135 140

Ile Ser Leu Asn Glu Asp Leu Arg Ser Trp Thr Ala Ala Asp Thr Val
145 150 155 160

Ala Gln Ile Thr Gln Arg Phe Tyr Glu Ala Glu Glu Tyr Ala Glu Glu
165 170 175

Phe Arg Thr Tyr Leu Glu Gly Glu Cys Leu Glu Leu Leu Arg Arg Tyr
180 185 190

Leu Glu Asn Gly Lys Glu Thr Leu Gln Arg Ala Asp Pro Pro Lys Ala
195 200 205

His Val Ala His His Pro Ile Ser Asp His Glu Ala Thr Leu Arg Cys
210 215 220

Trp Ala Leu Gly Phe Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg
225 230 235 240

Asp Gly Glu Glu Gln Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro
245 250 255

Ala Gly Asp Gly Thr Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser
260 265 270

Gly Glu Glu Gln Arg Tyr Thr Cys His Val Gln His Glu Gly Leu Pro
275 280 285

Gln Pro Leu Ile Leu Arg Trp Glu Gln Ser Pro Gln Pro Thr Ile Pro
290 295 300

Ile Val Gly Ile Val Ala Gly Leu Val Val Leu Gly Ala Val Val Thr
305 310 315 320

Gly Ala Val Val Ala Ala Val Met Trp Arg Lys Lys Ser Ser Asp Arg
325 330 335

Asn Arg Gly Ser Tyr Ser Gln Ala Ala Val Thr Asp Ser Ala Gln Gly
340 345 350

Ser Gly Val Ser Leu Thr Ala Asn Lys Val

355 360

<210> 2510
<211> 604
<212> PRT
<213> Homo sapiens

<400> 2510

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

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

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

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

Leu Phe Leu Lys Pro Thr Pro Asn Thr Val His Tyr Ile Leu Thr His
65 70 75 80

Phe Lys Gly Phe Trp Asn Val Val Asn Asn Ile Pro Phe Leu Arg Asn
85 90 95

Ala Ile Met Ser Tyr Val Leu Thr Ser Arg Ser His Leu Ile Asp Ser
100 105 110

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

Ser Asn Leu Ser Tyr Tyr Thr Arg Ala Leu Pro Pro Val Pro Asp Asp
130 135 140

Cys Pro Thr Pro Leu Gly Val Lys Gly Lys Lys Gln Leu Pro Asp Ser
145 150 155 160

Asn Glu Ile Val Glu Lys Leu Leu Leu Arg Arg Lys Phe Ile Pro Asp
165 170 175

Pro Gln Gly Ser Asn Met Met Phe Ala Phe Phe Ala Gln His Phe Thr
180 185 190

His Gln Phe Phe Lys Thr Asp His Lys Arg Gly Pro Ala Phe Thr Asn
195 200 205

Gly Leu Gly His Gly Val Asp Leu Asn His Ile Tyr Gly Glu Thr Leu
210 215 220

Ala Arg Gln Arg Lys Leu Arg Leu Phe Lys Asp Gly Lys Met Lys Tyr
225 230 235 240

Gln Ile Ile Asp Gly Glu Met Tyr Pro Pro Thr Val Lys Asp Thr Gln
245 250 255

Ala Glu Met Ile Tyr Pro Pro Gln Val Pro Glu His Leu Arg Phe Ala
260 265 270

Val Gly Gln Glu Val Phe Gly Leu Val Pro Gly Leu Met Met Tyr Ala
275 280 285

Thr Ile Trp Leu Arg Glu His Asn Arg Val Cys Asp Val Leu Lys Gln
290 295 300

Glu His Pro Glu Trp Gly Asp Glu Gln Leu Phe Gln Thr Ser Arg Leu
305 310 315 320

Ile Leu Ile Gly Glu Thr Ile Lys Ile Val Ile Glu Asp Tyr Val Gln
325 330 335

His Leu Ser Gly Tyr His Phe Lys Leu Lys Phe Asp Pro Glu Leu Leu
340 345 350

Phe Asn Lys Gln Phe Gln Tyr Gln Asn Arg Ile Ala Ala Glu Phe Asn
355 360 365

Thr Leu Tyr His Trp His Pro Leu Leu Pro Asp Thr Phe Gln Ile His
370 375 380

Asp Gln Lys Tyr Asn Tyr Gln Gln Phe Ile Tyr Asn Asn Ser Ile Leu
385 390 395 400

Leu Glu His Gly Ile Thr Gln Phe Val Glu Ser Phe Thr Arg Gln Ile
405 410 415

Ala Gly Arg Val Ala Gly Gly Arg Asn Val Pro Pro Ala Val Gln Lys
420 425 430

Val Ser Gln Ala Ser Ile Asp Gln Ser Arg Gln Met Lys Tyr Gln Ser
435 440 445

```
Phe Asn Glu Tyr Arg Lys Arg Phe Met Leu Lys Pro Tyr Glu Ser Phe
    450                 455                 460

Glu Glu Leu Thr Gly Glu Lys Glu Met Ser Ala Glu Leu Glu Ala Leu
465                 470                 475                 480

Tyr Gly Asp Ile Asp Ala Val Glu Leu Tyr Pro Ala Leu Leu Val Glu
                485                 490                 495

Lys Pro Arg Pro Asp Ala Ile Phe Gly Glu Thr Met Val Glu Val Gly
            500                 505                 510

Ala Pro Phe Ser Leu Lys Gly Leu Met Gly Asn Val Ile Cys Ser Pro
        515                 520                 525

Ala Tyr Trp Lys Pro Ser Thr Phe Gly Gly Glu Val Gly Phe Gln Ile
    530                 535                 540

Ile Asn Thr Ala Ser Ile Gln Ser Leu Ile Cys Asn Asn Val Lys Gly
545                 550                 555                 560

Cys Pro Phe Thr Ser Phe Ser Val Pro Asp Pro Glu Leu Ile Lys Thr
                565                 570                 575

Val Thr Ile Asn Ala Ser Ser Ser Arg Ser Gly Leu Asp Asp Ile Asn
            580                 585                 590

Pro Thr Val Leu Leu Lys Glu Arg Ser Thr Glu Leu
        595                 600
```

<210> 2511
<211> 343
<212> PRT
<213> Homo sapiens

<400> 2511

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

Leu Thr Leu Asn Glu Gly Ala Trp Tyr Ser Val Gly Ala Leu Met Ile
            20                  25                  30

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

Leu Pro Asp Ser Glu Leu Met Arg Arg Lys Tyr His Ser Val Arg Gln
    50                  55                  60
```

```
Glu Asp Leu Gln Arg Val Arg Leu Ser Arg Pro Glu Ala Val Ala Glu
65                  70                  75                  80

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

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

Val Ser Ser Gln Phe Tyr Gly Ala Leu Leu Gly Thr Val Cys Met Leu
        115                 120                 125

Tyr Leu Leu Pro Leu Cys Trp Val Leu Thr Leu Leu Asn Ser Thr Leu
    130                 135                 140

Phe Leu Gly Asn Val Glu Phe Phe Arg Val Val Ser Glu Tyr Arg Ala
145                 150                 155                 160

Ser Leu Gln Gln Arg Met Asn Pro Lys Gln Glu Glu His Ala Phe Glu
                165                 170                 175

Ser Pro Pro Pro Pro Asp Val Gly Gly Lys Asp Gly Leu Met Asp Ser
            180                 185                 190

Thr Pro Ala Leu Thr Pro Thr Glu Asp Leu Thr Pro Gly Ser Val Glu
        195                 200                 205

Glu Ala Glu Glu Ala Glu Pro Asp Glu Glu Phe Lys Asp Ala Ile Glu
    210                 215                 220

Glu Thr His Leu Val Val Leu Glu Asp Asp Glu Gly Ala Pro Cys Pro
225                 230                 235                 240

Ala Glu Asp Glu Leu Ala Leu Gln Asp Asn Gly Phe Leu Ser Lys Asn
                245                 250                 255

Glu Val Leu Arg Ser Lys Val Ser Arg Leu Thr Glu Arg Leu Arg Lys
            260                 265                 270

Arg Tyr Pro Thr Asn Asn Phe Gly Asn Cys Thr Gly Cys Ser Ala Thr
        275                 280                 285

Phe Ser Val Leu Lys Lys Arg Arg Ser Cys Ser Asn Cys Gly Asn Ser
    290                 295                 300
```

```
Phe Cys Ser Arg Cys Cys Ser Phe Lys Val Pro Lys Ser Ser Met Gly
305                 310                 315                 320

Ala Thr Ala Pro Glu Ala Gln Arg Glu Thr Val Phe Val Cys Ala Ser
                325                 330                 335

Cys Asn Gln Thr Leu Ser Lys
            340
```

<210> 2512
<211> 789
<212> PRT
<213> Homo sapiens

<400> 2512

```
Met Lys Met Asp Met Glu Asp Ala Asp Met Thr Leu Trp Thr Glu Ala
1               5                   10                  15

Glu Phe Glu Glu Lys Cys Thr Tyr Ile Val Asn Asp His Pro Trp Asp
            20                  25                  30

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

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

Val Met Ser Lys Glu Tyr Ile Pro Lys Gly Thr Arg Phe Gly Pro Leu
65                  70                  75                  80

Ile Gly Glu Ile Tyr Thr Asn Asp Thr Val Pro Lys Asn Ala Asn Arg
                85                  90                  95

Lys Tyr Phe Trp Arg Ile Tyr Ser Arg Gly Glu Leu His His Phe Ile
            100                 105                 110

Asp Gly Phe Asn Glu Glu Lys Ser Asn Trp Met Arg Tyr Val Asn Pro
        115                 120                 125

Ala His Ser Pro Arg Glu Gln Asn Leu Ala Ala Cys Gln Asn Gly Met
    130                 135                 140

Asn Ile Tyr Phe Tyr Thr Ile Lys Pro Ile Pro Ala Asn Gln Glu Leu
145                 150                 155                 160

Leu Val Trp Tyr Cys Arg Asp Phe Ala Glu Arg Leu His Tyr Pro Tyr
```

165 170 175

Pro Gly Glu Leu Thr Met Met Asn Leu Thr Gln Thr Gln Ser Ser Leu
180 185 190

Lys Gln Pro Ser Thr Glu Lys Asn Glu Leu Cys Pro Lys Asn Val Pro
195 200 205

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

Ser Lys Gly Lys Asp Leu Tyr Arg Ser Asn Ile Ser Pro Leu Thr Ser
225 230 235 240

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

Phe Tyr Pro Arg Val Val Tyr Pro Ile Arg Ala Pro Leu Pro Glu Asp
260 265 270

Phe Leu Lys Ala Ser Leu Ala Tyr Gly Ile Glu Arg Pro Thr Tyr Ile
275 280 285

Thr Arg Ser Pro Ile Pro Ser Ser Thr Thr Pro Ser Pro Ser Ala Arg
290 295 300

Ser Ser Pro Asp Gln Ser Leu Lys Ser Ser Ser Pro His Ser Ser Pro
305 310 315 320

Gly Asn Thr Val Ser Pro Val Gly Pro Gly Ser Gln Glu His Arg Asp
325 330 335

Ser Tyr Ala Tyr Leu Asn Ala Ser Tyr Gly Thr Glu Gly Leu Gly Ser
340 345 350

Tyr Pro Gly Tyr Ala Pro Leu Pro His Leu Pro Pro Ala Phe Ile Pro
355 360 365

Ser Tyr Asn Ala His Tyr Pro Lys Phe Leu Leu Pro Pro Tyr Gly Met
370 375 380

Asn Cys Asn Gly Leu Ser Ala Val Ser Ser Met Asn Gly Ile Asn Asn
385 390 395 400

Phe Gly Leu Phe Pro Arg Leu Cys Pro Val Tyr Ser Asn Leu Leu Gly
405 410 415

Gly Gly Ser Leu Pro His Pro Met Leu Asn Pro Thr Ser Leu Pro Ser
420 425 430

Ser Leu Pro Ser Asp Gly Ala Arg Arg Leu Leu Gln Pro Glu His Pro
435 440 445

Arg Glu Val Leu Val Pro Ala Pro His Ser Ala Phe Ser Phe Thr Gly
450 455 460

Ala Ala Ala Ser Met Lys Asp Lys Ala Cys Ser Pro Thr Ser Gly Ser
465 470 475 480

Pro Thr Ala Gly Thr Ala Ala Thr Ala Glu His Val Val Gln Pro Lys
485 490 495

Ala Thr Ser Ala Ala Met Ala Ala Pro Ser Ser Asp Glu Ala Met Asn
500 505 510

Leu Ile Lys Asn Lys Arg Asn Met Thr Gly Tyr Lys Thr Leu Pro Tyr
515 520 525

Pro Leu Lys Lys Gln Asn Gly Lys Ile Lys Tyr Glu Cys Asn Val Cys
530 535 540

Ala Lys Thr Phe Gly Gln Leu Ser Asn Leu Lys Val His Leu Arg Val
545 550 555 560

His Ser Gly Glu Arg Pro Phe Lys Cys Gln Thr Cys Asn Lys Gly Phe
565 570 575

Thr Gln Leu Ala His Leu Gln Lys His Tyr Leu Val His Thr Gly Glu
580 585 590

Lys Pro His Glu Cys Gln Val Cys His Lys Arg Phe Ser Ser Thr Ser
595 600 605

Asn Leu Lys Thr His Leu Arg Leu His Ser Gly Glu Lys Pro Tyr Gln
610 615 620

Cys Lys Val Cys Pro Ala Lys Phe Thr Gln Phe Val His Leu Lys Leu
625 630 635 640

His Lys Arg Leu His Thr Arg Glu Arg Pro His Lys Cys Ser Gln Cys
645 650 655

His Lys Asn Tyr Ile His Leu Cys Ser Leu Lys Val His Leu Lys Gly
660 665 670

Asn Cys Ala Ala Ala Pro Ala Pro Gly Leu Pro Leu Glu Asp Leu Thr
675 680 685

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

Arg Leu Glu Asp Val Glu Asp Asp Ile Ser Val Ile Ser Val Val Glu
705 710 715 720

Lys Glu Ile Leu Ala Val Val Arg Lys Glu Lys Glu Glu Thr Gly Leu
725 730 735

Lys Val Ser Leu Gln Arg Asn Met Gly Asn Gly Leu Leu Ser Ser Gly
740 745 750

Cys Ser Leu Tyr Glu Ser Ser Asp Leu Pro Leu Met Lys Leu Pro Pro
755 760 765

Ser Asn Pro Leu Pro Leu Val Pro Val Lys Val Lys Gln Glu Thr Val
770 775 780

Glu Pro Met Asp Pro
785

<210> 2513
<211> 381
<212> PRT
<213> Homo sapiens

<400> 2513

Met Pro Phe Ser Asn Ser His Asn Ala Leu Lys Leu Arg Phe Pro Ala
1 5 10 15

Glu Asp Glu Phe Pro Asp Leu Ser Ala His Asn Asn His Met Ala Lys
20 25 30

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

Ser Gly Phe Thr Leu Asp Asp Val Ile Gln Thr Gly Val Asp Asn Pro
50 55 60

Gly His Pro Tyr Ile Met Thr Val Gly Cys Val Ala Gly Asp Glu Glu

65 70 75 80

Ser Tyr Glu Val Phe Lys Asp Leu Phe Asp Pro Ile Ile Glu Asp Arg
85 90 95

His Gly Gly Tyr Lys Pro Ser Asp Glu His Lys Thr Asp Leu Asn Pro
100 105 110

Asp Asn Leu Gln Gly Gly Asp Asp Leu Asp Pro Asn Tyr Val Leu Ser
115 120 125

Ser Arg Val Arg Thr Gly Arg Ser Ile Arg Gly Phe Cys Leu Pro Pro
130 135 140

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

Ala Leu Ser Ser Leu Asp Gly Asp Leu Ala Gly Arg Tyr Tyr Ala Leu
165 170 175

Lys Ser Met Thr Glu Ala Glu Gln Gln Gln Leu Ile Asp Asp His Phe
180 185 190

Leu Phe Asp Lys Pro Val Ser Pro Leu Leu Leu Ala Ser Gly Met Ala
195 200 205

Arg Asp Trp Pro Asp Ala Arg Gly Ile Trp His Asn Asp Asn Lys Thr
210 215 220

Phe Leu Val Trp Val Asn Glu Glu Asp His Leu Arg Val Ile Ser Met
225 230 235 240

Gln Lys Gly Gly Asn Met Lys Glu Val Phe Thr Arg Phe Cys Thr Gly
245 250 255

Leu Thr Gln Ile Glu Thr Leu Phe Lys Ser Lys Asp Tyr Glu Phe Met
260 265 270

Trp Asn Pro His Leu Gly Tyr Ile Leu Thr Cys Pro Ser Asn Leu Gly
275 280 285

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

His Glu Lys Phe Ser Glu Val Leu Lys Arg Leu Arg Leu Gln Lys Arg
305 310 315 320

Gly Thr Gly Gly Val Asp Thr Ala Ala Val Gly Gly Val Phe Asp Val
325 330 335

Ser Asn Ala Asp Arg Leu Gly Phe Ser Glu Val Glu Leu Val Gln Met
340 345 350

Val Val Asp Gly Val Lys Leu Leu Ile Glu Met Glu Gln Arg Leu Glu
355 360 365

Gln Gly Gln Ala Ile Asp Asp Leu Met Pro Ala Gln Lys
370 375 380

<210> 2514
<211> 541
<212> PRT
<213> Homo sapiens

<400> 2514

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

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

Asp Pro Asp Ser Gln Ala Asp Thr Val His Ser Asn Pro Glu Leu Asp
35 40 45

Val Leu Leu Leu Gly Ser Val Asp Gly Arg His Leu Leu Arg Thr Leu
50 55 60

Ser Arg Ala Lys Phe Trp Pro Arg Arg Arg Phe Asn Phe Phe Val Leu
65 70 75 80

Glu Asn Asn Leu Glu Ala Val Ala Arg His Met Leu Ile Phe Ser Leu
85 90 95

Ala Leu Glu Glu Pro Glu Lys Met Gly Leu Gln Glu Arg Ser Glu Thr
100 105 110

Phe Leu Glu Val Trp Gly Asn Ala Leu Leu Arg Pro Pro Val Ala Ala
115 120 125

Phe Val Arg Ala Gln Ala Asp Leu Leu Ala His Leu Val Pro Glu Pro
130 135 140

Asp Arg Leu Glu Glu Gln Leu Pro Trp Leu Ser Leu Arg Ala Leu Lys
145 150 155 160

Phe Arg Glu Arg Asp Ala Leu Glu Ala Val Phe Arg Phe Trp Ala Gly
165 170 175

Gly Glu Lys Gly Pro Gln Ala Phe Pro Met Ser Arg Leu Trp Asp Ser
180 185 190

Arg Leu Arg His Tyr Leu Gly Ser Arg Tyr Asp Ala Arg Arg Gly Val
195 200 205

Ser Asp Trp Asp Leu Arg Met Lys Leu His Asp Arg Gly Ala Gln Val
210 215 220

Ile His Pro Gln Glu Phe Arg Arg Trp Arg Asp Thr Gly Val Ala Phe
225 230 235 240

Glu Leu Arg Asp Ser Ser Ala Tyr His Val Pro Asn Arg Thr Leu Ala
245 250 255

Ser Gly Arg Leu Leu Ser Tyr Arg Gly Glu Arg Val Ala Ala Arg Gly
260 265 270

Tyr Trp Gly Asp Ile Ala Thr Gly Pro Phe Val Ala Phe Gly Ile Glu
275 280 285

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

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

Val Ala Ala Trp Gly Arg Ala Arg Ala Thr Gly Gly Asp Leu Glu Glu
325 330 335

Gln Gln His Ala Glu Gly Ser Pro Glu Pro Gly Thr Pro Ala Ala Pro
340 345 350

Thr Pro Glu Ser Phe Thr Val His Phe Leu Pro Leu Asn Ser Ala Gln
355 360 365

Thr Leu His His Lys Ser Cys Tyr Asn Gly Arg Phe Gln Leu Leu Tyr
370 375 380

Val Ala Cys Gly Met Val His Leu Leu Ile Pro Glu Leu Gly Ala Cys

385 390 395 400

Val Ala Pro Gly Gly Asn Leu Ile Val Glu Leu Ala Arg Tyr Leu Val
405 410 415

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

Leu Ala Gln Ala Ala Gly Phe Ala Pro Gln Thr Gly Ala Arg Pro Ser
435 440 445

Glu Thr Phe Ala Arg Phe Cys Lys Ser Gln Glu Ser Ala Leu Gly Asn
450 455 460

Thr Val Pro Ala Val Glu Pro Gly Thr Pro Pro Leu Asp Ile Leu Ala
465 470 475 480

Gln Pro Leu Glu Ala Ser Asn Pro Ala Leu Glu Gly Leu Thr Gln Pro
485 490 495

Leu Gln Gly Gly Thr Pro His Cys Glu Pro Cys Gln Leu Pro Ser Glu
500 505 510

Ser Pro Gly Ser Leu Ser Glu Val Leu Ala Gln Pro Gln Gly Ala Leu
515 520 525

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

<210> 2515
<211> 288
<212> PRT
<213> Homo sapiens

<400> 2515

Met Ser Asp Ile Glu Glu Val Val Glu Glu Tyr Glu Glu Glu Glu Gln
1 5 10 15

Glu Glu Ala Ala Val Glu Glu Gln Glu Glu Ala Ala Glu Glu Asp Ala
20 25 30

Glu Ala Glu Ala Glu Thr Glu Glu Thr Arg Ala Glu Glu Asp Glu Glu
35 40 45

Glu Glu Glu Ala Lys Glu Ala Glu Asp Gly Pro Met Glu Glu Ser Lys
50 55 60

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

Asp Gly Glu Arg Val Asp Phe Asp Asp Ile His Arg Lys Arg Met Glu
85 90 95

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

Arg Lys Lys Glu Glu Glu Glu Leu Val Ser Leu Lys Asp Arg Ile Glu
115 120 125

Arg Arg Arg Ala Glu Arg Ala Glu Gln Gln Arg Ile Arg Asn Glu Arg
130 135 140

Glu Lys Glu Arg Gln Asn Arg Leu Ala Glu Glu Arg Ala Arg Arg Glu
145 150 155 160

Glu Glu Glu Asn Arg Arg Lys Ala Glu Asp Glu Ala Arg Lys Lys Lys
165 170 175

Ala Leu Ser Asn Met Met His Phe Gly Gly Tyr Ile Gln Lys Gln Ala
180 185 190

Gln Thr Glu Arg Lys Ser Gly Lys Arg Gln Thr Glu Arg Glu Lys Lys
195 200 205

Lys Lys Ile Leu Ala Glu Arg Arg Lys Val Leu Ala Ile Asp His Leu
210 215 220

Asn Glu Asp Gln Leu Arg Glu Lys Ala Lys Glu Leu Trp Gln Ser Ile
225 230 235 240

Tyr Asn Leu Glu Ala Glu Lys Phe Asp Leu Gln Glu Lys Phe Lys Gln
245 250 255

Gln Lys Tyr Glu Ile Asn Val Leu Arg Asn Arg Ile Asn Asp Asn Gln
260 265 270

Lys Val Ser Lys Thr Arg Gly Lys Ala Lys Val Thr Gly Arg Trp Lys
275 280 285

<210> 2516
<211> 154
<212> PRT
<213> Homo sapiens

<400> 2516

Met Gly Leu Ser Asp Gly Glu Trp Gln Leu Val Leu Asn Val Trp Gly
1 5 10 15

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

Leu Phe Lys Gly His Pro Glu Thr Leu Glu Lys Phe Asp Lys Phe Lys
35 40 45

His Leu Lys Ser Glu Asp Glu Met Lys Ala Ser Glu Asp Leu Lys Lys
50 55 60

His Gly Ala Thr Val Leu Thr Ala Leu Gly Gly Ile Leu Lys Lys Lys
65 70 75 80

Gly His His Glu Ala Glu Ile Lys Pro Leu Ala Gln Ser His Ala Thr
85 90 95

Lys His Lys Ile Pro Val Lys Tyr Leu Glu Phe Ile Ser Glu Cys Ile
100 105 110

Ile Gln Val Leu Gln Ser Lys His Pro Gly Asp Phe Gly Ala Asp Ala
115 120 125

Gln Gly Ala Met Asn Lys Ala Leu Glu Leu Phe Arg Lys Asp Met Ala
130 135 140

Ser Asn Tyr Lys Glu Leu Gly Phe Gln Gly
145 150

<210> 2517
<211> 501
<212> PRT
<213> Homo sapiens

<400> 2517

Met Val Arg Lys Pro Val Val Ser Thr Ile Ser Lys Gly Gly Tyr Leu
1 5 10 15

Gln Gly Asn Val Asn Gly Arg Leu Pro Ser Leu Gly Asn Lys Glu Pro
20 25 30

Pro Gly Gln Glu Lys Val Gln Leu Lys Arg Lys Val Thr Leu Leu Arg
35 40 45

Gly Val Ser Ile Ile Ile Gly Thr Ile Ile Gly Ala Gly Ile Phe Ile
50 55 60

Ser Pro Lys Gly Val Leu Gln Asn Thr Gly Ser Val Gly Met Ser Leu
65 70 75 80

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

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

Tyr Ile Leu Glu Val Phe Gly Pro Leu Pro Ala Phe Val Arg Val Trp
115 120 125

Val Glu Leu Leu Ile Ile Arg Pro Ala Ala Thr Ala Val Ile Ser Leu
130 135 140

Ala Phe Gly Arg Tyr Ile Leu Glu Pro Phe Phe Ile Gln Cys Glu Ile
145 150 155 160

Pro Glu Leu Ala Ile Lys Leu Ile Thr Ala Val Gly Ile Thr Val Val
165 170 175

Met Val Leu Asn Ser Met Ser Val Ser Trp Ser Ala Arg Ile Gln Ile
180 185 190

Phe Leu Thr Phe Cys Lys Leu Thr Ala Ile Leu Ile Ile Ile Val Pro
195 200 205

Gly Val Met Gln Leu Ile Lys Gly Gln Thr Gln Asn Phe Lys Asp Ala
210 215 220

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

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

Glu Glu Val Glu Asn Pro Glu Lys Thr Ile Pro Leu Ala Ile Cys Ile
260 265 270

Ser Met Ala Ile Val Thr Ile Gly Tyr Val Leu Thr Asn Val Ala Tyr
275 280 285

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

Val Thr Phe Ser Glu Arg Leu Leu Gly Asn Phe Ser Leu Ala Val Pro
305 310 315 320

Ile Phe Val Ala Leu Ser Cys Phe Gly Ser Met Asn Gly Gly Val Phe
325 330 335

Ala Val Ser Arg Leu Phe Tyr Val Ala Ser Arg Glu Gly His Leu Pro
340 345 350

Glu Ile Leu Ser Met Ile His Val Arg Lys His Thr Pro Leu Pro Ala
355 360 365

Val Ile Val Leu His Pro Leu Thr Met Ile Met Leu Phe Ser Gly Asp
370 375 380

Leu Asp Ser Leu Leu Asn Phe Leu Ser Phe Ala Arg Trp Leu Phe Ile
385 390 395 400

Gly Leu Ala Val Ala Gly Leu Ile Tyr Leu Arg Tyr Lys Cys Pro Asp
405 410 415

Met His Arg Pro Phe Lys Val Pro Leu Phe Ile Pro Ala Leu Phe Ser
420 425 430

Phe Thr Cys Leu Phe Met Val Ala Leu Ser Leu Tyr Ser Asp Pro Phe
435 440 445

Ser Thr Gly Ile Gly Phe Val Ile Thr Leu Thr Gly Val Pro Ala Tyr
450 455 460

Tyr Leu Phe Ile Ile Trp Asp Lys Lys Pro Arg Trp Phe Arg Ile Met
465 470 475 480

Ser Glu Lys Ile Thr Arg Thr Leu Gln Ile Ile Leu Glu Val Val Pro
485 490 495

Glu Glu Asp Lys Leu
500

<210> 2518
<211> 277
<212> PRT
<213> Homo sapiens

<400> 2518

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

Ala Val His Pro Glu Pro Pro Thr Ala Cys Arg Glu Lys Gln Tyr Leu
20 25 30

Ile Asn Ser Gln Cys Cys Ser Leu Cys Gln Pro Gly Gln Lys Leu Val
35 40 45

Ser Asp Cys Thr Glu Phe Thr Glu Thr Glu Cys Leu Pro Cys Gly Glu
50 55 60

Ser Glu Phe Leu Asp Thr Trp Asn Arg Glu Thr His Cys His Gln His
65 70 75 80

Lys Tyr Cys Asp Pro Asn Leu Gly Leu Arg Val Gln Gln Lys Gly Thr
85 90 95

Ser Glu Thr Asp Thr Ile Cys Thr Cys Glu Glu Gly Trp His Cys Thr
100 105 110

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

Phe Gly Val Lys Gln Ile Ala Thr Gly Val Ser Asp Thr Ile Cys Glu
130 135 140

Pro Cys Pro Val Gly Phe Phe Ser Asn Val Ser Ser Ala Phe Glu Lys
145 150 155 160

Cys His Pro Trp Thr Ser Cys Glu Thr Lys Asp Leu Val Val Gln Gln
165 170 175

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

Arg Ala Leu Val Val Ile Pro Ile Ile Phe Gly Ile Leu Phe Ala Ile
195 200 205

Leu Leu Val Leu Val Phe Ile Lys Lys Val Ala Lys Lys Pro Thr Asn
210 215 220

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

```
Asp Leu Pro Gly Ser Asn Thr Ala Ala Pro Val Gln Glu Thr Leu His
                245                 250                 255

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

Val Gln Glu Arg Gln
        275
```

<210> 2519
<211> 260
<212> PRT
<213> Homo sapiens

<400> 2519

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

Gly Leu Ser Ala Thr Pro Ala Pro Lys Ser Cys Pro Glu Arg His Tyr
            20                  25                  30

Trp Ala Gln Gly Lys Leu Cys Cys Gln Met Cys Glu Pro Gly Thr Phe
        35                  40                  45

Leu Val Lys Asp Cys Asp Gln His Arg Lys Ala Ala Gln Cys Asp Pro
    50                  55                  60

Cys Ile Pro Gly Val Ser Phe Ser Pro Asp His His Thr Arg Pro His
65                  70                  75                  80

Cys Glu Ser Cys Arg His Cys Asn Ser Gly Leu Leu Val Arg Asn Cys
                85                  90                  95

Thr Ile Thr Ala Asn Ala Glu Cys Ala Cys Arg Asn Gly Trp Gln Cys
            100                 105                 110

Arg Asp Lys Glu Cys Thr Glu Cys Asp Pro Leu Pro Asn Pro Ser Leu
        115                 120                 125

Thr Ala Arg Ser Ser Gln Ala Leu Ser Pro His Pro Gln Pro Thr His
    130                 135                 140

Leu Pro Tyr Val Ser Glu Met Leu Glu Ala Arg Thr Ala Gly His Met
145                 150                 155                 160

Gln Thr Leu Ala Asp Phe Arg Gln Leu Pro Ala Arg Thr Leu Ser Thr
```

165 170 175

His Trp Pro Pro Gln Arg Ser Leu Cys Ser Ser Asp Phe Ile Arg Ile
180 185 190

Leu Val Ile Phe Ser Gly Met Phe Leu Val Phe Thr Leu Ala Gly Ala
195 200 205

Leu Phe Leu His Gln Arg Arg Lys Tyr Arg Ser Asn Lys Gly Glu Ser
210 215 220

Pro Val Glu Pro Ala Glu Pro Cys Arg Tyr Ser Cys Pro Arg Glu Glu
225 230 235 240

Glu Gly Ser Thr Ile Pro Ile Gln Glu Asp Tyr Arg Lys Pro Glu Pro
245 250 255

Ala Cys Ser Pro
260

<210> 2520
<211> 329
<212> PRT
<213> Homo sapiens

<400> 2520

Met Asp Pro Gln Cys Thr Met Gly Leu Ser Asn Ile Leu Phe Val Met
1 5 10 15

Ala Phe Leu Leu Ser Gly Ala Ala Pro Leu Lys Ile Gln Ala Tyr Phe
20 25 30

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

Ser Leu Ser Glu Leu Val Val Phe Trp Gln Asp Gln Glu Asn Leu Val
50 55 60

Leu Asn Glu Val Tyr Leu Gly Lys Glu Lys Phe Asp Ser Val His Ser
65 70 75 80

Lys Tyr Met Gly Arg Thr Ser Phe Asp Ser Asp Ser Trp Thr Leu Arg
85 90 95

Leu His Asn Leu Gln Ile Lys Asp Lys Gly Leu Tyr Gln Cys Ile Ile
100 105 110

```
His His Lys Lys Pro Thr Gly Met Ile Arg Ile His Gln Met Asn Ser
        115                 120                 125

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

Ser Asn Ile Thr Glu Asn Val Tyr Ile Asn Leu Thr Cys Ser Ser Ile
145                 150                 155                 160

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

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

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

Asp Val Thr Ser Asn Met Thr Ile Phe Cys Ile Leu Glu Thr Asp Lys
    210                 215                 220

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

Pro Pro Pro Asp His Ile Pro Trp Ile Thr Ala Val Leu Pro Thr Val
                245                 250                 255

Ile Ile Cys Val Met Val Phe Cys Leu Ile Leu Trp Lys Trp Lys Lys
            260                 265                 270

Lys Lys Arg Pro Arg Asn Ser Tyr Lys Cys Gly Thr Asn Thr Met Glu
        275                 280                 285

Arg Glu Glu Ser Glu Gln Thr Lys Lys Arg Glu Lys Ile His Ile Pro
    290                 295                 300

Glu Arg Ser Asp Glu Ala Gln Arg Val Phe Lys Ser Ser Lys Thr Ser
305                 310                 315                 320

Ser Cys Asp Lys Ser Asp Thr Cys Phe
                325
```

<210> 2521
<211> 132
<212> PRT
<213> Homo sapiens

<400> 2521

Met Glu Phe Asp Leu Asn Gly Asn Gly Asp Ile Gly Glu Lys Arg Val
1 5 10 15

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

Pro Thr Cys Ser Ile Pro His Asp Leu Gly Gly Gly Pro Pro Thr Thr
35 40 45

Val Gly Gly Arg Arg Met Gly Met Arg Lys Trp Glu Arg Arg Glu Arg
50 55 60

Val Ser Pro Pro Ser Pro His Pro His Pro Leu Pro Pro Asp Ile Met
65 70 75 80

Ser Leu Lys Arg Met Leu Glu Lys Leu Gly Val Pro Lys Thr His Leu
85 90 95

Glu Leu Lys Lys Leu Ile Gly Glu Val Ser Ser Gly Ser Gly Glu Thr
100 105 110

Phe Ser Tyr Pro Asp Phe Leu Arg Met Met Leu Gly Lys Arg Ser Ala
115 120 125

Ile Leu Lys Met
130

<210> 2522
<211> 491
<212> PRT
<213> Homo sapiens

<400> 2522

Met Glu Ser Ser Ala Lys Arg Lys Met Asp Pro Asp Asn Pro Asp Glu
1 5 10 15

Gly Pro Ser Ser Lys Val Pro Arg Pro Glu Thr Pro Val Thr Lys Ala
20 25 30

Thr Thr Phe Leu Gln Thr Met Leu Arg Lys Glu Val Asn Ser Gln Leu
35 40 45

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

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

Val Leu Ala Glu Leu Val Lys Gln Ile Lys Val Arg Val Asp Met Val
85 90 95

Arg His Arg Ile Lys Glu His Met Leu Lys Lys Tyr Thr Gln Thr Glu
100 105 110

Glu Lys Phe Thr Gly Ala Phe Asn Met Met Gly Gly Cys Leu Gln Asn
115 120 125

Ala Leu Asp Ile Leu Asp Lys Val His Glu Pro Phe Glu Glu Met Lys
130 135 140

Cys Ile Gly Leu Thr Met Gln Ser Met Tyr Glu Asn Tyr Ile Val Pro
145 150 155 160

Glu Asp Lys Arg Glu Met Trp Met Ala Cys Ile Lys Glu Leu His Asp
165 170 175

Val Ser Lys Gly Ala Ala Asn Lys Leu Gly Gly Ala Leu Gln Ala Lys
180 185 190

Ala Arg Ala Lys Lys Asp Glu Leu Arg Arg Lys Met Met Tyr Met Cys
195 200 205

Tyr Arg Asn Ile Glu Phe Phe Thr Lys Asn Ser Ala Phe Pro Lys Thr
210 215 220

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

Cys Ser Pro Asp Glu Ile Met Ala Tyr Ala Gln Lys Ile Phe Lys Ile
245 250 255

Leu Asp Glu Glu Arg Asp Lys Val Leu Thr His Ile Asp His Ile Phe
260 265 270

Met Asp Ile Leu Thr Thr Cys Val Glu Thr Met Cys Asn Glu Tyr Lys
275 280 285

Val Thr Ser Asp Ala Cys Met Met Thr Met Tyr Gly Gly Ile Ser Leu
290 295 300

Leu Ser Glu Phe Cys Arg Val Leu Cys Cys Tyr Val Leu Glu Glu Thr
305 310 315 320

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

Ser Val Met Lys Arg Arg Ile Glu Glu Ile Cys Met Lys Val Phe Ala
340 345 350

Gln Tyr Ile Leu Gly Ala Asp Pro Leu Arg Val Cys Ser Pro Ser Val
355 360 365

Asp Asp Leu Arg Ala Ile Ala Glu Glu Ser Asp Glu Glu Glu Ala Ile
370 375 380

Val Ala Tyr Thr Leu Ala Thr Ala Gly Val Ser Ser Ser Asp Ser Leu
385 390 395 400

Val Ser Pro Pro Glu Ser Pro Val Pro Ala Thr Ile Pro Leu Ser Ser
405 410 415

Val Ile Val Ala Glu Asn Ser Asp Gln Glu Glu Ser Glu Gln Ser Asp
420 425 430

Glu Glu Glu Glu Glu Gly Ala Gln Glu Glu Arg Glu Asp Thr Val Ser
435 440 445

Val Lys Ser Glu Pro Val Ser Glu Ile Glu Glu Val Ala Pro Glu Glu
450 455 460

Glu Glu Asp Gly Ala Glu Glu Pro Thr Ala Ser Gly Gly Lys Ser Thr
465 470 475 480

His Pro Met Val Thr Arg Ser Lys Ala Asp Gln
485 490

<210> 2523
<211> 491
<212> PRT
<213> Homo sapiens

<400> 2523

Met Glu Ser Ser Ala Lys Arg Lys Met Asp Pro Asp Asn Pro Asp Glu
1 5 10 15

Gly Pro Ser Ser Lys Val Pro Arg Pro Glu Thr Pro Val Thr Lys Ala
20 25 30

Thr Thr Phe Leu Gln Thr Met Leu Arg Lys Glu Val Asn Ser Gln Leu
35 40 45

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

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

Val Leu Ala Glu Leu Val Lys Gln Ile Lys Val Arg Val Asp Met Val
85 90 95

Arg His Arg Ile Lys Glu His Met Leu Lys Lys Tyr Thr Gln Thr Glu
100 105 110

Glu Lys Phe Thr Gly Ala Phe Asn Met Met Gly Gly Cys Leu Gln Asn
115 120 125

Ala Leu Asp Ile Leu Asp Lys Val His Glu Pro Phe Glu Glu Met Lys
130 135 140

Cys Ile Gly Leu Thr Met Gln Ser Met Tyr Glu Asn Tyr Ile Val Pro
145 150 155 160

Glu Asp Lys Arg Glu Met Trp Met Ala Cys Ile Lys Glu Leu His Asp
165 170 175

Val Ser Lys Gly Ala Ala Asn Lys Leu Gly Gly Ala Leu Gln Ala Lys
180 185 190

Ala Arg Ala Lys Lys Asp Glu Leu Arg Arg Lys Met Met Tyr Met Cys
195 200 205

Tyr Arg Asn Ile Glu Phe Phe Thr Lys Asn Ser Ala Phe Pro Lys Thr
210 215 220

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

Cys Ser Pro Asp Glu Ile Met Ala Tyr Ala Gln Lys Ile Phe Lys Ile
245 250 255

Leu Asp Glu Glu Arg Asp Lys Val Leu Thr His Ile Asp His Ile Phe
260 265 270

Met Asp Ile Leu Thr Thr Cys Val Glu Thr Met Cys Asn Glu Tyr Lys
275 280 285

Val Thr Ser Asp Ala Cys Met Met Thr Met Tyr Gly Gly Ile Ser Leu
290 295 300

Leu Ser Glu Phe Cys Arg Val Leu Cys Cys Tyr Val Leu Glu Glu Thr
305 310 315 320

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

Ser Val Met Lys Arg Arg Ile Glu Glu Ile Cys Met Lys Val Phe Ala
340 345 350

Gln Tyr Ile Leu Gly Ala Asp Pro Leu Arg Val Cys Ser Pro Ser Val
355 360 365

Asp Asp Leu Arg Ala Ile Ala Glu Glu Ser Asp Glu Glu Glu Ala Ile
370 375 380

Val Ala Tyr Thr Leu Ala Thr Ala Gly Val Ser Ser Ser Asp Ser Leu
385 390 395 400

Val Ser Pro Pro Glu Ser Pro Val Pro Ala Thr Ile Pro Leu Ser Ser
405 410 415

Val Ile Val Ala Glu Asn Ser Asp Gln Glu Glu Ser Glu Gln Ser Asp
420 425 430

Glu Glu Glu Glu Glu Gly Ala Gln Glu Glu Arg Glu Asp Thr Val Ser
435 440 445

Val Lys Ser Glu Pro Val Ser Glu Ile Glu Glu Val Ala Pro Glu Glu
450 455 460

Glu Glu Asp Gly Ala Glu Glu Pro Thr Ala Ser Gly Gly Lys Ser Thr
465 470 475 480

His Pro Met Val Thr Arg Ser Lys Ala Asp Gln
485 490

<210> 2524
<211> 641
<212> PRT
<213> Homo sapiens

<400> 2524

```
Met Ser Asp Glu Gly Pro Gly Thr Gly Pro Gly Asn Gly Leu Gly Glu
1               5                  10                  15

Lys Gly Asp Thr Ser Gly Pro Glu Gly Ser Gly Gly Ser Gly Pro Gln
            20                  25                  30

Arg Arg Gly Gly Asp Asn His Gly Arg Gly Arg Gly Arg Gly Arg Gly
        35                  40                  45

Arg Gly Gly Gly Arg Pro Gly Ala Pro Gly Gly Ser Gly Ser Gly Pro
    50                  55                  60

Arg His Arg Asp Gly Val Arg Arg Pro Gln Lys Arg Pro Ser Cys Ile
65                  70                  75                  80

Gly Cys Lys Gly Thr His Gly Gly Thr Gly Ala Gly Ala Gly Ala Gly
                85                  90                  95

Gly Ala Gly Ala Gly Gly Ala Gly Ala Gly Gly Gly Ala Gly Ala Gly
            100                 105                 110

Gly Gly Ala Gly Gly Ala Gly Gly Ala Gly Gly Ala Gly Ala Gly Gly
        115                 120                 125

Gly Ala Gly Ala Gly Gly Gly Ala Gly Gly Ala Gly Gly Ala Gly Ala
    130                 135                 140

Gly Gly Gly Ala Gly Ala Gly Gly Gly Ala Gly Gly Ala Gly Ala Gly
145                 150                 155                 160

Gly Gly Ala Gly Gly Ala Gly Gly Ala Gly Ala Gly Gly Gly Ala Gly
                165                 170                 175

Ala Gly Gly Gly Ala Gly Gly Ala Gly Ala Gly Gly Gly Ala Gly Gly
            180                 185                 190

Ala Gly Gly Ala Gly Ala Gly Gly Gly Ala Gly Ala Gly Gly Ala Gly
        195                 200                 205

Gly Ala Gly Gly Ala Gly Ala Gly Gly Ala Gly Ala Gly Gly Gly Ala
    210                 215                 220

Gly Gly Ala Gly Gly Ala Gly Ala Gly Gly Ala Gly Ala Gly Gly Ala
225                 230                 235                 240
```

Gly Ala Gly Gly Ala Gly Ala Gly Gly Ala Gly Gly Ala Gly Ala Gly
245 250 255

Gly Ala Gly Gly Ala Gly Ala Gly Gly Ala Gly Gly Ala Gly Ala Gly
260 265 270

Gly Gly Ala Gly Gly Ala Gly Ala Gly Gly Gly Ala Gly Gly Ala Gly
275 280 285

Ala Gly Gly Ala Gly Gly Ala Gly Ala Gly Gly Ala Gly Gly Ala Gly
290 295 300

Ala Gly Gly Ala Gly Gly Ala Gly Ala Gly Gly Gly Ala Gly Ala Gly
305 310 315 320

Gly Ala Gly Ala Gly Gly Gly Gly Arg Gly Arg Gly Gly Ser Gly Gly
325 330 335

Arg Gly Arg Gly Gly Ser Gly Gly Arg Gly Arg Gly Gly Ser Gly Gly
340 345 350

Arg Arg Gly Arg Gly Arg Glu Arg Ala Arg Gly Gly Ser Arg Glu Arg
355 360 365

Ala Arg Gly Arg Gly Arg Gly Arg Gly Glu Lys Arg Pro Arg Ser Pro
370 375 380

Ser Ser Gln Ser Ser Ser Ser Gly Ser Pro Pro Arg Arg Pro Pro Pro
385 390 395 400

Gly Arg Arg Pro Phe Phe His Pro Val Gly Glu Ala Asp Tyr Phe Glu
405 410 415

Tyr His Gln Glu Gly Gly Pro Asp Gly Glu Pro Asp Val Pro Pro Gly
420 425 430

Ala Ile Glu Gln Gly Pro Ala Asp Asp Pro Gly Glu Gly Pro Ser Thr
435 440 445

Gly Pro Arg Gly Gln Gly Asp Gly Gly Arg Arg Lys Lys Gly Gly Trp
450 455 460

Phe Gly Lys His Arg Gly Gln Gly Gly Ser Asn Pro Lys Phe Glu Asn
465 470 475 480

Ile Ala Glu Gly Leu Arg Ala Leu Leu Ala Arg Ser His Val Glu Arg
485 490 495

Thr Thr Asp Glu Gly Thr Trp Val Ala Gly Val Phe Val Tyr Gly Gly
500 505 510

Ser Lys Thr Ser Leu Tyr Asn Leu Arg Arg Gly Thr Ala Leu Ala Ile
515 520 525

Pro Gln Cys Arg Leu Thr Pro Leu Ser Arg Leu Pro Phe Gly Met Ala
530 535 540

Pro Gly Pro Gly Pro Gln Pro Gly Pro Leu Arg Glu Ser Ile Val Cys
545 550 555 560

Tyr Phe Met Val Phe Leu Gln Thr His Ile Phe Ala Glu Val Leu Lys
565 570 575

Asp Ala Ile Lys Asp Leu Val Met Thr Lys Pro Ala Pro Thr Cys Asn
580 585 590

Ile Arg Val Thr Val Cys Ser Phe Asp Asp Gly Val Asp Leu Pro Pro
595 600 605

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

Asp Asp Gly Asp Glu Gly Gly Asp Gly Asp Glu Gly Glu Glu Gly Gln
625 630 635 640

Glu

<210> 2525
<211> 245
<212> PRT
<213> Homo sapiens

<400> 2525

Met Met Asp Pro Asn Ser Thr Ser Glu Asp Val Lys Phe Thr Pro Asp
1 5 10 15

Pro Tyr Gln Val Pro Phe Val Gln Ala Phe Asp Gln Ala Thr Arg Val
20 25 30

Tyr Gln Asp Leu Gly Gly Pro Ser Gln Ala Pro Leu Pro Cys Val Leu

```
        35                  40                  45

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

His Val Ser Thr Ala Pro Thr Gly Ser Trp Phe Ser Ala Pro Gln Pro
65                  70                  75                  80

Ala Pro Glu Asn Ala Tyr Gln Ala Tyr Ala Ala Pro Gln Leu Phe Pro
                85                  90                  95

Val Ser Asp Ile Thr Gln Asn Gln Gln Thr Asn Gln Ala Gly Gly Glu
            100                 105                 110

Ala Pro Gln Pro Gly Asp Asn Ser Thr Val Gln Thr Ala Ala Ala Val
        115                 120                 125

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

Gly Val Pro Gln Pro Ala Pro Val Ala Ala Pro Ala Arg Arg Thr Arg
145                 150                 155                 160

Lys Pro Gln Gln Pro Glu Ser Leu Glu Glu Cys Asp Ser Glu Leu Glu
                165                 170                 175

Ile Lys Arg Tyr Lys Asn Arg Val Ala Ser Arg Lys Cys Arg Ala Lys
            180                 185                 190

Phe Lys Gln Leu Leu Gln His Tyr Arg Glu Val Ala Ala Ala Lys Ser
        195                 200                 205

Ser Glu Asn Asp Arg Leu Arg Leu Leu Leu Lys Gln Met Cys Pro Ser
    210                 215                 220

Leu Asp Val Asp Ser Ile Ile Pro Arg Thr Pro Asp Val Leu His Glu
225                 230                 235                 240

Asp Leu Leu Asn Phe
                245
```

<210> 2526
<211> 491
<212> PRT
<213> Homo sapiens

<400> 2526

```
Met Glu Ser Ser Ala Lys Arg Lys Met Asp Pro Asp Asn Pro Asp Glu
1               5                  10                  15

Gly Pro Ser Ser Lys Val Pro Arg Pro Glu Thr Pro Val Thr Lys Ala
            20                  25                  30

Thr Thr Phe Leu Gln Thr Met Leu Arg Lys Glu Val Asn Ser Gln Leu
        35                  40                  45

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

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

Val Leu Ala Glu Leu Val Lys Gln Ile Lys Val Arg Val Asp Met Val
                85                  90                  95

Arg His Arg Ile Lys Glu His Met Leu Lys Lys Tyr Thr Gln Thr Glu
            100                 105                 110

Glu Lys Phe Thr Gly Ala Phe Asn Met Met Gly Gly Cys Leu Gln Asn
        115                 120                 125

Ala Leu Asp Ile Leu Asp Lys Val His Glu Pro Phe Glu Glu Met Lys
    130                 135                 140

Cys Ile Gly Leu Thr Met Gln Ser Met Tyr Glu Asn Tyr Ile Val Pro
145                 150                 155                 160

Glu Asp Lys Arg Glu Met Trp Met Ala Cys Ile Lys Glu Leu His Asp
                165                 170                 175

Val Ser Lys Gly Ala Ala Asn Lys Leu Gly Gly Ala Leu Gln Ala Lys
            180                 185                 190

Ala Arg Ala Lys Lys Asp Glu Leu Arg Arg Lys Met Met Tyr Met Cys
        195                 200                 205

Tyr Arg Asn Ile Glu Phe Phe Thr Lys Asn Ser Ala Phe Pro Lys Thr
    210                 215                 220

Thr Asn Gly Cys Ser Gln Ala Met Ala Ala Leu Gln Asn Leu Pro Gln
225                 230                 235                 240
```

Cys Ser Pro Asp Glu Ile Met Ala Tyr Ala Gln Lys Ile Phe Lys Ile
245 250 255

Leu Asp Glu Glu Arg Asp Lys Val Leu Thr His Ile Asp His Ile Phe
260 265 270

Met Asp Ile Leu Thr Thr Cys Val Glu Thr Met Cys Asn Glu Tyr Lys
275 280 285

Val Thr Ser Asp Ala Cys Met Met Thr Met Tyr Gly Gly Ile Ser Leu
290 295 300

Leu Ser Glu Phe Cys Arg Val Leu Cys Cys Tyr Val Leu Glu Glu Thr
305 310 315 320

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

Ser Val Met Lys Arg Arg Ile Glu Glu Ile Cys Met Lys Val Phe Ala
340 345 350

Gln Tyr Ile Leu Gly Ala Asp Pro Leu Arg Val Cys Ser Pro Ser Val
355 360 365

Asp Asp Leu Arg Ala Ile Ala Glu Glu Ser Asp Glu Glu Glu Ala Ile
370 375 380

Val Ala Tyr Thr Leu Ala Thr Ala Gly Val Ser Ser Ser Asp Ser Leu
385 390 395 400

Val Ser Pro Pro Glu Ser Pro Val Pro Ala Thr Ile Pro Leu Ser Ser
405 410 415

Val Ile Val Ala Glu Asn Ser Asp Gln Glu Glu Ser Glu Gln Ser Asp
420 425 430

Glu Glu Glu Glu Glu Gly Ala Gln Glu Glu Arg Glu Asp Thr Val Ser
435 440 445

Val Lys Ser Glu Pro Val Ser Glu Ile Glu Glu Val Ala Pro Glu Glu
450 455 460

Glu Glu Asp Gly Ala Glu Glu Pro Thr Ala Ser Gly Gly Lys Ser Thr
465 470 475 480

His Pro Met Val Thr Arg Ser Lys Ala Asp Gln

485 490

<210> 2527
<211> 491
<212> PRT
<213> Homo sapiens

<400> 2527

Met Glu Ser Ser Ala Lys Arg Lys Met Asp Pro Asp Asn Pro Asp Glu
1 5 10 15

Gly Pro Ser Ser Lys Val Pro Arg Pro Glu Thr Pro Val Thr Lys Ala
20 25 30

Thr Thr Phe Leu Gln Thr Met Leu Arg Lys Glu Val Asn Ser Gln Leu
35 40 45

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

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

Val Leu Ala Glu Leu Val Lys Gln Ile Lys Val Arg Val Asp Met Val
85 90 95

Arg His Arg Ile Lys Glu His Met Leu Lys Lys Tyr Thr Gln Thr Glu
100 105 110

Glu Lys Phe Thr Gly Ala Phe Asn Met Met Gly Gly Cys Leu Gln Asn
115 120 125

Ala Leu Asp Ile Leu Asp Lys Val His Glu Pro Phe Glu Glu Met Lys
130 135 140

Cys Ile Gly Leu Thr Met Gln Ser Met Tyr Glu Asn Tyr Ile Val Pro
145 150 155 160

Glu Asp Lys Arg Glu Met Trp Met Ala Cys Ile Lys Glu Leu His Asp
165 170 175

Val Ser Lys Gly Ala Ala Asn Lys Leu Gly Gly Ala Leu Gln Ala Lys
180 185 190

Ala Arg Ala Lys Lys Asp Glu Leu Arg Arg Lys Met Met Tyr Met Cys
195 200 205

Tyr Arg Asn Ile Glu Phe Phe Thr Lys Asn Ser Ala Phe Pro Lys Thr
210 215 220

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

Cys Ser Pro Asp Glu Ile Met Ala Tyr Ala Gln Lys Ile Phe Lys Ile
245 250 255

Leu Asp Glu Glu Arg Asp Lys Val Leu Thr His Ile Asp His Ile Phe
260 265 270

Met Asp Ile Leu Thr Thr Cys Val Glu Thr Met Cys Asn Glu Tyr Lys
275 280 285

Val Thr Ser Asp Ala Cys Met Met Thr Met Tyr Gly Gly Ile Ser Leu
290 295 300

Leu Ser Glu Phe Cys Arg Val Leu Cys Cys Tyr Val Leu Glu Glu Thr
305 310 315 320

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

Ser Val Met Lys Arg Arg Ile Glu Glu Ile Cys Met Lys Val Phe Ala
340 345 350

Gln Tyr Ile Leu Gly Ala Asp Pro Leu Arg Val Cys Ser Pro Ser Val
355 360 365

Asp Asp Leu Arg Ala Ile Ala Glu Glu Ser Asp Glu Glu Glu Ala Ile
370 375 380

Val Ala Tyr Thr Leu Ala Thr Ala Gly Val Ser Ser Ser Asp Ser Leu
385 390 395 400

Val Ser Pro Pro Glu Ser Pro Val Pro Ala Thr Ile Pro Leu Ser Ser
405 410 415

Val Ile Val Ala Glu Asn Ser Asp Gln Glu Glu Ser Glu Gln Ser Asp
420 425 430

Glu Glu Glu Glu Glu Gly Ala Gln Glu Glu Arg Glu Asp Thr Val Ser
435 440 445

Val Lys Ser Glu Pro Val Ser Glu Ile Glu Glu Val Ala Pro Glu Glu
450 455 460

Glu Glu Asp Gly Ala Glu Glu Pro Thr Ala Ser Gly Gly Lys Ser Thr
465 470 475 480

His Pro Met Val Thr Arg Ser Lys Ala Asp Gln
485 490

<210> 2528
<211> 142
<212> PRT
<213> Homo sapiens

<400> 2528

Met Ser Leu Leu Pro Val Pro Tyr Thr Glu Ala Ala Ser Leu Ser Thr
1 5 10 15

Gly Ser Thr Val Thr Ile Lys Gly Arg Pro Leu Ala Cys Phe Leu Asn
20 25 30

Glu Pro Tyr Leu Gln Val Asp Phe His Thr Glu Met Lys Glu Glu Ser
35 40 45

Asp Ile Val Phe His Phe Gln Val Cys Phe Gly Arg Arg Val Val Met
50 55 60

Asn Ser Arg Glu Tyr Gly Ala Trp Lys Gln Gln Val Glu Ser Lys Asn
65 70 75 80

Met Pro Phe Gln Asp Gly Gln Glu Phe Glu Leu Ser Ile Ser Val Leu
85 90 95

Pro Asp Lys Tyr Gln Val Met Val Asn Gly Gln Ser Ser Tyr Thr Phe
100 105 110

Asp His Arg Ile Lys Pro Glu Ala Val Lys Met Val Gln Val Trp Arg
115 120 125

Asp Ile Ser Leu Thr Lys Phe Asn Val Ser Tyr Leu Lys Arg
130 135 140

<210> 2529
<211> 298
<212> PRT
<213> Homo sapiens

<400> 2529

```
Met Ala Glu Ala Met Asp Leu Gly Lys Asp Pro Asn Gly Pro Thr His
1               5                  10                  15

Ser Ser Thr Leu Phe Val Arg Asp Asp Gly Ser Ser Met Ser Phe Tyr
            20                  25                  30

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

Gly Gly Gly Thr Val Cys Arg Val Gln Glu Pro Gly Ala Val Leu Leu
    50                  55                  60

Ala Gln Pro Gly Glu Ala Leu Ala Glu Ala Ser Gly Asp Phe Ile Ser
65                  70                  75                  80

Thr Gln His Ile Leu Asp Cys Val Glu Arg Asn Glu Arg Leu Glu Leu
                85                  90                  95

Glu Ala Tyr Arg Leu Gly Pro Ala Ser Ala Ala Asp Thr Gly Ser Glu
            100                 105                 110

Ala Lys Pro Gly Ala Leu Ala Glu Gly Ala Ala Glu Pro Glu Pro Gln
        115                 120                 125

Arg His Ala Gly Arg Ile Ala Phe Thr Asp Ala Asp Asp Val Ala Ile
    130                 135                 140

Leu Thr Tyr Val Lys Glu Asn Ala Arg Ser Pro Ser Ser Val Thr Gly
145                 150                 155                 160

Asn Ala Leu Trp Lys Ala Met Glu Lys Ser Ser Leu Thr Gln His Ser
                165                 170                 175

Trp Gln Ser Leu Lys Asp Arg Tyr Leu Lys His Leu Arg Gly Gln Glu
            180                 185                 190

His Lys Tyr Leu Leu Gly Asp Ala Pro Val Ser Pro Ser Ser Gln Lys
        195                 200                 205

Leu Lys Arg Lys Ala Glu Glu Asp Pro Glu Ala Ala Asp Ser Gly Glu
    210                 215                 220

Pro Gln Asn Lys Arg Thr Pro Asp Leu Pro Glu Glu Glu Tyr Val Lys
225                 230                 235                 240
```

Glu Glu Ile Gln Glu Asn Glu Glu Ala Val Lys Lys Met Leu Val Glu
245 250 255

Ala Thr Arg Glu Phe Glu Glu Val Val Val Asp Glu Ser Pro Pro Asp
260 265 270

Phe Glu Ile His Ile Thr Met Cys Asp Asp Asp Pro Pro Thr Pro Glu
275 280 285

Glu Asp Ser Glu Thr Gln Pro Asp Glu Glu
290 295

<210> 2530
<211> 365
<212> PRT
<213> Homo sapiens

<400> 2530

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

Leu Ala Leu Thr Gln Thr Trp Ala Gly Ser His Ser Met Arg Tyr Phe
20 25 30

Phe Thr Ser Val Ser Arg Pro Gly Arg Gly Glu Pro Arg Phe Ile Ala
35 40 45

Val Gly Tyr Val Asp Asp Thr Gln Phe Val Arg Phe Asp Ser Asp Ala
50 55 60

Ala Ser Gln Arg Met Glu Pro Arg Ala Pro Trp Ile Glu Gln Glu Gly
65 70 75 80

Pro Glu Tyr Trp Asp Gln Glu Thr Arg Asn Val Lys Ala Gln Ser Gln
85 90 95

Thr Asp Arg Val Asp Leu Gly Thr Leu Arg Gly Tyr Tyr Asn Gln Ser
100 105 110

Glu Ala Gly Ser His Thr Ile Gln Ile Met Tyr Gly Cys Asp Val Gly
115 120 125

Ser Asp Gly Arg Phe Leu Arg Gly Tyr Arg Gln Asp Ala Tyr Asp Gly
130 135 140

Lys Asp Tyr Ile Ala Leu Asn Glu Asp Leu Arg Ser Trp Thr Ala Ala
145 150 155 160

```
Asp Met Ala Ala Gln Ile Thr Lys Arg Lys Trp Glu Ala Ala His Glu
                165                 170                 175

Ala Glu Gln Leu Arg Ala Tyr Leu Asp Gly Thr Cys Val Glu Trp Leu
            180                 185                 190

Arg Arg Tyr Leu Glu Asn Gly Lys Glu Thr Leu Gln Arg Thr Asp Pro
        195                 200                 205

Pro Lys Thr His Met Thr His His Pro Ile Ser Asp His Glu Ala Thr
    210                 215                 220

Leu Arg Cys Trp Ala Leu Gly Phe Tyr Pro Ala Glu Ile Thr Leu Thr
225                 230                 235                 240

Trp Gln Arg Asp Gly Glu Asp Gln Thr Gln Asp Thr Glu Leu Val Glu
                245                 250                 255

Thr Arg Pro Ala Gly Asp Gly Thr Phe Gln Lys Trp Ala Ala Val Val
            260                 265                 270

Val Pro Ser Gly Glu Glu Gln Arg Tyr Thr Cys His Val Gln His Glu
        275                 280                 285

Gly Leu Pro Lys Pro Leu Thr Leu Arg Trp Glu Leu Ser Ser Gln Pro
    290                 295                 300

Thr Ile Pro Ile Val Gly Ile Ile Ala Gly Leu Val Leu Leu Gly Ala
305                 310                 315                 320

Val Ile Thr Gly Ala Val Val Ala Ala Val Met Trp Arg Arg Lys Ser
                325                 330                 335

Ser Asp Arg Lys Gly Gly Ser Tyr Thr Gln Ala Ala Ser Ser Asp Ser
            340                 345                 350

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

<210> 2531
<211> 155
<212> PRT
<213> Homo sapiens

<400> 2531

Met Glu Leu Arg Ser Gly Ser Val Gly Ser Gln Ala Val Ala Arg Arg
1 5 10 15

Met Asp Gly Asp Ser Arg Asp Gly Gly Gly Gly Lys Asp Ala Thr Gly
20 25 30

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

Met Thr Ala Gly Ala Met Ala Gly Ile Leu Glu His Ser Val Met Tyr
50 55 60

Pro Val Asp Ser Val Lys Thr Arg Met Gln Ser Leu Ser Pro Asp Pro
65 70 75 80

Lys Ala Gln Tyr Thr Ser Ile Tyr Gly Ala Leu Lys Lys Ile Met Arg
85 90 95

Thr Glu Gly Phe Trp Arg Pro Leu Arg Gly Val Asn Val Met Ile Met
100 105 110

Gly Ala Gly Pro Ala His Ala Met Tyr Phe Ala Cys Tyr Glu Asn Met
115 120 125

Lys Arg Thr Leu Asn Asp Val Phe His His Gln Gly Asn Ser His Leu
130 135 140

Ala Asn Gly Ile Leu Lys Ala Phe Val Trp Ser
145 150 155

<210> 2532
<211> 384
<212> PRT
<213> Homo sapiens

<400> 2532

Met Lys Val Thr Ser Leu Asp Gly Arg Gln Leu Arg Lys Met Leu Arg
1 5 10 15

Lys Glu Ala Ala Ala Arg Cys Val Val Leu Asp Cys Arg Pro Tyr Leu
20 25 30

Ala Phe Ala Ala Ser Asn Val Arg Gly Ser Leu Asn Val Asn Leu Asn
35 40 45

Ser Val Val Leu Arg Arg Ala Arg Gly Gly Ala Val Ser Ala Arg Tyr
50 55 60

Val Leu Pro Asp Glu Ala Ala Arg Ala Arg Leu Leu Gln Glu Gly Gly
65 70 75 80

Gly Gly Val Ala Ala Val Val Val Leu Asp Gln Gly Ser Arg His Trp
85 90 95

Gln Lys Leu Arg Glu Glu Ser Ala Ala Arg Val Val Leu Thr Ser Leu
100 105 110

Leu Ala Cys Leu Pro Ala Gly Pro Arg Val Tyr Phe Leu Lys Gly Gly
115 120 125

Tyr Glu Thr Phe Tyr Ser Glu Tyr Pro Glu Cys Cys Val Asp Val Lys
130 135 140

Pro Ile Ser Gln Glu Lys Ile Glu Ser Glu Arg Ala Leu Ile Ser Gln
145 150 155 160

Cys Gly Lys Pro Val Val Asn Val Ser Tyr Arg Pro Ala Tyr Asp Gln
165 170 175

Gly Gly Pro Val Glu Ile Leu Pro Phe Leu Tyr Leu Gly Ser Ala Tyr
180 185 190

His Ala Ser Lys Cys Glu Phe Leu Ala Asn Leu His Ile Thr Ala Leu
195 200 205

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

Tyr Lys Trp Ile Pro Val Glu Asp Ser His Thr Ala Asp Ile Ser Ser
225 230 235 240

His Phe Gln Glu Ala Ile Asp Phe Ile Asp Cys Val Arg Glu Lys Gly
245 250 255

Gly Lys Val Leu Val His Cys Glu Ala Gly Ile Ser Arg Ser Pro Thr
260 265 270

Ile Cys Met Ala Tyr Leu Met Lys Thr Lys Gln Phe Arg Leu Lys Glu
275 280 285

Ala Phe Asp Tyr Ile Lys Gln Arg Arg Ser Met Val Ser Pro Asn Phe
290 295 300

```
Gly Phe Met Gly Gln Leu Leu Gln Tyr Glu Ser Glu Ile Leu Pro Ser
305                 310                 315                 320

Thr Pro Asn Pro Gln Pro Pro Ser Cys Gln Gly Glu Ala Ala Gly Ser
                325                 330                 335

Ser Leu Ile Gly His Leu Gln Thr Leu Ser Pro Asp Met Gln Gly Ala
            340                 345                 350

Tyr Cys Thr Phe Pro Ala Ser Val Leu Ala Pro Val Pro Thr His Ser
        355                 360                 365

Thr Val Ser Glu Leu Ser Arg Ser Pro Val Ala Thr Ala Thr Ser Cys
    370                 375                 380
```

<210> 2533
<211> 99
<212> PRT
<213> Homo sapiens

<400> 2533

```
Met Ala Gln Gly Lys Val Ala Ser Leu Gly Pro Ile Lys Gln His Thr
1               5                   10                  15

Phe Leu Lys Asn Met Gly Ile Asp Val Arg Leu Lys Val Leu Leu Asp
            20                  25                  30

Lys Ser Asn Glu Pro Ser Val Arg Gln Gln Leu Leu Gln Gly Tyr Asp
        35                  40                  45

Met Leu Met Asn Pro Lys Lys Met Gly Glu Arg Phe Asn Phe Phe Ala
    50                  55                  60

Leu Leu Pro His Gln Arg Leu Gln Gly Gly Arg Tyr Gln Arg Asn Ala
65                  70                  75                  80

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

Ala Trp Gln
```

<210> 2534
<211> 529
<212> PRT
<213> Homo sapiens

<400> 2534

Met Gly Ser Ser Arg Ala Pro Trp Met Gly Arg Val Gly Gly His Gly
1 5 10 15

Met Met Ala Leu Leu Leu Ala Gly Leu Leu Leu Pro Gly Thr Leu Ala
20 25 30

Lys Ser Ile Gly Thr Phe Ser Asp Pro Cys Lys Asp Pro Thr Arg Ile
35 40 45

Thr Ser Pro Asn Asp Pro Cys Leu Thr Gly Lys Gly Asp Ser Ser Gly
50 55 60

Phe Ser Ser Tyr Ser Gly Ser Ser Ser Ser Gly Ser Ser Ile Ser Ser
65 70 75 80

Ala Arg Ser Ser Gly Gly Gly Ser Ser Gly Ser Ser Ser Gly Ser Ser
85 90 95

Ile Ala Gln Gly Gly Ser Ala Gly Ser Phe Lys Pro Gly Thr Gly Tyr
100 105 110

Ser Gln Val Ser Tyr Ser Ser Gly Ser Gly Ser Ser Leu Gln Gly Ala
115 120 125

Ser Gly Ser Ser Gln Leu Gly Ser Ser Ser Ser His Ser Gly Ser Ser
130 135 140

Gly Ser His Ser Gly Ser Ser Ser Ser His Ser Ser Ser Ser Ser Ser
145 150 155 160

Phe Gln Phe Ser Ser Ser Ser Phe Gln Val Gly Asn Gly Ser Ala Leu
165 170 175

Pro Thr Asn Asp Asn Ser Tyr Arg Gly Ile Leu Asn Pro Ser Gln Pro
180 185 190

Gly Gln Ser Ser Ser Ser Ser Gln Thr Ser Gly Val Ser Ser Ser Gly
195 200 205

Gln Ser Val Ser Ser Asn Gln Arg Pro Cys Ser Ser Asp Ile Pro Asp
210 215 220

Ser Pro Cys Ser Gly Gly Pro Ile Val Ser His Ser Gly Pro Tyr Ile
225 230 235 240

```
Pro Ser Ser His Ser Val Ser Gly Gly Gln Arg Pro Val Val Val Val
                245                 250                 255

Val Asp Gln His Gly Ser Gly Ala Pro Gly Val Val Gln Gly Pro Pro
            260                 265                 270

Cys Ser Asn Gly Gly Leu Pro Gly Lys Pro Cys Pro Pro Ile Thr Ser
        275                 280                 285

Val Asp Lys Ser Tyr Gly Gly Tyr Glu Val Val Gly Gly Ser Ser Asp
    290                 295                 300

Ser Tyr Leu Val Pro Gly Met Thr Tyr Ser Lys Gly Lys Ile Tyr Pro
305                 310                 315                 320

Val Gly Tyr Phe Thr Lys Glu Asn Pro Val Lys Gly Ser Pro Gly Val
                325                 330                 335

Pro Ser Phe Ala Ala Gly Pro Pro Ile Ser Glu Gly Lys Tyr Phe Ser
            340                 345                 350

Ser Asn Pro Ile Ile Pro Ser Gln Ser Ala Ala Ser Ser Ala Ile Ala
        355                 360                 365

Phe Gln Pro Val Gly Thr Gly Gly Val Gln Leu Cys Gly Gly Gly Ser
    370                 375                 380

Thr Gly Ser Lys Gly Pro Cys Ser Pro Ser Ser Ser Arg Val Pro Ser
385                 390                 395                 400

Ser Ser Ser Ile Ser Ser Ser Ser Gly Ser Pro Tyr His Pro Cys Gly
                405                 410                 415

Ser Ala Ser Gln Ser Pro Cys Ser Pro Pro Gly Thr Gly Ser Phe Ser
            420                 425                 430

Ser Ser Ser Ser Ser Gln Ser Ser Gly Lys Ile Ile Leu Gln Pro Cys
        435                 440                 445

Gly Ser Lys Ser Ser Ser Ser Gly His Pro Cys Met Ser Val Ser Ser
    450                 455                 460

Leu Thr Leu Thr Gly Gly Pro Asp Gly Ser Pro His Pro Asp Pro Ser
465                 470                 475                 480
```

Ala Gly Ala Lys Pro Cys Gly Ser Ser Ser Ala Gly Lys Ile Pro Cys
485 490 495

Arg Ser Ile Arg Asp Ile Leu Ala Gln Val Lys Pro Leu Gly Pro Gln
500 505 510

Leu Ala Asp Pro Glu Val Phe Leu Pro Gln Gly Glu Leu Leu Asp Ser
515 520 525

Pro

<210> 2535
<211> 125
<212> PRT
<213> Homo sapiens

<400> 2535

Met Pro Pro Lys Asp Asp Lys Lys Lys Lys Asp Ala Gly Lys Ser Ala
1 5 10 15

Lys Lys Asp Lys Asp Pro Val Asn Lys Ser Gly Gly Lys Ala Lys Lys
20 25 30

Lys Lys Trp Ser Lys Gly Lys Val Arg Asp Lys Leu Asn Asn Leu Val
35 40 45

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

Tyr Lys Leu Ile Thr Pro Ala Val Val Ser Glu Arg Leu Lys Ile Arg
65 70 75 80

Gly Ser Leu Ala Arg Ala Ala Leu Gln Glu Leu Leu Ser Lys Gly Leu
85 90 95

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

Thr Lys Gly Gly Asp Ala Pro Ala Ala Gly Glu Asp Ala
115 120 125

<210> 2536
<211> 335
<212> PRT
<213> Homo sapiens

<400> 2536

Met Gly Lys Val Lys Val Gly Val Asn Gly Phe Gly Arg Ile Gly Arg
1 5 10 15

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

Ile Asn Asp Pro Phe Ile Asp Leu Asn Tyr Met Val Tyr Met Phe Gln
35 40 45

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

Gly Lys Leu Val Ile Asn Gly Asn Pro Ile Thr Ile Phe Gln Glu Arg
65 70 75 80

Asp Pro Ser Lys Ile Lys Trp Gly Asp Ala Gly Ala Glu Tyr Val Val
85 90 95

Glu Ser Thr Gly Val Phe Thr Thr Met Glu Lys Ala Gly Ala His Leu
100 105 110

Gln Gly Gly Ala Lys Arg Val Ile Ile Ser Ala Pro Ser Ala Asp Ala
115 120 125

Pro Met Phe Val Met Gly Val Asn His Glu Lys Tyr Asp Asn Ser Leu
130 135 140

Lys Ile Ile Ser Asn Ala Ser Cys Thr Thr Asn Cys Leu Ala Pro Leu
145 150 155 160

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

Thr Val His Ala Ile Thr Ala Thr Gln Lys Thr Val Asp Gly Pro Ser
180 185 190

Gly Lys Leu Trp Arg Asp Gly Arg Gly Ala Leu Gln Asn Ile Ile Pro
195 200 205

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

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

```
Ser Val Val Asp Leu Thr Cys Arg Leu Glu Lys Pro Ala Lys Tyr Asp
                245                 250                 255

Asp Ile Lys Lys Val Val Lys Gln Ala Ser Glu Gly Pro Leu Lys Gly
            260                 265                 270

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

Asp Thr His Ser Ser Thr Phe Asp Ala Gly Ala Gly Ile Ala Leu Asn
    290                 295                 300

Asp His Phe Val Lys Leu Ile Ser Trp Tyr Asp Asn Glu Phe Gly Tyr
305                 310                 315                 320

Ser Asn Arg Val Val Asp Leu Met Ala His Met Ala Ser Lys Glu
                325                 330                 335
```

<210> 2537
<211> 114
<212> PRT
<213> Homo sapiens

<400> 2537

```
Met Ala Ser Val Ser Glu Leu Ala Cys Ile Tyr Ser Ala Leu Ile Leu
1               5                   10                  15

His Asp Asp Glu Val Thr Val Thr Glu Asp Lys Ile Asn Ala Leu Ile
            20                  25                  30

Lys Ala Ala Gly Val Asn Val Glu Pro Phe Trp Pro Gly Leu Phe Ala
        35                  40                  45

Lys Ala Leu Ala Asn Val Asn Ile Gly Ser Leu Ile Cys Asn Val Gly
    50                  55                  60

Ala Gly Gly Pro Ala Pro Ala Ala Gly Ala Ala Pro Ala Gly Gly Pro
65                  70                  75                  80

Ala Pro Ser Thr Ala Ala Ala Pro Ala Glu Glu Lys Lys Val Glu Ala
                85                  90                  95

Lys Lys Glu Glu Ser Glu Glu Ser Asp Asp Asp Met Gly Phe Gly Leu
            100                 105                 110

Phe Asp
```

<210> 2538
<211> 142
<212> PRT
<213> Homo sapiens

<400> 2538

Met Ala Ala Gly Gly Ser Asp Pro Arg Ala Gly Asp Val Glu Glu Asp
1 5 10 15

Ala Ser Gln Leu Ile Phe Pro Lys Glu Phe Glu Thr Ala Glu Thr Leu
20 25 30

Leu Asn Ser Glu Val His Met Leu Leu Glu His Arg Lys Gln Gln Asn
35 40 45

Glu Ser Ala Glu Asp Glu Gln Glu Leu Ser Glu Val Phe Met Lys Thr
50 55 60

Leu Asn Tyr Thr Ala Arg Phe Ser Arg Phe Lys Asn Arg Glu Thr Ile
65 70 75 80

Ala Ser Val Arg Ser Leu Leu Leu Gln Lys Lys Leu His Lys Phe Glu
85 90 95

Leu Ala Cys Leu Ala Asn Leu Cys Pro Glu Thr Ala Glu Glu Ser Lys
100 105 110

Ala Leu Ile Pro Ser Leu Glu Gly Arg Phe Glu Asp Glu Glu Leu Gln
115 120 125

Gln Ile Leu Asp Asp Ile Gln Thr Lys Arg Ser Phe Gln Tyr
130 135 140

<210> 2539
<211> 178
<212> PRT
<213> Homo sapiens

<400> 2539

Met Pro Ala Tyr His Ser Ser Leu Met Asp Pro Asp Thr Lys Leu Ile
1 5 10 15

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

Pro Arg Glu Thr Lys Asp Thr Asp Ile Val Asp Glu Ala Ile Tyr Tyr

35 40 45

Phe Lys Ala Asn Val Phe Phe Lys Asn Tyr Glu Ile Lys Asn Glu Ala
50 55 60

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

Lys Leu Gln Lys Cys Asn Ser Lys Ser Gln Gly Glu Lys Glu Met Tyr
85 90 95

Thr Leu Gly Ile Thr Asn Phe Pro Ile Pro Gly Glu Pro Gly Phe Pro
100 105 110

Leu Asn Ala Ile Tyr Ala Lys Pro Ala Asn Lys Gln Glu Asp Glu Val
115 120 125

Met Arg Ala Tyr Leu Gln Gln Leu Arg Gln Glu Thr Gly Leu Arg Leu
130 135 140

Cys Glu Lys Val Phe Asp Pro Gln Asn Asp Lys Pro Ser Lys Trp Trp
145 150 155 160

Thr Cys Phe Val Lys Arg Gln Phe Met Asn Lys Ser Leu Ser Gly Pro
165 170 175

Gly Gln

<210> 2540
<211> 351
<212> PRT
<213> Homo sapiens

<400> 2540

Met Glu Thr Asn Phe Ser Thr Pro Leu Asn Glu Tyr Glu Glu Val Ser
1 5 10 15

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

Leu Gly Val Thr Phe Val Leu Gly Val Leu Gly Asn Gly Leu Val Ile
35 40 45

Trp Val Ala Gly Phe Arg Met Thr Arg Thr Val Thr Thr Ile Cys Tyr
50 55 60

```
Leu Asn Leu Ala Leu Ala Asp Phe Ser Phe Thr Ala Thr Leu Pro Phe
65                  70                  75                  80

Leu Ile Val Ser Met Ala Met Gly Glu Lys Trp Pro Phe Gly Trp Phe
                85                  90                  95

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

Val Phe Leu Ile Gly Phe Ile Ala Leu Asp Arg Cys Ile Cys Val Leu
        115                 120                 125

His Pro Val Trp Ala Gln Asn His Arg Thr Val Ser Leu Ala Met Lys
    130                 135                 140

Val Ile Val Gly Pro Trp Ile Leu Ala Leu Val Leu Thr Leu Pro Val
145                 150                 155                 160

Phe Leu Phe Leu Thr Thr Val Thr Ile Pro Asn Gly Asp Thr Tyr Cys
                165                 170                 175

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

Val Ala Ile Thr Met Leu Thr Ala Arg Gly Ile Ile Arg Phe Val Ile
        195                 200                 205

Gly Phe Ser Leu Pro Met Ser Ile Val Ala Ile Cys Tyr Gly Leu Ile
    210                 215                 220

Ala Ala Lys Ile His Lys Lys Gly Met Ile Lys Ser Ser Arg Pro Leu
225                 230                 235                 240

Arg Val Leu Thr Ala Val Val Ala Ser Phe Phe Ile Cys Trp Phe Pro
                245                 250                 255

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

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

Ser Leu Ala Phe Phe Asn Ser Cys Leu Asn Pro Met Leu Tyr Val Phe
    290                 295                 300
```

Val Gly Gln Asp Phe Arg Glu Arg Leu Ile His Ser Leu Pro Thr Ser
305 310 315 320

Leu Glu Arg Ala Leu Ser Glu Asp Ser Ala Pro Thr Asn Asp Thr Ala
325 330 335

Ala Asn Ser Ala Ser Pro Pro Ala Glu Thr Glu Leu Gln Ala Met
340 345 350

<210> 2541
<211> 349
<212> PRT
<213> Homo sapiens

<400> 2541

Met Glu Thr Pro Pro Val Asn Thr Ile Gly Glu Lys Asp Thr Ser Gln
1 5 10 15

Pro Gln Gln Glu Trp Glu Lys Asn Leu Arg Glu Asn Leu Asp Ser Val
20 25 30

Ile Gln Ile Arg Gln Gln Pro Arg Asp Pro Pro Thr Glu Thr Leu Glu
35 40 45

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

Gly Ala Glu Lys Leu Val Ala Glu Leu Glu Gly Asp Ser His Lys Ser
65 70 75 80

His Gly Ser Thr Ser Gln Met Pro Glu Ala Leu Gln Ala Ser Asp Leu
85 90 95

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

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

Leu Gly Phe Pro Phe Gly Ser Gly Pro Pro Glu Gly Trp Thr Glu Leu
130 135 140

Thr Met Gly Val Gly Pro Trp Arg Glu Glu Thr Trp Gly Glu Leu Ile
145 150 155 160

Glu Lys Cys Leu Glu Ser Met Cys Gln Gly Glu Glu Ala Glu Leu Gln
165 170 175

Leu Pro Gly His Ser Gly Pro Pro Val Arg Leu Thr Leu Ala Ser Phe
180 185 190

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

Leu Ala Arg Glu Glu Arg Ala Arg Gly Thr Glu Leu Phe Arg Ala Gly
210 215 220

Asn Pro Glu Gly Ala Ala Arg Cys Tyr Gly Arg Ala Leu Arg Leu Leu
225 230 235 240

Leu Thr Leu Pro Pro Pro Gly Pro Pro Glu Arg Thr Val Leu His Ala
245 250 255

Asn Leu Ala Ala Cys Gln Leu Leu Leu Gly Gln Pro Gln Leu Ala Ala
260 265 270

Gln Ser Cys Asp Arg Val Leu Glu Arg Glu Pro Gly His Leu Lys Ala
275 280 285

Leu Tyr Arg Arg Gly Val Ala Gln Ala Ala Leu Gly Asn Leu Glu Lys
290 295 300

Ala Thr Ala Asp Leu Lys Lys Val Leu Ala Ile Asp Pro Lys Asn Arg
305 310 315 320

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

Asp Ala Gly Leu Ala Gln Gly Leu Arg Lys Met Phe Gly
340 345

<210> 2542
<211> 417
<212> PRT
<213> Homo sapiens

<400> 2542

Met Gly Arg Arg Arg Ala Pro Glu Leu Tyr Arg Ala Pro Phe Pro Leu
1 5 10 15

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

Gly Gly Gly Ala Ala Lys Thr Gly Ile Lys Asn Gly Val His Phe Leu
35 40 45

Gln Leu Glu Leu Ile Asn Gly Arg Leu Ser Ala Ser Leu Leu His Ser
50 55 60

His Asp Thr Glu Thr Arg Ala Thr Met Asn Leu Ala Leu Ala Gly Asp
65 70 75 80

Ile Leu Ala Ala Gly Gln Asp Ala His Cys Gln Leu Leu Arg Phe Gln
85 90 95

Ala His Gln Gln Gln Gly Asn Lys Ala Glu Lys Ala Gly Ser Lys Glu
100 105 110

Gln Gly Pro Arg Gln Arg Lys Gly Ala Ala Pro Ala Glu Lys Lys Cys
115 120 125

Gly Ala Glu Thr Gln His Glu Gly Leu Glu Leu Arg Val Glu Asn Leu
130 135 140

Gln Ala Val Gln Thr Asp Phe Ser Ser Asp Pro Leu Gln Lys Val Val
145 150 155 160

Cys Phe Asn His Asp Asn Thr Leu Leu Ala Thr Gly Gly Thr Asp Gly
165 170 175

Tyr Val Arg Val Trp Lys Val Pro Ser Leu Glu Lys Val Leu Glu Phe
180 185 190

Lys Ala His Glu Gly Glu Ile Glu Asp Leu Ala Leu Gly Pro Asp Gly
195 200 205

Lys Leu Val Thr Val Gly Arg Asp Leu Lys Ala Ser Val Trp Gln Lys
210 215 220

Asp Gln Leu Val Thr Gln Leu His Trp Gln Glu Asn Gly Pro Thr Phe
225 230 235 240

Ser Ser Thr Pro Tyr Arg Tyr Gln Ala Cys Arg Phe Gly Gln Val Pro
245 250 255

Asp Gln Pro Ala Gly Leu Arg Leu Phe Thr Val Gln Ile Pro His Lys
260 265 270

Arg Leu Arg Gln Pro Pro Pro Cys Tyr Leu Thr Ala Trp Asp Gly Ser

275 280 285

Asn Phe Leu Pro Leu Arg Thr Lys Ser Cys Gly His Glu Val Val Ser
290 295 300

Cys Leu Asp Val Ser Glu Ser Gly Thr Phe Leu Gly Leu Gly Thr Val
305 310 315 320

Thr Gly Ser Val Ala Ile Tyr Ile Ala Phe Ser Leu Gln Cys Leu Tyr
325 330 335

Tyr Val Arg Glu Ala His Gly Ile Val Val Thr Asp Val Ala Phe Leu
340 345 350

Pro Glu Lys Gly Arg Gly Pro Glu Leu Leu Gly Ser His Glu Thr Ala
355 360 365

Leu Phe Ser Val Ala Val Asp Ser Arg Cys Gln Leu His Leu Leu Pro
370 375 380

Ser Arg Arg Ser Val Pro Val Trp Leu Leu Leu Leu Leu Cys Val Gly
385 390 395 400

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

Leu

<210> 2543
<211> 309
<212> PRT
<213> Homo sapiens

<400> 2543

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

Arg Asp Arg Lys Asn Leu Cys Arg Ala Ile Asn Asp Phe Gln Gln Ser
20 25 30

Phe Gln Lys Pro Glu Thr Arg Arg Glu Phe Asp Leu Ser Asp Pro Leu
35 40 45

Ala Leu Lys Lys Asp Leu Pro Ala Arg Gln Ser Asp Asn Asp Val Arg
50 55 60

```
Asn Thr Ile Ser Gly Met Gln Lys Phe Met Gly Glu Asp Leu Asn Phe
65                  70                  75                  80

His Glu Arg Lys Lys Phe Gln Glu Glu Gln Asn Arg Glu Trp Ser Leu
                85                  90                  95

Gln Gln Gln Arg Glu Trp Lys Asn Ala Arg Ala Glu Gln Lys Cys Ala
            100                 105                 110

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

His Leu Gln Lys Leu Glu Ser Thr Thr Arg Lys Ala Val Cys Ala Ser
    130                 135                 140

Val Lys Asp Phe Asn Lys Ser Gln Ala Ile Glu Ser Val Glu Arg Lys
145                 150                 155                 160

Lys Gln Glu Lys Lys Gln Glu Gln Glu Asp Asn Leu Ala Glu Ile Thr
                165                 170                 175

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

Ser Ser Phe Gly Pro His Arg Val Val Pro Asp Arg Trp Lys Gly Met
        195                 200                 205

Thr Gln Glu Gln Leu Glu Gln Ile Arg Leu Val Gln Lys Gln Gln Ile
    210                 215                 220

Gln Glu Lys Leu Arg Leu Gln Glu Glu Lys Arg Gln Arg Asp Leu Asp
225                 230                 235                 240

Trp Asp Arg Arg Arg Ile Gln Gly Ala Arg Ala Thr Leu Leu Phe Glu
                245                 250                 255

Arg Gln Gln Trp Arg Arg Gln Arg Asp Leu Arg Arg Ala Leu Asp Ser
            260                 265                 270

Ser Asn Leu Ser Leu Ala Lys Glu Gln His Leu Gln Lys Lys Tyr Met
        275                 280                 285

Asn Glu Val Tyr Thr Asn Gln Pro Thr Gly Asp Tyr Phe Thr Gln Phe
    290                 295                 300
```

Asn Thr Gly Ser Arg
305

<210> 2544
<211> 838
<212> PRT
<213> Homo sapiens

<400> 2544

Met Gln Glu Gln Glu Ile Gly Phe Ile Ser Lys Tyr Asn Glu Gly Leu
1 5 10 15

Cys Val Asn Thr Asp Pro Val Ser Ile Leu Thr Ser Ile Leu Asp Met
20 25 30

Ser Leu His Arg Gln Met Gly Ser Asp Arg Asp Leu Gln Ser Ser Ala
35 40 45

Ser Ser Val Ser Leu Pro Ser Val Lys Lys Ala Pro Lys Lys Arg Arg
50 55 60

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

Ser Arg Glu Leu Asn Gly Gly Val Asp Gly Ile Ala Ser Ile Glu Ser
85 90 95

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

Thr Ser Ser Asp Asn Gly Leu Thr Ser Ile Ser Lys Gln Ile Gly Asp
115 120 125

Phe Ile Glu Cys Pro Leu Cys Leu Leu Arg His Ser Lys Asp Arg Phe
130 135 140

Pro Asp Ile Met Thr Cys His His Arg Ser Cys Val Asp Cys Leu Arg
145 150 155 160

Gln Tyr Leu Arg Ile Glu Ile Ser Glu Ser Arg Val Asn Ile Ser Cys
165 170 175

Pro Glu Cys Thr Glu Arg Phe Asn Pro His Asp Ile Arg Leu Ile Leu
180 185 190

Ser Asp Asp Val Leu Met Glu Lys Tyr Glu Glu Phe Met Leu Arg Arg
195 200 205

```
Trp Leu Val Ala Asp Pro Asp Cys Arg Trp Cys Pro Ala Pro Asp Cys
    210                 215                 220

Gly Tyr Ala Val Ile Ala Phe Gly Cys Ala Ser Cys Pro Lys Leu Thr
225                 230                 235                 240

Cys Gly Arg Glu Gly Cys Gly Thr Glu Phe Cys Tyr His Cys Lys Gln
                245                 250                 255

Ile Trp His Pro Asn Gln Thr Cys Asp Ala Ala Arg Gln Glu Arg Ala
            260                 265                 270

Gln Ser Leu Arg Leu Arg Thr Ile Arg Ser Ser Ser Ile Ser Tyr Ser
        275                 280                 285

Gln Glu Ser Gly Ala Ala Ala Asp Asp Ile Lys Pro Cys Pro Arg Cys
    290                 295                 300

Ala Ala Tyr Ile Ile Lys Met Asn Asp Gly Ser Cys Asn His Met Thr
305                 310                 315                 320

Cys Ala Val Cys Gly Cys Glu Phe Cys Trp Leu Cys Met Lys Glu Ile
                325                 330                 335

Ser Asp Leu His Tyr Leu Ser Pro Ser Gly Cys Thr Phe Trp Gly Lys
            340                 345                 350

Lys Pro Trp Ser Arg Lys Lys Lys Ile Leu Trp Gln Leu Gly Thr Leu
        355                 360                 365

Val Gly Ala Pro Val Gly Ile Ala Leu Ile Ala Gly Ile Ala Ile Pro
    370                 375                 380

Ala Met Ile Ile Gly Ile Pro Val Tyr Val Gly Arg Lys Ile His Asn
385                 390                 395                 400

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

Ala Gly Gly Val Thr Leu Ser Val Ile Val Ser Pro Val Val Ala Ala
            420                 425                 430

Val Thr Val Gly Ile Gly Val Pro Ile Met Leu Ala Tyr Val Tyr Gly
        435                 440                 445
```

```
Val Val Pro Ile Ser Leu Cys Arg Ser Gly Gly Cys Gly Val Ser Ala
    450                 455                 460

Gly Asn Gly Lys Gly Val Arg Ile Glu Phe Asp Asp Glu Asn Asp Ile
465                 470                 475                 480

Asn Val Gly Gly Thr Asn Thr Ala Val Asp Thr Thr Ser Val Ala Glu
                485                 490                 495

Ala Arg His Asn Pro Ser Ile Gly Glu Gly Ser Val Gly Gly Leu Thr
            500                 505                 510

Gly Ser Leu Ser Ala Ser Gly Ser His Met Asp Arg Ile Gly Ala Ile
        515                 520                 525

Arg Asp Asn Leu Ser Glu Thr Ala Ser Thr Met Ala Leu Ala Gly Ala
    530                 535                 540

Ser Ile Thr Gly Ser Leu Ser Gly Ser Ala Met Val Asn Cys Phe Asn
545                 550                 555                 560

Arg Leu Glu Val Gln Ala Asp Val Gln Lys Glu Arg Tyr Ser Leu Ser
                565                 570                 575

Gly Glu Ser Gly Thr Val Ser Leu Gly Thr Val Ser Asp Asn Ala Ser
            580                 585                 590

Thr Lys Ala Met Ala Gly Ser Ile Leu Asn Ser Tyr Ile Pro Leu Asp
        595                 600                 605

Lys Glu Gly Asn Ser Met Glu Val Gln Val Asp Ile Glu Ser Lys Pro
    610                 615                 620

Ser Lys Phe Arg His Asn Ser Gly Ser Ser Ser Val Asp Asp Gly Ser
625                 630                 635                 640

Ala Thr Arg Ser Tyr Ala Gly Gly Ser Ser Ser Gly Leu Pro Glu Gly
                645                 650                 655

Lys Ser Ser Ala Thr Lys Trp Ser Lys Glu Ala Thr Ala Gly Lys Lys
            660                 665                 670

Ser Lys Ser Gly Lys Leu Arg Lys Lys Gly Asn Met Lys Ile Asn Glu
        675                 680                 685
```

```
Thr Arg Glu Asp Met Asp Ala Gln Leu Leu Glu Gln Gln Ser Thr Asn
 690                 695                 700

Ser Ser Glu Phe Glu Ala Pro Ser Leu Ser Asp Ser Met Pro Ser Val
705                 710                 715                 720

Ala Asp Ser His Ser Ser His Phe Ser Glu Phe Ser Cys Ser Asp Leu
                725                 730                 735

Glu Ser Met Lys Thr Ser Cys Ser His Gly Ser Ser Asp Tyr His Thr
            740                 745                 750

Arg Phe Ala Thr Val Asn Ile Leu Pro Glu Val Glu Asn Asp Arg Leu
        755                 760                 765

Glu Asn Ser Pro His Gln Cys Ser Ile Ser Val Val Thr Gln Thr Ala
 770                 775                 780

Ser Cys Ser Glu Val Ser Gln Leu Asn His Ile Ala Glu Glu His Gly
785                 790                 795                 800

Asn Asn Gly Ile Lys Pro Asn Val Asp Leu Tyr Phe Gly Asp Ala Leu
                805                 810                 815

Lys Glu Thr Asn Asn Asn His Ser His Gln Thr Met Glu Leu Lys Val
            820                 825                 830

Ala Ile Gln Thr Glu Ile
        835

<210>  2545
<211>  1539
<212>  PRT
<213>  Homo sapiens

<400>  2545

Met Glu Pro Gly Cys Asp Glu Phe Leu Pro Pro Pro Glu Cys Pro Val
1               5                   10                  15

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

Lys Ile Arg Pro Ile Ala Glu Lys Ser Gly Ile Cys Lys Ile Arg Pro
        35                  40                  45

Pro Ala Asp Trp Gln Pro Pro Phe Ala Val Glu Val Asp Asn Phe Arg
 50                  55                  60
```

```
Phe Thr Pro Arg Val Gln Arg Leu Asn Glu Leu Glu Ala Gln Thr Arg
65                  70                  75                  80

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

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

Tyr Ser Leu Ser Lys Ile Val Ile Glu Glu Gly Gly Tyr Glu Ala Ile
        115                 120                 125

Cys Lys Asp Arg Arg Trp Ala Arg Val Ala Gln Arg Leu His Tyr Pro
    130                 135                 140

Pro Gly Lys Asn Ile Gly Ser Leu Leu Arg Ser His Tyr Glu Arg Ile
145                 150                 155                 160

Ile Tyr Pro Tyr Glu Met Phe Gln Ser Gly Ala Asn His Val Gln Cys
                165                 170                 175

Asn Thr His Pro Phe Asp Asn Glu Val Lys Asp Lys Glu Tyr Lys Pro
            180                 185                 190

His Ser Ile Pro Leu Arg Gln Ser Val Gln Pro Ser Lys Phe Ser Ser
        195                 200                 205

Tyr Ser Arg Arg Ala Lys Arg Leu Gln Pro Asp Pro Glu Pro Thr Glu
    210                 215                 220

Glu Asp Ile Glu Lys His Pro Glu Leu Lys Lys Leu Gln Ile Tyr Gly
225                 230                 235                 240

Pro Gly Pro Lys Met Met Gly Leu Gly Leu Met Ala Lys Asp Lys Asp
                245                 250                 255

Lys Thr Val His Lys Lys Val Thr Cys Pro Pro Thr Val Thr Val Lys
            260                 265                 270

Asp Glu Gln Ser Gly Gly Gly Asn Val Ser Ser Thr Leu Leu Lys Gln
        275                 280                 285

His Leu Ser Leu Glu Pro Cys Thr Lys Thr Thr Met Gln Leu Arg Lys
    290                 295                 300
```

```
Asn His Ser Ser Ala Gln Phe Ile Asp Ser Tyr Ile Cys Gln Val Cys
305                 310                 315                 320

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

Asp Asn Tyr His Ile Phe Cys Leu Leu Pro Pro Leu Pro Glu Ile Pro
            340                 345                 350

Arg Gly Ile Trp Arg Cys Pro Lys Cys Ile Leu Ala Glu Cys Lys Gln
        355                 360                 365

Pro Pro Glu Ala Phe Gly Phe Glu Gln Ala Thr Gln Glu Tyr Ser Leu
    370                 375                 380

Gln Ser Phe Gly Glu Met Ala Asp Ser Phe Lys Ser Asp Tyr Phe Asn
385                 390                 395                 400

Met Pro Val His Met Val Pro Thr Glu Leu Val Glu Lys Glu Phe Trp
                405                 410                 415

Arg Leu Val Ser Ser Ile Glu Glu Asp Val Thr Val Glu Tyr Gly Ala
            420                 425                 430

Asp Ile His Ser Lys Glu Phe Gly Ser Gly Phe Pro Val Ser Asn Ser
        435                 440                 445

Lys Gln Asn Leu Ser Pro Glu Glu Lys Glu Tyr Ala Thr Ser Gly Trp
    450                 455                 460

Asn Leu Asn Val Met Pro Val Leu Asp Gln Ser Val Leu Cys His Ile
465                 470                 475                 480

Asn Ala Asp Ile Ser Gly Met Lys Val Pro Trp Leu Tyr Val Gly Met
                485                 490                 495

Val Phe Ser Ala Phe Cys Trp His Ile Glu Asp His Trp Ser Tyr Ser
            500                 505                 510

Ile Asn Tyr Leu His Trp Gly Glu Pro Lys Thr Trp Tyr Gly Val Pro
        515                 520                 525

Ser Leu Ala Ala Glu His Leu Glu Glu Val Met Lys Met Leu Thr Pro
    530                 535                 540
```

```
Glu Leu Phe Asp Ser Gln Pro Asp Leu Leu His Gln Leu Val Thr Leu
545                 550                 555                 560

Met Asn Pro Asn Thr Leu Met Ser His Gly Val Pro Val Val Arg Thr
                565                 570                 575

Asn Gln Cys Ala Gly Glu Phe Val Ile Thr Phe Pro Arg Ala Tyr His
            580                 585                 590

Ser Gly Phe Asn Gln Gly Tyr Asn Phe Ala Glu Ala Val Asn Phe Cys
        595                 600                 605

Thr Ala Asp Trp Leu Pro Ala Gly Arg Gln Cys Ile Glu His Tyr Arg
    610                 615                 620

Arg Leu Arg Arg Tyr Cys Val Phe Ser His Glu Glu Leu Ile Cys Lys
625                 630                 635                 640

Met Ala Ala Phe Pro Glu Thr Leu Asp Leu Asn Leu Ala Val Ala Val
                645                 650                 655

His Lys Glu Met Phe Ile Met Val Gln Glu Glu Arg Arg Leu Arg Lys
            660                 665                 670

Ala Leu Leu Glu Lys Gly Val Thr Glu Ala Glu Arg Glu Ala Phe Glu
        675                 680                 685

Leu Leu Pro Asp Asp Glu Arg Gln Cys Ile Lys Cys Lys Thr Thr Cys
    690                 695                 700

Phe Leu Ser Ala Leu Ala Cys Tyr Asp Cys Pro Asp Gly Leu Val Cys
705                 710                 715                 720

Leu Ser His Ile Asn Asp Leu Cys Lys Cys Ser Ser Ser Arg Gln Tyr
                725                 730                 735

Leu Arg Tyr Arg Tyr Thr Leu Asp Glu Leu Pro Thr Met Leu His Lys
            740                 745                 750

Leu Lys Ile Arg Ala Glu Ser Phe Asp Thr Trp Ala Asn Lys Val Arg
        755                 760                 765

Val Ala Leu Glu Val Glu Asp Gly Arg Lys Arg Ser Phe Glu Glu Leu
    770                 775                 780

Arg Ala Leu Glu Ser Glu Ala Arg Glu Arg Arg Phe Pro Asn Ser Glu
```

785 790 795 800

Leu Leu Gln Arg Leu Lys Asn Cys Leu Ser Glu Val Glu Ala Cys Ile
805 810 815

Ala Gln Val Leu Gly Leu Val Ser Gly Gln Val Ala Arg Met Asp Thr
820 825 830

Pro Gln Leu Thr Leu Thr Glu Leu Arg Val Leu Leu Glu Gln Met Gly
835 840 845

Ser Leu Pro Cys Ala Met His Gln Ile Gly Asp Val Lys Asp Val Leu
850 855 860

Glu Gln Val Glu Ala Tyr Gln Ala Glu Ala Arg Glu Ala Leu Ala Thr
865 870 875 880

Leu Pro Ser Ser Pro Gly Leu Leu Arg Ser Leu Leu Glu Arg Gly Gln
885 890 895

Gln Leu Gly Val Glu Val Pro Glu Ala His Gln Leu Gln Gln Gln Val
900 905 910

Glu Gln Ala Gln Trp Leu Asp Glu Val Lys Gln Ala Leu Ala Pro Ser
915 920 925

Ala His Arg Gly Ser Leu Val Ile Met Gln Gly Leu Leu Val Met Gly
930 935 940

Ala Lys Ile Ala Ser Ser Pro Ser Val Asp Lys Ala Arg Ala Glu Leu
945 950 955 960

Gln Glu Leu Leu Thr Ile Ala Glu Arg Trp Glu Glu Lys Ala His Phe
965 970 975

Cys Leu Glu Ala Arg Gln Lys His Pro Pro Ala Thr Leu Glu Ala Ile
980 985 990

Ile Arg Glu Thr Glu Asn Ile Pro Val His Leu Pro Asn Ile Gln Ala
995 1000 1005

Leu Lys Glu Ala Leu Thr Lys Ala Gln Ala Trp Ile Ala Asp Val
1010 1015 1020

Asp Glu Ile Gln Asn Gly Asp His Tyr Pro Cys Leu Asp Asp Leu
1025 1030 1035

```
Glu Gly  Leu Val Ala Val Gly  Arg Asp Leu Pro Val  Gly Leu Glu
    1040                 1045                 1050

Glu Leu  Arg Gln Leu Glu Leu  Gln Val Leu Thr Ala  His Ser Trp
    1055                 1060                 1065

Arg Glu  Lys Ala Ser Lys Thr  Phe Leu Lys Lys Asn  Ser Cys Tyr
    1070                 1075                 1080

Thr Leu  Leu Glu Val Leu Cys  Pro Cys Ala Asp Ala  Gly Ser Asp
    1085                 1090                 1095

Ser Thr  Lys Arg Ser Arg Trp  Met Glu Lys Ala Leu  Gly Leu Tyr
    1100                 1105                 1110

Gln Cys  Asp Thr Glu Leu Leu  Gly Leu Ser Ala Gln  Asp Leu Arg
    1115                 1120                 1125

Asp Pro  Gly Ser Val Ile Val  Ala Phe Lys Glu Gly  Glu Gln Lys
    1130                 1135                 1140

Glu Lys  Glu Gly Ile Leu Gln  Leu Arg Arg Thr Asn  Ser Ala Lys
    1145                 1150                 1155

Pro Ser  Pro Leu Ala Pro Ser  Leu Met Ala Ser Ser  Pro Thr Ser
    1160                 1165                 1170

Ile Cys  Val Cys Gly Gln Val  Pro Ala Gly Val Gly  Leu Leu Gln
    1175                 1180                 1185

Cys Asp  Leu Cys Gln Asp Trp  Phe His Gly Gln Cys  Val Ser Val
    1190                 1195                 1200

Pro His  Leu Leu Thr Ser Pro  Lys Pro Ser Leu Thr  Ser Ser Pro
    1205                 1210                 1215

Leu Leu  Ala Trp Trp Glu Trp  Asp Thr Lys Phe Leu  Cys Pro Leu
    1220                 1225                 1230

Cys Met  Arg Ser Arg Arg Pro  Arg Leu Glu Thr Ile  Leu Ala Leu
    1235                 1240                 1245

Leu Val  Ala Leu Gln Arg Leu  Pro Val Arg Leu Pro  Glu Gly Glu
    1250                 1255                 1260
```

Ala Leu Gln Cys Leu Thr Glu Arg Ala Ile Gly Trp Gln Asp Arg
1265 1270 1275

Ala Arg Lys Ala Leu Ala Phe Glu Asp Val Thr Ala Leu Leu Arg
1280 1285 1290

Gln Leu Ala Glu Leu Arg Gln Gln Leu Gln Ala Lys Pro Arg Pro
1295 1300 1305

Glu Glu Ala Ser Val Tyr Thr Ser Ala Thr Ala Cys Asp Pro Ile
1310 1315 1320

Arg Glu Gly Ser Gly Asn Asn Ile Ser Lys Val Gln Gly Leu Leu
1325 1330 1335

Glu Asn Gly Asp Ser Val Thr Ser Pro Glu Asn Met Ala Pro Gly
1340 1345 1350

Lys Gly Ser Asp Leu Glu Leu Leu Ser Ser Leu Leu Pro Gln Leu
1355 1360 1365

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

Glu Glu Leu Met Met Glu Gly Gly Leu Leu Glu Val Thr Leu Asp
1385 1390 1395

Glu Asn His Ser Ile Trp Gln Leu Leu Gln Ala Gly Gln Pro Pro
1400 1405 1410

Asp Leu Asp Arg Ile Arg Thr Leu Leu Glu Leu Glu Lys Phe Glu
1415 1420 1425

His Gln Gly Ser Arg Thr Arg Ser Arg Ala Leu Glu Arg Arg Arg
1430 1435 1440

Arg Arg Gln Lys Val Asp Gln Gly Arg Asn Val Glu Asn Leu Val
1445 1450 1455

Gln Gln Glu Leu Gln Ser Lys Arg Ala Arg Ser Ser Gly Ile Met
1460 1465 1470

Ser Gln Val Gly Arg Glu Glu Glu His Tyr Gln Glu Lys Ala Asp
1475 1480 1485

```
Arg Glu  Asn Met Phe Leu Thr  Pro Ser Thr Asp His  Ser Pro Phe
    1490                 1495                 1500

Leu Lys  Gly Asn Gln Asn Ser  Leu Gln His Lys Asp  Ser Gly Ser
    1505                 1510                 1515

Ser Ala  Ala Cys Pro Ser Leu  Met Pro Leu Leu Gln  Leu Ser Tyr
    1520                 1525                 1530

Ser Asp  Glu Gln Gln Leu
    1535
```

<210> 2546
<211> 274
<212> PRT
<213> Homo sapiens

<400> 2546

```
Met Gly Val Ser Ala Gln Asp Ile Phe Asn Ala Val Ile Lys Glu His
1               5                  10                  15

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

Asp His Thr Leu Ala Glu Arg Cys Tyr Ser Glu Ala Ser Asp Leu Lys
        35                  40                  45

Val Ile His Trp Asn Ser Pro Lys Lys Leu Arg Val Lys Asn Lys His
    50                  55                  60

Val Glu Phe Phe Arg Asn Phe Tyr Leu Thr Phe Leu Glu Tyr Asp Gly
65                  70                  75                  80

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

Gly Ala Glu Gln Leu Gln Gln Ala Leu Ala Gln Leu Asp Gly Glu Asp
            100                 105                 110

Pro Cys Phe Glu Phe Arg Gln Gln Gln Leu Thr Val His Arg Val His
        115                 120                 125

Val Thr Phe Leu Pro His Glu Pro Pro Pro Pro Arg Pro His Asp Val
    130                 135                 140

Thr Leu Val Ala Gln Leu Ser Met Asp Arg Leu Gln Met Leu Glu Ala
145                 150                 155                 160
```

```
Leu Cys Arg His Trp Pro Gly Pro Met Ser Leu Ala Leu Tyr Leu Thr
                165                 170                 175

Asp Ala Glu Ala Gln Gln Phe Leu His Phe Val Glu Ala Ser Pro Val
            180                 185                 190

Leu Ala Ala Arg Gln Asp Val Ala Tyr His Val Val Tyr Arg Glu Gly
        195                 200                 205

Pro Leu Tyr Pro Val Asn Gln Leu Arg Asn Val Ala Leu Ala Gln Ala
    210                 215                 220

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

Ser Leu Tyr Asp Tyr Leu Arg Glu Ala Arg Ala Gly Phe Asn Ser Ser
                245                 250                 255

Ser Thr Cys Gly Cys Ala His Pro Ser His Gln Ala Arg Trp Pro Met
            260                 265                 270

Val Val
```

<210> 2547
<211> 504
<212> PRT
<213> Homo sapiens

<400> 2547

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

Phe Leu Leu Val Leu Val Asp Leu Gln Tyr Glu Gly Ala Glu Cys Gly
            20                  25                  30

Val Asn Ala Asp Val Glu Lys His Leu Glu Leu Gly Lys Lys Leu Leu
        35                  40                  45

Ala Ala Gly Gln Leu Ala Asp Ala Leu Ser Gln Phe His Ala Ala Val
    50                  55                  60

Asp Gly Asp Pro Asp Asn Tyr Ile Ala Tyr Tyr Arg Arg Ala Thr Val
65                  70                  75                  80
```

```
Phe Leu Ala Met Gly Lys Ser Lys Ala Ala Leu Pro Asp Leu Thr Lys
                85                  90                  95

Val Ile Gln Leu Lys Met Asp Phe Thr Ala Ala Arg Leu Gln Arg Gly
            100                 105                 110

His Leu Leu Leu Lys Gln Gly Lys Leu Asp Glu Ala Glu Asp Asp Phe
        115                 120                 125

Lys Lys Val Leu Lys Ser Asn Pro Ser Glu Asn Glu Glu Lys Glu Ala
    130                 135                 140

Gln Ser Gln Leu Ile Lys Ser Asp Glu Met Gln Arg Leu Arg Ser Gln
145                 150                 155                 160

Ala Leu Asn Ala Phe Gly Ser Gly Asp Tyr Thr Ala Ala Ile Ala Phe
                165                 170                 175

Leu Asp Lys Ile Leu Glu Val Cys Val Trp Asp Ala Glu Leu Arg Glu
            180                 185                 190

Leu Arg Ala Glu Cys Phe Ile Lys Glu Gly Glu Pro Arg Lys Ala Ile
        195                 200                 205

Ser Asp Leu Lys Ala Ala Ser Lys Leu Lys Asn Asp Asn Thr Glu Ala
    210                 215                 220

Phe Tyr Lys Ile Ser Thr Leu Tyr Tyr Gln Leu Gly Asp His Glu Leu
225                 230                 235                 240

Ser Leu Ser Glu Val Arg Glu Cys Leu Lys Leu Asp Gln Asp His Lys
                245                 250                 255

Arg Cys Phe Ala His Tyr Lys Gln Val Lys Lys Leu Asn Lys Leu Ile
            260                 265                 270

Glu Ser Ala Glu Glu Leu Ile Arg Asp Gly Arg Tyr Thr Asp Ala Thr
        275                 280                 285

Ser Lys Tyr Glu Ser Val Met Lys Thr Glu Pro Ser Ile Ala Glu Tyr
    290                 295                 300

Thr Val Arg Ser Lys Glu Arg Ile Cys His Cys Phe Ser Lys Asp Glu
305                 310                 315                 320

Lys Pro Val Glu Ala Ile Arg Val Cys Ser Glu Val Leu Gln Met Glu
```

325 330 335

Pro Asp Asn Val Asn Ala Leu Lys Asp Arg Ala Glu Ala Tyr Leu Ile
340 345 350

Glu Glu Met Tyr Asp Glu Ala Ile Gln Asp Tyr Glu Thr Ala Gln Glu
355 360 365

His Asn Glu Asn Asp Gln Gln Ile Arg Glu Gly Leu Glu Lys Ala Gln
370 375 380

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

Val Lys Arg Asn Ala Lys Lys Gln Glu Ile Ile Lys Ala Tyr Arg Lys
405 410 415

Leu Ala Leu Gln Trp His Pro Asp Asn Phe Gln Asn Glu Glu Glu Lys
420 425 430

Lys Lys Ala Glu Lys Lys Phe Ile Asp Ile Ala Ala Ala Lys Glu Val
435 440 445

Leu Ser Asp Pro Glu Met Arg Lys Lys Phe Asp Asp Gly Glu Asp Pro
450 455 460

Leu Asp Ala Glu Ser Gln Gln Gly Gly Gly Gly Asn Pro Phe His Arg
465 470 475 480

Ser Trp Asn Ser Trp Gln Gly Phe Asn Pro Phe Ser Ser Gly Gly Pro
485 490 495

Phe Arg Phe Lys Phe His Phe Asn
500

<210> 2548
<211> 258
<212> PRT
<213> Homo sapiens

<400> 2548

Met Pro Pro Gln Gln Gly Asp Pro Ala Phe Pro Asp Arg Cys Glu Ala
1 5 10 15

Pro Pro Val Pro Pro Arg Arg Glu Arg Gly Gly Arg Gly Gly Arg Gly
20 25 30

```
Pro Gly Glu Pro Gly Gly Arg Gly Arg Ala Gly Gly Ala Glu Gly Arg
        35                  40                  45

Gly Val Lys Cys Val Leu Val Gly Asp Gly Ala Val Gly Lys Thr Ser
    50                  55                  60

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

Thr Ala Phe Asp Asn Phe Ser Ala Val Val Ser Val Asp Gly Arg Pro
                85                  90                  95

Val Arg Leu Gln Leu Cys Asp Thr Ala Gly Gln Asp Glu Phe Asp Lys
            100                 105                 110

Leu Arg Pro Leu Cys Tyr Thr Asn Thr Asp Ile Phe Leu Leu Cys Phe
        115                 120                 125

Ser Val Val Ser Pro Ser Ser Phe Gln Asn Val Ser Glu Lys Trp Val
    130                 135                 140

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

Thr Gln Ser Asp Leu Arg Glu Asp Val Lys Val Leu Ile Glu Leu Asp
                165                 170                 175

Lys Cys Lys Glu Lys Pro Val Pro Glu Glu Ala Ala Lys Leu Cys Ala
            180                 185                 190

Glu Glu Ile Lys Ala Ala Ser Tyr Ile Glu Cys Ser Ala Leu Thr Gln
        195                 200                 205

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

Tyr Ser Asp Thr Gln Gln Gln Pro Lys Lys Ser Lys Ser Arg Thr Pro
225                 230                 235                 240

Asp Lys Met Lys Asn Leu Ser Lys Ser Trp Trp Lys Lys Tyr Cys Cys
                245                 250                 255

Phe Val
```

<210> 2549
<211> 394
<212> PRT
<213> Homo sapiens

<400> 2549

```
Met Phe Lys Lys Lys Ser His Val Arg Asn His Leu Arg Thr His Thr
1               5                   10                  15

Gly Glu Arg Pro Phe Pro Cys Pro Asp Cys Ser Lys Pro Phe Asn Ser
            20                  25                  30

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

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

Arg Gln His Arg Leu Val His Ala Gln His Phe Pro Tyr Arg Cys Gln
65                  70                  75                  80

Glu Cys Gly Val Arg Phe His Arg Pro Tyr Arg Leu Leu Met His Arg
                85                  90                  95

Tyr His His Thr Gly Glu Tyr Pro Tyr Lys Cys Arg Glu Cys Pro Arg
            100                 105                 110

Ser Phe Leu Leu Arg Arg Leu Leu Glu Val His Gln Leu Val Val His
        115                 120                 125

Ala Gly Arg Gln Pro His Arg Cys Pro Ser Cys Gly Ala Ala Phe Pro
    130                 135                 140

Ser Ser Leu Arg Leu Arg Glu His Arg Cys Ala Ala Ala Ala Ala Gln
145                 150                 155                 160

Ala Pro Arg Arg Phe Glu Cys Gly Thr Cys Gly Lys Lys Val Gly Ser
                165                 170                 175

Ala Ala Arg Leu Gln Ala His Glu Ala Ala His Ala Ala Ala Gly Pro
            180                 185                 190

Gly Glu Val Leu Ala Lys Glu Pro Pro Ala Pro Arg Ala Pro Arg Ala
        195                 200                 205

Thr Arg Ala Pro Val Ala Ser Pro Ala Ala Leu Gly Ser Thr Ala Thr
    210                 215                 220
```

```
Ala Ser Pro Ala Ala Pro Ala Arg Arg Arg Gly Leu Glu Cys Ser Glu
225                 230                 235                 240

Cys Lys Lys Leu Phe Ser Thr Glu Thr Ser Leu Gln Val His Arg Arg
                245                 250                 255

Ile His Thr Gly Glu Arg Pro Tyr Pro Cys Pro Asp Cys Gly Lys Ala
            260                 265                 270

Phe Arg Gln Ser Thr His Leu Lys Asp His Arg Arg Leu His Thr Gly
        275                 280                 285

Glu Arg Pro Phe Ala Cys Glu Val Cys Gly Lys Ala Phe Ala Ile Ser
    290                 295                 300

Met Arg Leu Ala Glu His Arg Arg Ile His Thr Gly Glu Arg Pro Tyr
305                 310                 315                 320

Ser Cys Pro Asp Cys Gly Lys Ser Tyr Arg Ser Phe Ser Asn Leu Trp
                325                 330                 335

Lys His Arg Lys Thr His Gln Gln Gln His Gln Ala Ala Val Arg Gln
            340                 345                 350

Gln Leu Ala Glu Ala Glu Ala Ala Val Gly Leu Ala Val Met Glu Thr
        355                 360                 365

Ala Val Glu Ala Leu Pro Leu Val Glu Ala Ile Glu Ile Tyr Pro Leu
    370                 375                 380

Ala Glu Ala Glu Gly Val Gln Ile Ser Gly
385                 390
```

<210> 2550
<211> 415
<212> PRT
<213> Homo sapiens

<400> 2550

```
Met Glu Asp Leu Cys Val Ala Asn Thr Leu Phe Ala Leu Asn Leu Phe
1               5                   10                  15

Lys His Leu Ala Lys Ala Ser Pro Thr Gln Asn Leu Phe Leu Ser Pro
            20                  25                  30
```

Trp Ser Ile Ser Ser Thr Met Ala Met Val Tyr Met Gly Ser Arg Gly
35 40 45

Ser Thr Glu Asp Gln Met Ala Lys Val Leu Gln Phe Asn Glu Val Gly
50 55 60

Ala Asn Ala Val Thr Pro Met Thr Pro Glu Asn Phe Thr Ser Cys Gly
65 70 75 80

Phe Met Gln Gln Ile Gln Lys Gly Ser Tyr Pro Asp Ala Ile Leu Gln
85 90 95

Ala Gln Ala Ala Asp Lys Ile His Ser Ser Phe Arg Ser Leu Ser Ser
100 105 110

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

Leu Phe Gly Glu Lys Ser Ala Ser Phe Arg Glu Glu Tyr Ile Arg Leu
130 135 140

Cys Gln Lys Tyr Tyr Ser Ser Glu Pro Gln Ala Val Asp Phe Leu Glu
145 150 155 160

Cys Ala Glu Glu Ala Arg Lys Lys Ile Asn Ser Trp Val Lys Thr Gln
165 170 175

Thr Lys Gly Lys Ile Pro Asn Leu Leu Pro Glu Gly Ser Val Asp Gly
180 185 190

Asp Thr Arg Met Val Leu Val Asn Ala Val Tyr Phe Lys Gly Lys Trp
195 200 205

Lys Thr Pro Phe Glu Lys Lys Leu Asn Gly Leu Tyr Pro Phe Arg Val
210 215 220

Asn Ser Ala Gln Arg Thr Pro Val Gln Met Met Tyr Leu Arg Glu Lys
225 230 235 240

Leu Asn Ile Gly Tyr Ile Glu Asp Leu Lys Ala Gln Ile Leu Glu Leu
245 250 255

Pro Tyr Ala Gly Asp Val Ser Met Phe Leu Leu Leu Pro Asp Glu Ile
260 265 270

Ala Asp Val Ser Thr Gly Leu Glu Leu Leu Glu Ser Glu Ile Thr Tyr

275 280 285

Asp Lys Leu Asn Lys Trp Thr Ser Lys Asp Lys Met Ala Glu Asp Glu
290 295 300

Val Glu Val Tyr Ile Pro Gln Phe Lys Leu Glu Glu His Tyr Glu Leu
305 310 315 320

Arg Ser Ile Leu Arg Ser Met Gly Met Glu Asp Ala Phe Asn Lys Gly
325 330 335

Arg Ala Asn Phe Ser Gly Met Ser Glu Arg Asn Asp Leu Phe Leu Ser
340 345 350

Glu Val Phe His Gln Ala Met Val Asp Val Asn Glu Glu Gly Thr Glu
355 360 365

Ala Ala Ala Gly Thr Gly Gly Val Met Thr Gly Arg Thr Gly His Gly
370 375 380

Gly Pro Gln Phe Val Ala Asp His Pro Phe Leu Phe Leu Ile Met His
385 390 395 400

Lys Ile Thr Asn Cys Ile Leu Phe Phe Gly Arg Phe Ser Ser Pro
405 410 415

<210> 2551
<211> 434
<212> PRT
<213> Homo sapiens

<400> 2551

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

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

Ala Ala Val Pro Ser Gly Ala Ser Thr Gly Ile Tyr Glu Ala Leu Glu
35 40 45

Leu Arg Asp Asn Asp Lys Thr Arg Tyr Met Gly Lys Gly Val Ser Lys
50 55 60

Ala Val Glu His Ile Asn Lys Thr Ile Ala Pro Ala Leu Val Ser Lys
65 70 75 80

```
Lys Leu Asn Val Thr Glu Gln Glu Lys Ile Asp Lys Leu Met Ile Glu
                85                  90                  95

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

Gly Val Ser Leu Ala Val Cys Lys Ala Gly Ala Val Glu Lys Gly Val
        115                 120                 125

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

Leu Pro Val Pro Ala Phe Asn Val Ile Asn Gly Gly Ser His Ala Gly
145                 150                 155                 160

Asn Lys Leu Ala Met Gln Glu Phe Met Ile Leu Pro Val Gly Ala Ala
                165                 170                 175

Asn Phe Arg Glu Ala Met Arg Ile Gly Ala Glu Val Tyr His Asn Leu
            180                 185                 190

Lys Asn Val Ile Lys Glu Lys Tyr Gly Lys Asp Ala Thr Asn Val Gly
        195                 200                 205

Asp Glu Gly Gly Phe Ala Pro Asn Ile Leu Glu Asn Lys Glu Gly Leu
    210                 215                 220

Glu Leu Leu Lys Thr Ala Ile Gly Lys Ala Gly Tyr Thr Asp Lys Val
225                 230                 235                 240

Val Ile Gly Met Asp Val Ala Ala Ser Glu Phe Phe Arg Ser Gly Lys
                245                 250                 255

Tyr Asp Leu Asp Phe Lys Ser Pro Asp Asp Pro Ser Arg Tyr Ile Ser
            260                 265                 270

Pro Asp Gln Leu Ala Asp Leu Tyr Lys Ser Phe Ile Lys Asp Tyr Pro
        275                 280                 285

Val Val Ser Ile Glu Asp Pro Phe Asp Gln Asp Asp Trp Gly Ala Trp
    290                 295                 300

Gln Lys Phe Thr Ala Ser Ala Gly Ile Gln Val Val Gly Asp Asp Leu
305                 310                 315                 320
```

```
Thr Val Thr Asn Pro Lys Arg Ile Ala Lys Ala Val Asn Glu Lys Ser
                325                 330                 335

Cys Asn Cys Leu Leu Leu Lys Val Asn Gln Ile Gly Ser Val Thr Glu
            340                 345                 350

Ser Leu Gln Ala Cys Lys Leu Ala Gln Ala Asn Gly Trp Gly Val Met
        355                 360                 365

Val Ser His Arg Ser Gly Glu Thr Glu Asp Thr Phe Ile Ala Asp Leu
    370                 375                 380

Val Val Gly Leu Cys Thr Gly Gln Ile Lys Thr Gly Ala Pro Cys Arg
385                 390                 395                 400

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

Leu Gly Ser Lys Ala Lys Phe Ala Gly Arg Asn Phe Arg Asn Pro Leu
            420                 425                 430

Ala Lys
```

<210> 2552
<211> 281
<212> PRT
<213> Homo sapiens

<400> 2552

```
Met Glu Val His Gln Gln Asn Ala Leu Phe Gln Tyr Phe Ala Asp Thr
1               5                   10                  15

Leu Thr Ala Val Val Gln Asn Ala Lys Lys Asn Gly Arg Tyr Asp Met
            20                  25                  30

Gly Ile Leu Asp Leu Gly Ser Gly Asp Glu Lys Val Arg Lys Ser Asp
        35                  40                  45

Val Lys Lys Phe Leu Thr Pro Gly Tyr Ser Thr Ser Gly His Val Glu
    50                  55                  60

Leu Tyr Thr Ile Ser Val Glu Arg Gly Met Ser Trp Glu Glu Ala Thr
65                  70                  75                  80

Lys Ile Trp Ala Glu Leu Thr Gly Pro Asp Asp Gly Phe Tyr Leu Ser
                85                  90                  95
```

```
Leu Gln Ile Arg Asn Asn Lys Lys Thr Ala Ile Leu Val Lys Glu Val
            100                 105                 110

Asn Pro Lys Lys Lys Leu Phe Leu Val Tyr Arg Pro Asn Thr Gly Lys
        115                 120                 125

Gln Leu Lys Leu Glu Ile Tyr Ala Asp Leu Lys Lys Lys Tyr Lys Lys
    130                 135                 140

Val Val Ser Asp Asp Ala Leu Met His Trp Leu Asp Gln Tyr Asn Ser
145                 150                 155                 160

Ser Ala Asp Thr Cys Thr His Ala Tyr Trp Arg Gly Asn Cys Lys Lys
                165                 170                 175

Ala Ser Leu Gly Leu Val Cys Glu Ile Gly Leu Arg Cys Arg Thr Tyr
            180                 185                 190

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

Val Leu Ala Ser Val Ser Gly Thr Asn Val Lys Met Gln Ile Val Arg
    210                 215                 220

Leu Arg Thr Glu Asp Gly Gln Arg Ile Val Gly Leu Ile Ile Pro Ala
225                 230                 235                 240

Asn Cys Val Ser Pro Leu Val Asn Leu Leu Ser Thr Ser Asp Gln Ser
                245                 250                 255

Gln Gln Leu Ala Val Gln Gln Lys Gln Leu Trp Gln Gln His His Pro
            260                 265                 270

Gln Ser Ile Thr Asn Leu Ser Asn Ala
        275                 280
```

<210> 2553
<211> 176
<212> PRT
<213> Homo sapiens

<400> 2553

```
Met Lys Ala Ser Gly Thr Leu Arg Glu Tyr Lys Val Val Gly Arg Cys
1               5                   10                  15
```

Leu Pro Thr Pro Lys Cys His Thr Pro Pro Leu Tyr Arg Met Arg Ile
20 25 30

Phe Ala Pro Asn His Val Val Ala Lys Ser Arg Phe Trp Tyr Phe Val
35 40 45

Ser Gln Leu Lys Lys Met Lys Lys Ser Ser Gly Glu Ile Val Tyr Cys
50 55 60

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

Trp Leu Arg Tyr Asp Ser Arg Ser Gly Thr His Asn Met Tyr Arg Glu
85 90 95

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

Met Gly Ala Arg His Arg Ala Arg Ala His Ser Ile Gln Ile Met Lys
115 120 125

Val Glu Glu Ile Ala Ala Ser Lys Cys Arg Arg Pro Ala Val Lys Gln
130 135 140

Phe His Asp Ser Lys Ile Lys Phe Pro Leu Pro His Arg Val Leu Arg
145 150 155 160

Arg Gln His Lys Pro Arg Phe Thr Thr Lys Arg Pro Asn Thr Phe Phe
165 170 175

<210> 2554
<211> 363
<212> PRT
<213> Homo sapiens

<400> 2554

Met Ala Leu His Cys Gln Glu Phe Gly Gly Lys Asn Tyr Glu Ala Ser
1 5 10 15

Met Ser His Val Asp Lys Phe Val Lys Glu Leu Leu Ser Ser Asp Ala
20 25 30

Met Lys Glu Tyr Asn Arg Ala Arg Val Tyr Leu Asp Glu Asn Tyr Lys
35 40 45

Ser Gln Glu His Phe Thr Ala Leu Gly Ser Phe Tyr Phe Leu His Glu
50 55 60

```
Ser Leu Lys Asn Ile Tyr Gln Phe Asp Phe Lys Ala Lys Lys Tyr Arg
65                  70                  75                  80

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

Met Leu Glu Lys Glu Lys Phe Arg Arg Leu Leu Pro Arg Val Gln Met
            100                 105                 110

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

Phe Asp Leu Val Asn Ile His Leu Phe His Asp Ala Ser Asn Leu Val
    130                 135                 140

Ala Trp Glu Thr Ser Pro Ser Val Tyr Ser Gly Ile Arg His Lys Ala
145                 150                 155                 160

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

Ser Tyr Phe Val Phe Gly Asp Phe Asn Phe Arg Leu Asp Ser Lys Ser
            180                 185                 190

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

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

Asp Arg Lys Val Met Leu Gln Leu Glu Lys Lys Leu Phe Asp Tyr Phe
225                 230                 235                 240

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

Asp Lys Glu Leu Ser Val Phe Lys Asp Arg Leu Tyr Glu Leu Asp Ile
            260                 265                 270

Ser Phe Pro Pro Ser Tyr Pro Tyr Ser Glu Asp Ala Arg Gln Gly Glu
        275                 280                 285

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

Ser Pro Ser Ala Lys Glu Leu Val Leu Arg Ser Glu Ser Glu Glu Lys
305 310 315 320

Val Val Thr Tyr Asp His Ile Gly Pro Asn Val Cys Met Gly Asp His
325 330 335

Lys Pro Val Phe Leu Ala Phe Arg Ile Met Pro Gly Ala Gly Lys Pro
340 345 350

His Ala His Val His Lys Cys Cys Val Val Gln
355 360

<210> 2555
<211> 56
<212> PRT
<213> Homo sapiens

<400> 2555

Met Gly His Gln Gln Leu Tyr Trp Ser His Pro Arg Lys Phe Gly Gln
1 5 10 15

Gly Ser Arg Ser Cys Arg Val Cys Ser Asn Arg His Gly Leu Ile Arg
20 25 30

Lys Tyr Gly Leu Asn Met Cys Arg Gln Cys Phe Arg Gln Tyr Ala Lys
35 40 45

Asp Ile Gly Phe Ile Lys Leu Asp
50 55

<210> 2556
<211> 520
<212> PRT
<213> Homo sapiens

<400> 2556

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

Thr Leu Gln Val Gly Thr Gln Asp Ser Phe Ile Ala Ala Val Tyr Glu
20 25 30

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

Asp Ala Leu Asn Leu Met Asn Glu Asn Ile Asp Ile Leu Glu Thr Ala
50 55 60

Ile Lys Gln Ala Ala Glu Gln Gly Ala Arg Ile Ile Val Thr Pro Glu
65 70 75 80

Asp Ala Leu Tyr Gly Trp Lys Phe Thr Arg Glu Thr Val Phe Pro Tyr
85 90 95

Leu Glu Asp Ile Pro Asp Pro Gln Val Asn Trp Ile Pro Cys Gln Asp
100 105 110

Pro His Arg Phe Gly His Thr Pro Val Gln Ala Arg Leu Ser Cys Leu
115 120 125

Ala Lys Asp Asn Ser Ile Tyr Val Leu Ala Asn Leu Gly Asp Lys Lys
130 135 140

Pro Cys Asn Ser Arg Asp Ser Thr Cys Pro Pro Asn Gly Tyr Phe Gln
145 150 155 160

Tyr Asn Thr Asn Val Val Tyr Asn Thr Glu Gly Lys Leu Val Ala Arg
165 170 175

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

Lys Pro Glu Leu Val Thr Phe Asn Thr Ala Phe Gly Arg Phe Gly Ile
195 200 205

Phe Thr Cys Phe Asp Ile Phe Phe Tyr Asp Pro Gly Val Thr Leu Val
210 215 220

Lys Asp Phe His Val Asp Thr Ile Leu Phe Pro Thr Ala Trp Met Asn
225 230 235 240

Val Leu Pro Leu Leu Thr Ala Ile Glu Phe His Ser Ala Trp Ala Met
245 250 255

Gly Met Gly Val Asn Leu Leu Val Ala Asn Thr His His Val Ser Leu
260 265 270

Asn Met Thr Gly Ser Gly Ile Tyr Ala Pro Asn Gly Pro Lys Val Tyr
275 280 285

His Tyr Asp Met Lys Thr Glu Leu Gly Lys Leu Leu Leu Ser Glu Val
290 295 300

Asp Ser His Pro Leu Ser Ser Leu Ala Tyr Pro Thr Ala Val Asn Trp
305 310 315 320

Asn Ala Tyr Ala Thr Thr Ile Lys Pro Phe Pro Val Gln Lys Asn Thr
325 330 335

Phe Arg Gly Phe Ile Ser Arg Asp Gly Phe Asn Phe Thr Glu Leu Phe
340 345 350

Glu Asn Ala Gly Asn Leu Thr Val Cys Gln Lys Glu Leu Cys Cys His
355 360 365

Leu Ser Tyr Arg Met Leu Gln Lys Glu Glu Asn Glu Val Tyr Val Leu
370 375 380

Gly Ala Phe Thr Gly Leu His Gly Arg Arg Arg Arg Glu Tyr Trp Gln
385 390 395 400

Val Cys Thr Met Leu Lys Cys Lys Thr Thr Asn Leu Thr Thr Cys Gly
405 410 415

Arg Pro Val Glu Thr Ala Ser Thr Arg Phe Glu Met Phe Ser Leu Ser
420 425 430

Gly Thr Phe Gly Thr Glu Tyr Val Phe Pro Glu Val Leu Leu Thr Glu
435 440 445

Ile His Leu Ser Pro Gly Lys Phe Glu Val Leu Lys Asp Gly Arg Leu
450 455 460

Val Asn Lys Asn Gly Ser Ser Gly Pro Ile Leu Thr Val Ser Leu Phe
465 470 475 480

Gly Arg Trp Tyr Thr Lys Asp Ser Leu Tyr Ser Ser Cys Gly Thr Ser
485 490 495

Asn Ser Ala Ile Thr Tyr Leu Leu Ile Phe Ile Leu Leu Met Ile Ile
500 505 510

Ala Leu Gln Asn Ile Val Met Leu
515 520

<210> 2557
<211> 564
<212> PRT
<213> Homo sapiens

<400> 2557

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

Lys Trp Asp Gln Pro Ala Pro Ala Pro Leu Leu Phe Leu Pro Pro Ala
20 25 30

Ala Pro Gly Gly Glu Val Thr Ser Ser Gly Gly Ser Pro Gly Gly Thr
35 40 45

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

Lys Ile Asn Ala Met Leu Met Ala Lys Gly Lys Leu Lys Pro Thr Gln
65 70 75 80

Asn Ala Ser Glu Lys Leu Gln Ala Pro Gly Lys Gly Leu Thr Ser Asn
85 90 95

Lys Ser Lys Asp Asp Leu Val Val Ala Glu Val Glu Ile Asn Asp Val
100 105 110

Pro Leu Thr Cys Arg Asn Leu Leu Thr Arg Gly Gln Thr Gln Asp Glu
115 120 125

Ile Ser Arg Leu Ser Gly Ala Ala Val Ser Thr Arg Gly Arg Phe Met
130 135 140

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

Leu His Val Gln Gly Gln Thr Arg Glu Leu Val Asp Arg Ala Val Asn
165 170 175

Arg Ile Lys Glu Ile Ile Thr Asn Gly Val Val Lys Ala Ala Thr Gly
180 185 190

Thr Ser Pro Thr Phe Asn Gly Ala Thr Val Thr Val Tyr His Gln Pro
195 200 205

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

Gln Ser Gly Met His Tyr Val Gln Asp Lys Leu Phe Val Gly Leu Glu
225 230 235 240

His Ala Val Pro Thr Phe Asn Val Lys Glu Lys Val Glu Gly Pro Gly
245 250 255

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

Leu Arg Gly Lys Gly Ser Gly Cys Ile Glu Pro Ala Ser Gly Arg Glu
275 280 285

Ala Phe Glu Pro Met Tyr Ile Tyr Ile Ser His Pro Lys Pro Glu Gly
290 295 300

Leu Ala Ala Ala Lys Lys Leu Cys Glu Asn Leu Leu Gln Thr Val His
305 310 315 320

Ala Glu Tyr Ser Arg Phe Val Asn Gln Ile Asn Thr Ala Val Pro Leu
325 330 335

Pro Gly Tyr Thr Gln Pro Ser Ala Ile Ser Ser Val Pro Pro Gln Pro
340 345 350

Pro Tyr Tyr Pro Ser Asn Gly Tyr Gln Ser Gly Tyr Pro Val Val Pro
355 360 365

Pro Pro Gln Gln Pro Val Gln Pro Pro Tyr Gly Val Pro Ser Ile Val
370 375 380

Pro Pro Ala Val Ser Leu Ala Pro Gly Val Leu Pro Ala Leu Pro Thr
385 390 395 400

Gly Val Pro Pro Val Pro Thr Gln Tyr Pro Ile Thr Gln Val Gln Pro
405 410 415

Pro Ala Ser Thr Gly Gln Ser Pro Met Gly Gly Pro Phe Ile Pro Ala
420 425 430

Ala Pro Val Lys Thr Ala Leu Pro Ala Gly Pro Gln Pro Gln Pro Gln
435 440 445

Pro Gln Pro Pro Leu Pro Ser Gln Pro Gln Ala Gln Lys Arg Arg Phe
450 455 460

Thr Glu Glu Leu Pro Asp Glu Arg Glu Ser Gly Leu Leu Gly Tyr Gln
465 470 475 480

```
His Gly Pro Ile His Met Thr Asn Leu Gly Thr Gly Phe Ser Ser Gln
                485                 490                 495

Asn Glu Ile Glu Gly Ala Gly Ser Lys Pro Ala Ser Ser Ser Gly Lys
            500                 505                 510

Glu Arg Glu Arg Asp Arg Gln Leu Met Pro Pro Pro Ala Phe Pro Val
        515                 520                 525

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

Thr Gly Ser His Gly Glu Cys Asp Ile Ala Gly Gly Thr Gly Glu Trp
545                 550                 555                 560

Leu Arg Leu Val
```

<210> 2558
<211> 462
<212> PRT
<213> Homo sapiens

<400> 2558

```
Met Gly Lys Glu Lys Thr His Ile Asn Ile Val Val Ile Gly His Val
1               5                   10                  15

Asp Ser Gly Lys Ser Thr Thr Thr Gly His Leu Ile Tyr Lys Cys Gly
            20                  25                  30

Gly Ile Asp Lys Arg Thr Ile Glu Lys Phe Glu Lys Glu Ala Ala Glu
        35                  40                  45

Met Gly Lys Gly Ser Phe Lys Tyr Ala Trp Val Leu Asp Lys Leu Lys
    50                  55                  60

Ala Glu Arg Glu Arg Gly Ile Thr Ile Asp Ile Ser Leu Trp Lys Phe
65                  70                  75                  80

Glu Thr Ser Lys Tyr Tyr Val Thr Ile Ile Asp Ala Pro Gly His Arg
                85                  90                  95

Asp Phe Ile Lys Asn Met Ile Thr Gly Thr Ser Gln Ala Asp Cys Ala
            100                 105                 110

Val Leu Ile Val Ala Ala Gly Val Gly Glu Phe Glu Ala Gly Ile Ser
```

115 120 125

Lys Asn Gly Gln Thr Arg Glu His Ala Leu Leu Ala Tyr Thr Leu Gly
130 135 140

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

Pro Tyr Ser Gln Lys Arg Tyr Glu Glu Ile Val Lys Glu Val Ser Thr
165 170 175

Tyr Ile Lys Lys Ile Gly Tyr Asn Pro Asp Thr Val Ala Phe Val Pro
180 185 190

Ile Ser Gly Trp Asn Gly Asp Asn Met Leu Glu Pro Ser Ala Asn Met
195 200 205

Pro Trp Phe Lys Gly Trp Lys Val Thr Arg Lys Asp Gly Asn Ala Ser
210 215 220

Gly Thr Thr Leu Leu Glu Ala Leu Asp Cys Ile Leu Pro Pro Thr Arg
225 230 235 240

Pro Thr Asp Lys Pro Leu Arg Leu Pro Leu Gln Asp Val Tyr Lys Ile
245 250 255

Gly Gly Ile Gly Thr Val Pro Val Gly Arg Val Glu Thr Gly Val Leu
260 265 270

Lys Pro Gly Met Val Val Thr Phe Ala Pro Val Asn Val Thr Thr Glu
275 280 285

Val Lys Ser Val Glu Met His His Glu Ala Leu Ser Glu Ala Leu Pro
290 295 300

Gly Asp Asn Val Gly Phe Asn Val Lys Asn Val Ser Val Lys Asp Val
305 310 315 320

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

Ala Ala Gly Phe Thr Ala Gln Val Ile Ile Leu Asn His Pro Gly Gln
340 345 350

Ile Ser Ala Gly Tyr Ala Pro Val Leu Asp Cys His Thr Ala His Ile
355 360 365

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

Lys Lys Leu Glu Asp Gly Pro Lys Phe Leu Lys Ser Gly Asp Ala Ala
385 390 395 400

Ile Val Asp Met Val Pro Gly Lys Pro Met Cys Val Glu Ser Phe Ser
405 410 415

Asp Tyr Pro Pro Leu Gly Arg Phe Ala Val Arg Asp Met Arg Gln Thr
420 425 430

Val Ala Val Gly Val Ile Lys Ala Val Asp Lys Lys Ala Ala Gly Ala
435 440 445

Gly Lys Val Thr Lys Ser Ala Gln Lys Ala Gln Lys Ala Lys
450 455 460

<210> 2559
<211> 394
<212> PRT
<213> Homo sapiens

<400> 2559

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

Val Val Thr Lys Tyr Lys Met Gly Gly Asp Ile Ala Asn Arg Val Leu
20 25 30

Arg Ser Leu Val Glu Ala Ser Ser Ser Gly Val Ser Val Leu Ser Leu
35 40 45

Cys Glu Lys Gly Asp Ala Met Ile Met Glu Glu Thr Gly Lys Ile Phe
50 55 60

Lys Lys Glu Lys Glu Met Lys Lys Gly Ile Ala Phe Pro Thr Ser Ile
65 70 75 80

Ser Val Asn Asn Cys Val Cys His Phe Ser Pro Leu Lys Ser Asp Gln
85 90 95

Asp Tyr Ile Leu Lys Glu Gly Asp Leu Val Lys Ile Asp Leu Gly Val
100 105 110

His Val Asp Gly Phe Ile Ala Asn Val Ala His Thr Phe Val Val Asp
115 120 125

Val Ala Gln Gly Thr Gln Val Thr Gly Arg Lys Ala Asp Val Ile Lys
130 135 140

Ala Ala His Leu Cys Ala Glu Ala Ala Leu Arg Leu Val Lys Pro Gly
145 150 155 160

Asn Gln Asn Thr Gln Val Thr Glu Ala Trp Asn Lys Val Ala His Ser
165 170 175

Phe Asn Cys Thr Pro Ile Glu Gly Met Leu Ser His Gln Leu Lys Gln
180 185 190

His Val Ile Asp Gly Glu Lys Thr Ile Ile Gln Asn Pro Thr Asp Gln
195 200 205

Gln Lys Lys Asp His Glu Lys Ala Glu Phe Glu Val His Glu Val Tyr
210 215 220

Ala Val Asp Val Leu Val Ser Ser Gly Glu Gly Lys Ala Lys Asp Ala
225 230 235 240

Gly Gln Arg Thr Thr Ile Tyr Lys Arg Asp Pro Ser Lys Gln Tyr Gly
245 250 255

Leu Lys Met Lys Thr Ser Arg Ala Phe Phe Ser Glu Val Glu Arg Arg
260 265 270

Phe Asp Ala Met Pro Phe Thr Leu Arg Ala Phe Glu Asp Glu Lys Lys
275 280 285

Ala Arg Met Gly Val Val Glu Cys Ala Lys His Glu Leu Leu Gln Pro
290 295 300

Phe Asn Val Leu Tyr Glu Lys Glu Gly Glu Phe Val Ala Gln Phe Lys
305 310 315 320

Phe Thr Val Leu Leu Met Pro Asn Gly Pro Met Arg Ile Thr Ser Gly
325 330 335

Pro Phe Glu Pro Asp Leu Tyr Lys Ser Glu Met Glu Val Gln Asp Ala
340 345 350

Glu Leu Lys Ala Leu Leu Gln Ser Ser Ala Ser Arg Lys Thr Gln Lys

355 360 365

Lys Lys Lys Lys Lys Ala Ser Lys Thr Ala Glu Asn Pro Thr Ser Gly
370 375 380

Glu Thr Leu Glu Glu Asn Glu Ala Gly Asp
385 390

<210> 2560
<211> 335
<212> PRT
<213> Homo sapiens

<400> 2560

Met Gly Lys Val Lys Val Gly Val Asn Gly Phe Gly Arg Ile Gly Arg
1 5 10 15

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

Ile Asn Asp Pro Phe Ile Asp Leu Asn Tyr Met Val Tyr Met Phe Gln
35 40 45

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

Gly Lys Leu Val Ile Asn Gly Asn Pro Ile Thr Ile Phe Gln Glu Arg
65 70 75 80

Asp Pro Ser Lys Ile Lys Trp Gly Asp Ala Gly Ala Glu Tyr Val Val
85 90 95

Glu Ser Thr Gly Val Phe Thr Thr Met Glu Lys Ala Gly Ala His Leu
100 105 110

Gln Gly Gly Ala Lys Arg Val Ile Ile Ser Ala Pro Ser Ala Asp Ala
115 120 125

Pro Met Phe Val Met Gly Val Asn His Glu Lys Tyr Asp Asn Ser Leu
130 135 140

Lys Ile Ile Ser Asn Ala Ser Cys Thr Thr Asn Cys Leu Ala Pro Leu
145 150 155 160

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

Thr Val His Ala Ile Thr Ala Thr Gln Lys Thr Val Asp Gly Pro Ser
180 185 190

Gly Lys Leu Trp Arg Asp Gly Arg Gly Ala Leu Gln Asn Ile Ile Pro
195 200 205

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

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

Ser Val Val Asp Leu Thr Cys Arg Leu Glu Lys Pro Ala Lys Tyr Asp
245 250 255

Asp Ile Lys Lys Val Val Lys Gln Ala Ser Glu Gly Pro Leu Lys Gly
260 265 270

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

Asp Thr His Ser Ser Thr Phe Asp Ala Gly Ala Gly Ile Ala Leu Asn
290 295 300

Asp His Phe Val Lys Leu Ile Ser Trp Tyr Asp Asn Glu Phe Gly Tyr
305 310 315 320

Ser Asn Arg Val Val Asp Leu Met Ala His Met Ala Ser Lys Glu
325 330 335

<210> 2561
<211> 1912
<212> PRT
<213> Homo sapiens

<400> 2561

Met Ala Ser Gly Leu Gly Ser Pro Ser Pro Cys Ser Ala Gly Ser Glu
1 5 10 15

Glu Glu Asp Met Asp Ala Leu Leu Asn Asn Ser Leu Pro Pro Pro His
20 25 30

Pro Glu Asn Glu Glu Asp Pro Glu Glu Asp Leu Ser Glu Thr Glu Thr
35 40 45

Pro Lys Leu Lys Lys Lys Lys Lys Pro Lys Lys Pro Arg Asp Pro Lys

50 55 60

Ile Pro Lys Ser Lys Arg Gln Lys Lys Glu Arg Met Leu Leu Cys Arg
65 70 75 80

Gln Leu Gly Asp Ser Ser Gly Glu Gly Pro Glu Phe Val Glu Glu Glu
85 90 95

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

Gly Lys Lys Lys Lys Lys Lys Leu Gly Pro Lys Lys Glu Lys Lys Ser
115 120 125

Lys Ser Lys Arg Lys Glu Glu Glu Glu Glu Asp Asp Asp Asp Asp Asp
130 135 140

Ser Lys Glu Pro Lys Ser Ser Ala Gln Leu Leu Glu Asp Trp Gly Met
145 150 155 160

Glu Asp Ile Asp His Val Phe Ser Glu Glu Asp Tyr Arg Thr Leu Thr
165 170 175

Asn Tyr Lys Ala Phe Ser Gln Phe Val Arg Pro Leu Ile Ala Ala Lys
180 185 190

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

Trp Arg Glu Phe Ser Thr Asn Asn Pro Phe Lys Gly Ser Ser Gly Ala
210 215 220

Ser Val Ala Ala Ala Ala Ala Ala Ala Val Ala Val Val Glu Ser Met
225 230 235 240

Val Thr Ala Thr Glu Val Ala Pro Pro Pro Pro Pro Val Glu Val Pro
245 250 255

Ile Arg Lys Ala Lys Thr Lys Glu Gly Lys Gly Pro Asn Ala Arg Arg
260 265 270

Lys Pro Lys Gly Ser Pro Arg Val Pro Asp Ala Lys Lys Pro Lys Pro
275 280 285

Lys Lys Val Ala Pro Leu Lys Ile Lys Leu Gly Gly Phe Gly Ser Lys
290 295 300

Arg Lys Arg Ser Ser Ser Glu Asp Asp Asp Leu Asp Val Glu Ser Asp
305 310 315 320

Phe Asp Asp Ala Ser Ile Asn Ser Tyr Ser Val Ser Asp Gly Ser Thr
325 330 335

Ser Arg Ser Ser Arg Ser Arg Lys Lys Leu Arg Thr Thr Lys Lys Lys
340 345 350

Lys Lys Gly Glu Glu Glu Val Thr Ala Val Asp Gly Tyr Glu Thr Asp
355 360 365

His Gln Asp Tyr Cys Glu Val Cys Gln Gln Gly Gly Glu Ile Ile Leu
370 375 380

Cys Asp Thr Cys Pro Arg Ala Tyr His Met Val Cys Leu Asp Pro Asp
385 390 395 400

Met Glu Lys Ala Pro Glu Gly Lys Trp Ser Cys Pro His Cys Glu Lys
405 410 415

Glu Gly Ile Gln Trp Glu Ala Lys Glu Asp Asn Ser Glu Gly Glu Glu
420 425 430

Ile Leu Glu Glu Val Gly Gly Asp Leu Glu Glu Glu Asp Asp His His
435 440 445

Met Glu Phe Cys Arg Val Cys Lys Asp Gly Gly Glu Leu Leu Cys Cys
450 455 460

Asp Thr Cys Pro Ser Ser Tyr His Ile His Cys Leu Asn Pro Pro Leu
465 470 475 480

Pro Glu Ile Pro Asn Gly Glu Trp Leu Cys Pro Arg Cys Thr Cys Pro
485 490 495

Ala Leu Lys Gly Lys Val Gln Lys Ile Leu Ile Trp Lys Trp Gly Gln
500 505 510

Pro Pro Ser Pro Thr Pro Val Pro Arg Pro Pro Asp Ala Asp Pro Asn
515 520 525

Thr Pro Ser Pro Lys Pro Leu Glu Gly Arg Pro Glu Arg Gln Phe Phe
530 535 540

Val Lys Trp Gln Gly Met Ser Tyr Trp His Cys Ser Trp Val Ser Glu
545 550 555 560

Leu Gln Leu Glu Leu His Cys Gln Val Met Phe Arg Asn Tyr Gln Arg
565 570 575

Lys Asn Asp Met Asp Glu Pro Pro Ser Gly Asp Phe Gly Gly Asp Glu
580 585 590

Glu Lys Ser Arg Lys Arg Lys Asn Lys Asp Pro Lys Phe Ala Glu Met
595 600 605

Glu Glu Arg Phe Tyr Arg Tyr Gly Ile Lys Pro Glu Trp Met Met Ile
610 615 620

His Arg Ile Leu Asn His Ser Val Asp Lys Lys Gly His Val His Tyr
625 630 635 640

Leu Ile Lys Trp Arg Asp Leu Pro Tyr Asp Gln Ala Ser Trp Glu Ser
645 650 655

Glu Asp Val Glu Ile Gln Asp Tyr Asp Leu Phe Lys Gln Ser Tyr Trp
660 665 670

Asn His Arg Glu Leu Met Arg Gly Glu Glu Gly Arg Pro Gly Lys Lys
675 680 685

Leu Lys Lys Val Lys Leu Arg Lys Leu Glu Arg Pro Pro Glu Thr Pro
690 695 700

Thr Val Asp Pro Thr Val Lys Tyr Glu Arg Gln Pro Glu Tyr Leu Asp
705 710 715 720

Ala Thr Gly Gly Thr Leu His Pro Tyr Gln Met Glu Gly Leu Asn Trp
725 730 735

Leu Arg Phe Ser Trp Ala Gln Gly Thr Asp Thr Ile Leu Ala Asp Glu
740 745 750

Met Gly Leu Gly Lys Thr Val Gln Thr Ala Val Phe Leu Tyr Ser Leu
755 760 765

Tyr Lys Glu Gly His Ser Lys Gly Pro Phe Leu Val Ser Ala Pro Leu
770 775 780

Ser Thr Ile Ile Asn Trp Glu Arg Glu Phe Glu Met Trp Ala Pro Asp
785 790 795 800

Met Tyr Val Val Thr Tyr Val Gly Asp Lys Asp Ser Arg Ala Ile Ile
805 810 815

Arg Glu Asn Glu Phe Ser Phe Glu Asp Asn Ala Ile Arg Gly Gly Lys
820 825 830

Lys Ala Ser Arg Met Lys Lys Glu Ala Ser Val Lys Phe His Val Leu
835 840 845

Leu Thr Ser Tyr Glu Leu Ile Thr Ile Asp Met Ala Ile Leu Gly Ser
850 855 860

Ile Asp Trp Ala Cys Leu Ile Val Asp Glu Ala His Arg Leu Lys Asn
865 870 875 880

Asn Gln Ser Lys Phe Phe Arg Val Leu Asn Gly Tyr Ser Leu Gln His
885 890 895

Lys Leu Leu Leu Thr Gly Thr Pro Leu Gln Asn Asn Leu Glu Glu Leu
900 905 910

Phe His Leu Leu Asn Phe Leu Thr Pro Glu Arg Phe His Asn Leu Glu
915 920 925

Gly Phe Leu Glu Glu Phe Ala Asp Ile Ala Lys Glu Asp Gln Ile Lys
930 935 940

Lys Leu His Asp Met Leu Gly Pro His Met Leu Arg Arg Leu Lys Ala
945 950 955 960

Asp Val Phe Lys Asn Met Pro Ser Lys Thr Glu Leu Ile Val Arg Val
965 970 975

Glu Leu Ser Pro Met Gln Lys Lys Tyr Tyr Lys Tyr Ile Leu Thr Arg
980 985 990

Asn Phe Glu Ala Leu Asn Ala Arg Gly Gly Gly Asn Gln Val Ser Leu
995 1000 1005

Leu Asn Val Val Met Asp Leu Lys Lys Cys Cys Asn His Pro Tyr
1010 1015 1020

Leu Phe Pro Val Ala Ala Met Glu Ala Pro Lys Met Pro Asn Gly

1025 1030 1035

Met Tyr Asp Gly Ser Ala Leu Ile Arg Ala Ser Gly Lys Leu Leu
1040 1045 1050

Leu Leu Gln Lys Met Leu Lys Asn Leu Lys Glu Gly Gly His Arg
1055 1060 1065

Val Leu Ile Phe Ser Gln Met Thr Lys Met Leu Asp Leu Leu Glu
1070 1075 1080

Asp Phe Leu Glu His Glu Gly Tyr Lys Tyr Glu Arg Ile Asp Gly
1085 1090 1095

Gly Ile Thr Gly Asn Met Arg Gln Glu Ala Ile Asp Arg Phe Asn
1100 1105 1110

Ala Pro Gly Ala Gln Gln Phe Cys Phe Leu Leu Ser Thr Arg Ala
1115 1120 1125

Gly Gly Leu Gly Ile Asn Leu Ala Thr Ala Asp Thr Val Ile Ile
1130 1135 1140

Tyr Asp Ser Asp Trp Asn Pro His Asn Asp Ile Gln Ala Phe Ser
1145 1150 1155

Arg Ala His Arg Ile Gly Gln Asn Lys Lys Val Met Ile Tyr Arg
1160 1165 1170

Phe Val Thr Arg Ala Ser Val Glu Glu Arg Ile Thr Gln Val Ala
1175 1180 1185

Lys Lys Lys Met Met Leu Thr His Leu Val Val Arg Pro Gly Leu
1190 1195 1200

Gly Ser Lys Thr Gly Ser Met Ser Lys Gln Glu Leu Asp Asp Ile
1205 1210 1215

Leu Lys Phe Gly Thr Glu Glu Leu Phe Lys Asp Glu Ala Thr Asp
1220 1225 1230

Gly Gly Gly Asp Asn Lys Glu Gly Glu Asp Ser Ser Val Ile His
1235 1240 1245

Tyr Asp Asp Lys Ala Ile Glu Arg Leu Leu Asp Arg Asn Gln Asp
1250 1255 1260

Glu Thr Glu Asp Thr Glu Leu Gln Gly Met Asn Glu Tyr Leu Ser
1265 1270 1275

Ser Phe Lys Val Ala Gln Tyr Val Val Arg Glu Glu Glu Met Gly
1280 1285 1290

Glu Glu Glu Glu Val Glu Arg Glu Ile Ile Lys Gln Glu Glu Ser
1295 1300 1305

Val Asp Pro Asp Tyr Trp Glu Lys Leu Leu Arg His His Tyr Glu
1310 1315 1320

Gln Gln Gln Glu Asp Leu Ala Arg Asn Leu Gly Lys Gly Lys Arg
1325 1330 1335

Ile Arg Lys Gln Val Asn Tyr Asn Asp Gly Ser Gln Glu Asp Arg
1340 1345 1350

Asp Trp Gln Asp Asp Gln Ser Asp Asn Gln Ser Asp Tyr Ser Val
1355 1360 1365

Ala Ser Glu Glu Gly Asp Glu Asp Phe Asp Glu Arg Ser Glu Ala
1370 1375 1380

Pro Arg Arg Pro Ser Arg Lys Gly Leu Arg Asn Asp Lys Asp Lys
1385 1390 1395

Pro Leu Pro Pro Leu Leu Ala Arg Val Gly Gly Asn Ile Glu Val
1400 1405 1410

Leu Gly Phe Asn Ala Arg Gln Arg Lys Ala Phe Leu Asn Ala Ile
1415 1420 1425

Met Arg Tyr Gly Met Pro Pro Gln Asp Ala Phe Thr Thr Gln Trp
1430 1435 1440

Leu Val Arg Asp Leu Arg Gly Lys Ser Glu Lys Glu Phe Lys Ala
1445 1450 1455

Tyr Val Ser Leu Phe Met Arg His Leu Cys Glu Pro Gly Ala Asp
1460 1465 1470

Gly Ala Glu Thr Phe Ala Asp Gly Val Pro Arg Glu Gly Leu Ser
1475 1480 1485

Arg Gln His Val Leu Thr Arg Ile Gly Val Met Ser Leu Ile Arg
1490 1495 1500

Lys Lys Val Gln Glu Phe Glu His Val Asn Gly Arg Trp Ser Met
1505 1510 1515

Pro Glu Leu Ala Glu Val Glu Glu Asn Lys Lys Met Ser Gln Pro
1520 1525 1530

Gly Ser Pro Ser Pro Lys Thr Pro Thr Pro Ser Thr Pro Gly Asp
1535 1540 1545

Thr Gln Pro Asn Thr Pro Ala Pro Val Pro Pro Ala Glu Asp Gly
1550 1555 1560

Ile Lys Ile Glu Glu Asn Ser Leu Lys Glu Glu Glu Ser Ile Glu
1565 1570 1575

Gly Glu Lys Glu Val Lys Ser Thr Ala Pro Glu Thr Ala Ile Glu
1580 1585 1590

Cys Thr Gln Ala Pro Ala Pro Ala Ser Glu Asp Glu Lys Val Val
1595 1600 1605

Val Glu Pro Pro Glu Gly Glu Glu Lys Val Glu Lys Ala Glu Val
1610 1615 1620

Lys Glu Arg Thr Glu Glu Pro Met Glu Thr Glu Pro Lys Gly Ala
1625 1630 1635

Ala Asp Val Glu Lys Val Glu Glu Lys Ser Ala Ile Asp Leu Thr
1640 1645 1650

Pro Ile Val Val Glu Asp Lys Glu Glu Lys Lys Glu Glu Glu Glu
1655 1660 1665

Lys Lys Glu Val Met Leu Gln Asn Gly Glu Thr Pro Lys Asp Leu
1670 1675 1680

Asn Asp Glu Lys Gln Lys Lys Asn Ile Lys Gln Arg Phe Met Phe
1685 1690 1695

Asn Ile Ala Asp Gly Gly Phe Thr Glu Leu His Ser Leu Trp Gln
1700 1705 1710

Asn Glu Glu Arg Ala Ala Thr Val Thr Lys Lys Thr Tyr Glu Ile
1715 1720 1725

Trp His Arg Arg His Asp Tyr Trp Leu Leu Ala Gly Ile Ile Asn
1730 1735 1740

His Gly Tyr Ala Arg Trp Gln Asp Ile Gln Asn Asp Pro Arg Tyr
1745 1750 1755

Ala Ile Leu Asn Glu Pro Phe Lys Gly Glu Met Asn Arg Gly Asn
1760 1765 1770

Phe Leu Glu Ile Lys Asn Lys Phe Leu Ala Arg Arg Phe Lys Leu
1775 1780 1785

Leu Glu Gln Ala Leu Val Ile Glu Glu Gln Leu Arg Arg Ala Ala
1790 1795 1800

Tyr Leu Asn Met Ser Glu Asp Pro Ser His Pro Ser Met Ala Leu
1805 1810 1815

Asn Thr Arg Phe Ala Glu Val Glu Cys Leu Ala Glu Ser His Gln
1820 1825 1830

His Leu Ser Lys Glu Ser Met Ala Gly Asn Lys Pro Ala Asn Ala
1835 1840 1845

Val Leu His Lys Val Leu Lys Gln Leu Glu Glu Leu Leu Ser Asp
1850 1855 1860

Met Lys Ala Asp Val Thr Arg Leu Pro Ala Thr Ile Ala Arg Ile
1865 1870 1875

Pro Pro Val Ala Val Arg Leu Gln Met Ser Glu Arg Asn Ile Leu
1880 1885 1890

Ser Arg Leu Ala Asn Arg Ala Pro Glu Pro Thr Pro Gln Gln Val
1895 1900 1905

Ala Gln Gln Gln
1910

<210> 2562
<211> 345
<212> PRT
<213> Homo sapiens

<400> 2562

Met Pro Gln Arg Pro Ala Ala Ser Asn Ile Pro Val Val Gly Ser Pro
1 5 10 15

Asn Pro Pro Ser Thr His Phe Ala Ser Gln Asn Gln His Ser Tyr Ser
20 25 30

Ser Pro Pro Trp Ala Gly Gln His Asn Arg Lys Gly Glu Lys Asn Gly
35 40 45

Met Gly Leu Cys Arg Leu Ser Met Lys Val Trp Glu Thr Val Gln Arg
50 55 60

Lys Gly Thr Thr Ser Cys Gln Glu Val Val Gly Glu Leu Val Ala Lys
65 70 75 80

Phe Arg Ala Ala Ser Asn His Ala Ser Pro Asn Glu Ser Ala Tyr Asp
85 90 95

Val Lys Asn Ile Lys Arg Arg Thr Tyr Asp Ala Leu Asn Val Leu Met
100 105 110

Ala Met Asn Ile Ile Ser Arg Glu Lys Lys Lys Ile Lys Trp Ile Gly
115 120 125

Leu Thr Thr Asn Ser Ala Gln Asn Cys Gln Asn Leu Arg Val Glu Arg
130 135 140

Gln Lys Arg Leu Glu Arg Ile Lys Gln Lys Gln Ser Glu Leu Gln Gln
145 150 155 160

Leu Ile Leu Gln Gln Ile Ala Phe Lys Asn Leu Val Leu Arg Asn Gln
165 170 175

Tyr Val Glu Glu Gln Val Ser Gln Arg Pro Leu Pro Asn Ser Val Ile
180 185 190

His Val Pro Phe Ile Ile Ile Ser Ser Ser Lys Lys Thr Val Ile Asn
195 200 205

Cys Ser Ile Ser Asp Asp Lys Ser Glu Tyr Leu Phe Lys Phe Asn Ser
210 215 220

Ser Phe Glu Ile His Asp Asp Thr Glu Val Leu Met Trp Met Gly Met
225 230 235 240

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

Ala Arg Asn Leu Val Pro Lys Ala Leu Glu Pro Tyr Val Thr Glu Met
260 265 270

Ala Gln Gly Thr Phe Gly Gly Val Phe Thr Thr Ala Gly Ser Arg Ser
275 280 285

Asn Gly Thr Trp Leu Ser Ala Ser Asp Leu Thr Asn Ile Ala Ile Gly
290 295 300

Met Leu Ala Thr Ser Ser Gly Gly Ser Gln Tyr Ser Gly Ser Arg Val
305 310 315 320

Glu Thr Pro Ala Val Glu Glu Glu Glu Glu Glu Asp Asn Asn Asp Asp
325 330 335

Asp Leu Ser Glu Asn Asp Glu Asp Asp
340 345

<210> 2563
<211> 553
<212> PRT
<213> Homo sapiens

<400> 2563

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

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

Lys Arg Phe Lys Gly Glu Gly Val Arg Tyr Lys Ala Lys Leu Ile Gly
35 40 45

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

Met Met Lys Leu Lys Gly Val Val Ala Gly Ala Arg Ser Lys Gly Glu
65 70 75 80

His Lys Gln Lys Ile Phe Leu Thr Ile Ser Phe Gly Gly Ile Lys Ile
85 90 95

Phe Asp Glu Lys Thr Gly Ala Leu Gln His His His Ala Val His Glu

100 105 110

Ile Ser Tyr Ile Ala Lys Asp Ile Thr Asp His Arg Ala Phe Gly Tyr
115 120 125

Val Cys Gly Lys Glu Gly Asn His Arg Phe Val Ala Ile Lys Thr Ala
130 135 140

Gln Ala Ala Glu Pro Val Ile Leu Asp Leu Arg Asp Leu Phe Gln Leu
145 150 155 160

Ile Tyr Glu Leu Lys Gln Arg Glu Glu Leu Glu Lys Lys Ala Gln Lys
165 170 175

Asp Lys Gln Cys Glu Gln Ala Val Tyr Gln Thr Ile Leu Glu Glu Asp
180 185 190

Val Glu Asp Pro Val Tyr Gln Tyr Ile Val Phe Glu Ala Gly His Glu
195 200 205

Pro Ile Arg Asp Pro Glu Thr Glu Glu Asn Ile Tyr Gln Val Pro Thr
210 215 220

Ser Gln Lys Lys Glu Gly Val Tyr Asp Val Pro Lys Ser Gln Pro Ala
225 230 235 240

Val Thr Gln Leu Glu Leu Phe Gly Asp Met Ser Thr Pro Pro Asp Ile
245 250 255

Thr Ser Pro Pro Thr Pro Ala Thr Pro Gly Asp Ala Phe Ile Pro Ser
260 265 270

Ser Ser Gln Thr Leu Pro Ala Ser Ala Asp Val Phe Ser Ser Val Pro
275 280 285

Phe Gly Thr Ala Ala Val Pro Ser Gly Tyr Val Ala Met Gly Ala Val
290 295 300

Leu Pro Ser Phe Trp Gly Gln Gln Pro Leu Val Gln Gln Gln Met Val
305 310 315 320

Met Gly Ala Gln Pro Pro Val Ala Gln Val Met Pro Gly Ala Gln Pro
325 330 335

Ile Ala Trp Gly Gln Pro Gly Leu Phe Pro Ala Thr Gln Gln Pro Trp
340 345 350

Pro Thr Val Ala Gly Gln Phe Pro Pro Ala Ala Phe Met Pro Thr Gln
355 360 365

Thr Val Met Pro Leu Pro Ala Ala Met Phe Gln Gly Pro Leu Thr Pro
370 375 380

Leu Ala Thr Val Pro Gly Thr Ser Asp Ser Thr Arg Ser Ser Pro Gln
385 390 395 400

Thr Asp Lys Pro Arg Gln Lys Met Gly Lys Glu Thr Phe Lys Asp Phe
405 410 415

Gln Met Ala Gln Pro Pro Pro Val Pro Ser Arg Lys Pro Asp Gln Pro
420 425 430

Ser Leu Thr Cys Thr Ser Glu Ala Phe Ser Ser Tyr Phe Asn Lys Val
435 440 445

Gly Val Ala Gln Asp Thr Asp Asp Cys Asp Asp Phe Asp Ile Ser Gln
450 455 460

Leu Asn Leu Thr Pro Val Thr Ser Thr Thr Pro Ser Thr Asn Ser Pro
465 470 475 480

Pro Thr Pro Ala Pro Arg Gln Ser Ser Pro Ser Lys Ser Ser Ala Ser
485 490 495

His Ala Ser Asp Pro Thr Thr Asp Asp Ile Phe Glu Glu Gly Phe Glu
500 505 510

Ser Pro Ser Lys Ser Glu Glu Gln Glu Ala Pro Asp Gly Ser Gln Ala
515 520 525

Ser Ser Asn Ser Asp Pro Phe Gly Glu Pro Ser Gly Glu Pro Ser Gly
530 535 540

Asp Asn Ile Ser Pro Gln Ala Gly Ser
545 550

<210> 2564
<211> 1336
<212> PRT
<213> Homo sapiens

<400> 2564

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

Arg Gly Pro Val Gly Pro Ser Gly Gly Gly Ser Thr Arg Asp Gln Val
20 25 30

Arg Thr Val Val Met Arg Pro Ser Val Ser Trp Glu Lys Ala Gly Pro
35 40 45

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

Val Ala Gly Pro Ala Ala Gly Thr Pro Pro Cys Gln Met Gly Val Tyr
65 70 75 80

Pro Thr Asp Leu Thr Leu Gln Leu Leu Ala Val Arg Arg Lys Ser Arg
85 90 95

Leu Arg Asp Pro Gly Leu Gln Gln Thr Leu Arg Gly Gln Leu Arg Leu
100 105 110

Leu Glu Asn Asp Ser Arg Glu Met Ala Arg Val Leu Gly Glu Leu Ser
115 120 125

Ala Arg Leu Leu Ser Ile His Ser Asp Gln Asp Arg Ile Val Val Thr
130 135 140

Phe Lys Thr Phe Glu Glu Ile Trp Lys Phe Ser Thr Tyr His Ala Leu
145 150 155 160

Gly Phe Thr His His Cys Leu Ala Asn Leu Leu Met Asp Gln Ala Phe
165 170 175

Trp Leu Leu Leu Pro Ser Glu Glu Glu Glu Thr Ala Ile Gln Val His
180 185 190

Val Asp Glu Asn Ala Leu Arg Leu Thr His Glu Ser Leu Leu Ile Gln
195 200 205

Glu Gly Pro Phe Phe Val Leu Cys Pro Asp His His Val Arg Val Met
210 215 220

Thr Gly Pro Arg Asp Ala Gly Asn Gly Pro Gln Ala Leu Arg Gln Ala
225 230 235 240

Ser Gly Ala Pro Gln Gly Glu Ala Ala Pro Glu Thr Asp Ser Ser Pro

245 250 255

Pro Ser Pro Ser Val Ser Ser Glu Glu Val Ala Val Ala Ala Ala Pro
260 265 270

Glu Pro Leu Ile Pro Phe His Gln Trp Ala Leu Arg Ile Pro Gln Asp
275 280 285

Pro Ile Asp Asp Ala Met Gly Gly Pro Val Met Pro Gly Asn Pro Leu
290 295 300

Met Ala Val Gly Leu Ala Ser Ala Leu Ala Asp Phe Gln Gly Ser Gly
305 310 315 320

Pro Glu Glu Met Thr Phe Arg Gly Gly Asp Leu Ile Glu Ile Leu Gly
325 330 335

Ala Gln Val Pro Ser Leu Pro Trp Cys Val Gly Arg His Ala Ala Ser
340 345 350

Gly Arg Val Gly Phe Val Arg Ser Ser Leu Ile Ser Met Gln Gly Pro
355 360 365

Val Ser Glu Leu Glu Ser Ala Ile Phe Leu Asn Glu Glu Glu Lys Ser
370 375 380

Phe Phe Ser Glu Gly Cys Phe Ser Glu Glu Asp Ala Arg Gln Leu Leu
385 390 395 400

Arg Arg Met Ser Gly Thr Asp Val Cys Ser Val Tyr Ser Leu Asp Ser
405 410 415

Val Glu Glu Ala Glu Thr Glu Gln Pro Gln Glu Lys Glu Ile Pro Pro
420 425 430

Pro Cys Leu Ser Pro Glu Pro Gln Glu Thr Leu Gln Lys Val Lys Asn
435 440 445

Val Leu Glu Gln Cys Lys Thr Cys Pro Gly Cys Pro Gln Glu Pro Ala
450 455 460

Ser Trp Gly Leu Cys Ala Ala Ser Ser Asp Val Ser Leu Gln Asp Pro
465 470 475 480

Glu Glu Pro Ser Phe Cys Leu Glu Ala Glu Asp Asp Trp Glu Asp Pro
485 490 495

Glu Ala Leu Ser Ser Leu Leu Leu Phe Leu Asn Ala Pro Gly Tyr Lys
500 505 510

Ala Ser Phe Arg Gly Leu Tyr Asp Val Ala Leu Pro Trp Leu Ser Ser
515 520 525

Val Phe Arg Ser Phe Ser Asp Glu Glu Glu Leu Thr Gly Arg Leu Ala
530 535 540

Gln Ala Arg Gly Ala Ala Lys Lys Ala Gly Leu Leu Met Ala Leu Ala
545 550 555 560

Arg Leu Cys Phe Leu Leu Gly Arg Leu Cys Ser Arg Arg Leu Lys Leu
565 570 575

Ser Gln Ala Arg Val Tyr Phe Glu Glu Ala Leu Gly Ala Leu Glu Gly
580 585 590

Ser Phe Gly Asp Leu Phe Leu Val Val Ala Val Tyr Ala Asn Leu Ala
595 600 605

Ser Ile Tyr Arg Lys Gln Lys Asn Arg Glu Lys Cys Ala Gln Val Val
610 615 620

Pro Lys Ala Met Ala Leu Leu Leu Gly Thr Pro Asp His Ile Cys Ser
625 630 635 640

Thr Glu Ala Glu Gly Glu Leu Leu Gln Leu Ala Leu Arg Arg Ala Val
645 650 655

Gly Gly Gln Ser Leu Gln Ala Glu Ala Arg Ala Cys Phe Leu Leu Ala
660 665 670

Arg His His Val His Leu Lys Gln Pro Glu Glu Ala Leu Pro Phe Leu
675 680 685

Glu Arg Leu Leu Leu Leu His Arg Asp Ser Gly Ala Pro Glu Ala Ala
690 695 700

Trp Leu Ser Asp Cys Tyr Leu Leu Leu Ala Asp Ile Tyr Ser Arg Lys
705 710 715 720

Cys Leu Pro His Leu Val Leu Ser Cys Val Lys Val Ala Ser Leu Arg
725 730 735

Thr Arg Gly Ser Leu Ala Gly Ser Leu Arg Ser Val Asn Leu Val Leu
740 745 750

Gln Asn Ala Pro Gln Pro His Ser Leu Pro Ala Gln Thr Ser His Tyr
755 760 765

Leu Arg Gln Ala Leu Ala Ser Leu Thr Pro Gly Thr Gly Gln Ala Leu
770 775 780

Arg Gly Pro Leu Tyr Thr Ser Leu Ala Gln Leu Tyr Ser His His Gly
785 790 795 800

Cys His Gly Pro Ala Ile Thr Phe Met Thr Gln Ala Val Glu Ala Ser
805 810 815

Ala Ile Ala Gly Val Arg Ala Ile Val Asp His Leu Val Ala Leu Ala
820 825 830

Trp Leu His Val Leu His Gly Gln Ser Pro Val Ala Leu Asp Ile Leu
835 840 845

Gln Ser Val Arg Asp Ala Val Val Ala Ser Glu Asp Gln Glu Gly Val
850 855 860

Ile Ala Asn Met Val Ala Val Ala Leu Lys Arg Thr Gly Arg Thr Arg
865 870 875 880

Gln Ala Ala Glu Ser Tyr Tyr Arg Ala Leu Arg Val Ala Arg Asp Leu
885 890 895

Gly Gln Gln Arg Asn Gln Ala Val Gly Leu Ala Asn Phe Gly Ala Leu
900 905 910

Cys Leu His Ala Gly Ala Ser Arg Leu Ala Gln His Tyr Leu Leu Glu
915 920 925

Ala Val Arg Leu Phe Ser Arg Leu Pro Leu Gly Glu Cys Gly Arg Asp
930 935 940

Phe Thr His Val Leu Leu Gln Leu Gly His Leu Cys Thr Arg Gln Gly
945 950 955 960

Pro Ala Gln Gln Gly Lys Gly Tyr Tyr Glu Trp Ala Leu Leu Val Ala
965 970 975

Val Glu Met Gly His Val Glu Ser Gln Leu Arg Ala Val Gln Arg Leu
980 985 990

Cys His Phe Tyr Ser Ala Val Met Pro Ser Glu Ala Gln Cys Val Ile
995 1000 1005

Tyr His Glu Leu Gln Leu Ser Pro Ala Cys Lys Val Ala Asp Lys
1010 1015 1020

Val Leu Glu Gly Gln Leu Leu Glu Thr Ile Ser Gln Leu Tyr Leu
1025 1030 1035

Ser Leu Gly Thr Glu Arg Ala Tyr Lys Ser Ala Leu Asp Tyr Thr
1040 1045 1050

Lys Arg Ser Leu Gly Ile Phe Ile Asp Leu Gln Lys Lys Glu Lys
1055 1060 1065

Glu Ala His Ala Trp Leu Gln Ala Gly Lys Ile Tyr Tyr Ile Leu
1070 1075 1080

Arg Gln Ser Glu Leu Val Asp Leu Tyr Ile Gln Val Ala Gln Asn
1085 1090 1095

Val Ala Leu Tyr Thr Gly Asp Pro Asn Leu Gly Leu Glu Leu Phe
1100 1105 1110

Glu Ala Ala Gly Asp Ile Phe Phe Asp Gly Ala Trp Glu Arg Glu
1115 1120 1125

Lys Ala Val Ser Phe Tyr Arg Asp Arg Ala Leu Pro Leu Ala Val
1130 1135 1140

Thr Thr Gly Asn Arg Lys Ala Glu Leu Arg Leu Cys Asn Lys Leu
1145 1150 1155

Val Ala Leu Leu Ala Thr Leu Glu Glu Pro Gln Glu Gly Leu Glu
1160 1165 1170

Phe Ala His Met Ala Leu Ala Leu Ser Ile Thr Leu Gly Asp Arg
1175 1180 1185

Leu Asn Glu Arg Val Ala Tyr His Arg Leu Ala Ala Leu Gln His
1190 1195 1200

Arg Leu Gly His Gly Glu Leu Ala Glu His Phe Tyr Leu Lys Ala

1205 1210 1215

Leu Ser Leu Cys Asn Ser Pro Leu Glu Phe Asp Glu Glu Thr Leu
1220 1225 1230

Tyr Tyr Val Lys Val Tyr Leu Val Leu Gly Asp Ile Ile Phe Tyr
1235 1240 1245

Asp Leu Lys Asp Pro Phe Asp Ala Ala Gly Tyr Tyr Gln Leu Ala
1250 1255 1260

Leu Ala Ala Ala Val Asp Leu Gly Asn Lys Lys Ala Gln Leu Lys
1265 1270 1275

Ile Tyr Thr Arg Leu Ala Thr Ile Tyr His Asn Phe Leu Leu Asp
1280 1285 1290

Arg Glu Lys Ser Leu Phe Phe Tyr Gln Lys Ala Arg Thr Phe Ala
1295 1300 1305

Thr Glu Leu Asn Val Arg Arg Val Asn Leu Pro Pro Leu Pro Leu
1310 1315 1320

Cys Gly Trp Ala Pro Trp Leu Ala Pro Ser His Pro Arg
1325 1330 1335

<210> 2565
<211> 93
<212> PRT
<213> Homo sapiens

<400> 2565

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
65 70 75 80

Ala Ala His Lys Lys Ser His Glu Glu Ser His Lys Glu
85 90

<210> 2566
<211> 1186
<212> PRT
<213> Homo sapiens

<400> 2566

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

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

Ile Trp Leu Asn Gln Ala Leu Lys Gly Val Arg Asp Arg His Gly Asn
35 40 45

Ser Ile Glu Asn Pro His Leu Leu Thr Leu Phe His Arg Leu Cys Lys
50 55 60

Leu Leu Phe Phe Arg Ile Arg Pro Ile Phe Val Phe Asp Gly Asp Ala
65 70 75 80

Pro Leu Leu Lys Lys Gln Thr Leu Val Lys Arg Arg Gln Arg Lys Asp
85 90 95

Leu Ala Ser Ser Asp Ser Arg Lys Thr Thr Glu Lys Leu Leu Lys Thr
100 105 110

Phe Leu Lys Arg Gln Ala Ile Lys Thr Ala Phe Arg Ser Lys Arg Asp
115 120 125

Glu Ala Leu Pro Ser Leu Thr Gln Val Arg Arg Glu Asn Asp Leu Tyr
130 135 140

Val Leu Pro Pro Leu Gln Glu Glu Glu Lys His Ser Ser Glu Glu Glu
145 150 155 160

Asp Glu Lys Glu Trp Gln Glu Arg Met Asn Gln Lys Gln Ala Leu Gln
165 170 175

Glu Glu Phe Phe His Asn Pro Gln Ala Ile Asp Ile Glu Ser Glu Asp
180 185 190

Phe Ser Ser Leu Pro Pro Glu Val Lys His Glu Ile Leu Thr Asp Met

195 200 205

Lys Glu Phe Thr Lys Arg Arg Arg Thr Leu Phe Glu Ala Met Pro Glu
210 215 220

Glu Ser Asp Asp Phe Ser Gln Tyr Gln Leu Lys Gly Leu Leu Lys Lys
225 230 235 240

Asn Tyr Leu Asn Gln His Ile Glu His Val Gln Lys Glu Met Asn Gln
245 250 255

Gln His Ser Gly His Ile Arg Arg Gln Tyr Glu Asp Glu Gly Gly Phe
260 265 270

Leu Lys Glu Val Glu Ser Arg Arg Val Val Ser Glu Asp Thr Ser His
275 280 285

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

Ser Glu Ser Leu Pro Ser Ser Ser Lys Met His Gly Met Ser Phe Asp
305 310 315 320

Val Lys Ser Ser Pro Cys Glu Lys Leu Lys Thr Glu Lys Glu Pro Asp
325 330 335

Ala Thr Pro Pro Ser Pro Arg Thr Leu Leu Ala Met Gln Ala Ala Leu
340 345 350

Leu Gly Ser Ser Ser Glu Glu Glu Leu Glu Ser Glu Asn Arg Arg Gln
355 360 365

Ala Arg Gly Arg Asn Ala Pro Ala Ala Val Asp Glu Gly Ser Ile Ser
370 375 380

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

Val Lys Val Cys Ala Gly Asp Asp Val Gln Thr Gly Gly Pro Gly Ala
405 410 415

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

Lys Val Arg Asp Gly Lys Gly Ile Pro Phe Thr Ala Thr Leu Ala Ser
435 440 445

Ser Ser Val Asn Ser Ala Glu Glu His Val Ala Ser Thr Asn Glu Gly
450 455 460

Arg Glu Pro Thr Asp Ser Val Pro Lys Glu Gln Met Ser Leu Val His
465 470 475 480

Val Gly Thr Glu Ala Phe Pro Ile Ser Asp Glu Ser Met Ile Lys Asp
485 490 495

Arg Lys Asp Arg Leu Pro Leu Glu Ser Ala Val Val Arg His Ser Asp
500 505 510

Ala Pro Gly Leu Pro Asn Gly Arg Glu Leu Thr Pro Ala Ser Pro Thr
515 520 525

Cys Thr Asn Ser Val Ser Lys Asn Glu Thr His Ala Glu Val Leu Glu
530 535 540

Gln Gln Asn Glu Leu Cys Pro Tyr Glu Ser Lys Phe Asp Ser Ser Leu
545 550 555 560

Leu Ser Ser Asp Asp Glu Thr Lys Cys Lys Pro Asn Ser Ala Ser Glu
565 570 575

Val Ile Gly Pro Val Ser Leu Gln Glu Thr Ser Ser Ile Val Ser Val
580 585 590

Pro Ser Glu Ala Val Asp Asn Val Glu Asn Val Val Ser Phe Asn Ala
595 600 605

Lys Glu His Glu Asn Phe Leu Glu Thr Ile Gln Glu Gln Gln Thr Thr
610 615 620

Glu Ser Ala Gly Gln Asp Leu Ile Ser Ile Pro Lys Ala Val Glu Pro
625 630 635 640

Met Glu Ile Asp Ser Glu Glu Ser Glu Ser Asp Gly Ser Phe Ile Glu
645 650 655

Val Gln Ser Val Ile Ser Asp Glu Glu Leu Gln Ala Glu Phe Pro Glu
660 665 670

Thr Ser Lys Pro Pro Ser Glu Gln Gly Glu Glu Glu Leu Val Gly Thr
675 680 685

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Arg Glu Gly Glu Ala Pro Ala Glu Ser Glu Ser Leu Leu Arg Asp Asn
    690                 695                 700

Ser Glu Arg Asp Asp Val Asp Gly Glu Pro Gln Glu Ala Glu Lys Asp
705                 710                 715                 720

Ala Glu Asp Ser Leu His Glu Trp Gln Asp Ile Asn Leu Glu Glu Leu
                725                 730                 735

Glu Thr Leu Glu Ser Asn Leu Leu Ala Gln Gln Asn Ser Leu Lys Ala
            740                 745                 750

Gln Lys Gln Gln Gln Glu Arg Ile Ala Ala Thr Val Thr Gly Gln Met
        755                 760                 765

Phe Leu Glu Ser Gln Glu Leu Leu Arg Leu Phe Gly Ile Pro Tyr Ile
    770                 775                 780

Gln Ala Pro Met Glu Ala Glu Ala Gln Cys Ala Ile Leu Asp Leu Thr
785                 790                 795                 800

Asp Gln Thr Ser Gly Thr Ile Thr Asp Asp Ser Asp Ile Trp Leu Phe
                805                 810                 815

Gly Ala Arg His Val Tyr Arg Asn Phe Phe Asn Lys Asn Lys Phe Val
            820                 825                 830

Glu Tyr Tyr Gln Tyr Val Asp Phe His Asn Gln Leu Gly Leu Asp Arg
        835                 840                 845

Asn Lys Leu Ile Asn Leu Ala Tyr Leu Leu Gly Ser Asp Tyr Thr Glu
    850                 855                 860

Gly Ile Pro Thr Val Gly Cys Val Thr Ala Met Glu Ile Leu Asn Glu
865                 870                 875                 880

Phe Pro Gly His Gly Leu Glu Pro Leu Leu Lys Phe Ser Glu Trp Trp
                885                 890                 895

His Glu Ala Gln Lys Asn Pro Lys Ile Arg Pro Asn Pro His Asp Thr
            900                 905                 910

Lys Val Lys Lys Lys Leu Arg Thr Leu Gln Leu Thr Pro Gly Phe Pro
        915                 920                 925
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Asn Pro Ala Val Ala Glu Ala Tyr Leu Lys Pro Val Val Asp Asp Ser
930 935 940

Lys Gly Ser Phe Leu Trp Gly Lys Pro Asp Leu Asp Lys Ile Arg Glu
945 950 955 960

Phe Cys Gln Arg Tyr Phe Gly Trp Asn Arg Thr Lys Thr Asp Glu Ser
965 970 975

Leu Phe Pro Val Leu Lys Gln Leu Asp Ala Gln Gln Thr Gln Leu Arg
980 985 990

Ile Asp Ser Phe Phe Arg Leu Ala Gln Gln Glu Lys Glu Asp Ala Lys
995 1000 1005

Arg Ile Lys Ser Gln Arg Leu Asn Arg Ala Val Thr Cys Met Leu
1010 1015 1020

Arg Lys Glu Lys Glu Ala Ala Ala Ser Glu Ile Glu Ala Val Ser
1025 1030 1035

Val Ala Met Glu Lys Glu Phe Glu Leu Leu Asp Lys Ala Lys Arg
1040 1045 1050

Lys Thr Gln Lys Arg Gly Ile Thr Asn Thr Leu Glu Glu Ser Ser
1055 1060 1065

Ser Leu Lys Arg Lys Arg Leu Ser Asp Ser Lys Arg Lys Asn Thr
1070 1075 1080

Cys Gly Gly Phe Leu Gly Glu Thr Cys Leu Ser Glu Ser Ser Asp
1085 1090 1095

Gly Ser Ser Ser Glu His Ala Glu Ser Ser Ser Leu Met Asn Val
1100 1105 1110

Gln Arg Arg Thr Ala Ala Lys Glu Pro Lys Thr Ser Ala Ser Asp
1115 1120 1125

Ser Gln Asn Ser Val Lys Glu Ala Pro Val Lys Asn Gly Gly Ala
1130 1135 1140

Thr Thr Ser Ser Ser Ser Asp Ser Asp Asp Asp Gly Gly Lys Glu
1145 1150 1155

Lys Met Val Leu Val Thr Ala Arg Ser Val Phe Gly Lys Lys Arg

1160 1165 1170

Arg Lys Leu Arg Arg Ala Arg Gly Arg Lys Arg Lys Thr
1175 1180 1185

<210> 2567
<211> 84
<212> PRT
<213> Homo sapiens

<400> 2567

Met Pro Leu Ala Lys Asp Leu Leu His Pro Ser Pro Glu Glu Glu Lys
1 5 10 15

Arg Lys His Lys Lys Lys Arg Leu Val Gln Ser Pro Asn Ser Tyr Phe
20 25 30

Met Asp Val Lys Cys Pro Gly Cys Tyr Lys Ile Thr Thr Val Phe Ser
35 40 45

His Ala Gln Thr Val Val Leu Cys Val Gly Cys Ser Thr Val Leu Cys
50 55 60

Gln Pro Thr Gly Gly Lys Ala Arg Leu Thr Glu Gly Cys Ser Phe Arg
65 70 75 80

Arg Lys Gln His

<210> 2568
<211> 691
<212> PRT
<213> Homo sapiens

<400> 2568

Met Asp Gly Cys Lys Lys Glu Leu Pro Arg Leu Gln Glu Pro Glu Glu
1 5 10 15

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

Ser Gly Ser Ser Val Ala Arg Arg Ala Pro Lys Arg Gln Ala Ser Cys
35 40 45

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

Ala Arg Arg Ala Pro Lys Arg Gln Ala Ser Ser Val Val Val Ile Asp
65 70 75 80

Ser Asp Ser Asp Glu Glu Cys His Thr His Glu Glu Lys Lys Ala Lys
85 90 95

Leu Leu Glu Ile Asn Ser Asp Asp Glu Ser Pro Glu Cys Cys His Val
100 105 110

Lys Pro Ala Ile Gln Glu Pro Pro Ile Val Ile Ser Asp Asp Asp Asn
115 120 125

Asp Asp Asp Asn Gly Asn Asp Leu Glu Val Pro Asp Asp Asn Ser Asp
130 135 140

Asp Ser Glu Ala Pro Asp Asp Asn Ser Asp Asp Ser Glu Ala Pro Asp
145 150 155 160

Asp Asn Ser Asp Asp Ser Glu Ala Pro Asp Asp Asn Ser Asp Asp Ser
165 170 175

Glu Ala Pro Asp Asp Asn Ser Asp Asp Ser Asp Val Pro Asp Asp Asn
180 185 190

Ser Asp Asp Ser Ser Asp Asp Asn Ser Asp Asp Ser Ser Asp Asp Asn
195 200 205

Ser Asp Asp Ser Asp Val Pro Asp Asp Lys Ser Asp Asp Ser Asp Val
210 215 220

Pro Asp Asp Ser Ser Asp Asp Ser Asp Val Pro Asp Asp Ser Ser Asp
225 230 235 240

Asp Ser Glu Ala Pro Asp Asp Ser Ser Asp Asp Ser Glu Ala Pro Asp
245 250 255

Asp Ser Ser Asp Asp Ser Glu Ala Pro Asp Asp Ser Ser Asp Asp Ser
260 265 270

Glu Ala Pro Asp Asp Ser Ser Asp Asp Ser Glu Ala Ser Asp Asp Ser
275 280 285

Ser Asp Asp Ser Glu Ala Ser Asp Asp Ser Ser Asp Asp Ser Glu Ala
290 295 300

Pro Asp Asp Lys Ser Asp Asp Ser Asp Val Pro Glu Asp Lys Ser Asp

305 310 315 320

Asp Ser Asp Val Pro Asp Asp Asn Ser Asp Asp Leu Glu Val Pro Val
325 330 335

Pro Ala Glu Asp Leu Cys Asn Glu Gly Gln Ile Ala Ser Asp Glu Glu
340 345 350

Glu Leu Val Glu Ala Ala Ala Ala Val Ser Gln His Asp Ser Ser Asp
355 360 365

Asp Ala Gly Glu Gln Asp Leu Gly Glu Asn Leu Ser Lys Pro Pro Ser
370 375 380

Asp Pro Glu Ala Asn Pro Glu Val Ser Glu Arg Lys Leu Pro Thr Glu
385 390 395 400

Glu Glu Pro Ala Pro Val Val Glu Gln Ser Gly Lys Arg Lys Ser Lys
405 410 415

Thr Lys Thr Ile Val Glu Pro Pro Arg Lys Arg Gln Thr Lys Thr Lys
420 425 430

Asn Ile Val Glu Pro Pro Arg Lys Arg Gln Thr Lys Thr Lys Asn Ile
435 440 445

Val Glu Pro Leu Arg Lys Arg Lys Ala Lys Thr Lys Asn Val Ser Val
450 455 460

Thr Pro Gly His Lys Lys Arg Gly Pro Ser Lys Lys Lys Pro Gly Ala
465 470 475 480

Ala Lys Val Glu Lys Arg Lys Thr Arg Thr Pro Lys Cys Lys Val Pro
485 490 495

Gly Cys Phe Leu Gln Asp Leu Glu Lys Ser Lys Lys Tyr Ser Gly Lys
500 505 510

Asn Leu Lys Arg Asn Lys Asp Glu Leu Val Gln Arg Ile Tyr Asp Leu
515 520 525

Phe Asn Arg Ser Val Cys Asp Lys Lys Leu Pro Glu Lys Leu Arg Ile
530 535 540

Gly Trp Asn Asn Lys Met Val Lys Thr Ala Gly Leu Cys Ser Thr Gly
545 550 555 560

Glu Met Trp Tyr Pro Lys Trp Arg Arg Phe Ala Lys Ile Gln Ile Gly
565 570 575

Leu Lys Val Cys Asp Ser Ala Asp Arg Ile Arg Asp Thr Leu Ile His
580 585 590

Glu Met Cys His Ala Ala Ser Trp Leu Ile Asp Gly Ile His Asp Ser
595 600 605

His Gly Asp Ala Trp Lys Tyr Tyr Ala Arg Lys Ser Asn Arg Ile His
610 615 620

Pro Glu Leu Pro Arg Val Thr Arg Cys His Asn Tyr Lys Ile Asn Tyr
625 630 635 640

Lys Val His Tyr Glu Cys Thr Gly Cys Lys Thr Arg Ile Gly Cys Tyr
645 650 655

Thr Lys Ser Leu Asp Thr Ser Arg Phe Ile Cys Ala Lys Cys Lys Gly
660 665 670

Ser Leu Val Met Val Pro Leu Thr Gln Lys Asp Gly Thr Arg Ile Val
675 680 685

Pro His Val
690

<210> 2569
<211> 101
<212> PRT
<213> Homo sapiens

<400> 2569

Met Ser Asp Gln Glu Ala Lys Pro Ser Thr Glu Asp Leu Gly Asp Lys
1 5 10 15

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

Glu Ile His Phe Lys Val Lys Met Thr Thr His Leu Lys Lys Leu Lys
35 40 45

Glu Ser Tyr Cys Gln Arg Gln Gly Val Pro Met Asn Ser Leu Arg Phe
50 55 60

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

Gly Met Glu Glu Glu Asp Val Ile Glu Val Tyr Gln Glu Gln Thr Gly
85 90 95

Gly His Ser Thr Val
100

<210> 2570
<211> 93
<212> PRT
<213> Homo sapiens

<400> 2570

Met Ser Gly Leu Arg Val Tyr Ser Thr Ser Val Thr Gly Ser Arg Glu
1 5 10 15

Ile Lys Ser Gln Gln Ser Glu Val Thr Arg Ile Leu Asp Gly Lys Arg
20 25 30

Ile Gln Tyr Gln Leu Val Asp Ile Ser Gln Asp Asn Ala Leu Arg Asp
35 40 45

Glu Met Arg Ala Leu Ala Gly Asn Pro Lys Ala Thr Pro Pro Gln Ile
50 55 60

Val Asn Gly Asp Gln Tyr Cys Gly Asp Tyr Glu Leu Phe Val Glu Ala
65 70 75 80

Val Glu Gln Asn Thr Leu Gln Glu Phe Leu Lys Leu Ala
85 90

<210> 2571
<211> 666
<212> PRT
<213> Homo sapiens

<400> 2571

Met Thr Pro Pro Pro Pro Gly Arg Ala Ala Pro Ser Ala Pro Arg Ala
1 5 10 15

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

Leu Leu Leu Leu Leu Trp Ala Ala Ala Ala Ser Ala Gln Gly His Leu
35 40 45

Arg Ser Gly Pro Arg Ile Phe Ala Val Trp Lys Gly His Val Gly Gln
50 55 60

Asp Arg Val Asp Phe Gly Gln Thr Glu Pro His Thr Val Leu Phe His
65 70 75 80

Glu Pro Gly Ser Ser Ser Val Trp Val Gly Gly Arg Gly Lys Val Tyr
85 90 95

Leu Phe Asp Phe Pro Glu Gly Lys Asn Ala Ser Val Arg Thr Val Asn
100 105 110

Ile Gly Ser Thr Lys Gly Ser Cys Leu Asp Lys Arg Asp Cys Glu Asn
115 120 125

Tyr Ile Thr Leu Leu Glu Arg Arg Ser Glu Gly Leu Leu Ala Cys Gly
130 135 140

Thr Asn Ala Arg His Pro Ser Cys Trp Asn Leu Val Asn Gly Thr Val
145 150 155 160

Val Pro Leu Gly Glu Met Arg Gly Tyr Ala Pro Phe Ser Pro Asp Glu
165 170 175

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

Lys Gln Glu Tyr Asn Gly Lys Ile Pro Arg Phe Arg Arg Ile Arg Gly
195 200 205

Glu Ser Glu Leu Tyr Thr Ser Asp Thr Val Met Gln Asn Pro Gln Phe
210 215 220

Ile Lys Ala Thr Ile Val His Gln Asp Gln Ala Tyr Asp Asp Lys Ile
225 230 235 240

Tyr Tyr Phe Phe Arg Glu Asp Asn Pro Asp Lys Asn Pro Glu Ala Pro
245 250 255

Leu Asn Val Ser Arg Val Ala Gln Leu Cys Arg Gly Asp Gln Gly Gly
260 265 270

Glu Ser Ser Leu Ser Val Ser Lys Trp Asn Thr Phe Leu Lys Ala Met
275 280 285

Leu Val Cys Ser Asp Ala Ala Thr Asn Lys Asn Phe Asn Arg Leu Gln
290 295 300

Asp Val Phe Leu Leu Pro Asp Pro Ser Gly Gln Trp Arg Asp Thr Arg
305 310 315 320

Val Tyr Gly Val Phe Ser Asn Pro Trp Asn Tyr Ser Ala Val Cys Val
325 330 335

Tyr Ser Leu Gly Asp Ile Asp Lys Val Phe Arg Thr Ser Ser Leu Lys
340 345 350

Gly Tyr His Ser Ser Leu Pro Asn Pro Arg Pro Gly Lys Cys Leu Pro
355 360 365

Asp Gln Gln Pro Ile Pro Thr Glu Thr Phe Gln Val Ala Asp Arg His
370 375 380

Pro Glu Val Ala Gln Arg Val Glu Pro Met Gly Pro Leu Lys Thr Pro
385 390 395 400

Leu Phe His Ser Lys Tyr His Tyr Gln Lys Val Ala Val His Arg Met
405 410 415

Gln Ala Ser His Gly Glu Thr Phe His Val Leu Tyr Leu Thr Thr Asp
420 425 430

Arg Gly Thr Ile His Lys Val Val Glu Pro Gly Glu Gln Glu His Ser
435 440 445

Phe Ala Phe Asn Ile Met Glu Ile Gln Pro Phe Arg Arg Ala Ala Ala
450 455 460

Ile Gln Thr Met Ser Leu Asp Ala Glu Arg Arg Lys Leu Tyr Val Ser
465 470 475 480

Ser Gln Trp Glu Val Ser Gln Val Pro Leu Asp Leu Cys Glu Val Tyr
485 490 495

Gly Gly Gly Cys His Gly Cys Leu Met Ser Arg Asp Pro Tyr Cys Gly
500 505 510

Trp Asp Gln Gly Arg Cys Ile Ser Ile Tyr Ser Ser Glu Arg Ser Val
515 520 525

Leu Gln Ser Ile Asn Pro Ala Glu Pro His Lys Glu Cys Pro Asn Pro

530 535 540

Lys Pro Asp Lys Ala Pro Leu Gln Lys Val Ser Leu Ala Pro Asn Ser
545 550 555 560

Arg Tyr Tyr Leu Ser Cys Pro Met Glu Ser Arg His Ala Thr Tyr Ser
565 570 575

Trp Arg His Lys Glu Asn Val Glu Gln Ser Cys Glu Pro Gly His Gln
580 585 590

Ser Pro Asn Cys Ile Leu Phe Ile Glu Asn Leu Thr Ala Gln Gln Tyr
595 600 605

Gly His Tyr Phe Cys Glu Ala Gln Glu Gly Ser Tyr Phe Arg Glu Ala
610 615 620

Gln His Trp Gln Leu Leu Pro Glu Asp Gly Ile Met Ala Glu His Leu
625 630 635 640

Leu Gly His Ala Cys Ala Leu Ala Ala Ser Leu Trp Leu Gly Val Leu
645 650 655

Pro Thr Leu Thr Leu Gly Leu Leu Val His
660 665

<210> 2572
<211> 162
<212> PRT
<213> Homo sapiens

<400> 2572

Met Arg Ser Ser Pro Gly Asn Met Glu Arg Ile Val Ile Cys Leu Met
1 5 10 15

Val Ile Phe Leu Gly Thr Leu Val His Lys Ser Ser Ser Gln Gly Gln
20 25 30

Asp Arg His Met Ile Arg Met Arg Gln Leu Ile Asp Ile Val Asp Gln
35 40 45

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

Glu Asp Val Glu Thr Asn Cys Glu Trp Ser Ala Phe Ser Cys Phe Gln
65 70 75 80

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

Asn Val Ser Ile Lys Lys Leu Lys Arg Lys Pro Pro Ser Thr Asn Ala
100 105 110

Gly Arg Arg Gln Lys His Arg Leu Thr Cys Pro Ser Cys Asp Ser Tyr
115 120 125

Glu Lys Lys Pro Pro Lys Glu Phe Leu Glu Arg Phe Lys Ser Leu Leu
130 135 140

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

Asp Ser

<210> 2573
<211> 1050
<212> PRT
<213> Homo sapiens

<400> 2573

Met Leu Cys Trp Gly Tyr Trp Ser Leu Gly Gln Pro Gly Ile Ser Thr
1 5 10 15

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

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

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

Gln Leu Gly His Glu Arg Glu Gly Asn Lys Pro Glu Gln Ile Gly Ala
65 70 75 80

Leu Ala Asp Gln His Ile Ile His Val Ala Cys Gly Glu Ser His Ser
85 90 95

Leu Ala Leu Ser Asp Arg Gly Gln Leu Phe Ser Trp Gly Ala Gly Ser
100 105 110

Asp Gly Gln Leu Gly Leu Met Thr Thr Glu Asp Ser Val Ala Val Pro

115 120 125

Arg Leu Ile Gln Lys Leu Asn Gln Gln Thr Ile Leu Gln Val Ser Cys
130 135 140

Gly Asn Trp His Cys Leu Ala Leu Ala Ala Asp Gly Gln Phe Phe Thr
145 150 155 160

Trp Gly Lys Asn Ser His Gly Gln Leu Gly Leu Gly Lys Glu Phe Pro
165 170 175

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

Ala Gln Val Ala Ala Gly Gly Ala His Ser Phe Ala Leu Ser Leu Ser
195 200 205

Gly Ala Val Phe Gly Trp Gly Met Asn Asn Ala Gly Gln Leu Gly Leu
210 215 220

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

Thr Gln Lys Val Val Tyr Ile Ser Cys Gly Glu Glu His Thr Ala Val
245 250 255

Leu Thr Lys Ser Gly Gly Val Phe Thr Phe Gly Ala Gly Ser Cys Gly
260 265 270

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

Leu Glu Leu Met Gly Ser Glu Val Thr Gln Ile Ala Cys Gly Arg Gln
290 295 300

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

Cys Gly Ala Arg Gly Gln Leu Gly Thr Gly His Thr Cys Asn Val Lys
325 330 335

Cys Pro Ser Pro Val Lys Gly Tyr Trp Ala Ala His Ser Gly Gln Leu
340 345 350

Ser Ala Arg Ala Asp Arg Phe Lys Tyr His Ile Val Lys Gln Ile Phe
355 360 365

Ser Gly Gly Asp Gln Thr Phe Val Leu Cys Ser Lys Tyr Glu Asn Tyr
370 375 380

Ser Pro Ala Val Asp Phe Arg Thr Met Asn Gln Ala His Tyr Thr Ser
385 390 395 400

Leu Ile Asn Asp Glu Thr Ile Ala Val Trp Arg Gln Lys Leu Ser Glu
405 410 415

His Asn Asn Ala Asn Thr Ile Asn Gly Val Val Gln Ile Leu Ser Ser
420 425 430

Ala Ala Cys Trp Asn Gly Ser Phe Leu Glu Lys Lys Ile Asp Glu His
435 440 445

Phe Lys Thr Ser Pro Lys Ile Pro Gly Ile Asp Leu Asn Ser Thr Arg
450 455 460

Val Leu Phe Glu Lys Leu Met Asn Ser Gln His Ser Met Ile Leu Glu
465 470 475 480

Gln Ile Leu Asn Ser Phe Glu Ser Cys Leu Ile Pro Gln Leu Ser Ser
485 490 495

Ser Pro Pro Asp Val Glu Ala Met Arg Ile Tyr Leu Ile Leu Pro Glu
500 505 510

Phe Pro Leu Leu Gln Asp Ser Lys Tyr Tyr Ile Thr Leu Thr Ile Pro
515 520 525

Leu Ala Met Ala Ile Leu Arg Leu Asp Thr Asn Pro Ser Lys Val Leu
530 535 540

Asp Asn Trp Trp Ser Gln Val Cys Pro Lys Tyr Phe Met Lys Leu Val
545 550 555 560

Asn Leu Tyr Lys Gly Ala Val Leu Tyr Leu Leu Arg Gly Arg Lys Thr
565 570 575

Phe Leu Ile Pro Val Leu Phe Asn Asn Tyr Ile Thr Ala Ala Leu Lys
580 585 590

Leu Leu Glu Lys Leu Tyr Lys Val Asn Leu Lys Val Lys His Val Glu
595 600 605

```
Tyr Asp Thr Phe Tyr Ile Pro Glu Ile Ser Asn Leu Val Asp Ile Gln
    610                 615                 620

Glu Asp Tyr Leu Met Trp Phe Leu His Gln Ala Gly Met Lys Ala Arg
625                 630                 635                 640

Pro Ser Ile Ile Gln Asp Thr Val Thr Leu Cys Ser Tyr Pro Phe Ile
                645                 650                 655

Phe Asp Ala Gln Ala Lys Thr Lys Met Leu Gln Thr Asp Ala Glu Leu
            660                 665                 670

Gln Met Gln Val Ala Val Asn Gly Ala Asn Leu Gln Asn Val Phe Met
        675                 680                 685

Leu Leu Thr Leu Glu Pro Leu Leu Ala Arg Ser Pro Phe Leu Val Leu
    690                 695                 700

His Val Arg Arg Asn Asn Leu Val Gly Asp Ala Leu Arg Glu Leu Ser
705                 710                 715                 720

Ile His Ser Asp Ile Asp Leu Lys Lys Pro Leu Lys Val Ile Phe Asp
                725                 730                 735

Gly Glu Glu Ala Val Asp Ala Gly Gly Val Thr Lys Glu Phe Phe Leu
            740                 745                 750

Leu Leu Leu Lys Glu Leu Leu Asn Pro Ile Tyr Gly Met Phe Thr Tyr
        755                 760                 765

Tyr Gln Asp Ser Asn Leu Leu Trp Phe Ser Asp Thr Cys Phe Val Glu
    770                 775                 780

His Asn Trp Phe His Leu Ile Gly Ile Thr Cys Gly Leu Ala Ile Tyr
785                 790                 795                 800

Asn Ser Thr Val Val Asp Leu His Phe Pro Leu Ala Leu Tyr Lys Lys
                805                 810                 815

Leu Leu Asn Val Lys Pro Gly Leu Glu Asp Leu Lys Glu Leu Ser Pro
            820                 825                 830

Thr Glu Gly Arg Ser Leu Gln Glu Leu Leu Asp Tyr Pro Gly Glu Asp
        835                 840                 845
```

```
Val Glu Glu Thr Phe Cys Leu Asn Phe Thr Ile Cys Arg Glu Ser Tyr
    850                 855                 860

Gly Val Ile Glu Gln Lys Lys Leu Ile Pro Gly Gly Asp Asn Val Thr
865                 870                 875                 880

Val Cys Lys Asp Asn Arg Gln Glu Phe Val Asp Ala Tyr Val Asn Tyr
                885                 890                 895

Val Phe Gln Ile Ser Val His Glu Trp Tyr Thr Ala Phe Ser Ser Gly
            900                 905                 910

Phe Leu Lys Val Cys Gly Gly Lys Val Leu Glu Leu Phe Gln Pro Ser
        915                 920                 925

Glu Leu Arg Ala Met Met Val Gly Asn Ser Asn Tyr Asn Trp Glu Glu
    930                 935                 940

Leu Glu Glu Thr Ala Ile Tyr Lys Gly Asp Tyr Ser Ala Thr His Pro
945                 950                 955                 960

Thr Val Lys Leu Phe Trp Glu Thr Phe His Glu Phe Pro Leu Glu Lys
                965                 970                 975

Lys Lys Lys Phe Leu Leu Phe Leu Thr Gly Ser Asp Arg Ile Pro Ile
            980                 985                 990

Tyr Gly Met Ala Ser Leu Gln Ile  Val Ile Gln Ser Thr  Ala Ser Gly
        995                 1000                1005

Glu Glu  Tyr Leu Pro Val Ala  His Thr Cys Tyr Asn  Leu Leu Asp
    1010                1015                1020

Leu Pro  Lys Tyr Ser Ser Lys  Glu Ile Leu Ser Ala  Arg Leu Thr
    1025                1030                1035

Gln Ala  Leu Asp Asn Tyr Glu  Gly Phe Ser Leu Ala
    1040                1045                1050
```

<210> 2574
<211> 369
<212> PRT
<213> Homo sapiens

<400> 2574

```
Met Arg Ala Cys Ile Ser Leu Val Leu Ala Val Leu Cys Gly Leu Ala
1               5                   10                  15
```

```
Trp Ala Glu Asp His Lys Glu Ser Glu Pro Leu Pro Gln Leu Glu Glu
            20                  25                  30

Glu Thr Glu Glu Ala Leu Ala Ser Asn Leu Tyr Ser Ala Pro Thr Ser
        35                  40                  45

Cys Gln Gly Arg Cys Tyr Glu Ala Phe Asp Lys His His Gln Cys His
    50                  55                  60

Cys Asn Ala Arg Cys Gln Glu Phe Gly Asn Cys Cys Lys Asp Phe Glu
65                  70                  75                  80

Ser Leu Cys Ser Asp His Glu Val Ser His Ser Ser Asp Ala Ile Thr
                85                  90                  95

Lys Glu Glu Ile Gln Ser Ile Ser Glu Lys Ile Tyr Arg Ala Asp Thr
            100                 105                 110

Asn Lys Ala Gln Lys Glu Asp Ile Val Leu Asn Ser Gln Asn Cys Ile
        115                 120                 125

Ser Pro Ser Glu Thr Arg Asn Gln Val Asp Arg Cys Pro Lys Pro Leu
    130                 135                 140

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

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

His Phe Ser Ala Gln Glu Leu Ala Glu Gln Asp Ala Phe Leu Arg Glu
            180                 185                 190

Ile Met Lys Thr Ala Val Met Lys Glu Leu Tyr Ser Phe Leu His His
        195                 200                 205

Gln Asn Arg Tyr Gly Ser Glu Gln Glu Phe Val Asp Asp Leu Lys Asn
    210                 215                 220

Met Trp Phe Gly Leu Tyr Ser Arg Gly Asn Glu Glu Gly Asp Ser Ser
225                 230                 235                 240

Gly Phe Glu His Val Phe Ser Gly Glu Val Lys Lys Gly Lys Val Thr
                245                 250                 255
```

Gly Phe His Asn Trp Ile Arg Phe Tyr Leu Glu Glu Lys Glu Gly Leu
260 265 270

Val Asp Tyr Tyr Ser His Ile Tyr Asp Gly Pro Trp Asp Ser Tyr Pro
275 280 285

Asp Val Leu Ala Met Gln Phe Asn Trp Asp Gly Tyr Tyr Lys Glu Val
290 295 300

Gly Ser Ala Phe Ile Gly Ser Ser Pro Glu Phe Glu Phe Ala Leu Tyr
305 310 315 320

Ser Leu Cys Phe Ile Ala Arg Pro Gly Lys Val Cys Gln Leu Ser Leu
325 330 335

Gly Gly Tyr Pro Leu Ala Val Arg Thr Tyr Thr Trp Asp Lys Ser Thr
340 345 350

Tyr Gly Asn Gly Lys Lys Tyr Ile Ala Thr Ala Tyr Ile Val Ser Ser
355 360 365

Thr

<210> 2575
<211> 90
<212> PRT
<213> Homo sapiens

<400> 2575

Met Asp Pro Leu Arg Ala Gln Gln Leu Ala Ala Glu Leu Glu Val Glu
1 5 10 15

Met Met Ala Asp Met Tyr Asn Arg Met Thr Ser Ala Cys His Arg Lys
20 25 30

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

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

Met Gly Lys Lys Leu Thr Glu Leu Ser Met Gln Asp Glu Glu Leu Met
65 70 75 80

Lys Arg Val Gln Gln Ser Ser Gly Pro Ala

85 90

<210> 2576
<211> 426
<212> PRT
<213> Homo sapiens

<400> 2576

Met Ala Asn Asp Ser Gly Gly Pro Gly Gly Pro Ser Pro Ser Glu Arg
1 5 10 15

Asp Arg Gln Tyr Cys Glu Leu Cys Gly Lys Met Glu Asn Leu Leu Arg
20 25 30

Cys Ser Arg Cys Arg Ser Ser Phe Tyr Cys Cys Lys Glu His Gln Arg
35 40 45

Gln Asp Trp Lys Lys His Lys Leu Val Cys Gln Gly Ser Glu Gly Ala
50 55 60

Leu Gly His Gly Val Gly Pro His Gln His Ser Gly Pro Ala Pro Pro
65 70 75 80

Ala Ala Val Pro Pro Pro Arg Ala Gly Ala Arg Glu Pro Arg Lys Ala
85 90 95

Ala Ala Arg Arg Asp Asn Ala Ser Gly Asp Ala Ala Lys Gly Lys Val
100 105 110

Lys Ala Lys Pro Pro Ala Asp Pro Ala Ala Ala Ala Ser Pro Cys Arg
115 120 125

Ala Ala Ala Gly Gly Gln Gly Ser Ala Val Ala Ala Glu Ala Glu Pro
130 135 140

Gly Lys Glu Glu Pro Pro Ala Arg Ser Ser Leu Phe Gln Glu Lys Ala
145 150 155 160

Asn Leu Tyr Pro Pro Ser Asn Thr Pro Gly Asp Ala Leu Ser Pro Gly
165 170 175

Gly Gly Leu Arg Pro Asn Gly Gln Thr Lys Pro Leu Pro Ala Leu Lys
180 185 190

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

```
Val Val Asp Asp Phe Leu Gly Lys Glu Thr Gly Gln Gln Ile Gly Asp
    210                 215                 220

Glu Val Arg Ala Leu His Asp Thr Gly Lys Phe Thr Asp Gly Gln Leu
225                 230                 235                 240

Val Ser Gln Lys Ser Asp Ser Ser Lys Asp Ile Arg Gly Asp Lys Ile
                245                 250                 255

Thr Trp Ile Glu Gly Lys Glu Pro Gly Cys Glu Thr Ile Gly Leu Leu
            260                 265                 270

Met Ser Ser Met Asp Asp Leu Ile Arg His Cys Asn Gly Lys Leu Gly
        275                 280                 285

Ser Tyr Lys Ile Asn Gly Arg Thr Lys Ala Met Val Ala Cys Tyr Pro
    290                 295                 300

Gly Asn Gly Thr Gly Tyr Val Arg His Val Asp Asn Pro Asn Gly Asp
305                 310                 315                 320

Gly Arg Cys Val Thr Cys Ile Tyr Tyr Leu Asn Lys Asp Trp Asp Ala
                325                 330                 335

Lys Val Ser Gly Gly Ile Leu Arg Ile Phe Pro Glu Gly Lys Ala Gln
            340                 345                 350

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

Asp Arg Arg Asn Pro His Glu Val Gln Pro Ala Tyr Ala Thr Arg Tyr
    370                 375                 380

Ala Ile Thr Val Trp Tyr Phe Asp Ala Asp Glu Arg Ala Arg Ala Lys
385                 390                 395                 400

Val Lys Tyr Leu Thr Gly Glu Lys Gly Val Arg Val Glu Leu Asn Lys
                405                 410                 415

Pro Ser Asp Ser Val Gly Lys Asp Val Phe
            420                 425
```

<210> 2577
<211> 346
<212> PRT
<213> Homo sapiens

<400> 2577

```
Met Glu Ser Val Ser Cys Ser Ala Ala Ala Val Arg Thr Gly Asp Met
1               5                  10                  15

Glu Ser Gln Arg Asp Leu Ser Leu Val Pro Glu Arg Leu Gln Arg Arg
            20                  25                  30

Glu Gln Glu Arg Gln Leu Glu Val Glu Arg Arg Lys Gln Lys Arg Gln
        35                  40                  45

Asn Gln Glu Val Glu Lys Glu Asn Ser His Phe Phe Val Ala Thr Phe
    50                  55                  60

Ala Arg Glu Arg Ala Ala Val Glu Glu Leu Leu Glu Arg Ala Glu Ser
65                  70                  75                  80

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

Leu Ile Asn Asp Ser Val Phe Phe Leu Ala Ala Tyr Asp Leu Arg Gln
            100                 105                 110

Gly Gln Glu Ala Leu Ala Arg Leu Gln Ala Ala Leu Ala Glu Arg Arg
        115                 120                 125

Arg Gly Leu Gln Pro Lys Lys Arg Phe Ala Phe Lys Thr Arg Gly Lys
    130                 135                 140

Asp Ala Ala Ser Ser Thr Lys Val Asp Ala Ala Pro Gly Ile Pro Pro
145                 150                 155                 160

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

Asp Leu Gly Pro Ser Trp Val Cys Gly Phe Ser Asn Leu Glu Ser Gln
            180                 185                 190

Val Leu Glu Lys Arg Ala Ser Glu Leu His Gln Arg Asp Val Leu Leu
        195                 200                 205

Thr Glu Leu Ser Asn Cys Thr Val Arg Leu Tyr Gly Asn Pro Asn Thr
    210                 215                 220

Leu Arg Leu Thr Lys Ala His Ser Cys Lys Leu Leu Cys Gly Pro Val
225                 230                 235                 240
```

Ser Thr Ser Val Phe Leu Glu Asp Cys Ser Asp Cys Val Leu Ala Val
245 250 255

Ala Cys Gln Gln Leu Arg Ile His Ser Thr Lys Asp Thr Arg Ile Phe
260 265 270

Leu Gln Val Thr Ser Arg Ala Ile Val Glu Asp Cys Ser Gly Ile Gln
275 280 285

Phe Ala Pro Tyr Thr Trp Ser Tyr Pro Glu Ile Asp Lys Asp Phe Glu
290 295 300

Ser Ser Gly Leu Asp Arg Ser Lys Asn Asn Trp Asn Asp Val Asp Asp
305 310 315 320

Phe Asn Trp Leu Ala Arg Asp Met Ala Ser Pro Asn Trp Ser Ile Leu
325 330 335

Pro Glu Glu Glu Arg Asn Ile Gln Trp Asp
340 345

<210> 2578
<211> 247
<212> PRT
<213> Homo sapiens

<400> 2578

Met Glu Phe Pro Lys Met Leu Thr Arg Lys Ile Lys Leu Trp Asp Ile
1 5 10 15

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

Thr Thr Val Thr Glu Cys Leu His Thr Phe Cys Arg Ser Cys Leu Val
35 40 45

Lys Tyr Leu Glu Glu Asn Asn Thr Cys Pro Thr Cys Arg Ile Val Ile
50 55 60

His Gln Ser His Pro Leu Gln Tyr Ile Gly His Asp Arg Thr Met Gln
65 70 75 80

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

```
Lys Gln Arg Glu Phe Tyr His Lys Leu Gly Met Glu Val Pro Gly Asp
            100                 105                 110

Ile Lys Gly Glu Thr Cys Ser Ala Lys Gln His Leu Asp Ser His Arg
        115                 120                 125

Asn Gly Glu Thr Lys Ala Asp Asp Ser Ser Asn Lys Glu Ala Ala Glu
    130                 135                 140

Glu Lys Pro Glu Glu Asp Asn Asp Tyr His Arg Ser Asp Glu Gln Val
145                 150                 155                 160

Ser Ile Cys Leu Glu Cys Asn Ser Ser Lys Leu Arg Gly Leu Lys Arg
                165                 170                 175

Lys Trp Ile Arg Cys Ser Ala Gln Ala Thr Val Leu His Leu Lys Lys
            180                 185                 190

Phe Ile Ala Lys Lys Leu Asn Leu Ser Ser Phe Asn Glu Leu Asp Ile
        195                 200                 205

Leu Cys Asn Glu Glu Ile Leu Gly Lys Asp His Thr Leu Lys Phe Val
    210                 215                 220

Val Val Thr Arg Trp Arg Phe Lys Lys Ala Pro Leu Leu Leu His Tyr
225                 230                 235                 240

Arg Pro Lys Met Asp Leu Leu
                245
```

<210> 2579
<211> 360
<212> PRT
<213> Homo sapiens

<400> 2579

```
Met Ala Ser Ala Thr Ala Pro Ala Ala Ala Val Pro Thr Leu Ala Ser
1               5                   10                  15

Pro Leu Glu Gln Leu Arg His Leu Ala Glu Glu Leu Arg Leu Leu Leu
            20                  25                  30

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

Arg Glu Met Phe Trp Arg Arg Leu Asn Glu Ala Ala Val Thr Val Ser
    50                  55                  60
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Arg Glu Ala Thr Thr Leu Thr Ile Val Phe Ser Gln Leu Pro Leu Pro
65                  70                  75                  80

Ser Pro Gln Glu Thr Gln Lys Phe Cys Glu Gln Val His Ala Ala Ile
                85                  90                  95

Lys Ala Phe Ile Ala Val Tyr Tyr Leu Leu Pro Lys Asp Gln Gly Ile
            100                 105                 110

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

Met Ala Gln Leu Met Glu Val Leu Ser Val Thr Pro Thr Gln Ser Pro
    130                 135                 140

Glu Asn Asn Asp Leu Ile Ser Tyr Asn Ser Val Trp Val Ala Cys Gln
145                 150                 155                 160

Gln Met Pro Gln Ile Pro Arg Asp Asn Lys Ala Ala Ala Leu Leu Met
                165                 170                 175

Leu Thr Lys Asn Val Asp Phe Val Lys Asp Ala His Glu Glu Met Glu
            180                 185                 190

Gln Ala Val Glu Glu Cys Asp Pro Tyr Ser Gly Leu Leu Asn Asp Thr
        195                 200                 205

Glu Glu Asn Asn Ser Asp Asn His Asn His Glu Asp Asp Val Leu Gly
    210                 215                 220

Phe Pro Ser Asn Gln Asp Leu Tyr Trp Ser Glu Asp Asp Gln Glu Leu
225                 230                 235                 240

Ile Ile Pro Cys Leu Ala Leu Val Arg Ala Ser Lys Ala Cys Leu Lys
                245                 250                 255

Lys Ile Arg Met Leu Val Ala Glu Asn Gly Lys Lys Asp Gln Val Ala
            260                 265                 270

Gln Met Ala Asp Ile Val Asp Ile Ser Asp Glu Ile Ser Pro Ser Val
        275                 280                 285

Asp Asp Leu Ala Leu Ser Ile Tyr Pro Pro Met Cys His Leu Thr Val
    290                 295                 300
```

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

Ile Thr Lys Ala Ser His Val Thr Pro Gln Pro Glu Asp Ser Trp Ile
325 330 335

Pro Leu Leu Ile Asn Ala Ile Asp His Cys Met Asn Arg Ile Lys Glu
340 345 350

Leu Thr Gln Ser Glu Leu Glu Leu
355 360

<210> 2580
<211> 412
<212> PRT
<213> Homo sapiens

<400> 2580

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

Asn Gln Leu Gln Asp Leu Cys Arg Leu Ala Lys Leu Ser Cys Pro Ala
20 25 30

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

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

Arg Gly Tyr Pro Asp Ser Glu Ser Thr Trp Glu Pro Arg Gln Asn Leu
65 70 75 80

Lys Cys Val Arg Ile Leu Lys Gln Phe His Lys Asp Leu Glu Arg Glu
85 90 95

Leu Leu Arg Arg His His Arg Ser Lys Thr Pro Arg His Leu Asp Pro
100 105 110

Ser Leu Ala Asn Tyr Leu Val Gln Lys Ala Lys Gln Arg Arg Ala Leu
115 120 125

Arg Arg Trp Glu Gln Glu Leu Asn Ala Lys Arg Ser His Leu Gly Arg
130 135 140

Ile Thr Val Glu Asn Glu Val Asp Leu Asp Gly Pro Pro Arg Ala Phe

```
145                 150                 155                 160

Val Tyr Ile Asn Glu Tyr Arg Val Gly Glu Gly Ile Thr Leu Asn Gln
                165                 170                 175

Val Ala Val Gly Cys Glu Cys Gln Asp Cys Leu Trp Ala Pro Thr Gly
            180                 185                 190

Gly Cys Cys Pro Gly Ala Ser Leu His Lys Phe Ala Tyr Asn Asp Gln
        195                 200                 205

Gly Gln Val Arg Leu Arg Ala Gly Leu Pro Ile Tyr Glu Cys Asn Ser
    210                 215                 220

Arg Cys Arg Cys Gly Tyr Asp Cys Pro Asn Arg Val Val Gln Lys Gly
225                 230                 235                 240

Ile Arg Tyr Asp Leu Cys Ile Phe Arg Thr Asp Asp Gly Arg Gly Trp
                245                 250                 255

Gly Val Arg Thr Leu Glu Lys Ile Arg Lys Asn Ser Phe Val Met Glu
            260                 265                 270

Tyr Val Gly Glu Ile Ile Thr Ser Glu Glu Ala Glu Arg Arg Gly Gln
        275                 280                 285

Ile Tyr Asp Arg Gln Gly Ala Thr Tyr Leu Phe Asp Leu Asp Tyr Val
    290                 295                 300

Glu Asp Val Tyr Thr Val Asp Ala Ala Tyr Tyr Gly Asn Ile Ser His
305                 310                 315                 320

Phe Val Asn His Ser Cys Asp Pro Asn Leu Gln Val Tyr Asn Val Phe
                325                 330                 335

Ile Asp Asn Leu Asp Glu Arg Leu Pro Arg Ile Ala Phe Phe Ala Thr
            340                 345                 350

Arg Thr Ile Arg Ala Gly Glu Glu Leu Thr Phe Asp Tyr Asn Met Gln
        355                 360                 365

Val Asp Pro Val Asp Met Glu Ser Thr Arg Met Asp Ser Asn Phe Gly
    370                 375                 380

Leu Ala Gly Leu Pro Gly Ser Pro Lys Lys Arg Val Arg Ile Glu Cys
385                 390                 395                 400
```

Lys Cys Gly Thr Glu Ser Cys Arg Lys Tyr Leu Phe
405 410

<210> 2581
<211> 110
<212> PRT
<213> Homo sapiens

<400> 2581

Met Val Tyr Glu Arg Ala Gly Glu Ala Val Pro Pro Arg Gly Leu Arg
1 5 10 15

Glu Lys Phe Pro Arg Ala Leu Phe Gly Trp Ala Gly Glu Arg Pro Ser
20 25 30

Ala Leu Cys Ala Ser Asn Pro Pro Gln Leu Ser Cys Ser Gly Arg Gly
35 40 45

Ala Arg Tyr Phe Arg Leu Gly Glu Val Leu Gly Thr Asp Val Gly Ser
50 55 60

Ser Val Gly Asp Phe Ser Gly Phe Trp Pro Phe Gln Thr Leu Val Ile
65 70 75 80

Val Phe Ser Val Gln Ser Ser Phe Gly Val Trp Gly Phe Pro Ser Ser
85 90 95

Cys Ala Arg His Arg Glu Ala Trp Pro Glu Gly Pro Val Ser
100 105 110

<210> 2582
<211> 471
<212> PRT
<213> Homo sapiens

<400> 2582

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

Ala Thr Gln Gly Glu Leu Val Arg Ser Leu Lys Ala Gly Asn Ala Ser
20 25 30

Lys Asp Glu Ile Asp Ser Ala Val Lys Met Leu Val Ser Leu Lys Met
35 40 45

Ser Tyr Lys Ala Ala Ala Gly Glu Asp Tyr Lys Ala Asp Cys Pro Pro

```
    50                  55                  60

Gly Asn Pro Ala Pro Thr Ser Asn His Gly Pro Asp Ala Thr Glu Ala
65                  70                  75                  80

Glu Glu Asp Phe Val Asp Pro Trp Thr Val Gln Thr Ser Ser Ala Lys
                85                  90                  95

Gly Ile Asp Tyr Asp Lys Leu Ile Val Arg Phe Gly Ser Ser Lys Ile
            100                 105                 110

Asp Lys Glu Leu Ile Asn Arg Ile Glu Arg Ala Thr Gly Gln Arg Pro
        115                 120                 125

His His Phe Leu Arg Arg Gly Ile Phe Phe Ser His Arg Asp Met Asn
    130                 135                 140

Gln Val Leu Asp Ala Tyr Glu Asn Lys Lys Pro Phe Tyr Leu Tyr Thr
145                 150                 155                 160

Gly Arg Gly Pro Ser Ser Glu Ala Met His Val Gly His Leu Ile Pro
                165                 170                 175

Phe Ile Phe Thr Lys Trp Leu Gln Asp Val Phe Asn Val Pro Leu Val
            180                 185                 190

Ile Gln Met Thr Asp Asp Glu Lys Tyr Leu Trp Lys Asp Leu Thr Leu
        195                 200                 205

Asp Gln Ala Tyr Gly Asp Ala Val Glu Asn Ala Lys Asp Ile Ile Ala
    210                 215                 220

Cys Gly Phe Asp Ile Asn Lys Thr Phe Ile Phe Ser Asp Leu Asp Tyr
225                 230                 235                 240

Met Gly Met Ser Ser Gly Phe Tyr Lys Asn Val Val Lys Ile Gln Lys
                245                 250                 255

His Val Thr Phe Asn Gln Val Lys Gly Ile Phe Gly Phe Thr Asp Ser
            260                 265                 270

Asp Cys Ile Gly Lys Ile Ser Phe Pro Ala Ile Gln Ala Ala Pro Ser
        275                 280                 285

Phe Ser Asn Ser Phe Pro Gln Ile Phe Arg Asp Arg Thr Asp Ile Gln
    290                 295                 300
```

```
Cys Leu Ile Pro Cys Ala Ile Asp Gln Asp Pro Tyr Phe Arg Met Thr
305                 310                 315                 320

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

Ser Thr Phe Phe Pro Ala Leu Gln Gly Ala Gln Thr Lys Met Ser Ala
            340                 345                 350

Ser Asp Pro Asn Ser Ser Ile Phe Leu Thr Asp Thr Ala Lys Gln Ile
        355                 360                 365

Lys Thr Lys Val Asn Lys His Ala Phe Ser Gly Gly Arg Asp Thr Ile
    370                 375                 380

Glu Glu His Arg Gln Phe Gly Gly Asn Cys Asp Val Asp Val Ser Phe
385                 390                 395                 400

Met Tyr Leu Thr Phe Phe Leu Glu Asp Asp Asp Lys Leu Glu Gln Ile
                405                 410                 415

Arg Lys Asp Tyr Thr Ser Gly Ala Met Leu Thr Gly Glu Leu Lys Lys
            420                 425                 430

Ala Leu Ile Glu Val Leu Gln Pro Leu Ile Ala Glu His Gln Ala Arg
        435                 440                 445

Arg Lys Glu Val Thr Asp Glu Ile Val Lys Glu Phe Met Thr Pro Arg
    450                 455                 460

Lys Leu Ser Phe Asp Phe Gln
465                 470


<210>  2583
<211>  392
<212>  PRT
<213>  Homo sapiens

<400>  2583

Met Gly Ser Leu Ser Thr Ala Asn Val Glu Phe Cys Leu Asp Val Phe
1               5                   10                  15

Lys Glu Leu Asn Ser Asn Asn Ile Gly Asp Asn Ile Phe Phe Ser Ser
            20                  25                  30
```

Leu Ser Leu Leu Tyr Ala Leu Ser Met Val Leu Leu Gly Ala Arg Gly
35 40 45

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

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

Gly Arg Ile His Ser Glu Phe Gly Val Glu Phe Ser Gln Ile Asn Gln
85 90 95

Pro Asp Ser Asn Cys Thr Leu Ser Ile Ala Asn Arg Leu Tyr Gly Thr
100 105 110

Lys Thr Met Ala Phe His Gln Gln Tyr Leu Ser Cys Ser Glu Lys Trp
115 120 125

Tyr Gln Ala Arg Leu Gln Thr Val Asp Phe Glu Gln Ser Thr Glu Glu
130 135 140

Thr Arg Lys Met Ile Asn Ala Trp Val Glu Asn Lys Thr Asn Gly Lys
145 150 155 160

Val Ala Asn Leu Phe Gly Lys Ser Thr Ile Asp Pro Ser Ser Val Met
165 170 175

Val Leu Val Asn Thr Ile Tyr Phe Lys Gly Gln Arg Gln Asn Lys Phe
180 185 190

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

Asn Val Thr Val Glu Met Met Tyr Gln Ile Gly Thr Phe Lys Leu Ala
210 215 220

Phe Val Lys Glu Pro Gln Met Gln Val Leu Glu Leu Pro Tyr Val Asn
225 230 235 240

Asn Lys Leu Ser Met Ile Ile Leu Leu Pro Val Gly Ile Ala Asn Leu
245 250 255

Lys Gln Ile Glu Lys Gln Leu Asn Ser Gly Thr Phe His Glu Trp Thr
260 265 270

Ser Ser Ser Asn Met Met Glu Arg Glu Val Glu Val His Leu Pro Arg

275 280 285

Phe Lys Leu Glu Ile Lys Tyr Glu Leu Asn Ser Leu Leu Lys Pro Leu
290 295 300

Gly Val Thr Asp Leu Phe Asn Gln Val Lys Ala Asp Leu Ser Gly Met
305 310 315 320

Ser Pro Thr Lys Gly Leu Tyr Leu Ser Lys Ala Ile His Lys Ser Tyr
325 330 335

Leu Asp Val Ser Glu Glu Gly Thr Glu Ala Ala Ala Ala Thr Gly Asp
340 345 350

Ser Ile Ala Val Lys Ser Leu Pro Met Arg Ala Gln Phe Lys Ala Asn
355 360 365

His Pro Phe Leu Phe Phe Ile Arg His Thr His Thr Asn Thr Ile Leu
370 375 380

Phe Cys Gly Lys Leu Ala Ser Pro
385 390

<210> 2584
<211> 811
<212> PRT
<213> Homo sapiens

<400> 2584

Met Pro Leu Ser Ser Pro Asn Ala Ala Ala Thr Ala Ser Asp Met Asp
1 5 10 15

Lys Asn Ser Gly Ser Asn Ser Ser Ser Ala Ser Ser Gly Ser Ser Lys
20 25 30

Gly Gln Gln Pro Pro Arg Ser Ala Ser Ala Gly Pro Ala Gly Glu Ser
35 40 45

Lys Pro Lys Ser Asp Gly Lys Asn Ser Ser Gly Ser Lys Arg Tyr Asn
50 55 60

Arg Lys Arg Glu Leu Ser Tyr Pro Lys Asn Glu Ser Phe Asn Asn Gln
65 70 75 80

Ser Arg Arg Ser Ser Ser Gln Lys Ser Lys Thr Phe Asn Lys Met Pro
85 90 95

```
Pro Gln Arg Gly Gly Gly Ser Ser Lys Leu Phe Ser Ser Ser Phe Asn
            100                 105                 110

Gly Gly Arg Arg Asp Glu Val Ala Glu Ala Gln Arg Ala Glu Phe Ser
        115                 120                 125

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

Asn Phe Thr Phe Glu Pro Arg Gly Gln Thr Gly His Phe Glu Gly Ser
145                 150                 155                 160

Gly His Gly Ser Trp Gly Lys Arg Asn Lys Trp Gly His Lys Pro Phe
                165                 170                 175

Asn Lys Glu Leu Phe Leu Gln Ala Asn Cys Gln Phe Val Val Ser Glu
            180                 185                 190

Asp Gln Asp Tyr Thr Ala His Phe Ala Asp Pro Asp Thr Leu Val Asn
        195                 200                 205

Trp Asp Phe Val Glu Gln Val Arg Ile Cys Ser His Glu Val Pro Ser
    210                 215                 220

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

Gly His Ile Phe Cys Trp Ala Cys Ile Leu His Tyr Leu Ser Leu Ser
                245                 250                 255

Glu Lys Thr Trp Ser Lys Cys Pro Ile Cys Tyr Ser Ser Val His Lys
            260                 265                 270

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

Gly Asp Thr Ile Thr Met Gln Leu Met Lys Arg Glu Lys Gly Val Leu
    290                 295                 300

Val Ala Leu Pro Lys Ser Lys Trp Met Asn Val Asp His Pro Ile His
305                 310                 315                 320

Leu Gly Asp Glu Gln His Ser Gln Tyr Ser Lys Phe Leu Leu Ala Ser
                325                 330                 335
```

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Lys Glu Gln Val Leu His Arg Val Val Leu Glu Glu Lys Val Ala Leu
            340                 345                 350

Glu Gln Gln Leu Ala Glu Glu Lys His Thr Pro Glu Ser Cys Phe Ile
        355                 360                 365

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

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

Gln Leu Val Leu Met Ala Pro Leu Ala Lys Glu Ser Val Phe Gln Pro
                405                 410                 415

Arg Lys Gly Val Leu Glu Tyr Leu Ser Ala Phe Asp Glu Glu Thr Thr
            420                 425                 430

Glu Val Cys Ser Leu Asp Thr Pro Ser Arg Pro Leu Ala Leu Pro Leu
        435                 440                 445

Val Glu Glu Glu Glu Ala Val Ser Glu Pro Glu Pro Glu Gly Leu Pro
    450                 455                 460

Glu Ala Cys Asp Asp Leu Glu Leu Ala Asp Asp Asn Leu Lys Glu Gly
465                 470                 475                 480

Thr Ile Cys Thr Glu Ser Ser Gln Gln Glu Pro Ile Thr Lys Ser Gly
                485                 490                 495

Phe Thr Arg Leu Ser Ser Ser Pro Cys Tyr Tyr Phe Tyr Gln Ala Glu
            500                 505                 510

Asp Gly Gln His Met Phe Leu His Pro Val Asn Val Arg Cys Leu Val
        515                 520                 525

Arg Glu Tyr Gly Ser Leu Glu Arg Ser Pro Glu Lys Ile Ser Ala Thr
    530                 535                 540

Val Val Glu Ile Ala Gly Tyr Ser Met Ser Glu Asp Val Arg Gln Arg
545                 550                 555                 560

His Arg Tyr Leu Ser His Leu Pro Leu Thr Cys Glu Phe Ser Ile Cys
                565                 570                 575

Glu Leu Ala Leu Gln Pro Pro Val Val Ser Lys Glu Thr Leu Glu Met
```

580 585 590

Phe Ser Asp Asp Ile Glu Lys Arg Lys Arg Gln Arg Gln Lys Lys Ala
595 600 605

Arg Glu Glu Arg Arg Arg Glu Arg Arg Ile Glu Ile Glu Glu Asn Lys
610 615 620

Lys Gln Gly Lys Tyr Pro Glu Val His Ile Pro Leu Glu Asn Leu Gln
625 630 635 640

Gln Phe Pro Ala Phe Asn Ser Tyr Thr Cys Ser Ser Asp Ser Ala Leu
645 650 655

Gly Pro Thr Ser Thr Glu Gly His Gly Ala Leu Ser Ile Ser Pro Leu
660 665 670

Ser Arg Ser Pro Gly Ser His Ala Asp Phe Leu Leu Thr Pro Leu Ser
675 680 685

Pro Thr Ala Ser Gln Gly Ser Pro Ser Phe Cys Val Gly Ser Leu Glu
690 695 700

Glu Asp Ser Pro Phe Pro Ser Phe Ala Gln Met Leu Arg Val Gly Lys
705 710 715 720

Ala Lys Ala Asp Val Trp Pro Lys Thr Ala Pro Lys Lys Asp Glu Asn
725 730 735

Ser Leu Val Pro Pro Ala Pro Val Asp Ser Asp Gly Glu Ser Asp Asn
740 745 750

Ser Asp Arg Val Pro Val Pro Ser Phe Gln Asn Ser Phe Ser Gln Ala
755 760 765

Ile Glu Ala Ala Phe Met Lys Leu Asp Thr Pro Ala Thr Ser Asp Pro
770 775 780

Leu Ser Glu Glu Lys Gly Gly Lys Lys Arg Lys Lys Gln Lys Gln Lys
785 790 795 800

Leu Leu Phe Ser Thr Ser Val Val His Thr Lys
805 810

<210> 2585
<211> 482

<212> PRT
<213> Homo sapiens

<400> 2585

Met Ala Glu Ala Ala Thr Pro Gly Thr Thr Ala Thr Thr Ser Gly Ala
1 5 10 15

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

Thr Val Thr Ala Pro Ser Leu Gly Ala Gly Gly Gly Gly Gly Gly Ser
35 40 45

Asp Gly Ser Gly Gly Gly Trp Thr Lys Gln Val Thr Cys Arg Tyr Phe
50 55 60

Met His Gly Val Cys Lys Glu Gly Asp Asn Cys Arg Tyr Ser His Asp
65 70 75 80

Leu Ser Asp Ser Pro Tyr Ser Val Val Cys Lys Tyr Phe Gln Arg Gly
85 90 95

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

Lys Gln Glu Glu Ala Thr Ala Thr Glu Leu Thr Thr Lys Ser Ser Leu
115 120 125

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

Asn Thr Gly Glu Ala Glu Ser Arg Asn Ser Asn Phe Ala Thr Val Gly
145 150 155 160

Ala Gly Ser Glu Asp Trp Val Asn Ala Ile Glu Phe Val Pro Gly Gln
165 170 175

Pro Tyr Cys Gly Arg Thr Ala Pro Ser Cys Thr Glu Ala Pro Leu Gln
180 185 190

Gly Ser Val Thr Lys Glu Glu Ser Glu Lys Glu Gln Thr Ala Val Glu
195 200 205

Thr Lys Lys Gln Leu Cys Pro Tyr Ala Ala Val Gly Glu Cys Arg Tyr
210 215 220

Gly Glu Asn Cys Val Tyr Leu His Gly Asp Ser Cys Asp Met Cys Gly
225 230 235 240

Leu Gln Leu Leu His Pro Met Asp Ala Ala Gln Arg Ser Gln His Ile
245 250 255

Lys Ser Cys Ile Glu Ala His Glu Lys Asp Met Glu Leu Ser Phe Ala
260 265 270

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

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

Cys Asn His Thr Tyr Cys Leu Lys Cys Ile Arg Lys Trp Arg Ser Ala
305 310 315 320

Lys Gln Phe Glu Ser Lys Ile Ile Lys Ser Cys Pro Glu Cys Arg Ile
325 330 335

Thr Ser Asn Phe Val Ile Pro Ser Glu Tyr Trp Val Glu Glu Lys Glu
340 345 350

Glu Lys Gln Lys Leu Ile Leu Lys Tyr Lys Glu Ala Met Ser Asn Lys
355 360 365

Ala Cys Arg Tyr Phe Asp Glu Gly Arg Gly Ser Cys Pro Phe Gly Gly
370 375 380

Asn Cys Phe Tyr Lys His Ala Tyr Pro Asp Gly Arg Arg Glu Glu Pro
385 390 395 400

Gln Arg Gln Lys Val Gly Thr Ser Ser Arg Tyr Arg Ala Gln Arg Arg
405 410 415

Asn His Phe Trp Glu Leu Ile Glu Glu Arg Glu Asn Ser Asn Pro Phe
420 425 430

Asp Asn Asp Glu Glu Glu Val Val Thr Phe Glu Leu Gly Glu Met Leu
435 440 445

Leu Met Leu Leu Ala Ala Gly Gly Asp Asp Glu Leu Thr Asp Ser Glu
450 455 460

Asp Glu Trp Asp Leu Phe His Asp Glu Leu Glu Asp Phe Tyr Asp Leu

465 470 475 480

Asp Leu

<210> 2586
<211> 146
<212> PRT
<213> Homo sapiens

<400> 2586

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

Lys Thr Ala Thr Ala Val Ala His Cys Lys Arg Gly Asn Gly Leu Ile
20 25 30

Lys Val Asn Gly Arg Pro Leu Glu Met Ile Glu Pro Arg Thr Leu Gln
35 40 45

Tyr Lys Leu Leu Glu Pro Val Leu Leu Leu Gly Lys Glu Arg Phe Ala
50 55 60

Gly Val Asp Ile Arg Val Arg Val Lys Gly Gly Gly His Val Ala Gln
65 70 75 80

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

Gln Lys Tyr Val Asp Glu Ala Ser Lys Lys Glu Ile Lys Asp Ile Leu
100 105 110

Ile Gln Tyr Asp Arg Thr Leu Leu Val Ala Asp Pro Arg Arg Cys Glu
115 120 125

Ser Lys Lys Phe Gly Gly Pro Gly Ala Arg Ala Arg Tyr Gln Lys Ser
130 135 140

Tyr Arg
145

<210> 2587
<211> 1674
<212> PRT
<213> Homo sapiens

<400> 2587

```
Met Glu Asp Ala Ser Glu Ser Ser Arg Gly Val Ala Pro Leu Ile Asn
1               5                  10                  15

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

Gly Cys Lys Ser His Arg Val Ala Asn Lys Lys Val Glu Ala Arg Ser
        35                  40                  45

Glu Lys Leu Leu Pro Thr Ala Leu Pro Pro Ser Glu Pro Lys Val Asp
    50                  55                  60

Gln Lys Leu Pro Arg Ser Ser Glu Arg Arg Gly Ser Gly Gly Gly Thr
65                  70                  75                  80

Gln Phe Pro Ala Arg Ser Arg Ala Val Ala Ala Gly Glu Ala Ala Ala
                85                  90                  95

Arg Gly Ala Ala Gly Pro Glu Arg Gly Ser Pro Leu Gly Arg Arg Val
            100                 105                 110

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

Val Ile Ala Gly Lys Arg Gly Arg Arg Gly Arg Asp Gly Ser Arg Arg
    130                 135                 140

Ala Pro Gly Gly Arg Glu Met Pro Leu Leu His Arg Lys Pro Phe Val
145                 150                 155                 160

Arg Gln Lys Pro Pro Ala Asp Leu Arg Pro Asp Glu Glu Val Phe Tyr
                165                 170                 175

Cys Lys Val Thr Asn Glu Ile Phe Arg His Tyr Asp Asp Phe Phe Glu
            180                 185                 190

Arg Thr Ile Leu Cys Asn Ser Leu Val Trp Ser Cys Ala Val Thr Gly
        195                 200                 205

Arg Pro Gly Leu Thr Tyr Gln Glu Ala Leu Glu Ser Glu Lys Lys Ala
    210                 215                 220

Arg Gln Asn Leu Gln Ser Phe Pro Glu Pro Leu Ile Ile Pro Val Leu
225                 230                 235                 240

Tyr Leu Thr Ser Leu Thr His Arg Ser Arg Leu His Glu Ile Cys Asp
```

245 250 255

Asp Ile Phe Ala Tyr Val Lys Asp Arg Tyr Phe Val Glu Glu Thr Val
260 265 270

Glu Val Ile Arg Asn Asn Gly Ala Arg Leu Gln Cys Thr Ile Leu Glu
275 280 285

Val Leu Pro Pro Ser His Gln Asn Gly Phe Ala Asn Gly His Val Asn
290 295 300

Ser Val Asp Gly Glu Thr Ile Ile Ile Ser Asp Ser Asp Asp Ser Glu
305 310 315 320

Thr Gln Ser Cys Ser Phe Gln Asn Gly Lys Lys Lys Asp Ala Ile Asp
325 330 335

Pro Leu Leu Phe Lys Tyr Lys Val Gln Pro Thr Lys Lys Glu Leu His
340 345 350

Glu Ser Ala Ile Val Lys Ala Thr Gln Ile Ser Arg Arg Lys His Leu
355 360 365

Phe Ser Arg Asp Lys Leu Lys Leu Phe Leu Lys Gln His Cys Glu Pro
370 375 380

Gln Glu Gly Val Ile Lys Ile Lys Ala Ser Ser Leu Ser Thr Tyr Lys
385 390 395 400

Ile Ala Glu Gln Asp Phe Ser Tyr Phe Phe Pro Asp Asp Pro Pro Thr
405 410 415

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

Ile His Ile Ser Gln Glu Asp Asn Val Ala Asn Lys Gln Thr Leu Ala
435 440 445

Ser Tyr Arg Ser Lys Ala Thr Lys Glu Arg Asp Lys Leu Leu Lys Gln
450 455 460

Glu Glu Met Lys Ser Leu Ala Phe Glu Lys Ala Lys Leu Lys Arg Glu
465 470 475 480

Lys Ala Asp Ala Leu Glu Ala Lys Lys Lys Glu Lys Glu Asp Lys Glu
485 490 495

Lys Lys Arg Glu Glu Leu Lys Lys Ile Val Glu Glu Glu Arg Leu Lys
500 505 510

Lys Lys Glu Glu Lys Glu Arg Leu Lys Val Glu Arg Glu Lys Glu Arg
515 520 525

Glu Lys Leu Arg Glu Glu Lys Arg Lys Tyr Val Glu Tyr Leu Lys Gln
530 535 540

Trp Ser Lys Pro Arg Glu Asp Met Glu Cys Asp Asp Leu Lys Glu Leu
545 550 555 560

Pro Glu Pro Thr Pro Val Lys Thr Arg Leu Pro Pro Glu Ile Phe Gly
565 570 575

Asp Ala Leu Met Val Leu Glu Phe Leu Asn Ala Phe Gly Glu Leu Phe
580 585 590

Asp Leu Gln Asp Glu Phe Pro Asp Gly Val Thr Leu Glu Val Leu Glu
595 600 605

Glu Ala Leu Val Gly Asn Asp Ser Glu Gly Pro Leu Cys Glu Leu Leu
610 615 620

Phe Phe Phe Leu Thr Ala Ile Phe Gln Ala Ile Ala Glu Glu Glu Glu
625 630 635 640

Glu Val Ala Lys Glu Gln Leu Thr Asp Ala Asp Thr Lys Gly Cys Ser
645 650 655

Leu Lys Ser Leu Asp Leu Asp Ser Cys Thr Leu Ser Glu Ile Leu Arg
660 665 670

Leu His Ile Leu Ala Ser Gly Ala Asp Val Thr Ser Ala Asn Ala Lys
675 680 685

Tyr Arg Tyr Gln Lys Arg Gly Gly Phe Asp Ala Thr Asp Asp Ala Cys
690 695 700

Met Glu Leu Arg Leu Ser Asn Pro Ser Leu Val Lys Lys Leu Ser Ser
705 710 715 720

Thr Ser Val Tyr Asp Leu Thr Pro Gly Glu Lys Met Lys Ile Leu His
725 730 735

Ala Leu Cys Gly Lys Leu Leu Thr Leu Val Ser Thr Arg Asp Phe Ile
740 745 750

Glu Asp Tyr Val Asp Ile Leu Arg Gln Ala Lys Gln Glu Phe Arg Glu
755 760 765

Leu Lys Ala Glu Gln His Arg Lys Glu Arg Glu Glu Ala Ala Ala Arg
770 775 780

Ile Arg Lys Arg Lys Glu Glu Lys Leu Lys Glu Gln Glu Gln Lys Met
785 790 795 800

Lys Glu Lys Gln Glu Lys Leu Lys Glu Asp Glu Gln Arg Asn Ser Thr
805 810 815

Ala Asp Ile Ser Ile Gly Glu Glu Glu Arg Glu Asp Phe Asp Thr Ser
820 825 830

Ile Glu Ser Lys Asp Thr Glu Gln Lys Glu Leu Asp Gln Asp Met Phe
835 840 845

Thr Glu Asp Glu Asp Asp Pro Gly Ser His Lys Arg Gly Arg Arg Gly
850 855 860

Lys Arg Gly Gln Asn Gly Phe Lys Glu Phe Thr Arg Gln Glu Gln Ile
865 870 875 880

Asn Cys Val Thr Arg Glu Leu Leu Thr Ala Asp Glu Glu Glu Ala Leu
885 890 895

Lys Gln Glu His Gln Arg Lys Glu Lys Glu Leu Leu Glu Lys Ile Gln
900 905 910

Ser Ala Ile Ala Cys Thr Asn Ile Phe Pro Leu Gly Arg Asp Arg Met
915 920 925

Tyr Arg Arg Tyr Trp Ile Phe Pro Ser Ile Pro Gly Leu Phe Ile Glu
930 935 940

Glu Asp Tyr Ser Gly Leu Thr Glu Asp Met Leu Leu Pro Arg Pro Ser
945 950 955 960

Ser Phe Gln Asn Asn Val Gln Ser Gln Asp Pro Gln Val Ser Thr Lys
965 970 975

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Thr Gly Glu Pro Leu Met Ser Glu Ser Thr Ser Asn Ile Asp Gln Gly
            980                 985                 990

Pro Arg Asp His Ser Val Gln Leu  Pro Lys Pro Val His  Lys Pro Asn
        995                 1000                1005

Arg Trp  Cys Phe Tyr Ser Ser  Cys Glu Gln Leu Asp  Gln Leu Ile
    1010                1015                1020

Glu Ala  Leu Asn Ser Arg Gly  His Arg Glu Ser Ala  Leu Lys Glu
    1025                1030                1035

Thr Leu  Leu Gln Glu Lys Ser  Arg Ile Cys Ala Gln  Leu Ala Arg
    1040                1045                1050

Phe Ser  Glu Glu Lys Phe His  Phe Ser Asp Lys Pro  Gln Pro Asp
    1055                1060                1065

Ser Lys  Pro Thr Tyr Ser Arg  Gly Arg Ser Ser Asn  Ala Tyr Asp
    1070                1075                1080

Pro Ser  Gln Met Cys Ala Glu  Lys Gln Leu Glu Leu  Arg Leu Arg
    1085                1090                1095

Asp Phe  Leu Leu Asp Ile Glu  Asp Arg Ile Tyr Gln  Gly Thr Leu
    1100                1105                1110

Gly Ala  Ile Lys Val Thr Asp  Arg His Ile Trp Arg  Ser Ala Leu
    1115                1120                1125

Glu Ser  Gly Arg Tyr Glu Leu  Leu Ser Glu Glu Asn  Lys Glu Asn
    1130                1135                1140

Gly Ile  Ile Lys Thr Val Asn  Glu Asp Val Glu Glu  Met Glu Ile
    1145                1150                1155

Asp Glu  Gln Thr Lys Val Ile  Val Lys Asp Arg Leu  Leu Gly Ile
    1160                1165                1170

Lys Thr  Glu Thr Pro Ser Thr  Val Ser Thr Asn Ala  Ser Thr Pro
    1175                1180                1185

Gln Ser  Val Ser Ser Val Val  His Tyr Leu Ala Met  Ala Leu Phe
    1190                1195                1200

Gln Ile  Glu Gln Gly Ile Glu  Arg Arg Phe Leu Lys  Ala Pro Leu
```

1205 1210 1215

Asp Ala Ser Asp Ser Gly Arg Ser Tyr Lys Thr Val Leu Asp Arg
1220 1225 1230

Trp Arg Glu Ser Leu Leu Ser Ser Ala Ser Leu Ser Gln Val Phe
1235 1240 1245

Leu His Leu Ser Thr Leu Asp Arg Ser Val Ile Trp Ser Lys Ser
1250 1255 1260

Ile Leu Asn Ala Arg Cys Lys Ile Cys Arg Lys Lys Gly Asp Ala
1265 1270 1275

Glu Asn Met Val Leu Cys Asp Gly Cys Asp Arg Gly His His Thr
1280 1285 1290

Tyr Cys Val Arg Pro Lys Leu Lys Thr Val Pro Glu Gly Asp Trp
1295 1300 1305

Phe Cys Pro Glu Cys Arg Pro Lys Gln Arg Cys Arg Arg Leu Ser
1310 1315 1320

Phe Arg Gln Arg Pro Ser Leu Glu Ser Asp Glu Asp Val Glu Asp
1325 1330 1335

Ser Met Gly Gly Glu Asp Asp Glu Val Asp Gly Asp Glu Glu Glu
1340 1345 1350

Gly Gln Ser Glu Glu Glu Glu Tyr Glu Val Glu Gln Asp Glu Asp
1355 1360 1365

Asp Ser Gln Glu Glu Glu Glu Val Ser Leu Pro Lys Arg Gly Arg
1370 1375 1380

Pro Gln Val Arg Leu Pro Val Lys Thr Arg Gly Lys Leu Ser Ser
1385 1390 1395

Ser Phe Ser Ser Arg Gly Gln Gln Gln Glu Pro Gly Arg Tyr Pro
1400 1405 1410

Ser Arg Ser Gln Gln Ser Thr Pro Lys Thr Thr Val Ser Ser Lys
1415 1420 1425

Thr Gly Arg Ser Leu Arg Lys Ile Asn Ser Ala Pro Pro Thr Glu
1430 1435 1440

Thr Lys Ser Leu Arg Ile Ala Ser Arg Ser Thr Arg His Ser His
1445 1450 1455

Gly Pro Leu Gln Ala Asp Val Phe Val Glu Leu Leu Ser Pro Arg
1460 1465 1470

Arg Lys Arg Arg Gly Arg Lys Ser Ala Asn Asn Thr Pro Glu Asn
1475 1480 1485

Ser Pro Asn Phe Pro Asn Phe Arg Val Ile Ala Thr Lys Ser Ser
1490 1495 1500

Glu Gln Ser Arg Ser Val Asn Ile Ala Ser Lys Leu Ser Leu Gln
1505 1510 1515

Glu Ser Glu Ser Lys Arg Arg Cys Arg Lys Arg Gln Ser Pro Glu
1520 1525 1530

Pro Ser Pro Val Thr Leu Gly Arg Arg Ser Ser Gly Arg Gln Gly
1535 1540 1545

Gly Val His Glu Leu Ser Ala Phe Glu Gln Leu Val Val Glu Leu
1550 1555 1560

Val Arg His Asp Asp Ser Trp Pro Phe Leu Lys Leu Val Ser Lys
1565 1570 1575

Ile Gln Val Pro Asp Tyr Tyr Asp Ile Ile Lys Lys Pro Ile Ala
1580 1585 1590

Leu Asn Ile Ile Arg Glu Lys Val Asn Lys Cys Glu Tyr Lys Leu
1595 1600 1605

Ala Ser Glu Phe Ile Asp Asp Ile Glu Leu Met Phe Ser Asn Cys
1610 1615 1620

Phe Glu Tyr Asn Pro Arg Asn Thr Ser Glu Ala Lys Ala Gly Thr
1625 1630 1635

Arg Leu Gln Ala Phe Phe His Ile Gln Ala Gln Lys Leu Gly Leu
1640 1645 1650

His Val Thr Pro Ser Asn Val Asp Gln Val Ser Thr Pro Pro Ala
1655 1660 1665

Ala Lys Lys Ser Arg Ile
1670

<210> 2588
<211> 103
<212> PRT
<213> Homo sapiens

<400> 2588

Met Ala Gln Phe Val Arg Asn Leu Val Glu Lys Thr Pro Ala Leu Val
1 5 10 15

Asn Ala Ala Val Thr Tyr Ser Lys Pro Arg Leu Ala Thr Phe Trp Tyr
20 25 30

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

Ala Ile Gln Ser Leu Lys Lys Ile Ala Asn Ser Ala Gln Thr Gly Ser
50 55 60

Phe Lys Gln Leu Thr Val Lys Glu Ala Val Leu Asn Gly Leu Val Ala
65 70 75 80

Thr Glu Val Leu Met Trp Phe Tyr Val Gly Glu Ile Ile Gly Lys Arg
85 90 95

Gly Ile Ile Gly Tyr Asp Val
100

<210> 2589
<211> 156
<212> PRT
<213> Homo sapiens

<400> 2589

Met Ser Gly Gly Leu Leu Lys Ala Leu Arg Ser Asp Ser Tyr Val Glu
1 5 10 15

Leu Ser Gln Tyr Arg Asp Gln His Phe Arg Gly Asp Asn Glu Glu Gln
20 25 30

Glu Lys Leu Leu Lys Lys Ser Cys Thr Leu Tyr Val Gly Asn Leu Ser
35 40 45

Phe Tyr Thr Thr Glu Glu Gln Ile Tyr Glu Leu Phe Ser Lys Ser Gly
50 55 60

```
Asp Ile Lys Lys Ile Ile Met Gly Leu Asp Lys Met Lys Lys Thr Ala
65                  70                  75                  80

Cys Gly Phe Cys Phe Val Glu Tyr Tyr Ser Arg Ala Asp Ala Glu Asn
                85                  90                  95

Ala Met Arg Tyr Ile Asn Gly Thr Arg Leu Asp Asp Arg Ile Ile Arg
            100                 105                 110

Thr Asp Trp Asp Ala Gly Phe Lys Glu Gly Arg Gln Tyr Gly Arg Gly
        115                 120                 125

Arg Ser Gly Gly Gln Val Arg Asp Glu Tyr Arg Gln Asp Tyr Asp Ala
    130                 135                 140

Gly Arg Gly Gly Tyr Gly Lys Leu Ala Gln Asn Gln
145                 150                 155
```

<210> 2590
<211> 436
<212> PRT
<213> Homo sapiens

<400> 2590

```
Met Asp Ser Val Ala Phe Glu Asp Val Ala Val Asn Phe Thr Gln Glu
1               5                   10                  15

Glu Trp Ala Leu Leu Ser Pro Ser Gln Lys Asn Leu Tyr Arg Asp Val
            20                  25                  30

Thr Leu Glu Thr Phe Arg Asn Leu Ala Ser Val Gly Ile Gln Trp Lys
        35                  40                  45

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

Ser Leu Val Glu Arg Leu Cys Gly Arg Lys Glu Gly Asn Glu His Arg
65                  70                  75                  80

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

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

Arg His Ser Phe Leu Asp Arg His Met Arg Ala His Ala Gly His Lys
115 120 125

Arg Ser Glu Cys Gly Gly Glu Trp Arg Glu Thr Pro Arg Lys Gln Lys
130 135 140

Gln His Gly Lys Ala Ser Ile Ser Pro Ser Ser Gly Ala Arg Arg Thr
145 150 155 160

Val Thr Pro Thr Arg Lys Arg Pro Tyr Glu Cys Lys Val Cys Gly Lys
165 170 175

Ala Phe Asn Ser Pro Asn Leu Phe Gln Ile His Gln Arg Thr His Thr
180 185 190

Gly Lys Arg Ser Tyr Lys Cys Arg Glu Ile Val Arg Ala Phe Thr Val
195 200 205

Ser Ser Phe Phe Arg Lys His Gly Lys Met His Thr Gly Glu Lys Arg
210 215 220

Tyr Glu Cys Lys Tyr Cys Gly Lys Pro Ile Asp Tyr Pro Ser Leu Phe
225 230 235 240

Gln Ile His Val Arg Thr His Thr Gly Glu Lys Pro Tyr Lys Cys Lys
245 250 255

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

Ile Arg Ser His Ala Leu Glu Lys Ser His Gln Cys Gln Glu Cys Gly
275 280 285

Lys Lys Leu Ser Cys Ser Ser Ser Leu His Arg His Glu Arg Thr His
290 295 300

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

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

Pro Tyr Glu Cys Asn Lys Cys Gly Lys Thr Phe Asn Tyr Pro Ser Cys
340 345 350

Phe Arg Arg His Lys Lys Thr His Ser Gly Glu Lys Pro Tyr Glu Cys

355 360 365

Thr Arg Cys Gly Lys Ala Phe Gly Trp Cys Ser Ser Leu Arg Arg His
370 375 380

Glu Met Thr His Thr Gly Glu Lys Pro Phe Asp Cys Lys Gln Cys Gly
385 390 395 400

Lys Val Phe Thr Phe Ser Asn Tyr Leu Arg Leu His Glu Arg Thr His
405 410 415

Leu Ala Gly Arg Ser Gln Cys Phe Gly Arg Arg Gln Gly Asp His Leu
420 425 430

Ser Pro Gly Val
435

<210> 2591
<211> 92
<212> PRT
<213> Homo sapiens

<400> 2591

Met Gln Val Ser Thr Ala Ala Leu Ala Val Leu Leu Cys Thr Met Ala
1 5 10 15

Leu Cys Asn Gln Phe Ser Ala Ser Leu Ala Ala Asp Thr Pro Thr Ala
20 25 30

Cys Cys Phe Ser Tyr Thr Ser Arg Gln Ile Pro Gln Asn Phe Ile Ala
35 40 45

Asp Tyr Phe Glu Thr Ser Ser Gln Cys Ser Lys Pro Gly Val Ile Phe
50 55 60

Leu Thr Lys Arg Ser Arg Gln Val Cys Ala Asp Pro Ser Glu Glu Trp
65 70 75 80

Val Gln Lys Tyr Val Ser Asp Leu Glu Leu Ser Ala
85 90

<210> 2592
<211> 271
<212> PRT
<213> Homo sapiens

<400> 2592

```
Met Glu Ala Leu Pro Leu Leu Ala Ala Thr Thr Pro Asp His Gly Arg
1               5                  10                  15

His Arg Arg Leu Leu Leu Leu Pro Leu Leu Leu Phe Leu Leu Pro Ala
            20                  25                  30

Gly Ala Val Gln Gly Trp Glu Thr Glu Glu Arg Pro Arg Thr Arg Glu
        35                  40                  45

Glu Glu Cys His Phe Tyr Ala Gly Gly Gln Val Tyr Pro Gly Glu Ala
    50                  55                  60

Ser Arg Val Ser Val Ala Asp His Ser Leu His Leu Ser Lys Ala Lys
65                  70                  75                  80

Ile Ser Lys Pro Ala Pro Tyr Trp Glu Gly Thr Ala Val Ile Asp Gly
                85                  90                  95

Glu Phe Lys Glu Leu Lys Leu Thr Asp Tyr Arg Gly Lys Tyr Leu Val
            100                 105                 110

Phe Phe Phe Tyr Pro Leu Asp Phe Thr Phe Val Cys Pro Thr Glu Ile
        115                 120                 125

Ile Ala Phe Gly Asp Arg Leu Glu Glu Phe Arg Ser Ile Asn Thr Glu
    130                 135                 140

Val Val Ala Cys Ser Val Asp Ser Gln Phe Thr His Leu Ala Trp Ile
145                 150                 155                 160

Asn Thr Pro Arg Arg Gln Gly Gly Leu Gly Pro Ile Arg Ile Pro Leu
                165                 170                 175

Leu Ser Asp Leu Thr His Gln Ile Ser Lys Asp Tyr Gly Val Tyr Leu
            180                 185                 190

Glu Asp Ser Gly His Thr Leu Arg Gly Leu Phe Ile Ile Asp Asp Lys
        195                 200                 205

Gly Ile Leu Arg Gln Ile Thr Leu Asn Asp Leu Pro Val Gly Arg Ser
    210                 215                 220

Val Asp Glu Thr Leu Arg Leu Val Gln Ala Phe Gln Tyr Thr Asp Lys
225                 230                 235                 240

His Gly Glu Val Cys Pro Ala Gly Trp Lys Pro Gly Ser Glu Thr Ile
```

245 250 255

Ile Pro Asp Pro Ala Gly Lys Leu Lys Tyr Phe Asp Lys Leu Asn
260 265 270

<210> 2593
<211> 659
<212> PRT
<213> Homo sapiens

<400> 2593

Met Ala Ala Val Ile Leu Glu Ser Ile Phe Leu Lys Arg Ser Gln Gln
1 5 10 15

Lys Lys Lys Thr Ser Pro Leu Asn Phe Lys Lys Arg Leu Phe Leu Leu
20 25 30

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

Arg Gly Ser Lys Lys Gly Ser Ile Asp Val Glu Lys Ile Thr Cys Val
50 55 60

Glu Thr Val Val Pro Glu Lys Asn Pro Pro Pro Glu Arg Gln Ile Pro
65 70 75 80

Arg Arg Gly Glu Glu Ser Ser Glu Met Glu Gln Ile Ser Ile Ile Glu
85 90 95

Arg Phe Pro Tyr Pro Phe Gln Val Val Tyr Asp Glu Gly Pro Leu Tyr
100 105 110

Val Phe Ser Pro Thr Glu Glu Leu Arg Lys Arg Trp Ile His Gln Leu
115 120 125

Lys Asn Val Ile Arg Tyr Asn Ser Asp Leu Val Gln Lys Tyr His Pro
130 135 140

Cys Phe Trp Ile Asp Gly Gln Tyr Leu Cys Cys Ser Gln Thr Ala Lys
145 150 155 160

Asn Ala Met Gly Cys Gln Ile Leu Glu Asn Arg Asn Gly Ser Leu Lys
165 170 175

Pro Gly Ser Ser His Arg Lys Thr Lys Lys Pro Leu Pro Pro Thr Pro
180 185 190

Glu Glu Asp Gln Ile Leu Lys Lys Pro Leu Pro Pro Glu Pro Ala Ala
195 200 205

Ala Pro Val Ser Thr Ser Glu Leu Lys Lys Val Val Ala Leu Tyr Asp
210 215 220

Tyr Met Pro Met Asn Ala Asn Asp Leu Gln Leu Arg Lys Gly Asp Glu
225 230 235 240

Tyr Phe Ile Leu Glu Glu Ser Asn Leu Pro Trp Trp Arg Ala Arg Asp
245 250 255

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

Glu Asp Ser Ile Glu Met Tyr Glu Trp Tyr Ser Lys His Met Thr Arg
275 280 285

Ser Gln Ala Glu Gln Leu Leu Lys Gln Glu Gly Lys Glu Gly Gly Phe
290 295 300

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

Ala Lys Ser Thr Gly Asp Pro Gln Gly Val Ile Arg His Tyr Val Val
325 330 335

Cys Ser Thr Pro Gln Ser Gln Tyr Tyr Leu Ala Glu Lys His Leu Phe
340 345 350

Ser Thr Ile Pro Glu Leu Ile Asn Tyr His Gln His Asn Ser Ala Gly
355 360 365

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

Pro Ser Thr Ala Gly Leu Gly Tyr Gly Ser Trp Glu Ile Asp Pro Lys
385 390 395 400

Asp Leu Thr Phe Leu Lys Glu Leu Gly Thr Gly Gln Phe Gly Val Val
405 410 415

Lys Tyr Gly Lys Trp Arg Gly Gln Tyr Asp Val Ala Ile Lys Met Ile
420 425 430

Lys Glu Gly Ser Met Ser Glu Asp Glu Phe Ile Glu Glu Ala Lys Val
435 440 445

Met Met Asn Leu Ser His Glu Lys Leu Val Gln Leu Tyr Gly Val Cys
450 455 460

Thr Lys Gln Arg Pro Ile Phe Ile Ile Thr Glu Tyr Met Ala Asn Gly
465 470 475 480

Cys Leu Leu Asn Tyr Leu Arg Glu Met Arg His Arg Phe Gln Thr Gln
485 490 495

Gln Leu Leu Glu Met Cys Lys Asp Val Cys Glu Ala Met Glu Tyr Leu
500 505 510

Glu Ser Lys Gln Phe Leu His Arg Asp Leu Ala Ala Arg Asn Cys Leu
515 520 525

Val Asn Asp Gln Gly Val Val Lys Val Ser Asp Phe Gly Leu Ser Arg
530 535 540

Tyr Val Leu Asp Asp Glu Tyr Thr Ser Ser Val Gly Ser Lys Phe Pro
545 550 555 560

Val Arg Trp Ser Pro Pro Glu Val Leu Met Tyr Ser Lys Phe Ser Ser
565 570 575

Lys Ser Asp Ile Trp Ala Phe Gly Val Leu Met Trp Glu Ile Tyr Ser
580 585 590

Leu Gly Lys Met Pro Tyr Glu Arg Phe Thr Asn Ser Glu Thr Ala Glu
595 600 605

His Ile Ala Gln Gly Leu Arg Leu Tyr Arg Pro His Leu Ala Ser Glu
610 615 620

Lys Val Tyr Thr Ile Met Tyr Ser Cys Trp His Glu Lys Ala Asp Glu
625 630 635 640

Arg Pro Thr Phe Lys Ile Leu Leu Ser Asn Ile Leu Asp Val Met Asp
645 650 655

Glu Glu Ser

<210> 2594

<211> 417
<212> PRT
<213> Homo sapiens

<400> 2594

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

Lys Arg Val Val Met Arg Val Asp Phe Asn Val Pro Met Lys Asn Asn
20 25 30

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

Phe Cys Leu Asp Asn Gly Ala Lys Ser Val Val Leu Met Ser His Leu
50 55 60

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

Val Ala Val Glu Leu Lys Ser Leu Leu Gly Lys Asp Val Leu Phe Leu
85 90 95

Lys Asp Cys Val Gly Pro Glu Val Glu Lys Ala Cys Ala Asn Pro Ala
100 105 110

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

Glu Gly Lys Gly Lys Asp Ala Ser Gly Asn Lys Val Lys Ala Glu Pro
130 135 140

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

Tyr Val Asn Asp Ala Phe Gly Thr Ala His Arg Ala His Ser Ser Met
165 170 175

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

Glu Leu Asn Tyr Phe Ala Lys Ala Leu Glu Ser Pro Glu Arg Pro Phe
195 200 205

Leu Ala Ile Leu Gly Gly Ala Lys Val Ala Asp Lys Ile Gln Leu Ile
210 215 220

```
Asn Asn Met Leu Asp Lys Val Asn Glu Met Ile Ile Gly Gly Gly Met
225                 230                 235                 240

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

Leu Phe Asp Glu Glu Gly Ala Lys Ile Val Lys Asp Leu Met Ser Lys
            260                 265                 270

Ala Glu Lys Asn Gly Val Lys Ile Thr Leu Pro Val Asp Phe Val Thr
        275                 280                 285

Ala Asp Lys Phe Asp Glu Asn Ala Lys Thr Gly Gln Ala Thr Val Ala
    290                 295                 300

Ser Gly Ile Pro Ala Gly Trp Met Gly Leu Asp Cys Gly Pro Glu Ser
305                 310                 315                 320

Ser Lys Lys Tyr Ala Glu Ala Val Thr Arg Ala Lys Gln Ile Val Trp
                325                 330                 335

Asn Gly Pro Val Gly Val Phe Glu Trp Glu Ala Phe Ala Arg Gly Thr
            340                 345                 350

Lys Ala Leu Met Asp Glu Val Val Lys Ala Thr Ser Arg Gly Cys Ile
        355                 360                 365

Thr Ile Ile Gly Gly Gly Asp Thr Ala Thr Cys Cys Ala Lys Trp Asn
    370                 375                 380

Thr Glu Asp Lys Val Ser His Val Ser Thr Gly Gly Gly Ala Ser Leu
385                 390                 395                 400

Glu Leu Leu Glu Gly Lys Val Leu Pro Gly Val Asp Ala Leu Ser Asn
                405                 410                 415

Ile
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<210> 2595
<211> 468
<212> PRT
<213> Homo sapiens

<400> 2595

```
Met Ala Pro Pro Pro Ala Arg Val His Leu Gly Ala Phe Leu Ala Val
```

1 5 10 15

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

Thr Pro Ser Lys Val Trp Gly Ser Ser Ala Gly Arg Ile Glu Pro Arg
35 40 45

Gly Gly Gly Arg Gly Ala Leu Pro Thr Ser Met Gly Gln His Gly Pro
50 55 60

Ser Ala Arg Ala Arg Ala Gly Arg Ala Pro Gly Pro Arg Pro Ala Arg
65 70 75 80

Glu Ala Ser Pro Arg Leu Arg Val His Lys Thr Phe Lys Phe Val Val
85 90 95

Val Gly Val Leu Leu Gln Val Val Pro Ser Ser Ala Ala Thr Ile Lys
100 105 110

Leu His Asp Gln Ser Ile Gly Thr Gln Gln Trp Glu His Ser Pro Leu
115 120 125

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

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

Leu Phe Ala Cys Leu Pro Cys Thr Ala Cys Lys Ser Asp Glu Glu Glu
165 170 175

Arg Ser Pro Cys Thr Thr Thr Arg Asn Thr Ala Cys Gln Cys Lys Pro
180 185 190

Gly Thr Phe Arg Asn Asp Asn Ser Ala Glu Met Cys Arg Lys Cys Ser
195 200 205

Arg Gly Cys Pro Arg Gly Met Val Lys Val Lys Asp Cys Thr Pro Trp
210 215 220

Ser Asp Ile Glu Cys Val His Lys Glu Ser Gly Asn Gly His Asn Ile
225 230 235 240

Trp Val Ile Leu Val Val Thr Leu Val Val Pro Leu Leu Leu Val Ala
245 250 255

Val Leu Ile Val Cys Cys Cys Ile Gly Ser Gly Cys Gly Gly Asp Pro
260 265 270

Lys Cys Met Asp Arg Val Cys Phe Trp Arg Leu Gly Leu Leu Arg Gly
275 280 285

Pro Gly Ala Glu Asp Asn Ala His Asn Glu Ile Leu Ser Asn Ala Asp
290 295 300

Ser Leu Ser Thr Phe Val Ser Glu Gln Gln Met Glu Ser Gln Glu Pro
305 310 315 320

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

Leu Leu Gly Pro Ala Glu Ala Glu Gly Ser Gln Arg Arg Arg Leu Leu
340 345 350

Val Pro Ala Asn Gly Ala Asp Pro Thr Glu Thr Leu Met Leu Phe Phe
355 360 365

Asp Lys Phe Ala Asn Ile Val Pro Phe Asp Ser Trp Asp Gln Leu Met
370 375 380

Arg Gln Leu Asp Leu Thr Lys Asn Glu Ile Asp Val Val Arg Ala Gly
385 390 395 400

Thr Ala Gly Pro Gly Asp Ala Leu Tyr Ala Met Leu Met Lys Trp Val
405 410 415

Asn Lys Thr Gly Arg Asn Ala Ser Ile His Thr Leu Leu Asp Ala Leu
420 425 430

Glu Arg Met Glu Glu Arg His Ala Lys Glu Lys Ile Gln Asp Leu Leu
435 440 445

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

Val Ser Leu Glu
465

<210> 2596
<211> 185
<212> PRT

<213> Homo sapiens

<400> 2596

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

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

Lys Trp Asn Lys Trp Ala Leu Ser Arg Gly Lys Arg Glu Leu Arg Met
35 40 45

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

Gln Thr Leu Ile Arg Pro Gln Asp Met Lys Gly Ala Ser Arg Ser Pro
65 70 75 80

Glu Asp Ser Ser Pro Asp Ala Ala Arg Ile Arg Val Lys Arg Tyr Arg
85 90 95

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

Gly Thr Cys Thr Val Gln Lys Leu Ala His Gln Ile Tyr Gln Phe Thr
115 120 125

Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Lys Ile Ser Pro Gln
130 135 140

Gly Tyr Gly Arg Arg Arg Arg Arg Ser Leu Pro Glu Ala Gly Pro Gly
145 150 155 160

Arg Thr Leu Val Ser Ser Lys Pro Gln Ala His Gly Ala Pro Ala Pro
165 170 175

Pro Ser Gly Ser Ala Pro His Phe Leu
180 185

<210> 2597
<211> 851
<212> PRT
<213> Homo sapiens

<400> 2597

Met Ser Ser Lys Gln Glu Ile Met Ser Asp Gln Arg Phe Arg Arg Val
1 5 10 15

Ala Lys Asp Pro Arg Phe Trp Glu Met Pro Glu Lys Asp Arg Lys Val
20 25 30

Lys Ile Asp Lys Arg Phe Arg Ala Met Phe His Asp Lys Lys Phe Lys
35 40 45

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

Thr Glu Asp Leu Lys Arg Phe Tyr Asp Leu Ser Asp Ser Asp Ser Asn
65 70 75 80

Leu Ser Gly Glu Asp Ser Lys Ala Leu Ser Gln Lys Lys Ile Lys Lys
85 90 95

Lys Lys Thr Gln Thr Lys Lys Glu Ile Asp Ser Lys Asn Leu Val Glu
100 105 110

Lys Lys Lys Glu Thr Lys Lys Ala Asn His Lys Gly Ser Glu Asn Lys
115 120 125

Thr Asp Leu Asp Asn Ser Ile Gly Ile Lys Lys Met Lys Thr Ser Cys
130 135 140

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

Phe Thr Gln Lys Asn Lys Lys Glu Lys Lys Asn Ile Val Gln His Thr
165 170 175

Thr Asp Ser Ser Leu Glu Glu Lys Gln Arg Thr Leu Asp Ser Gly Thr
180 185 190

Ser Glu Ile Val Lys Ser Pro Arg Ile Glu Cys Ser Lys Thr Arg Arg
195 200 205

Glu Met Gln Ser Val Val Gln Leu Ile Met Thr Arg Asp Ser Asp Gly
210 215 220

Tyr Glu Asn Ser Thr Asp Gly Glu Met Cys Asp Lys Asp Ala Leu Glu
225 230 235 240

Glu Asp Ser Glu Ser Val Ser Glu Ile Gly Ser Asp Glu Glu Ser Glu
245 250 255

Asn Glu Ile Thr Ser Val Gly Arg Ala Ser Gly Asp Asp Asp Gly Ser
260 265 270

Glu Asp Asp Glu Glu Glu Asp Glu Asp Glu Glu Glu Asp Glu Asp Glu
275 280 285

Asp Ser Glu Asp Asp Asp Lys Ser Asp Ser Gly Pro Asp Leu Ala Arg
290 295 300

Gly Lys Gly Asn Ile Glu Thr Ser Ser Glu Asp Glu Asp Asp Thr Ala
305 310 315 320

Asp Leu Phe Pro Glu Glu Ser Gly Phe Glu His Ala Trp Arg Glu Leu
325 330 335

Asp Lys Asp Ala Pro Arg Ala Asp Glu Ile Thr Arg Arg Leu Ala Val
340 345 350

Cys Asn Met Asp Trp Asp Arg Leu Lys Ala Lys Asp Leu Leu Ala Leu
355 360 365

Phe Asn Ser Phe Lys Pro Lys Gly Gly Val Ile Phe Ser Val Lys Ile
370 375 380

Tyr Pro Ser Glu Phe Gly Lys Glu Arg Met Lys Glu Glu Gln Val Gln
385 390 395 400

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

Trp Thr Ser Arg Glu Lys Leu Arg Asp Tyr Gln Phe Lys Arg Leu Lys
420 425 430

Tyr Tyr Tyr Ala Val Val Asp Cys Asp Ser Pro Glu Thr Ala Ser Lys
435 440 445

Ile Tyr Glu Asp Cys Asp Gly Leu Glu Phe Glu Ser Ser Cys Ser Phe
450 455 460

Ile Asp Leu Arg Phe Ile Pro Asp Asp Ile Thr Phe Asp Asp Glu Pro
465 470 475 480

Lys Asp Val Ala Ser Glu Val Asn Leu Thr Ala Tyr Lys Pro Lys Tyr
485 490 495

Phe Thr Ser Ala Ala Met Gly Thr Ser Thr Val Glu Ile Thr Trp Asp
500 505 510

Glu Thr Asp His Glu Arg Ile Thr Met Leu Asn Arg Lys Phe Lys Lys
515 520 525

Glu Glu Leu Leu Asp Met Asp Phe Gln Ala Tyr Leu Ala Ser Ser Ser
530 535 540

Glu Asp Glu Glu Glu Ile Glu Glu Glu Leu Gln Gly Asp Asp Gly Val
545 550 555 560

Asn Val Glu Glu Asp Gly Lys Thr Lys Lys Ser Gln Lys Asp Asp Glu
565 570 575

Glu Gln Ile Ala Lys Tyr Arg Gln Leu Leu Gln Val Ile Gln Glu Lys
580 585 590

Glu Lys Lys Gly Lys Glu Asn Asp Met Glu Met Glu Ile Lys Trp Val
595 600 605

Pro Gly Leu Lys Glu Ser Ala Glu Glu Met Val Lys Asn Lys Leu Glu
610 615 620

Gly Lys Asp Lys Leu Thr Pro Trp Glu Gln Phe Leu Glu Lys Lys Lys
625 630 635 640

Glu Lys Lys Arg Leu Lys Arg Lys Gln Lys Ala Leu Ala Glu Glu Ala
645 650 655

Ser Glu Glu Glu Leu Pro Ser Asp Val Asp Leu Asn Asp Pro Tyr Phe
660 665 670

Ala Glu Glu Val Lys Gln Ile Gly Ile Asn Lys Lys Ser Val Lys Ser
675 680 685

Ala Lys Asp Gly Thr Ser Pro Glu Glu Glu Ile Glu Ile Glu Arg Gln
690 695 700

Lys Ala Glu Met Ala Leu Leu Met Met Asp Glu Asp Glu Asp Ser Lys
705 710 715 720

Lys His Phe Asn Tyr Asn Lys Ile Val Glu His Gln Asn Leu Ser Lys
725 730 735

Lys Lys Lys Lys Gln Leu Met Lys Lys Lys Glu Leu Ile Glu Asp Asp

740 745 750

Phe Glu Val Asn Val Asn Asp Ala Arg Phe Gln Ala Met Tyr Thr Ser
755 760 765

His Leu Phe Asn Leu Asp Pro Ser Asp Pro Asn Phe Lys Lys Thr Lys
770 775 780

Ala Met Glu Lys Ile Leu Glu Glu Lys Ala Arg Gln Arg Glu Arg Lys
785 790 795 800

Glu Gln Glu Leu Thr Gln Ala Ile Lys Lys Lys Glu Ser Glu Ile Glu
805 810 815

Lys Glu Ser Gln Arg Lys Ser Ile Asp Pro Ala Leu Ser Met Leu Ile
820 825 830

Lys Ser Ile Lys Thr Lys Thr Glu Gln Phe Gln Ala Arg Lys Lys Gln
835 840 845

Lys Val Lys
850

<210> 2598
<211> 244
<212> PRT
<213> Homo sapiens

<400> 2598

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

Arg Val Gln Ser Leu Pro Thr Ser Ala Pro Leu Ser Val Ser Leu Pro
20 25 30

Thr Asn Ile Val Pro Pro Thr Thr Ile Trp Thr Ser Ser Pro Gln Asn
35 40 45

Thr Asp Ala Asp Thr Ala Ser Pro Ser Asn Gly Thr His Asn Asn Ser
50 55 60

Val Leu Pro Val Thr Ala Ser Ala Pro Thr Ser Leu Leu Pro Lys Asn
65 70 75 80

Ile Ser Ile Glu Ser Arg Glu Glu Glu Ile Thr Ser Pro Gly Ser Asn
85 90 95

Trp Glu Gly Thr Asn Thr Asp Pro Ser Pro Ser Gly Phe Ser Ser Thr
100 105 110

Ser Gly Gly Val His Leu Thr Thr Thr Leu Glu Glu His Ser Leu Gly
115 120 125

Thr Pro Glu Ala Gly Val Ala Ala Thr Leu Ser Gln Ser Ala Ala Glu
130 135 140

Pro Pro Thr Leu Ile Ser Pro Gln Ala Pro Ala Ser Ser Pro Ser Ser
145 150 155 160

Leu Ser Thr Ser Pro Pro Glu Val Phe Ser Ala Ser Val Thr Thr Asn
165 170 175

His Ser Ser Thr Val Thr Ser Thr Gln Pro Thr Gly Ala Pro Thr Ala
180 185 190

Pro Glu Ser Pro Thr Glu Glu Ser Ser Ser Asp His Thr Pro Thr Ser
195 200 205

His Ala Thr Ala Glu Pro Val Pro Gln Glu Lys Thr Pro Pro Thr Thr
210 215 220

Val Ser Gly Lys Val Met Cys Glu Leu Ile Asp Met Glu Thr Pro Pro
225 230 235 240

Pro Phe Pro Gly

<210> 2599
<211> 395
<212> PRT
<213> Homo sapiens

<400> 2599

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

Ser Cys Ala Val Ala Gln His Ala Pro Pro Trp Thr Glu Asp Cys Arg
20 25 30

Lys Ser Thr Tyr Pro Pro Ser Gly Pro Thr Tyr Arg Gly Ala Val Pro
35 40 45

Trp Tyr Thr Ile Asn Leu Asp Leu Pro Pro Tyr Lys Arg Trp His Glu

```
    50                  55                  60

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

Lys Asn Met Ile Asn Thr Phe Val Pro Ser Gly Lys Val Met Gln Val
                85                  90                  95

Val Asp Glu Lys Leu Pro Gly Leu Leu Gly Asn Phe Pro Gly Pro Phe
            100                 105                 110

Glu Glu Glu Met Lys Gly Ile Ala Ala Val Thr Asp Ile Pro Leu Gly
        115                 120                 125

Glu Ile Ile Ser Phe Asn Ile Phe Tyr Glu Leu Phe Thr Ile Cys Thr
    130                 135                 140

Ser Ile Val Ala Glu Asp Lys Lys Gly His Leu Ile His Gly Arg Asn
145                 150                 155                 160

Met Asp Phe Gly Val Phe Leu Gly Trp Asn Ile Asn Asn Asp Thr Trp
                165                 170                 175

Val Ile Thr Glu Gln Leu Lys Pro Leu Thr Val Asn Leu Asp Phe Gln
            180                 185                 190

Arg Asn Asn Lys Thr Val Phe Lys Ala Ser Ser Phe Ala Gly Tyr Val
        195                 200                 205

Gly Met Leu Thr Gly Phe Lys Pro Gly Leu Phe Ser Leu Thr Leu Asn
    210                 215                 220

Glu Arg Phe Ser Ile Asn Gly Gly Tyr Leu Gly Ile Leu Glu Trp Ile
225                 230                 235                 240

Leu Gly Lys Lys Asp Ala Met Trp Ile Gly Phe Leu Thr Arg Thr Val
                245                 250                 255

Leu Glu Asn Ser Thr Ser Tyr Glu Glu Ala Lys Asn Leu Leu Thr Lys
            260                 265                 270

Thr Lys Ile Leu Ala Pro Ala Tyr Phe Ile Leu Gly Gly Asn Gln Ser
        275                 280                 285

Gly Glu Gly Cys Val Ile Thr Arg Asp Arg Lys Glu Ser Leu Asp Val
    290                 295                 300
```

Tyr Glu Leu Asp Ala Lys Gln Gly Arg Trp Tyr Val Val Gln Thr Asn
305 310 315 320

Tyr Asp Arg Trp Lys His Pro Phe Phe Leu Asp Asp Arg Arg Thr Pro
325 330 335

Ala Lys Met Cys Leu Asn Arg Thr Ser Gln Glu Asn Ile Ser Phe Glu
340 345 350

Thr Met Tyr Asp Val Leu Ser Thr Lys Pro Val Leu Asn Lys Leu Thr
355 360 365

Val Tyr Thr Thr Leu Ile Asp Val Thr Lys Gly Gln Phe Glu Thr Tyr
370 375 380

Leu Arg Asp Cys Pro Asp Pro Cys Ile Gly Trp
385 390 395

<210> 2600
<211> 282
<212> PRT
<213> Homo sapiens

<400> 2600

Met Ser Leu Leu Ala Thr Leu Gly Leu Glu Leu Asp Arg Ala Leu Leu
1 5 10 15

Pro Ala Ser Gly Leu Gly Trp Leu Val Asp Tyr Gly Lys Leu Pro Pro
20 25 30

Ala Pro Ala Pro Leu Ala Pro Tyr Glu Val Leu Gly Gly Ala Leu Glu
35 40 45

Gly Gly Leu Pro Val Gly Gly Glu Pro Leu Ala Gly Asp Gly Phe Ser
50 55 60

Asp Trp Met Thr Glu Arg Val Asp Phe Thr Ala Leu Leu Pro Leu Glu
65 70 75 80

Pro Pro Leu Pro Pro Gly Thr Leu Pro Gln Pro Ser Pro Thr Pro Pro
85 90 95

Asp Leu Glu Ala Met Ala Ser Leu Leu Lys Lys Glu Leu Glu Gln Met
100 105 110

Glu Asp Phe Phe Leu Asp Ala Pro Pro Leu Pro Pro Pro Ser Pro Pro
115 120 125

Pro Leu Pro Pro Pro Pro Leu Pro Pro Ala Pro Ser Leu Pro Leu Ser
130 135 140

Leu Pro Ser Phe Asp Leu Pro Gln Pro Pro Val Leu Asp Thr Leu Asp
145 150 155 160

Leu Leu Ala Ile Tyr Cys Arg Asn Glu Ala Gly Gln Glu Glu Val Gly
165 170 175

Met Pro Pro Leu Pro Pro Pro Gln Gln Pro Pro Pro Pro Ser Pro Pro
180 185 190

Gln Pro Ser Arg Leu Ala Pro Tyr Pro His Pro Ala Thr Thr Arg Gly
195 200 205

Asp Arg Lys Gln Lys Lys Arg Asp Gln Asn Lys Ser Ala Ala Leu Arg
210 215 220

Tyr Arg Gln Arg Lys Arg Ala Glu Gly Glu Ala Leu Glu Gly Glu Cys
225 230 235 240

Gln Gly Leu Glu Ala Arg Asn Arg Glu Leu Lys Glu Arg Ala Glu Ser
245 250 255

Val Glu Arg Glu Ile Gln Tyr Val Lys Asp Leu Leu Ile Glu Val Tyr
260 265 270

Lys Ala Arg Ser Gln Arg Thr Arg Ser Cys
275 280

<210> 2601
<211> 23
<212> PRT
<213> Homo sapiens

<400> 2601

Met Glu Thr Ser Glu Gly Pro Gly Leu Glu Ser Thr Gly Ser Tyr Leu
1 5 10 15

Gly Ile Gln Gln Arg Ser Pro
20

<210> 2602
<211> 491

<212> PRT
<213> Homo sapiens

<400> 2602

```
Met Cys Asn Thr Asn Met Ser Val Pro Thr Asp Gly Ala Val Thr Thr
1               5                  10                  15

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

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

Thr Met Lys Glu Val Leu Phe Tyr Leu Gly Gln Tyr Ile Met Thr Lys
    50                  55                  60

Arg Leu Tyr Asp Glu Lys Gln Gln His Ile Val Tyr Cys Ser Asn Asp
65                  70                  75                  80

Leu Leu Gly Asp Leu Phe Gly Val Pro Ser Phe Ser Val Lys Glu His
                85                  90                  95

Arg Lys Ile Tyr Thr Met Ile Tyr Arg Asn Leu Val Val Val Asn Gln
            100                 105                 110

Gln Glu Ser Ser Asp Ser Gly Thr Ser Val Ser Glu Asn Arg Cys His
        115                 120                 125

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

Glu Lys Pro Ser Ser Ser His Leu Val Ser Arg Pro Ser Thr Ser Ser
145                 150                 155                 160

Arg Arg Arg Ala Ile Ser Glu Thr Glu Glu Asn Ser Asp Glu Leu Ser
                165                 170                 175

Gly Glu Arg Gln Arg Lys Arg His Lys Ser Asp Ser Ile Ser Leu Ser
            180                 185                 190

Phe Asp Glu Ser Leu Ala Leu Cys Val Ile Arg Glu Ile Cys Cys Glu
        195                 200                 205

Arg Ser Ser Ser Ser Glu Ser Thr Gly Thr Pro Ser Asn Pro Asp Leu
    210                 215                 220
```

Asp Ala Gly Val Ser Glu His Ser Gly Asp Trp Leu Asp Gln Asp Ser
225 230 235 240

Val Ser Asp Gln Phe Ser Val Glu Phe Glu Val Glu Ser Leu Asp Ser
245 250 255

Glu Asp Tyr Ser Leu Ser Glu Glu Gly Gln Glu Leu Ser Asp Glu Asp
260 265 270

Asp Glu Val Tyr Gln Val Thr Val Tyr Gln Ala Gly Glu Ser Asp Thr
275 280 285

Asp Ser Phe Glu Glu Asp Pro Glu Ile Ser Leu Ala Asp Tyr Trp Lys
290 295 300

Cys Thr Ser Cys Asn Glu Met Asn Pro Pro Leu Pro Ser His Cys Asn
305 310 315 320

Arg Cys Trp Ala Leu Arg Glu Asn Trp Leu Pro Glu Asp Lys Gly Lys
325 330 335

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

Ala Glu Glu Gly Phe Asp Val Pro Asp Cys Lys Lys Thr Ile Val Asn
355 360 365

Asp Ser Arg Glu Ser Cys Val Glu Glu Asn Asp Asp Lys Ile Thr Gln
370 375 380

Ala Ser Gln Ser Gln Glu Ser Glu Asp Tyr Ser Gln Pro Ser Thr Ser
385 390 395 400

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

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

Asn Ala Ile Glu Pro Cys Val Ile Cys Gln Gly Arg Pro Lys Asn Gly
435 440 445

Cys Ile Val His Gly Lys Thr Gly His Leu Met Ala Cys Phe Thr Cys
450 455 460

Ala Lys Lys Leu Lys Lys Arg Asn Lys Pro Cys Pro Val Cys Arg Gln

465 470 475 480

Pro Ile Gln Met Ile Val Leu Thr Tyr Phe Pro
485 490

<210> 2603
<211> 950
<212> PRT
<213> Homo sapiens

<400> 2603

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

Ile Ile Val Asn Cys Val Glu Glu Lys Pro Lys Glu Cys Asn Gly Val
20 25 30

Lys Ile Pro Val Asp Ala Ser Lys Pro Asn Pro Asn Asp Val Glu Phe
35 40 45

Asp Asn Leu Tyr Leu Asp Met Asn Gly Ile Ile His Pro Cys Thr His
50 55 60

Pro Glu Asp Lys Pro Ala Pro Lys Asn Glu Asp Glu Met Met Val Ala
65 70 75 80

Ile Phe Glu Tyr Ile Asp Arg Leu Phe Ser Ile Val Arg Pro Arg Arg
85 90 95

Leu Leu Tyr Met Ala Ile Asp Gly Val Ala Pro Arg Ala Lys Met Asn
100 105 110

Gln Gln Arg Ser Arg Arg Phe Arg Ala Ser Lys Glu Gly Met Glu Ala
115 120 125

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

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

Thr Pro Gly Thr Glu Phe Met Asp Asn Leu Ala Lys Cys Leu Arg Tyr
165 170 175

Tyr Ile Ala Asp Arg Leu Asn Asn Asp Pro Gly Trp Lys Asn Leu Thr
180 185 190

Val Ile Leu Ser Asp Ala Ser Ala Pro Gly Glu Gly Glu His Lys Ile
195 200 205

Met Asp Tyr Ile Arg Arg Gln Arg Ala Gln Pro Asn His Asp Pro Asn
210 215 220

Thr His His Cys Leu Cys Gly Ala Asp Ala Asp Leu Ile Met Leu Gly
225 230 235 240

Leu Ala Thr His Glu Pro Asn Phe Thr Ile Ile Arg Glu Glu Phe Lys
245 250 255

Pro Asn Lys Pro Lys Pro Cys Gly Leu Cys Asn Gln Phe Gly His Glu
260 265 270

Val Lys Asp Cys Glu Gly Leu Pro Arg Glu Lys Lys Gly Lys His Asp
275 280 285

Glu Leu Ala Asp Ser Leu Pro Cys Ala Glu Gly Glu Phe Ile Phe Leu
290 295 300

Arg Leu Asn Val Leu Arg Glu Tyr Leu Glu Arg Glu Leu Thr Met Ala
305 310 315 320

Ser Leu Pro Phe Thr Phe Asp Val Glu Arg Ser Ile Asp Asp Trp Val
325 330 335

Phe Met Cys Phe Phe Val Gly Asn Asp Phe Leu Pro His Leu Pro Ser
340 345 350

Leu Glu Ile Arg Glu Asn Ala Ile Asp Arg Leu Val Asn Ile Tyr Lys
355 360 365

Asn Val Val His Lys Thr Gly Gly Tyr Leu Thr Glu Ser Gly Tyr Val
370 375 380

Asn Leu Gln Arg Val Gln Met Ile Met Leu Ala Val Gly Glu Val Glu
385 390 395 400

Asp Ser Ile Phe Lys Lys Arg Lys Asp Asp Glu Asp Ser Phe Arg Arg
405 410 415

Arg Gln Lys Glu Lys Arg Lys Arg Met Lys Arg Asp Gln Pro Ala Phe
420 425 430

```
Thr Pro Ser Gly Ile Leu Thr Pro His Ala Leu Gly Ser Arg Asn Ser
        435                 440                 445

Pro Gly Ser Gln Val Ala Ser Asn Pro Arg Gln Ala Ala Tyr Glu Met
    450                 455                 460

Arg Met Gln Asn Asn Ser Ser Pro Ser Ile Ser Pro Asn Thr Ser Phe
465                 470                 475                 480

Thr Ser Asp Gly Ser Pro Ser Pro Leu Gly Gly Ile Lys Arg Lys Ala
                485                 490                 495

Glu Asp Ser Asp Ser Glu Pro Glu Pro Glu Asp Asn Val Arg Leu Trp
            500                 505                 510

Glu Ala Gly Trp Lys Gln Arg Tyr Tyr Lys Asn Lys Phe Asp Val Asp
        515                 520                 525

Ala Ala Asp Glu Lys Phe Arg Arg Lys Val Val Gln Ser Tyr Val Glu
    530                 535                 540

Gly Leu Cys Trp Val Leu Arg Tyr Tyr Tyr Gln Gly Cys Ala Ser Trp
545                 550                 555                 560

Lys Trp Tyr Tyr Pro Phe His Tyr Ala Pro Phe Ala Ser Asp Phe Glu
                565                 570                 575

Gly Ile Ala Asp Met Pro Ser Asp Phe Glu Lys Gly Thr Lys Pro Phe
            580                 585                 590

Lys Pro Leu Glu Gln Leu Met Gly Val Phe Pro Ala Ala Ser Gly Asn
        595                 600                 605

Phe Leu Pro Pro Ser Trp Arg Lys Leu Met Ser Asp Pro Asp Ser Ser
    610                 615                 620

Ile Ile Asp Phe Tyr Pro Glu Asp Phe Ala Ile Asp Leu Asn Gly Lys
625                 630                 635                 640

Lys Tyr Ala Trp Gln Gly Val Ala Leu Leu Pro Phe Val Asp Glu Arg
                645                 650                 655

Arg Leu Arg Ala Ala Leu Glu Glu Val Tyr Pro Asp Leu Thr Pro Glu
            660                 665                 670

Glu Thr Arg Arg Asn Ser Leu Gly Gly Asp Val Leu Phe Val Gly Lys
```

675 680 685

His His Pro Leu His Asp Phe Ile Leu Glu Leu Tyr Gln Thr Gly Ser
690 695 700

Thr Glu Pro Val Glu Val Pro Pro Glu Leu Cys His Gly Ile Gln Gly
705 710 715 720

Lys Phe Ser Leu Asp Glu Glu Ala Ile Leu Pro Asp Gln Ile Val Cys
725 730 735

Ser Pro Val Pro Met Leu Arg Asp Leu Thr Gln Asn Thr Val Val Ser
740 745 750

Ile Asn Phe Lys Asp Pro Gln Phe Ala Glu Asp Tyr Ile Phe Lys Ala
755 760 765

Val Met Leu Pro Gly Ala Arg Lys Pro Ala Ala Val Leu Lys Pro Ser
770 775 780

Asp Trp Glu Lys Ser Ser Asn Gly Arg Gln Trp Lys Pro Gln Leu Gly
785 790 795 800

Phe Asn Arg Asp Arg Arg Pro Val His Leu Asp Gln Ala Ala Phe Arg
805 810 815

Thr Leu Gly His Val Met Pro Arg Gly Ser Gly Thr Gly Ile Tyr Ser
820 825 830

Asn Ala Ala Pro Pro Pro Val Thr Tyr Gln Gly Asn Leu Tyr Arg Pro
835 840 845

Leu Leu Arg Gly Gln Ala Gln Ile Pro Lys Leu Met Ser Asn Met Arg
850 855 860

Pro Gln Asp Ser Trp Arg Gly Pro Pro Pro Leu Phe Gln Gln Gln Arg
865 870 875 880

Phe Asp Arg Gly Val Gly Ala Glu Pro Leu Leu Pro Trp Asn Arg Met
885 890 895

Leu Gln Thr Gln Asn Ala Ala Phe Gln Pro Asn Gln Tyr Gln Met Leu
900 905 910

Ala Gly Pro Gly Gly Tyr Pro Pro Arg Arg Asp Asp Arg Gly Gly Arg
915 920 925

Gln Gly Tyr Pro Arg Glu Gly Arg Lys Tyr Pro Leu Pro Pro Pro Ser
930 935 940

Gly Arg Tyr Asn Trp Asn
945 950

<210> 2604
<211> 313
<212> PRT
<213> Homo sapiens

<400> 2604

Met Ser Gln Ser Arg His Arg Ala Glu Ala Pro Pro Leu Glu Arg Glu
1 5 10 15

Asp Ser Gly Thr Phe Ser Leu Gly Lys Met Ile Thr Ala Lys Pro Gly
20 25 30

Lys Thr Pro Ile Gln Val Leu His Glu Tyr Gly Met Lys Thr Lys Asn
35 40 45

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

Thr Phe Thr Phe Arg Val Thr Val Gly Asp Ile Thr Cys Thr Gly Glu
65 70 75 80

Gly Thr Ser Lys Lys Leu Ala Lys His Arg Ala Ala Glu Ala Ala Ile
85 90 95

Asn Ile Leu Lys Ala Asn Ala Ser Ile Cys Phe Ala Val Pro Asp Pro
100 105 110

Leu Met Pro Asp Pro Ser Lys Gln Pro Lys Asn Gln Leu Asn Pro Ile
115 120 125

Gly Ser Leu Gln Glu Leu Ala Ile His His Gly Trp Arg Leu Pro Glu
130 135 140

Tyr Thr Leu Ser Gln Glu Gly Gly Pro Ala His Lys Arg Glu Tyr Thr
145 150 155 160

Thr Ile Cys Arg Leu Glu Ser Phe Met Glu Thr Gly Lys Gly Ala Ser
165 170 175

```
Lys Lys Gln Ala Lys Arg Asn Ala Ala Glu Lys Phe Leu Ala Lys Phe
            180                 185                 190

Ser Asn Ile Ser Pro Glu Asn His Ile Ser Leu Thr Asn Val Val Gly
        195                 200                 205

His Ser Leu Gly Cys Thr Trp His Ser Leu Arg Asn Ser Pro Gly Glu
    210                 215                 220

Lys Ile Asn Leu Leu Lys Arg Ser Leu Leu Ser Ile Pro Asn Thr Asp
225                 230                 235                 240

Tyr Ile Gln Leu Leu Ser Glu Ile Ala Lys Glu Gln Gly Phe Asn Ile
                245                 250                 255

Thr Tyr Leu Asp Ile Asp Glu Leu Ser Ala Asn Gly Gln Tyr Gln Cys
            260                 265                 270

Leu Ala Glu Leu Ser Thr Ser Pro Ile Thr Val Cys His Gly Ser Gly
        275                 280                 285

Ile Ser Cys Gly Asn Ala Gln Ser Asp Ala Ala His Asn Ala Leu Gln
    290                 295                 300

Tyr Leu Lys Ile Ile Ala Glu Arg Lys
305                 310
```

<210> 2605
<211> 198
<212> PRT
<213> Homo sapiens

<400> 2605

```
Met Ser Asn Val Arg Val Ser Asn Gly Ser Pro Ser Leu Glu Arg Met
1               5                   10                  15

Asp Ala Arg Gln Ala Glu His Pro Lys Pro Ser Ala Cys Arg Asn Leu
            20                  25                  30

Phe Gly Pro Val Asp His Glu Glu Leu Thr Arg Asp Leu Glu Lys His
        35                  40                  45

Cys Arg Asp Met Glu Glu Ala Ser Gln Arg Lys Trp Asn Phe Asp Phe
    50                  55                  60

Gln Asn His Lys Pro Leu Glu Gly Lys Tyr Glu Trp Gln Glu Val Glu
65                  70                  75                  80
```

Lys Gly Ser Leu Pro Glu Phe Tyr Tyr Arg Pro Pro Arg Pro Pro Lys
85 90 95

Gly Ala Cys Lys Val Pro Ala Gln Glu Ser Gln Asp Val Ser Gly Ser
100 105 110

Arg Pro Ala Ala Pro Leu Ile Gly Ala Pro Ala Asn Ser Glu Asp Thr
115 120 125

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

Ala Glu Gln Cys Ala Gly Ile Arg Lys Arg Pro Ala Thr Asp Asp Ser
145 150 155 160

Ser Thr Gln Asn Lys Arg Ala Asn Arg Thr Glu Glu Asn Val Ser Asp
165 170 175

Gly Ser Pro Asn Ala Gly Ser Val Glu Gln Thr Pro Lys Lys Pro Gly
180 185 190

Leu Arg Arg Arg Gln Thr
195

<210> 2606
<211> 727
<212> PRT
<213> Homo sapiens

<400> 2606

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

Glu Ala Lys Gly Asp Ala Lys Pro Glu Asp Asn Leu Leu Val Leu Thr
20 25 30

Val Ala Thr Lys Glu Thr Glu Gly Phe Arg Arg Phe Lys Arg Ser Ala
35 40 45

Gln Phe Phe Asn Tyr Lys Ile Gln Ala Leu Gly Leu Gly Glu Asp Trp
50 55 60

Asn Val Glu Lys Gly Thr Ser Ala Gly Gly Gly Gln Lys Val Arg Leu
65 70 75 80

Leu Lys Lys Ala Leu Glu Lys His Ala Asp Lys Glu Asp Leu Val Ile
85 90 95

Leu Phe Thr Asp Ser Tyr Asp Val Leu Phe Ala Ser Gly Pro Arg Glu
100 105 110

Leu Leu Lys Lys Phe Arg Gln Ala Arg Ser Gln Val Val Phe Ser Ala
115 120 125

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

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

Ala Pro Asn Leu Ser Lys Leu Val Ala Glu Trp Glu Gly Gln Asp Ser
165 170 175

Asp Ser Asp Gln Leu Phe Tyr Thr Lys Ile Phe Leu Asp Pro Glu Lys
180 185 190

Arg Glu Gln Ile Asn Ile Thr Leu Asp His Arg Cys Arg Ile Phe Gln
195 200 205

Asn Leu Asp Gly Ala Leu Asp Glu Val Val Leu Lys Phe Glu Met Gly
210 215 220

His Val Arg Ala Arg Asn Leu Ala Tyr Asp Thr Leu Pro Val Leu Ile
225 230 235 240

His Gly Asn Gly Pro Thr Lys Leu Gln Leu Asn Tyr Leu Gly Asn Tyr
245 250 255

Ile Pro Arg Phe Trp Thr Phe Glu Thr Gly Cys Thr Val Cys Asp Glu
260 265 270

Gly Leu Arg Ser Leu Lys Gly Ile Gly Asp Glu Ala Leu Pro Thr Val
275 280 285

Leu Val Gly Val Phe Ile Glu Gln Pro Thr Pro Phe Val Ser Leu Phe
290 295 300

Phe Gln Arg Leu Leu Arg Leu His Tyr Pro Gln Lys His Met Arg Leu
305 310 315 320

Phe Ile His Asn His Glu Gln His His Lys Ala Gln Val Glu Glu Phe

325 330 335

Leu Ala Gln His Gly Ser Glu Tyr Gln Ser Val Lys Leu Val Gly Pro
340 345 350

Glu Val Arg Met Ala Asn Ala Asp Ala Arg Asn Met Gly Ala Asp Leu
355 360 365

Cys Arg Gln Asp Arg Ser Cys Thr Tyr Tyr Phe Ser Val Asp Ala Asp
370 375 380

Val Ala Leu Thr Glu Pro Asn Ser Leu Arg Leu Leu Ile Gln Gln Asn
385 390 395 400

Lys Asn Val Ile Ala Pro Leu Met Thr Arg His Gly Arg Leu Trp Ser
405 410 415

Asn Phe Trp Gly Ala Leu Ser Ala Asp Gly Tyr Tyr Ala Arg Ser Glu
420 425 430

Asp Tyr Val Asp Ile Val Gln Gly Arg Arg Val Gly Val Trp Asn Val
435 440 445

Pro Tyr Ile Ser Asn Ile Tyr Leu Ile Lys Gly Ser Ala Leu Arg Gly
450 455 460

Glu Leu Gln Ser Ser Asp Leu Phe His His Ser Lys Leu Asp Pro Asp
465 470 475 480

Met Ala Phe Cys Ala Asn Ile Arg Gln Gln Asp Val Phe Met Phe Leu
485 490 495

Thr Asn Arg His Thr Leu Gly His Leu Leu Ser Leu Asp Ser Tyr Arg
500 505 510

Thr Thr His Leu His Asn Asp Leu Trp Glu Val Phe Ser Asn Pro Glu
515 520 525

Asp Trp Lys Glu Lys Tyr Ile His Gln Asn Tyr Thr Lys Ala Leu Ala
530 535 540

Gly Lys Leu Val Glu Thr Pro Cys Pro Asp Val Tyr Trp Phe Pro Ile
545 550 555 560

Phe Thr Glu Val Ala Cys Asp Glu Leu Val Glu Glu Met Glu His Phe
565 570 575

Gly Gln Trp Ser Leu Gly Asn Asn Lys Asp Asn Arg Ile Gln Gly Gly
580 585 590

Tyr Glu Asn Val Pro Thr Ile Asp Ile His Met Asn Gln Ile Gly Phe
595 600 605

Glu Arg Glu Trp His Lys Phe Leu Leu Glu Tyr Ile Ala Pro Met Thr
610 615 620

Glu Lys Leu Tyr Pro Gly Tyr Tyr Thr Arg Ala Gln Phe Asp Leu Ala
625 630 635 640

Phe Val Val Arg Tyr Lys Pro Asp Glu Gln Pro Ser Leu Met Pro His
645 650 655

His Asp Ala Ser Thr Phe Thr Ile Asn Ile Ala Leu Asn Arg Val Gly
660 665 670

Val Asp Tyr Glu Gly Gly Gly Cys Arg Phe Leu Arg Tyr Asn Cys Ser
675 680 685

Ile Arg Ala Pro Arg Lys Gly Trp Thr Leu Met His Pro Gly Arg Leu
690 695 700

Thr His Tyr His Glu Gly Leu Pro Thr Thr Arg Gly Thr Arg Tyr Ile
705 710 715 720

Ala Val Ser Phe Val Asp Pro
725

<210> 2607
<211> 537
<212> PRT
<213> Homo sapiens

<400> 2607

Met Ala Trp Arg Gly Ala Gly Pro Ser Val Pro Gly Ala Pro Gly Gly
1 5 10 15

Val Gly Leu Ser Leu Gly Leu Leu Leu Gln Leu Leu Leu Leu Leu Gly
20 25 30

Pro Ala Arg Gly Phe Gly Asp Glu Glu Glu Arg Arg Cys Asp Pro Ile
35 40 45

```
Arg Ile Ser Met Cys Gln Asn Leu Gly Tyr Asn Val Thr Lys Met Pro
    50                  55                  60

Asn Leu Val Gly His Glu Leu Gln Thr Asp Ala Glu Leu Gln Leu Thr
65                  70                  75                  80

Thr Phe Thr Pro Leu Ile Gln Tyr Gly Cys Ser Ser Gln Leu Gln Phe
                85                  90                  95

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

Pro Ile Gly Pro Cys Gly Gly Met Cys Leu Ser Val Lys Arg Arg Cys
        115                 120                 125

Glu Pro Val Leu Lys Glu Phe Gly Phe Ala Trp Pro Glu Ser Leu Asn
    130                 135                 140

Cys Ser Lys Phe Pro Pro Gln Asn Asp His Asn His Met Cys Met Glu
145                 150                 155                 160

Gly Pro Gly Asp Glu Glu Val Pro Leu Pro His Lys Thr Pro Ile Gln
                165                 170                 175

Pro Gly Glu Glu Cys His Ser Val Gly Thr Asn Ser Asp Gln Tyr Ile
            180                 185                 190

Trp Val Lys Arg Ser Leu Asn Cys Val Leu Lys Cys Gly Tyr Asp Ala
        195                 200                 205

Gly Leu Tyr Ser Arg Ser Ala Lys Glu Phe Thr Asp Ile Trp Met Ala
    210                 215                 220

Val Trp Ala Ser Leu Cys Phe Ile Ser Thr Ala Phe Thr Val Leu Thr
225                 230                 235                 240

Phe Leu Ile Asp Ser Ser Arg Phe Ser Tyr Pro Glu Arg Pro Ile Ile
                245                 250                 255

Phe Leu Ser Met Cys Tyr Asn Ile Tyr Ser Ile Ala Tyr Ile Val Arg
            260                 265                 270

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

Glu Pro Val Leu Ile Gln Glu Gly Leu Lys Asn Thr Gly Cys Ala Ile
```

290 295 300

Ile Phe Leu Leu Met Tyr Phe Phe Gly Met Ala Ser Ser Ile Trp Trp
305 310 315 320

Val Ile Leu Thr Leu Thr Trp Phe Leu Ala Ala Gly Leu Lys Trp Gly
325 330 335

His Glu Ala Ile Glu Met His Ser Ser Tyr Phe His Ile Ala Ala Trp
340 345 350

Ala Ile Pro Ala Val Lys Thr Ile Val Ile Leu Ile Met Arg Leu Val
355 360 365

Asp Ala Asp Glu Leu Thr Gly Leu Cys Tyr Val Gly Asn Gln Asn Leu
370 375 380

Asp Ala Leu Thr Gly Phe Val Val Ala Pro Leu Phe Thr Tyr Leu Val
385 390 395 400

Ile Gly Thr Leu Phe Ile Ala Ala Gly Leu Val Ala Leu Phe Lys Ile
405 410 415

Arg Ser Asn Leu Gln Lys Asp Gly Thr Lys Thr Asp Lys Leu Glu Arg
420 425 430

Leu Met Val Lys Ile Gly Val Phe Ser Val Leu Tyr Thr Val Pro Ala
435 440 445

Thr Cys Val Ile Ala Cys Tyr Phe Tyr Glu Ile Ser Asn Trp Ala Leu
450 455 460

Phe Arg Tyr Ser Ala Asp Asp Ser Asn Met Ala Val Glu Met Leu Lys
465 470 475 480

Ile Phe Met Ser Leu Leu Val Gly Ile Thr Ser Gly Met Trp Ile Trp
485 490 495

Ser Ala Lys Thr Leu His Thr Trp Gln Lys Cys Ser Asn Arg Leu Val
500 505 510

Asn Ser Gly Lys Val Lys Arg Glu Lys Arg Gly Asn Gly Trp Val Lys
515 520 525

Pro Gly Lys Gly Ser Glu Thr Val Val
530 535

<210> 2608
<211> 362
<212> PRT
<213> Homo sapiens

<400> 2608

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

Leu Ala Leu Thr Glu Thr Trp Ala Gly Ser His Ser Met Arg Tyr Phe
20 25 30

Tyr Thr Ser Val Ser Arg Pro Gly Arg Gly Glu Pro Arg Phe Ile Ser
35 40 45

Val Gly Tyr Val Asp Asp Thr Gln Phe Val Arg Phe Asp Ser Asp Ala
50 55 60

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

Pro Glu Tyr Trp Asp Arg Asn Thr Gln Ile Tyr Lys Ala Gln Ala Gln
85 90 95

Thr Asp Arg Glu Ser Leu Arg Asn Leu Arg Gly Tyr Tyr Asn Gln Ser
100 105 110

Glu Ala Gly Ser His Thr Leu Gln Ser Met Tyr Gly Cys Asp Val Gly
115 120 125

Pro Asp Gly Arg Leu Leu Arg Gly His Asp Gln Tyr Ala Tyr Asp Gly
130 135 140

Lys Asp Tyr Ile Ala Leu Asn Glu Asp Leu Arg Ser Trp Thr Ala Ala
145 150 155 160

Asp Thr Ala Ala Gln Ile Thr Gln Arg Lys Trp Glu Ala Ala Arg Glu
165 170 175

Ala Glu Gln Arg Arg Ala Tyr Leu Glu Gly Glu Cys Val Glu Trp Leu
180 185 190

Arg Arg Tyr Leu Glu Asn Gly Lys Asp Lys Leu Glu Arg Ala Asp Pro
195 200 205

Pro Lys Thr His Val Thr His His Pro Ile Ser Asp His Glu Ala Thr
210 215 220

Leu Arg Cys Trp Ala Leu Gly Phe Tyr Pro Ala Glu Ile Thr Leu Thr
225 230 235 240

Trp Gln Arg Asp Gly Glu Asp Gln Thr Gln Asp Thr Glu Leu Val Glu
245 250 255

Thr Arg Pro Ala Gly Asp Arg Thr Phe Gln Lys Trp Ala Ala Val Val
260 265 270

Val Pro Ser Gly Glu Glu Gln Arg Tyr Thr Cys His Val Gln His Glu
275 280 285

Gly Leu Pro Lys Pro Leu Thr Leu Arg Trp Glu Pro Ser Ser Gln Ser
290 295 300

Thr Val Pro Ile Val Gly Ile Val Ala Gly Leu Ala Val Leu Ala Val
305 310 315 320

Val Val Ile Gly Ala Val Val Ala Ala Val Met Cys Arg Arg Lys Ser
325 330 335

Ser Gly Gly Lys Gly Gly Ser Tyr Ser Gln Ala Ala Cys Ser Asp Ser
340 345 350

Ala Gln Gly Ser Asp Val Ser Leu Thr Ala
355 360

<210> 2609
<211> 350
<212> PRT
<213> Homo sapiens

<400> 2609

Met Glu Thr Asn Ser Ser Leu Pro Thr Asn Ile Ser Gly Gly Thr Pro
1 5 10 15

Ala Val Ser Ala Gly Tyr Leu Phe Leu Asp Ile Ile Thr Tyr Leu Val
20 25 30

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

Trp Val Ala Gly Phe Arg Met Thr His Thr Val Thr Thr Ile Ser Tyr
50 55 60

Leu Asn Leu Ala Val Ala Asp Phe Cys Phe Thr Ser Thr Leu Pro Phe
65 70 75 80

Phe Met Val Arg Lys Ala Met Gly Gly His Trp Pro Phe Gly Trp Phe
85 90 95

Leu Cys Lys Phe Val Phe Thr Ile Val Asp Ile Asn Leu Phe Gly Ser
100 105 110

Val Phe Leu Ile Ala Leu Ile Ala Leu Asp Arg Cys Val Cys Val Leu
115 120 125

His Pro Val Trp Thr Gln Asn His Arg Thr Val Ser Leu Ala Lys Lys
130 135 140

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

Ile Ile Arg Val Thr Thr Val Pro Gly Lys Thr Gly Thr Val Ala Cys
165 170 175

Thr Phe Asn Phe Ser Pro Trp Thr Asn Asp Pro Lys Glu Arg Ile Asn
180 185 190

Val Ala Val Ala Met Leu Thr Val Arg Gly Ile Ile Arg Phe Ile Ile
195 200 205

Gly Phe Ser Ala Pro Met Ser Ile Val Ala Val Ser Tyr Gly Leu Ile
210 215 220

Ala Thr Lys Ile His Lys Gln Gly Leu Ile Lys Ser Ser Arg Pro Leu
225 230 235 240

Arg Val Leu Ser Phe Val Ala Ala Ala Phe Phe Leu Cys Trp Ser Pro
245 250 255

Tyr Gln Val Val Ala Leu Ile Ala Thr Val Arg Ile Arg Glu Leu Leu
260 265 270

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

Leu Ala Phe Phe Asn Ser Cys Leu Asn Pro Met Leu Tyr Val Phe Met
290 295 300

Gly Gln Asp Phe Arg Glu Arg Leu Ile His Ala Leu Pro Ala Ser Leu
305 310 315 320

Glu Arg Ala Leu Thr Glu Asp Ser Thr Gln Thr Ser Asp Thr Ala Thr
325 330 335

Asn Ser Thr Leu Pro Ser Ala Glu Val Glu Leu Gln Ala Lys
340 345 350

<210> 2610
<211> 638
<212> PRT
<213> Homo sapiens

<400> 2610

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

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

Cys Gly Ala Pro Ser Val Thr Val Thr Lys Ser His Lys Arg Gly Met
35 40 45

Lys Gly Asp Thr Val Asn Val Arg Arg Ser Val Arg Val Lys Thr Lys
50 55 60

Asn Pro Pro His Cys Leu Glu Ile Thr Pro Pro Ser Ser Glu Lys Leu
65 70 75 80

Val Ser Val Met Arg Leu Ser Asp Leu Ser Thr Glu Asp Asp Asp Ser
85 90 95

Gly His Cys Lys Met Asn Arg Tyr Asp Lys Lys Ile Asp Ser Leu Met
100 105 110

Asn Ala Val Gly Cys Leu Lys Ser Glu Val Lys Met Gln Lys Gly Glu
115 120 125

Arg Gln Met Ala Lys Arg Phe Leu Glu Glu Arg Lys Glu Glu Leu Glu
130 135 140

Glu Val Ala His Glu Leu Ala Glu Thr Glu His Glu Asn Thr Val Leu
145 150 155 160

Arg His Asn Ile Glu Arg Met Lys Glu Glu Lys Asp Phe Thr Ile Leu

```
                165                 170                 175

Gln Lys Lys His Leu Gln Gln Glu Lys Glu Cys Leu Met Ser Lys Leu
            180                 185                 190

Val Glu Ala Glu Met Asp Gly Ala Ala Ala Ala Lys Gln Val Met Ala
        195                 200                 205

Leu Lys Asp Thr Ile Gly Lys Leu Lys Thr Glu Lys Gln Met Thr Cys
    210                 215                 220

Thr Asp Ile Asn Thr Leu Thr Arg Gln Lys Glu Leu Leu Leu Gln Lys
225                 230                 235                 240

Leu Ser Thr Phe Glu Glu Thr Asn Arg Thr Leu Arg Asp Leu Leu Arg
                245                 250                 255

Glu Gln His Cys Lys Glu Asp Ser Glu Arg Leu Met Glu Gln Gln Gly
            260                 265                 270

Ala Leu Leu Lys Arg Leu Ala Glu Ala Asp Ser Glu Lys Ala Arg Leu
        275                 280                 285

Leu Leu Leu Leu Gln Asp Lys Asp Lys Glu Val Glu Glu Leu Leu Gln
    290                 295                 300

Glu Ile Gln Cys Glu Lys Ala Gln Ala Lys Thr Ala Ser Glu Leu Ser
305                 310                 315                 320

Lys Ser Met Glu Ser Met Arg Gly His Leu Gln Ala Gln Leu Arg Ser
                325                 330                 335

Lys Glu Ala Glu Asn Ser Arg Leu Cys Met Gln Ile Lys Asn Leu Glu
            340                 345                 350

Arg Ser Gly Asn Gln His Lys Ala Glu Val Glu Ala Ile Met Glu Gln
        355                 360                 365

Leu Lys Glu Leu Lys Gln Lys Gly Asp Arg Asp Lys Glu Ser Leu Lys
    370                 375                 380

Lys Ala Ile Arg Ala Gln Lys Glu Arg Ala Glu Lys Ser Glu Glu Tyr
385                 390                 395                 400

Ala Glu Gln Leu His Val Gln Leu Ala Asp Lys Asp Leu Tyr Val Ala
                405                 410                 415
```

```
Glu Ala Leu Ser Thr Leu Glu Ser Trp Arg Ser Arg Tyr Asn Gln Val
            420                 425                 430

Val Lys Glu Lys Gly Asp Leu Glu Leu Glu Ile Ile Val Leu Asn Asp
        435                 440                 445

Arg Val Thr Asp Leu Val Asn Gln Gln Gln Thr Leu Glu Glu Lys Met
    450                 455                 460

Arg Glu Asp Arg Asp Ser Leu Val Glu Arg Leu His Arg Gln Thr Ala
465                 470                 475                 480

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

Ala Pro Met Glu Asp Lys Leu Asn Gln Ala His Leu Glu Val Gln Gln
            500                 505                 510

Leu Lys Ala Ser Val Lys Asn Tyr Glu Gly Met Ile Asp Asn Tyr Lys
        515                 520                 525

Ser Gln Val Met Lys Thr Arg Leu Glu Ala Asp Glu Val Ala Ala Gln
    530                 535                 540

Leu Glu Arg Cys Asp Lys Glu Asn Lys Ile Leu Lys Asp Glu Met Asn
545                 550                 555                 560

Lys Glu Ile Glu Ala Ala Arg Arg Gln Phe Gln Ser Gln Leu Ala Asp
                565                 570                 575

Leu Gln Gln Leu Pro Asp Ile Leu Lys Ile Thr Glu Ala Lys Leu Ala
            580                 585                 590

Glu Cys Gln Asp Gln Leu Gln Gly Tyr Glu Arg Lys Asn Ile Asp Leu
        595                 600                 605

Thr Ala Ile Ile Ser Asp Leu Arg Ser Arg Val Arg Asp Trp Gln Lys
    610                 615                 620

Gly Ser His Glu Leu Thr Arg Ala Gly Ala Arg Ile Pro Arg
625                 630                 635
```

<210> 2611
<211> 197
<212> PRT

<213> Homo sapiens

<400> 2611

```
Met Thr Leu Leu Pro Gly Leu Leu Phe Leu Thr Trp Leu His Thr Cys
1               5                  10                  15

Leu Ala His His Asp Pro Ser Leu Arg Gly His Pro His Ser His Gly
            20                  25                  30

Thr Pro His Cys Tyr Ser Ala Glu Glu Leu Pro Leu Gly Gln Ala Pro
        35                  40                  45

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

Ala Leu Val Ser Ser Leu Glu Ala Ala Ser His Arg Gly Arg His Glu
65                  70                  75                  80

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

Leu Glu Ala Asp Thr His Gln Arg Ser Ile Ser Pro Trp Arg Tyr Arg
            100                 105                 110

Val Asp Thr Asp Glu Asp Arg Tyr Pro Gln Lys Leu Ala Phe Ala Glu
        115                 120                 125

Cys Leu Cys Arg Gly Cys Ile Asp Ala Arg Thr Gly Arg Glu Thr Ala
    130                 135                 140

Ala Leu Asn Ser Val Arg Leu Leu Gln Ser Leu Leu Val Leu Arg Arg
145                 150                 155                 160

Arg Pro Cys Ser Arg Asp Gly Ser Gly Leu Pro Thr Pro Gly Ala Phe
                165                 170                 175

Ala Phe His Thr Glu Phe Ile His Val Pro Val Gly Cys Thr Cys Val
            180                 185                 190

Leu Pro Arg Ser Val
        195
```

<210> 2612
<211> 570
<212> PRT
<213> Homo sapiens

<400> 2612

```
Met Asn Val Val Phe Ala Val Lys Gln Tyr Ile Ser Lys Met Ile Glu
1               5                   10                  15

Asp Ser Gly Pro Gly Met Lys Val Leu Leu Met Asp Lys Glu Thr Thr
            20                  25                  30

Gly Ile Val Ser Met Val Tyr Thr Gln Ser Glu Ile Leu Gln Lys Glu
        35                  40                  45

Val Tyr Leu Phe Glu Arg Ile Asp Ser Gln Asn Arg Glu Ile Met Lys
    50                  55                  60

His Leu Lys Ala Ile Cys Phe Leu Arg Pro Thr Lys Glu Asn Val Asp
65                  70                  75                  80

Tyr Ile Ile Gln Glu Leu Arg Arg Pro Lys Tyr Thr Ile Tyr Phe Ile
                85                  90                  95

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

Ala Asp Glu Gln Glu Val Val Ala Glu Val Gln Glu Phe Tyr Gly Asp
        115                 120                 125

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

Cys Gln Gly Arg Asn Trp Asp Pro Ala Gln Leu Ser Arg Thr Thr Gln
145                 150                 155                 160

Gly Leu Thr Ala Leu Leu Leu Ser Leu Lys Lys Cys Pro Met Ile Arg
                165                 170                 175

Tyr Gln Leu Ser Ser Glu Ala Ala Lys Arg Leu Ala Glu Cys Val Lys
            180                 185                 190

Gln Val Ile Thr Lys Glu Tyr Glu Leu Phe Glu Phe Arg Arg Thr Glu
        195                 200                 205

Val Pro Pro Leu Leu Leu Ile Leu Asp Arg Cys Asp Asp Ala Ile Thr
    210                 215                 220

Pro Leu Leu Asn Gln Trp Thr Tyr Gln Ala Met Val His Glu Leu Leu
225                 230                 235                 240
```

```
Gly Ile Asn Asn Asn Arg Ile Asp Leu Ser Arg Val Pro Gly Ile Ser
                245                 250                 255

Lys Asp Leu Arg Glu Val Val Leu Ser Ala Glu Asn Asp Glu Phe Tyr
            260                 265                 270

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

Asn Leu Met Glu Asp Phe Gln Lys Lys Lys Pro Lys Glu Gln Gln Lys
    290                 295                 300

Leu Glu Ser Ile Ala Asp Met Lys Ala Phe Val Glu Asn Tyr Pro Gln
305                 310                 315                 320

Phe Lys Lys Met Ser Gly Thr Val Ser Lys His Val Thr Val Val Gly
                325                 330                 335

Glu Leu Ser Arg Leu Val Ser Glu Arg Asn Leu Leu Glu Val Ser Glu
            340                 345                 350

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

Asn Ile Lys Arg Leu Leu Gln Asn Pro Lys Val Thr Glu Phe Asp Ala
    370                 375                 380

Ala Arg Leu Val Met Leu Tyr Ala Leu His Tyr Glu Arg His Ser Ser
385                 390                 395                 400

Asn Ser Leu Pro Gly Leu Met Met Asp Leu Arg Asn Lys Gly Val Ser
                405                 410                 415

Glu Lys Tyr Arg Lys Leu Val Ser Ala Val Val Glu Tyr Gly Gly Lys
            420                 425                 430

Arg Val Arg Gly Ser Asp Leu Phe Ser Pro Lys Asp Ala Val Ala Ile
        435                 440                 445

Thr Lys Gln Phe Leu Lys Gly Leu Lys Gly Val Glu Asn Val Tyr Thr
    450                 455                 460

Gln His Gln Pro Phe Leu His Glu Thr Leu Asp His Leu Ile Lys Gly
465                 470                 475                 480
```

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

Asp Arg Pro Gln Asp Ile Ile Val Phe Val Ile Gly Gly Ala Thr Tyr
            500                 505                 510

Glu Glu Ala Leu Thr Val Tyr Asn Leu Asn Arg Thr Thr Pro Gly Val
        515                 520                 525

Arg Ile Val Leu Gly Gly Thr Thr Val His Asn Thr Lys Ser Phe Leu
    530                 535                 540

Glu Glu Val Leu Ala Ser Gly Leu His Ser Arg Ser Lys Glu Ser Ser
545                 550                 555                 560

Gln Val Thr Ser Arg Ser Ala Ser Arg Arg
                565                 570
```

<210> 2613
<211> 474
<212> PRT
<213> Homo sapiens

<400> 2613

```
Met Thr Ile Leu Thr Tyr Pro Phe Lys Asn Leu Pro Thr Ala Ser Lys
1               5                   10                  15

Trp Ala Leu Arg Phe Ser Ile Arg Pro Leu Ser Cys Ser Ser Gln Leu
            20                  25                  30

Arg Ala Ala Pro Ala Val Gln Thr Lys Thr Lys Lys Thr Leu Ala Lys
        35                  40                  45

Pro Asn Ile Arg Asn Val Val Val Val Asp Gly Val Arg Thr Pro Phe
    50                  55                  60

Leu Leu Ser Gly Thr Ser Tyr Lys Asp Leu Met Pro His Asp Leu Ala
65                  70                  75                  80

Arg Ala Ala Leu Thr Gly Leu Leu His Arg Thr Ser Val Pro Lys Glu
                85                  90                  95

Val Val Asp Tyr Ile Ile Phe Gly Thr Val Ile Gln Glu Val Lys Thr
            100                 105                 110

Ser Asn Val Ala Arg Glu Ala Ala Leu Gly Ala Gly Phe Ser Asp Lys
        115                 120                 125
```

```
Thr Pro Ala His Thr Val Thr Met Ala Cys Ile Ser Ala Asn Gln Ala
    130                 135                 140

Met Thr Thr Gly Val Gly Leu Ile Ala Ser Gly Gln Cys Asp Val Ile
145                 150                 155                 160

Val Ala Gly Gly Val Glu Leu Met Ser Asp Val Pro Ile Arg His Ser
                165                 170                 175

Arg Lys Met Arg Lys Leu Met Leu Asp Leu Asn Lys Ala Lys Ser Met
            180                 185                 190

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

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

His Ser Ala Asp Arg Leu Ala Ala Ala Phe Ala Val Ser Arg Leu Glu
225                 230                 235                 240

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

Asp Glu Gly Leu Leu Ser Asp Val Val Pro Phe Lys Val Pro Gly Lys
            260                 265                 270

Asp Thr Val Thr Lys Asp Asn Gly Ile Arg Pro Ser Ser Leu Glu Gln
        275                 280                 285

Met Ala Lys Leu Lys Pro Ala Phe Ile Lys Pro Tyr Gly Thr Val Thr
    290                 295                 300

Ala Ala Asn Ser Ser Phe Leu Thr Asp Gly Ala Ser Ala Met Leu Ile
305                 310                 315                 320

Met Ala Glu Glu Lys Ala Leu Ala Met Gly Tyr Lys Pro Lys Ala Tyr
                325                 330                 335

Leu Arg Asp Phe Met Tyr Val Ser Gln Asp Pro Lys Asp Gln Leu Leu
            340                 345                 350

Leu Gly Pro Thr Tyr Ala Thr Pro Lys Val Leu Glu Lys Ala Gly Leu
        355                 360                 365
```

```
Thr Met Asn Asp Ile Asp Ala Phe Glu Phe His Glu Ala Phe Ser Gly
    370                 375                 380

Gln Ile Leu Ala Asn Phe Lys Ala Met Asp Ser Asp Trp Phe Ala Glu
385                 390                 395                 400

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

Phe Asn Asn Trp Gly Gly Ser Leu Ser Leu Gly His Pro Phe Gly Ala
            420                 425                 430

Thr Gly Cys Arg Leu Val Met Ala Ala Ala Asn Arg Leu Arg Lys Glu
        435                 440                 445

Gly Gly Gln Tyr Gly Leu Val Ala Ala Cys Ala Ala Gly Gly Gln Gly
    450                 455                 460

His Ala Met Ile Val Glu Ala Tyr Pro Lys
465                 470
```

<210> 2614
<211> 793
<212> PRT
<213> Homo sapiens

<400> 2614

```
Met Glu Ser Arg Ala Glu Gly Gly Ser Pro Ala Val Phe Asp Trp Phe
1               5                   10                  15

Phe Glu Ala Ala Cys Pro Ala Ser Leu Gln Glu Asp Pro Pro Ile Leu
            20                  25                  30

Arg Gln Phe Pro Pro Asp Phe Arg Asp Gln Glu Ala Met Gln Met Val
        35                  40                  45

Pro Lys Phe Cys Phe Pro Phe Asp Val Glu Arg Glu Pro Pro Ser Pro
    50                  55                  60

Ala Val Gln His Phe Thr Phe Ala Leu Thr Asp Leu Ala Gly Asn Arg
65                  70                  75                  80

Arg Phe Gly Phe Cys Arg Leu Arg Ala Gly Thr Gln Ser Cys Leu Cys
                85                  90                  95

Ile Leu Ser His Leu Pro Trp Phe Glu Val Phe Tyr Lys Leu Leu Asn
```

100 105 110

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

Leu Leu Gln Asn Leu Phe Gln Gln Ser Leu Ser Gly Pro Gln Ala Ser
130 135 140

Val Gly Leu Glu Leu Gly Ser Gly Val Thr Val Ser Ser Gly Gln Gly
145 150 155 160

Ile Pro Pro Pro Thr Arg Gly Asn Ser Lys Pro Leu Ser Cys Phe Val
165 170 175

Ala Pro Asp Ser Gly Arg Leu Pro Ser Ile Pro Glu Asn Arg Asn Leu
180 185 190

Thr Glu Leu Val Val Ala Val Thr Asp Glu Asn Ile Val Gly Leu Phe
195 200 205

Ala Ala Leu Leu Ala Glu Arg Arg Val Leu Leu Thr Ala Ser Lys Leu
210 215 220

Ser Thr Leu Thr Ser Cys Val His Ala Ser Cys Ala Leu Leu Tyr Pro
225 230 235 240

Met Arg Trp Glu His Val Leu Ile Pro Thr Leu Pro Pro His Leu Leu
245 250 255

Asp Tyr Cys Cys Ala Pro Met Pro Tyr Leu Ile Gly Val His Ala Ser
260 265 270

Leu Ala Glu Arg Val Arg Glu Lys Ala Leu Glu Asp Val Val Val Leu
275 280 285

Asn Val Asp Ala Asn Thr Leu Glu Thr Thr Phe Asn Asp Val Gln Ala
290 295 300

Leu Pro Pro Asp Val Val Ser Leu Leu Arg Leu Arg Leu Arg Lys Val
305 310 315 320

Ala Leu Ala Pro Gly Glu Gly Val Ser Arg Leu Phe Leu Lys Ala Gln
325 330 335

Ala Leu Leu Phe Gly Gly Tyr Arg Asp Ala Leu Val Cys Ser Pro Gly
340 345 350

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

Ala Pro Leu Gln Ala Phe His Arg Arg Ala Val His Leu Gln Leu Phe
370 375 380

Lys Gln Phe Ile Glu Ala Arg Leu Glu Lys Leu Asn Lys Gly Glu Gly
385 390 395 400

Phe Ser Asp Gln Phe Glu Gln Glu Ile Thr Gly Cys Gly Ala Ser Pro
405 410 415

Gly Ala Leu Arg Ser Tyr Gln Leu Trp Ala Asp Asn Leu Lys Lys Gly
420 425 430

Gly Gly Ala Leu Leu His Ser Val Lys Ala Lys Thr Gln Pro Ala Val
435 440 445

Lys Asn Met Tyr Arg Ser Ala Lys Ser Gly Leu Lys Gly Val Gln Ser
450 455 460

Leu Leu Met Tyr Lys Asp Gly Asp Ser Val Leu Gln Arg Gly Gly Ser
465 470 475 480

Leu Arg Ala Pro Ala Leu Pro Ser Arg Ser Asp Arg Leu Gln Gln Arg
485 490 495

Leu Pro Ile Thr Gln His Phe Gly Lys Asn Arg Pro Leu Arg Pro Ser
500 505 510

Arg Arg Arg Gln Leu Glu Glu Gly Thr Ser Glu Pro Pro Gly Ala Gly
515 520 525

Thr Pro Pro Leu Ser Pro Glu Asp Glu Gly Cys Pro Trp Ala Glu Glu
530 535 540

Ala Leu Asp Ser Ser Phe Leu Gly Ser Gly Glu Glu Leu Asp Leu Leu
545 550 555 560

Ser Glu Ile Leu Asp Ser Leu Ser Met Gly Ala Lys Ser Ala Gly Ser
565 570 575

Leu Arg Pro Ser Gln Ser Leu Asp Cys Cys His Arg Gly Asp Leu Asp
580 585 590

Ser Cys Phe Ser Leu Pro Asn Ile Leu Arg Trp Gln Pro Asp Asp Lys
595 600 605

Lys Leu Pro Glu Pro Glu Pro Gln Pro Leu Ser Leu Pro Ser Leu Gln
610 615 620

Asn Ala Ser Ser Leu Asp Ala Thr Ser Ser Ser Lys Asp Ser Arg Ser
625 630 635 640

Gln Leu Ile Pro Ser Glu Ser Asp Gln Glu Val Thr Ser Pro Ser Gln
645 650 655

Ser Ser Thr Ala Ser Ala Asp Pro Ser Ile Trp Gly Asp Pro Lys Pro
660 665 670

Ser Pro Leu Thr Glu Pro Leu Ile Leu His Leu Thr Pro Ser His Lys
675 680 685

Ala Ala Glu Asp Phe Thr Ala Gln Glu Asn Pro Thr Pro Trp Leu Ser
690 695 700

Thr Ala Pro Thr Glu Pro Ser Pro Pro Glu Ser Pro Gln Ile Leu Ala
705 710 715 720

Pro Thr Lys Pro Asn Phe Asp Ile Ala Trp Thr Ser Gln Pro Leu Asp
725 730 735

Pro Ser Ser Asp Pro Ser Ser Leu Glu Asp Pro Arg Ala Arg Pro Pro
740 745 750

Lys Ala Leu Leu Ala Glu Arg Ala His Leu Gln Pro Arg Glu Glu Pro
755 760 765

Gly Ala Leu Asn Ser Pro Ala Thr Pro Thr Ser Asn Cys Gln Lys Ser
770 775 780

Gln Pro Ser Lys Pro Ala Gln Ser Arg
785 790

<210> 2615
<211> 83
<212> PRT
<213> Homo sapiens

<400> 2615

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

1 5 10 15

Val Val Phe Met Thr Val Ala Ala Gly Gly Ala Ser Ser Phe Ala Val
20 25 30

Tyr Ser Leu Trp Lys Thr Asp Val Ile Leu Asp Arg Lys Lys Asn Pro
35 40 45

Glu Pro Trp Glu Thr Val Asp Pro Thr Val Pro Gln Lys Leu Ile Thr
50 55 60

Ile Asn Gln Gln Trp Lys Pro Ile Glu Glu Leu Gln Asn Val Gln Arg
65 70 75 80

Val Thr Lys

<210> 2616
<211> 2413
<212> PRT
<213> Homo sapiens

<400> 2616

Met Gly Ile Ser Thr Val Ile Leu Glu Met Cys Leu Leu Trp Gly Gln
1 5 10 15

Val Leu Ser Thr Gly Gly Trp Ile Pro Arg Thr Thr Asp Tyr Ala Ser
20 25 30

Leu Ile Pro Ser Glu Val Pro Leu Asp Gln Thr Val Ala Glu Gly Ser
35 40 45

Pro Phe Pro Ser Glu Ser Thr Leu Glu Ser Thr Ala Ala Glu Gly Ser
50 55 60

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

Leu Ile Pro Ser Glu Ser Thr Leu Glu Ser Thr Val Ala Glu Gly Ser
85 90 95

Asp Ser Gly Leu Ala Leu Arg Leu Val Asn Gly Asp Gly Arg Cys Gln
100 105 110

Gly Arg Val Glu Ile Leu Tyr Arg Gly Ser Trp Gly Thr Val Cys Asp
115 120 125

Asp Ser Trp Asp Thr Asn Asp Ala Asn Val Val Cys Arg Gln Leu Gly
130 135 140

Cys Gly Trp Ala Met Ser Ala Pro Gly Asn Ala Trp Phe Gly Gln Gly
145 150 155 160

Ser Gly Pro Ile Ala Leu Asp Asp Val Arg Cys Ser Gly His Glu Ser
165 170 175

Tyr Leu Trp Ser Cys Pro His Asn Gly Trp Leu Ser His Asn Cys Gly
180 185 190

His Gly Glu Asp Ala Gly Val Ile Cys Ser Ala Ala Gln Pro Gln Ser
195 200 205

Thr Leu Arg Pro Glu Ser Trp Pro Val Arg Ile Ser Pro Pro Val Pro
210 215 220

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

Asp Arg Cys Arg Gly Arg Val Glu Val Leu Tyr Arg Gly Ser Trp Gly
245 250 255

Thr Val Cys Asp Asp Tyr Trp Asp Thr Asn Asp Ala Asn Val Val Cys
260 265 270

Arg Gln Leu Gly Cys Gly Trp Ala Met Ser Ala Pro Gly Asn Ala Gln
275 280 285

Phe Gly Gln Gly Ser Gly Pro Ile Val Leu Asp Asp Val Arg Cys Ser
290 295 300

Gly His Glu Ser Tyr Leu Trp Ser Cys Pro His Asn Gly Trp Leu Thr
305 310 315 320

His Asn Cys Gly His Ser Glu Asp Ala Gly Val Ile Cys Ser Ala Pro
325 330 335

Gln Ser Arg Pro Thr Pro Ser Pro Asp Thr Trp Pro Thr Ser His Ala
340 345 350

Ser Thr Ala Gly Pro Glu Ser Ser Leu Ala Leu Arg Leu Val Asn Gly
355 360 365

```
Gly Asp Arg Cys Gln Gly Arg Val Glu Val Leu Tyr Arg Gly Ser Trp
    370                 375                 380

Gly Thr Val Cys Asp Asp Ser Trp Asp Thr Ser Asp Ala Asn Val Val
385                 390                 395                 400

Cys Arg Gln Leu Gly Cys Gly Trp Ala Thr Ser Ala Pro Gly Asn Ala
                405                 410                 415

Arg Phe Gly Gln Gly Ser Gly Pro Ile Val Leu Asp Asp Val Arg Cys
            420                 425                 430

Ser Gly Tyr Glu Ser Tyr Leu Trp Ser Cys Pro His Asn Gly Trp Leu
        435                 440                 445

Ser His Asn Cys Gln His Ser Glu Asp Ala Gly Val Ile Cys Ser Ala
    450                 455                 460

Ala His Ser Trp Ser Thr Pro Ser Pro Asp Thr Leu Pro Thr Ile Thr
465                 470                 475                 480

Leu Pro Ala Ser Thr Val Gly Ser Glu Ser Ser Leu Ala Leu Arg Leu
                485                 490                 495

Val Asn Gly Gly Asp Arg Cys Gln Gly Arg Val Glu Val Leu Tyr Arg
            500                 505                 510

Gly Ser Trp Gly Thr Val Cys Asp Asp Ser Trp Asp Thr Asn Asp Ala
        515                 520                 525

Asn Val Val Cys Arg Gln Leu Gly Cys Gly Trp Ala Met Leu Ala Pro
    530                 535                 540

Gly Asn Ala Arg Phe Gly Gln Gly Ser Gly Pro Ile Val Leu Asp Asp
545                 550                 555                 560

Val Arg Cys Ser Gly Asn Glu Ser Tyr Leu Trp Ser Cys Pro His Asn
                565                 570                 575

Gly Trp Leu Ser His Asn Cys Gly His Ser Glu Asp Ala Gly Val Ile
            580                 585                 590

Cys Ser Gly Pro Glu Ser Ser Leu Ala Leu Arg Leu Val Asn Gly Gly
        595                 600                 605

Asp Arg Cys Gln Gly Arg Val Glu Val Leu Tyr Arg Gly Ser Trp Gly
```

610 615 620

Thr Val Cys Asp Asp Ser Trp Asp Thr Asn Asp Ala Asn Val Val Cys
625 630 635 640

Arg Gln Leu Gly Cys Gly Trp Ala Met Ser Ala Pro Gly Asn Ala Arg
645 650 655

Phe Gly Gln Gly Ser Gly Pro Ile Val Leu Asp Asp Val Arg Cys Ser
660 665 670

Gly His Glu Ser Tyr Leu Trp Ser Cys Pro Asn Asn Gly Trp Leu Ser
675 680 685

His Asn Cys Gly His His Glu Asp Ala Gly Val Ile Cys Ser Ala Ala
690 695 700

Gln Ser Arg Ser Thr Pro Arg Pro Asp Thr Leu Ser Thr Ile Thr Leu
705 710 715 720

Pro Pro Ser Thr Val Gly Ser Glu Ser Ser Leu Thr Leu Arg Leu Val
725 730 735

Asn Gly Ser Asp Arg Cys Gln Gly Arg Val Glu Val Leu Tyr Arg Gly
740 745 750

Ser Trp Gly Thr Val Cys Asp Asp Ser Trp Asp Thr Asn Asp Ala Asn
755 760 765

Val Val Cys Arg Gln Leu Gly Cys Gly Trp Ala Met Ser Ala Pro Gly
770 775 780

Asn Ala Arg Phe Gly Gln Gly Ser Gly Pro Ile Val Leu Asp Asp Val
785 790 795 800

Arg Cys Ser Gly His Glu Ser Tyr Leu Trp Ser Cys Pro His Asn Gly
805 810 815

Trp Leu Ser His Asn Cys Gly His His Glu Asp Ala Gly Val Ile Cys
820 825 830

Ser Val Ser Gln Ser Arg Pro Thr Pro Ser Pro Asp Thr Trp Pro Thr
835 840 845

Ser His Ala Ser Thr Ala Gly Ser Glu Ser Ser Leu Ala Leu Arg Leu
850 855 860

Val Asn Gly Gly Asp Arg Cys Gln Gly Arg Val Glu Val Leu Tyr Arg
865 870 875 880

Gly Ser Trp Gly Thr Val Cys Asp Asp Ser Trp Asp Thr Ser Asp Ala
885 890 895

Asn Val Val Cys Arg Gln Leu Gly Cys Gly Trp Ala Thr Ser Ala Pro
900 905 910

Gly Asn Ala Arg Phe Gly Gln Gly Ser Gly Pro Ile Val Leu Asp Asp
915 920 925

Val Arg Cys Ser Gly Tyr Glu Ser Tyr Leu Trp Ser Cys Pro His Asn
930 935 940

Gly Trp Leu Ser His Asn Cys Gln His Ser Glu Asp Ala Gly Val Ile
945 950 955 960

Cys Ser Ala Ala His Ser Trp Ser Thr Pro Ser Pro Asp Thr Leu Pro
965 970 975

Thr Ile Thr Leu Pro Ala Ser Thr Val Gly Ser Glu Ser Ser Leu Ala
980 985 990

Leu Arg Leu Val Asn Gly Gly Asp Arg Cys Gln Gly Arg Val Glu Val
995 1000 1005

Leu Tyr Gln Gly Ser Trp Gly Thr Val Cys Asp Asp Ser Trp Asp
1010 1015 1020

Thr Asn Asp Ala Asn Val Val Cys Arg Gln Pro Gly Cys Gly Trp
1025 1030 1035

Ala Met Ser Ala Pro Gly Asn Ala Arg Phe Gly Gln Gly Ser Gly
1040 1045 1050

Pro Ile Val Leu Asp Asp Val Arg Cys Ser Gly His Glu Ser Tyr
1055 1060 1065

Pro Trp Ser Cys Pro His Asn Gly Trp Leu Ser His Asn Cys Gly
1070 1075 1080

His Ser Glu Asp Ala Gly Val Ile Cys Ser Ala Ser Gln Ser Arg
1085 1090 1095

```
Pro Thr  Pro Ser Pro Asp Thr  Trp Pro Thr Ser His  Ala Ser Thr
1100                 1105                 1110

Ala Gly  Ser Glu Ser Ser Leu  Ala Leu Arg Leu Val  Asn Gly Gly
1115                 1120                 1125

Asp Arg  Cys Gln Gly Arg Val  Glu Val Leu Tyr Arg  Gly Ser Trp
1130                 1135                 1140

Gly Thr  Val Cys Asp Asp Tyr  Trp Asp Thr Asn Asp  Ala Asn Val
1145                 1150                 1155

Val Cys  Arg Gln Leu Gly Cys  Gly Trp Ala Met Ser  Ala Pro Gly
1160                 1165                 1170

Asn Ala  Arg Phe Gly Gln Gly  Ser Gly Pro Ile Val  Leu Asp Asp
1175                 1180                 1185

Val Arg  Cys Ser Gly His Glu  Ser Tyr Leu Trp Ser  Cys Pro His
1190                 1195                 1200

Asn Gly  Trp Leu Ser His Asn  Cys Gly His His Glu  Asp Ala Gly
1205                 1210                 1215

Val Ile  Cys Ser Ala Ser Gln  Ser Gln Pro Thr Pro  Ser Pro Asp
1220                 1225                 1230

Thr Trp  Pro Thr Ser His Ala  Ser Thr Ala Gly Ser  Glu Ser Ser
1235                 1240                 1245

Leu Ala  Leu Arg Leu Val Asn  Gly Gly Asp Arg Cys  Gln Gly Arg
1250                 1255                 1260

Val Glu  Val Leu Tyr Arg Gly  Ser Trp Gly Thr Val  Cys Asp Asp
1265                 1270                 1275

Tyr Trp  Asp Thr Asn Asp Ala  Asn Val Val Cys Arg  Gln Leu Gly
1280                 1285                 1290

Cys Gly  Trp Ala Thr Ser Ala  Pro Gly Asn Ala Arg  Phe Gly Gln
1295                 1300                 1305

Gly Ser  Gly Pro Ile Val Leu  Asp Asp Val Arg Cys  Ser Gly His
1310                 1315                 1320
```

```
Glu Ser  Tyr Leu Trp Ser Cys  Pro His Asn Gly Trp  Leu Ser His
     1325                 1330                 1335

Asn Cys  Gly His His Glu Asp  Ala Gly Val Ile Cys  Ser Ala Ser
     1340                 1345                 1350

Gln Ser  Gln Pro Thr Pro Ser  Pro Asp Thr Trp Pro  Thr Ser His
     1355                 1360                 1365

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

Asn Gly  Gly Asp Arg Cys Gln  Gly Arg Val Glu Val  Leu Tyr Arg
     1385                 1390                 1395

Gly Ser  Trp Gly Thr Val Cys  Asp Asp Tyr Trp Asp  Thr Asn Asp
     1400                 1405                 1410

Ala Asn  Val Val Cys Arg Gln  Leu Gly Cys Gly Trp  Ala Thr Ser
     1415                 1420                 1425

Ala Pro  Gly Asn Ala Arg Phe  Gly Gln Gly Ser Gly  Pro Ile Val
     1430                 1435                 1440

Leu Asp  Asp Val Arg Cys Ser  Gly His Glu Ser Tyr  Leu Trp Ser
     1445                 1450                 1455

Cys Pro  His Asn Gly Trp Leu  Ser His Asn Cys Gly  His His Glu
     1460                 1465                 1470

Asp Ala  Gly Val Ile Cys Ser  Ala Ser Gln Ser Gln  Pro Thr Pro
     1475                 1480                 1485

Ser Pro  Asp Thr Trp Pro Thr  Ser Arg Ala Ser Thr  Ala Gly Ser
     1490                 1495                 1500

Glu Ser  Thr Leu Ala Leu Arg  Leu Val Asn Gly Gly  Asp Arg Cys
     1505                 1510                 1515

Arg Gly  Arg Val Glu Val Leu  Tyr Gln Gly Ser Trp  Gly Thr Val
     1520                 1525                 1530

Cys Asp  Asp Tyr Trp Asp Thr  Asn Asp Ala Asn Val  Val Cys Arg
     1535                 1540                 1545

Gln Leu  Gly Cys Gly Trp Ala  Met Ser Ala Pro Gly  Asn Ala Gln
```

1550 1555 1560

Phe Gly Gln Gly Ser Gly Pro Ile Val Leu Asp Asp Val Arg Cys
1565 1570 1575

Ser Gly His Glu Ser Tyr Leu Trp Ser Cys Pro His Asn Gly Trp
1580 1585 1590

Leu Ser His Asn Cys Gly His His Glu Asp Ala Gly Val Ile Cys
1595 1600 1605

Ser Ala Ala Gln Ser Gln Ser Thr Pro Arg Pro Asp Thr Trp Leu
1610 1615 1620

Thr Thr Asn Leu Pro Ala Leu Thr Val Gly Ser Glu Ser Ser Leu
1625 1630 1635

Ala Leu Arg Leu Val Asn Gly Gly Asp Arg Cys Arg Gly Arg Val
1640 1645 1650

Glu Val Leu Tyr Arg Gly Ser Trp Gly Thr Val Cys Asp Asp Ser
1655 1660 1665

Trp Asp Thr Asn Asp Ala Asn Val Val Cys Arg Gln Leu Gly Cys
1670 1675 1680

Gly Trp Ala Met Ser Ala Pro Gly Asn Ala Arg Phe Gly Gln Gly
1685 1690 1695

Ser Gly Pro Ile Val Leu Asp Asp Val Arg Cys Ser Gly Asn Glu
1700 1705 1710

Ser Tyr Leu Trp Ser Cys Pro His Lys Gly Trp Leu Thr His Asn
1715 1720 1725

Cys Gly His His Glu Asp Ala Gly Val Ile Cys Ser Ala Thr Gln
1730 1735 1740

Ile Asn Ser Thr Thr Thr Asp Trp Trp His Pro Thr Thr Thr Thr
1745 1750 1755

Thr Ala Arg Pro Ser Ser Asn Cys Gly Gly Phe Leu Phe Tyr Ala
1760 1765 1770

Ser Gly Thr Phe Ser Ser Pro Ser Tyr Pro Ala Tyr Tyr Pro Asn
1775 1780 1785

Asn Ala Lys Cys Val Trp Glu Ile Glu Val Asn Ser Gly Tyr Arg
1790 1795 1800

Ile Asn Leu Gly Phe Ser Asn Leu Lys Leu Glu Ala His His Asn
1805 1810 1815

Cys Ser Phe Asp Tyr Val Glu Ile Phe Asp Gly Ser Leu Asn Ser
1820 1825 1830

Ser Leu Leu Leu Gly Lys Ile Cys Asn Asp Thr Arg Gln Ile Phe
1835 1840 1845

Thr Ser Ser Tyr Asn Arg Met Thr Ile His Phe Arg Ser Asp Ile
1850 1855 1860

Ser Phe Gln Asn Thr Gly Phe Leu Ala Trp Tyr Asn Ser Phe Pro
1865 1870 1875

Ser Asp Ala Thr Leu Arg Leu Val Asn Leu Asn Ser Ser Tyr Gly
1880 1885 1890

Leu Cys Ala Gly Arg Val Glu Ile Tyr His Gly Gly Thr Trp Gly
1895 1900 1905

Thr Val Cys Asp Asp Ser Trp Thr Ile Gln Glu Ala Glu Val Val
1910 1915 1920

Cys Arg Gln Leu Gly Cys Gly Arg Ala Val Ser Ala Leu Gly Asn
1925 1930 1935

Ala Tyr Phe Gly Ser Gly Ser Gly Pro Ile Thr Leu Asp Asp Val
1940 1945 1950

Glu Cys Ser Gly Thr Glu Ser Thr Leu Trp Gln Cys Arg Asn Arg
1955 1960 1965

Gly Trp Phe Ser His Asn Cys Asn His Arg Glu Asp Ala Gly Val
1970 1975 1980

Ile Cys Ser Gly Asn His Leu Ser Thr Pro Ala Pro Phe Leu Asn
1985 1990 1995

Ile Thr Arg Pro Asn Thr Asp Tyr Ser Cys Gly Gly Phe Leu Ser
2000 2005 2010

Gln Pro Ser Gly Asp Phe Ser Ser Pro Phe Tyr Pro Gly Asn Tyr
2015 2020 2025

Pro Asn Asn Ala Lys Cys Val Trp Asp Ile Glu Val Gln Asn Asn
2030 2035 2040

Tyr Arg Val Thr Val Ile Phe Arg Asp Val Gln Leu Glu Gly Gly
2045 2050 2055

Cys Asn Tyr Asp Tyr Ile Glu Val Phe Asp Gly Pro Tyr Arg Ser
2060 2065 2070

Ser Pro Leu Ile Ala Arg Val Cys Asp Gly Ala Arg Gly Ser Phe
2075 2080 2085

Thr Ser Ser Ser Asn Phe Met Ser Ile Arg Phe Ile Ser Asp His
2090 2095 2100

Ser Ile Thr Arg Arg Gly Phe Arg Ala Glu Tyr Tyr Ser Ser Pro
2105 2110 2115

Ser Asn Asp Ser Thr Asn Leu Leu Cys Leu Pro Asn His Met Gln
2120 2125 2130

Ala Ser Val Ser Arg Ser Tyr Leu Gln Ser Leu Gly Phe Ser Ala
2135 2140 2145

Ser Asp Leu Val Ile Ser Thr Trp Asn Gly Tyr Tyr Glu Cys Arg
2150 2155 2160

Pro Gln Ile Thr Pro Asn Leu Val Ile Phe Thr Ile Pro Tyr Ser
2165 2170 2175

Gly Cys Gly Thr Phe Lys Gln Ala Asp Asn Asp Thr Ile Asp Tyr
2180 2185 2190

Ser Asn Phe Leu Thr Ala Ala Val Ser Gly Gly Ile Ile Lys Arg
2195 2200 2205

Arg Thr Asp Leu Arg Ile His Val Ser Cys Arg Met Leu Gln Asn
2210 2215 2220

Thr Trp Val Asp Thr Met Tyr Ile Ala Asn Asp Thr Ile His Val
2225 2230 2235

```
Ala Asn  Asn Thr Ile Gln Val  Glu Glu Val Gln Tyr  Gly Asn Phe
     2240                 2245                 2250

Asp Val  Asn Ile Ser Phe Tyr  Thr Ser Ser Ser Phe  Leu Tyr Pro
     2255                 2260                 2265

Val Thr  Ser Arg Pro Tyr Tyr  Val Asp Leu Asn Gln  Asp Leu Tyr
     2270                 2275                 2280

Val Gln  Ala Glu Ile Leu His  Ser Asp Ala Val Leu  Thr Leu Phe
     2285                 2290                 2295

Val Asp  Thr Cys Val Ala Ser  Pro Tyr Ser Asn Asp  Phe Thr Ser
     2300                 2305                 2310

Leu Thr  Tyr Asp Leu Ile Arg  Ser Gly Cys Val Arg  Asp Asp Thr
     2315                 2320                 2325

Tyr Gly  Pro Tyr Ser Ser Pro  Ser Leu Arg Ile Ala  Arg Phe Arg
     2330                 2335                 2340

Phe Arg  Ala Phe His Phe Leu  Asn Arg Phe Pro Ser  Val Tyr Leu
     2345                 2350                 2355

Arg Cys  Lys Met Val Val Cys  Arg Ala Tyr Asp Pro  Ser Ser Arg
     2360                 2365                 2370

Cys Tyr  Arg Gly Cys Val Leu  Arg Ser Lys Arg Asp  Val Gly Ser
     2375                 2380                 2385

Tyr Gln  Glu Lys Val Asp Val  Val Leu Gly Pro Ile  Gln Leu Gln
     2390                 2395                 2400

Thr Pro  Pro Arg Arg Glu Glu  Glu Pro Arg
     2405                 2410
```

<210> 2617
<211> 143
<212> PRT
<213> Homo sapiens

<400> 2617

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

Arg Arg Asp Gln Lys Trp His Asp Lys Gln Tyr Lys Lys Ala His Leu
            20                  25                  30
```

```
Gly Thr Ala Leu Lys Ala Asn Pro Phe Gly Gly Ala Ser His Ala Lys
        35                  40                  45

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

Ala Ile Arg Lys Cys Val Arg Val Gln Leu Ile Lys Asn Gly Lys Lys
65                  70                  75                  80

Ile Thr Ala Phe Val Pro Asn Asp Gly Cys Leu Asn Phe Ile Glu Glu
                85                  90                  95

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

Gly Asp Ile Pro Gly Val Arg Phe Lys Val Val Lys Val Ala Asn Val
        115                 120                 125

Ser Leu Leu Ala Leu Tyr Lys Gly Lys Lys Glu Arg Pro Arg Ser
    130                 135                 140
```

<210> 2618
<211> 272
<212> PRT
<213> Homo sapiens

<400> 2618

```
Met Glu Glu Glu Ala Ile Ala Ser Leu Pro Gly Glu Glu Thr Glu Asp
1               5                   10                  15

Met Asp Phe Leu Ser Gly Leu Glu Leu Ala Asp Leu Leu Asp Pro Arg
            20                  25                  30

Gln Pro Asp Trp His Leu Asp Pro Gly Leu Ser Ser Pro Gly Pro Leu
        35                  40                  45

Ser Ser Ser Gly Gly Gly Ser Asp Ser Gly Gly Leu Trp Arg Gly Asp
    50                  55                  60

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

Leu Gln Arg Leu Leu Asn Gly Ile Gly Gly Cys Ser Ser Ser Ser Asp
                85                  90                  95
```

```
Ser Gly Ser Ala Glu Lys Arg Arg Arg Lys Ser Pro Gly Gly Gly Gly
            100                 105                 110

Gly Gly Gly Ser Gly Asn Asp Asn Asn Gln Ala Ala Thr Lys Ser Pro
        115                 120                 125

Arg Lys Ala Ala Ala Ala Ala Ala Arg Leu Asn Arg Leu Lys Lys Lys
    130                 135                 140

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

Asn Gln Glu Leu Arg Ala Glu Asn Arg Glu Leu Gly Lys Arg Val Gln
                165                 170                 175

Ala Leu Gln Glu Glu Ser Arg Tyr Leu Arg Ala Val Leu Ala Asn Glu
            180                 185                 190

Thr Gly Leu Ala Arg Leu Leu Ser Arg Leu Ser Gly Val Gly Leu Arg
        195                 200                 205

Leu Thr Thr Ser Leu Phe Arg Asp Ser Pro Ala Gly Asp His Asp Tyr
    210                 215                 220

Ala Leu Pro Val Gly Lys Gln Lys Gln Asp Leu Leu Glu Glu Asp Asp
225                 230                 235                 240

Ser Ala Gly Gly Val Cys Leu His Val Asp Lys Asp Lys Val Ser Val
                245                 250                 255

Glu Phe Cys Ser Ala Cys Ala Arg Lys Ala Ser Ser Ser Leu Lys Met
            260                 265                 270
```

<210> 2619
<211> 694
<212> PRT
<213> Homo sapiens

<400> 2619

```
Met Lys His Leu Lys Arg Trp Trp Ser Ala Gly Gly Gly Leu Leu His
1               5                   10                  15

Leu Thr Leu Leu Leu Ser Leu Ala Gly Leu Arg Val Asp Leu Asp Leu
            20                  25                  30

Tyr Leu Leu Leu Pro Pro Pro Thr Leu Leu Gln Asp Glu Leu Leu Phe
        35                  40                  45
```

Leu Gly Gly Pro Ala Ser Ser Ala Tyr Ala Leu Ser Pro Phe Ser Ala
50 55 60

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

Leu Asp Pro Ala Ala Pro Pro Glu Gly Gln Leu Leu Arg Glu Val Arg
85 90 95

Ala Leu Gly Val Pro Phe Val Pro Arg Thr Ser Val Asp Ala Trp Leu
100 105 110

Val His Ser Val Ala Ala Gly Ser Ala Asp Glu Ala His Gly Leu Leu
115 120 125

Gly Ala Ala Ala Ala Ser Ser Thr Gly Gly Ala Gly Ala Ser Val Asp
130 135 140

Gly Gly Ser Gln Ala Val Gln Gly Gly Gly Gly Asp Pro Arg Ala Ala
145 150 155 160

Arg Ser Gly Pro Leu Asp Ala Gly Glu Glu Glu Lys Ala Pro Ala Glu
165 170 175

Pro Thr Ala Gln Val Pro Asp Ala Gly Gly Cys Ala Ser Glu Glu Asn
180 185 190

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

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

Gln Asn Asp Asp Asp Glu Asn Lys Ile Ala Glu Lys Pro Asp Trp Glu
225 230 235 240

Ala Glu Lys Thr Thr Glu Ser Arg Asn Glu Arg His Leu Asn Gly Thr
245 250 255

Asp Thr Ser Phe Ser Leu Glu Asp Leu Phe Gln Leu Leu Ser Ser Gln
260 265 270

Pro Glu Asn Ser Leu Glu Gly Ile Ser Leu Gly Asp Ile Pro Leu Pro
275 280 285

Gly Ser Ile Ser Asp Gly Met Asn Ser Ser Ala His Tyr His Val Asn
290 295 300

Phe Ser Gln Ala Ile Ser Gln Asp Val Asn Leu His Glu Ala Ile Leu
305 310 315 320

Leu Cys Pro Asn Asn Thr Phe Arg Arg Asp Pro Thr Ala Arg Thr Ser
325 330 335

Gln Ser Gln Glu Pro Phe Leu Gln Leu Asn Ser His Thr Thr Asn Pro
340 345 350

Glu Gln Thr Leu Pro Gly Thr Asn Leu Thr Gly Phe Leu Ser Pro Val
355 360 365

Asp Asn His Met Arg Asn Leu Thr Ser Gln Asp Leu Leu Tyr Asp Leu
370 375 380

Asp Ile Asn Ile Phe Asp Glu Ile Asn Leu Met Ser Leu Ala Thr Glu
385 390 395 400

Asp Asn Phe Asp Pro Ile Asp Val Ser Gln Leu Phe Asp Glu Pro Asp
405 410 415

Ser Asp Ser Gly Leu Ser Leu Asp Ser Ser His Asn Asn Thr Ser Val
420 425 430

Ile Lys Ser Asn Ser Ser His Ser Val Cys Asp Glu Gly Ala Ile Gly
435 440 445

Tyr Cys Thr Asp His Glu Ser Ser Ser His His Asp Leu Glu Gly Ala
450 455 460

Val Gly Gly Tyr Tyr Pro Glu Pro Ser Lys Leu Cys His Leu Asp Gln
465 470 475 480

Ser Asp Ser Asp Phe His Gly Asp Leu Thr Phe Gln His Val Phe His
485 490 495

Asn His Thr Tyr His Leu Gln Pro Thr Ala Pro Glu Ser Thr Ser Glu
500 505 510

Pro Phe Pro Trp Pro Gly Lys Ser Gln Lys Ile Arg Ser Arg Tyr Leu
515 520 525

```
Glu Asp Thr Asp Arg Asn Leu Ser Arg Asp Glu Gln Arg Ala Lys Ala
    530                 535                 540

Leu His Ile Pro Phe Ser Val Asp Glu Ile Val Gly Met Pro Val Asp
545                 550                 555                 560

Ser Phe Asn Ser Met Leu Ser Arg Tyr Tyr Leu Thr Asp Leu Gln Val
                565                 570                 575

Ser Leu Ile Arg Asp Ile Arg Arg Arg Gly Lys Asn Lys Val Ala Ala
            580                 585                 590

Gln Asn Cys Arg Lys Arg Lys Leu Asp Ile Ile Leu Asn Leu Glu Asp
        595                 600                 605

Asp Val Cys Asn Leu Gln Ala Lys Lys Glu Thr Leu Lys Arg Glu Gln
    610                 615                 620

Ala Gln Cys Asn Lys Ala Ile Asn Ile Met Lys Gln Lys Leu His Asp
625                 630                 635                 640

Leu Tyr His Asp Ile Phe Ser Arg Leu Arg Asp Asp Gln Gly Arg Pro
                645                 650                 655

Val Asn Pro Asn His Tyr Ala Leu Gln Cys Thr His Asp Gly Ser Ile
            660                 665                 670

Leu Ile Val Pro Lys Glu Leu Val Ala Ser Gly His Lys Lys Glu Thr
        675                 680                 685

Gln Lys Gly Lys Arg Lys
    690
```

<210> 2620
<211> 391
<212> PRT
<213> Homo sapiens

<400> 2620

```
Met Lys Cys Leu Val Thr Gly Gly Asn Val Lys Val Leu Gly Lys Ala
1               5                   10                  15

Val His Ser Leu Ser Arg Ile Gly Asp Glu Leu Tyr Leu Glu Pro Leu
            20                  25                  30

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

```
Ala Cys Phe Leu Phe Ala Pro Leu Phe Phe Gln Gln Tyr Gln Ala Ala
    50                  55                  60

Thr Pro Gly Gln Asp Leu Leu Arg Cys Lys Ile Leu Met Lys Ser Phe
65                  70                  75                  80

Leu Ser Val Phe Arg Ser Leu Ala Met Leu Glu Lys Thr Val Glu Lys
                85                  90                  95

Cys Cys Ile Ser Leu Asn Gly Arg Ser Ser Arg Leu Val Val Gln Leu
            100                 105                 110

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

Cys Glu Ser Leu Gln Ala Val Phe Asp Pro Ala Ser Cys Pro His Met
    130                 135                 140

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

Pro Ala Leu Ala Glu Val Thr Leu Gly Ile Gly Arg Gly Arg Arg Val
                165                 170                 175

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

Met Val Thr Glu Met Cys Leu Gly Glu Glu Asp Phe Gln Gln Leu Gln
        195                 200                 205

Ala Gln Glu Gly Val Ala Ile Thr Phe Cys Leu Lys Glu Phe Arg Gly
    210                 215                 220

Leu Leu Ser Phe Ala Glu Ser Ala Asn Leu Asn Leu Ser Ile His Phe
225                 230                 235                 240

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

Asp Gly His Phe Val Leu Ala Thr Leu Ser Asp Thr Asp Ser His Ser
            260                 265                 270

Gln Asp Leu Gly Ser Pro Glu Arg His Gln Pro Val Pro Gln Leu Gln
        275                 280                 285
```

Ala His Ser Thr Pro His Pro Asp Asp Phe Ala Asn Asp Asp Ile Asp
290 295 300

Ser Tyr Met Ile Ala Met Glu Thr Thr Ile Gly Asn Glu Gly Ser Arg
305 310 315 320

Val Leu Pro Ser Ile Ser Leu Ser Pro Gly Pro Gln Pro Pro Lys Ser
325 330 335

Pro Gly Pro His Ser Glu Glu Glu Asp Glu Ala Glu Pro Ser Thr Val
340 345 350

Pro Gly Thr Pro Pro Pro Lys Lys Phe Arg Ser Leu Phe Phe Gly Ser
355 360 365

Ile Leu Ala Pro Val Arg Ser Pro Gln Gly Pro Ser Pro Val Leu Ala
370 375 380

Glu Asp Ser Glu Gly Glu Gly
385 390

<210> 2621
<211> 1429
<212> PRT
<213> Homo sapiens

<400> 2621

Met Ala Gly Gly Ala Trp Gly Arg Leu Ala Cys Tyr Leu Glu Phe Leu
1 5 10 15

Lys Lys Glu Glu Leu Lys Glu Phe Gln Leu Leu Leu Ala Asn Lys Ala
20 25 30

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

Ser Gly Met Glu Val Ala Ser Tyr Leu Val Ala Gln Tyr Gly Glu Gln
50 55 60

Arg Ala Trp Asp Leu Ala Leu His Thr Trp Glu Gln Met Gly Leu Arg
65 70 75 80

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

Pro Tyr Ser Pro Ser Glu Pro His Leu Gly Ser Pro Ser Gln Pro Thr

100 105 110

Ser Thr Ala Val Leu Met Pro Trp Ile His Glu Leu Pro Ala Gly Cys
115 120 125

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

Gly Arg Arg Trp Arg Glu Ile Ser Ala Ser Leu Leu Tyr Gln Ala Leu
145 150 155 160

Pro Ser Ser Pro Asp His Glu Ser Pro Ser Gln Glu Ser Pro Asn Ala
165 170 175

Pro Thr Ser Thr Ala Val Leu Gly Ser Trp Gly Ser Pro Pro Gln Pro
180 185 190

Ser Leu Ala Pro Arg Glu Gln Glu Ala Pro Gly Thr Gln Trp Pro Leu
195 200 205

Asp Glu Thr Ser Gly Ile Tyr Tyr Thr Glu Ile Arg Glu Arg Glu Arg
210 215 220

Glu Lys Ser Glu Lys Gly Arg Pro Pro Trp Ala Ala Val Val Gly Thr
225 230 235 240

Pro Pro Gln Ala His Thr Ser Leu Gln Pro His His His Pro Trp Glu
245 250 255

Pro Ser Val Arg Glu Ser Leu Cys Ser Thr Trp Pro Trp Lys Asn Glu
260 265 270

Asp Phe Asn Gln Lys Phe Thr Gln Leu Leu Leu Leu Gln Arg Pro His
275 280 285

Pro Arg Ser Gln Asp Pro Leu Val Lys Arg Ser Trp Pro Asp Tyr Val
290 295 300

Glu Glu Asn Arg Gly His Leu Ile Glu Ile Arg Asp Leu Phe Gly Pro
305 310 315 320

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

Gly Ile Gly Lys Ser Thr Leu Ala Arg Gln Val Lys Glu Ala Trp Gly
340 345 350

```
Arg Gly Gln Leu Tyr Gly Asp Arg Phe Gln His Val Phe Tyr Phe Ser
        355                 360                 365

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

Gly Lys Asp Gly Thr Ala Thr Pro Ala Pro Ile Arg Gln Ile Leu Ser
385                 390                 395                 400

Arg Pro Glu Arg Leu Leu Phe Ile Leu Asp Gly Val Asp Glu Pro Gly
                405                 410                 415

Trp Val Leu Gln Glu Pro Ser Ser Glu Leu Cys Leu His Trp Ser Gln
            420                 425                 430

Pro Gln Pro Ala Asp Ala Leu Leu Gly Ser Leu Leu Gly Lys Thr Ile
        435                 440                 445

Leu Pro Glu Ala Ser Phe Leu Ile Thr Ala Arg Thr Thr Ala Leu Gln
    450                 455                 460

Asn Leu Ile Pro Ser Leu Glu Gln Ala Arg Trp Val Glu Val Leu Gly
465                 470                 475                 480

Phe Ser Glu Ser Ser Arg Lys Glu Tyr Phe Tyr Arg Tyr Phe Thr Asp
                485                 490                 495

Glu Arg Gln Ala Ile Arg Ala Phe Arg Leu Val Lys Ser Asn Lys Glu
            500                 505                 510

Leu Trp Ala Leu Cys Leu Val Pro Trp Val Ser Trp Leu Ala Cys Thr
        515                 520                 525

Cys Leu Met Gln Gln Met Lys Arg Lys Glu Lys Leu Thr Leu Thr Ser
    530                 535                 540

Lys Thr Thr Thr Thr Leu Cys Leu His Tyr Leu Ala Gln Ala Leu Gln
545                 550                 555                 560

Ala Gln Pro Leu Gly Pro Gln Leu Arg Asp Leu Cys Ser Leu Ala Ala
                565                 570                 575

Glu Gly Ile Trp Gln Lys Lys Thr Leu Phe Ser Pro Asp Asp Leu Arg
            580                 585                 590
```

```
Lys His Gly Leu Asp Gly Ala Ile Ile Ser Thr Phe Leu Lys Met Gly
        595                 600                 605

Ile Leu Gln Glu His Pro Ile Pro Leu Ser Tyr Ser Phe Ile His Leu
    610                 615                 620

Cys Phe Gln Glu Phe Phe Ala Ala Met Ser Tyr Val Leu Glu Asp Glu
625                 630                 635                 640

Lys Gly Arg Gly Lys His Ser Asn Cys Ile Ile Asp Leu Glu Lys Thr
                645                 650                 655

Leu Glu Ala Tyr Gly Ile His Gly Leu Phe Gly Ala Ser Thr Thr Arg
            660                 665                 670

Phe Leu Leu Gly Leu Leu Ser Asp Glu Gly Glu Arg Glu Met Glu Asn
        675                 680                 685

Ile Phe His Cys Arg Leu Ser Gln Gly Arg Asn Leu Met Gln Trp Val
    690                 695                 700

Pro Ser Leu Gln Leu Leu Leu Gln Pro His Ser Leu Glu Ser Leu His
705                 710                 715                 720

Cys Leu Tyr Glu Thr Arg Asn Lys Thr Phe Leu Thr Gln Val Met Ala
                725                 730                 735

His Phe Glu Glu Met Gly Met Cys Val Glu Thr Asp Met Glu Leu Leu
            740                 745                 750

Val Cys Thr Phe Cys Ile Lys Phe Ser Arg His Val Lys Lys Leu Gln
        755                 760                 765

Leu Ile Glu Gly Arg Gln His Arg Ser Thr Trp Ser Pro Thr Met Val
    770                 775                 780

Val Leu Phe Arg Trp Val Pro Val Thr Asp Ala Tyr Trp Gln Ile Leu
785                 790                 795                 800

Phe Ser Val Leu Lys Val Thr Arg Asn Leu Lys Glu Leu Asp Leu Ser
                805                 810                 815

Gly Asn Ser Leu Ser His Ser Ala Val Lys Ser Leu Cys Lys Thr Leu
            820                 825                 830
```

Arg Arg Pro Arg Cys Leu Leu Glu Thr Leu Arg Leu Ala Gly Cys Gly
835 840 845

Leu Thr Ala Glu Asp Cys Lys Asp Leu Ala Phe Gly Leu Arg Ala Asn
850 855 860

Gln Thr Leu Thr Glu Leu Asp Leu Ser Phe Asn Val Leu Thr Asp Ala
865 870 875 880

Gly Ala Lys His Leu Cys Gln Arg Leu Arg Gln Pro Ser Cys Lys Leu
885 890 895

Gln Arg Leu Gln Leu Val Ser Cys Gly Leu Thr Ser Asp Cys Cys Gln
900 905 910

Asp Leu Ala Ser Val Leu Ser Ala Ser Pro Ser Leu Lys Glu Leu Asp
915 920 925

Leu Gln Gln Asn Asn Leu Asp Asp Val Gly Val Arg Leu Leu Cys Glu
930 935 940

Gly Leu Arg His Pro Ala Cys Lys Leu Ile Arg Leu Gly Leu Asp Gln
945 950 955 960

Thr Thr Leu Ser Asp Glu Met Arg Gln Glu Leu Arg Ala Leu Glu Gln
965 970 975

Glu Lys Pro Gln Leu Leu Ile Phe Ser Arg Arg Lys Pro Ser Val Met
980 985 990

Thr Pro Thr Glu Gly Leu Asp Thr Gly Glu Met Ser Asn Ser Thr Ser
995 1000 1005

Ser Leu Lys Arg Gln Arg Leu Gly Ser Glu Arg Ala Ala Ser His
1010 1015 1020

Val Ala Gln Ala Asn Leu Lys Leu Leu Asp Val Ser Lys Ile Phe
1025 1030 1035

Pro Ile Ala Glu Ile Ala Glu Glu Ser Ser Pro Glu Val Val Pro
1040 1045 1050

Val Glu Leu Leu Cys Val Pro Ser Pro Ala Ser Gln Gly Asp Leu
1055 1060 1065

His Thr Lys Pro Leu Gly Thr Asp Asp Asp Phe Trp Gly Pro Thr

1070 1075 1080

Gly Pro Val Ala Thr Glu Val Val Asp Lys Glu Lys Asn Leu Tyr
1085 1090 1095

Arg Val His Phe Pro Val Ala Gly Ser Tyr Arg Trp Pro Asn Thr
1100 1105 1110

Gly Leu Cys Phe Val Met Arg Glu Ala Val Thr Val Glu Ile Glu
1115 1120 1125

Phe Cys Val Trp Asp Gln Phe Leu Gly Glu Ile Asn Pro Gln His
1130 1135 1140

Ser Trp Met Val Ala Gly Pro Leu Leu Asp Ile Lys Ala Glu Pro
1145 1150 1155

Gly Ala Val Glu Ala Val His Leu Pro His Phe Val Ala Leu Gln
1160 1165 1170

Gly Gly His Val Asp Thr Ser Leu Phe Gln Met Ala His Phe Lys
1175 1180 1185

Glu Glu Gly Met Leu Leu Glu Lys Pro Ala Arg Val Glu Leu His
1190 1195 1200

His Ile Val Leu Glu Asn Pro Ser Phe Ser Pro Leu Gly Val Leu
1205 1210 1215

Leu Lys Met Ile His Asn Ala Leu Arg Phe Ile Pro Val Thr Ser
1220 1225 1230

Val Val Leu Leu Tyr His Arg Val His Pro Glu Glu Val Thr Phe
1235 1240 1245

His Leu Tyr Leu Ile Pro Ser Asp Cys Ser Ile Arg Lys Glu Leu
1250 1255 1260

Glu Leu Cys Tyr Arg Ser Pro Gly Glu Asp Gln Leu Phe Ser Glu
1265 1270 1275

Phe Tyr Val Gly His Leu Gly Ser Gly Ile Arg Leu Gln Val Lys
1280 1285 1290

Asp Lys Lys Asp Glu Thr Leu Val Trp Glu Ala Leu Val Lys Pro
1295 1300 1305

Gly Asp Leu Met Pro Ala Thr Thr Leu Ile Pro Pro Ala Arg Ile
1310 1315 1320

Ala Val Pro Ser Pro Leu Asp Ala Pro Gln Leu Leu His Phe Val
1325 1330 1335

Asp Gln Tyr Arg Glu Gln Leu Ile Ala Arg Val Thr Ser Val Glu
1340 1345 1350

Val Val Leu Asp Lys Leu His Gly Gln Val Leu Ser Gln Glu Gln
1355 1360 1365

Tyr Glu Arg Val Leu Ala Glu Asn Thr Arg Pro Ser Gln Met Arg
1370 1375 1380

Lys Leu Phe Ser Leu Ser Gln Ser Trp Asp Arg Lys Cys Lys Asp
1385 1390 1395

Gly Leu Tyr Gln Ala Leu Lys Glu Thr His Pro His Leu Ile Met
1400 1405 1410

Glu Leu Trp Glu Lys Gly Ser Lys Lys Gly Leu Leu Pro Leu Ser
1415 1420 1425

Ser

<210> 2622
<211> 179
<212> PRT
<213> Homo sapiens

<400> 2622

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

Ala Thr Ser Cys Leu Leu Leu Leu Ala Leu Leu Val Gln Gly Gly Ala
20 25 30

Ala Ala Pro Ile Ser Ser His Cys Arg Leu Asp Lys Ser Asn Phe Gln
35 40 45

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

Leu Ala Asp Asn Asn Thr Asp Val Arg Leu Ile Gly Glu Lys Leu Phe
65 70 75 80

His Gly Val Ser Met Ser Glu Arg Cys Tyr Leu Met Lys Gln Val Leu
85 90 95

Asn Phe Thr Leu Glu Glu Val Leu Phe Pro Gln Ser Asp Arg Phe Gln
100 105 110

Pro Tyr Met Gln Glu Val Val Pro Phe Leu Ala Arg Leu Ser Asn Arg
115 120 125

Leu Ser Thr Cys His Ile Glu Gly Asp Asp Leu His Ile Gln Arg Asn
130 135 140

Val Gln Lys Leu Lys Asp Thr Val Lys Lys Leu Gly Glu Ser Gly Glu
145 150 155 160

Ile Lys Ala Ile Gly Glu Leu Asp Leu Leu Phe Met Ser Leu Arg Asn
165 170 175

Ala Cys Ile

<210> 2623
<211> 261
<212> PRT
<213> Homo sapiens

<400> 2623

Met Ser Arg Arg Tyr Asp Ser Arg Thr Thr Ile Phe Ser Pro Glu Gly
1 5 10 15

Arg Leu Tyr Gln Val Glu Tyr Ala Met Glu Ala Ile Gly His Ala Gly
20 25 30

Thr Cys Leu Gly Ile Leu Ala Asn Asp Gly Val Leu Leu Ala Ala Glu
35 40 45

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

Ile Tyr Lys Leu Asn Glu Asp Met Ala Cys Ser Val Ala Gly Ile Thr
65 70 75 80

Ser Asp Ala Asn Val Leu Thr Asn Glu Leu Arg Leu Ile Ala Gln Arg
85 90 95

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Tyr Leu Leu Gln Tyr Gln Glu Pro Ile Pro Cys Glu Gln Leu Val Thr
            100                 105                 110

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

Pro Phe Gly Val Ser Leu Leu Tyr Ile Gly Trp Asp Lys His Tyr Gly
    130                 135                 140

Phe Gln Leu Tyr Gln Ser Asp Pro Ser Gly Asn Tyr Gly Gly Trp Lys
145                 150                 155                 160

Ala Thr Cys Ile Gly Asn Asn Ser Ala Ala Ala Val Ser Met Leu Lys
                165                 170                 175

Gln Asp Tyr Lys Glu Gly Glu Met Thr Leu Lys Ser Ala Leu Ala Leu
            180                 185                 190

Ala Ile Lys Val Leu Asn Lys Thr Met Asp Val Ser Lys Leu Ser Ala
        195                 200                 205

Glu Lys Val Glu Ile Ala Thr Leu Thr Arg Glu Asn Gly Lys Thr Val
    210                 215                 220

Ile Arg Val Leu Lys Gln Lys Glu Val Glu Gln Leu Ile Lys Lys His
225                 230                 235                 240

Glu Glu Glu Glu Ala Lys Ala Glu Arg Glu Lys Lys Glu Lys Glu Gln
                245                 250                 255

Lys Glu Lys Asp Lys
            260
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<210> 2624
<211> 377
<212> PRT
<213> Homo sapiens

<400> 2624

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Met Lys Phe Pro Gly Pro Leu Glu Asn Gln Arg Leu Ser Phe Leu Leu
1               5                   10                  15

Glu Lys Ala Ile Thr Arg Glu Ala Gln Met Trp Lys Val Asn Val Arg
            20                  25                  30
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Lys Met Pro Ser Asn Gln Asn Val Ser Pro Ser Gln Arg Asp Glu Val
35 40 45

Ile Gln Trp Leu Ala Lys Leu Lys Tyr Gln Phe Asn Leu Tyr Pro Glu
50 55 60

Thr Phe Ala Leu Ala Ser Ser Leu Leu Asp Arg Phe Leu Ala Thr Val
65 70 75 80

Lys Ala His Pro Lys Tyr Leu Ser Cys Ile Ala Ile Ser Cys Phe Phe
85 90 95

Leu Ala Ala Lys Thr Val Glu Glu Asp Glu Arg Ile Pro Val Leu Lys
100 105 110

Val Leu Ala Arg Asp Ser Phe Cys Gly Cys Ser Ser Ser Glu Ile Leu
115 120 125

Arg Met Glu Arg Ile Ile Leu Asp Lys Leu Asn Trp Asp Leu His Thr
130 135 140

Ala Thr Pro Leu Asp Phe Leu His Ile Phe His Ala Ile Ala Val Ser
145 150 155 160

Thr Arg Pro Gln Leu Leu Phe Ser Leu Pro Lys Leu Ser Pro Ser Gln
165 170 175

His Leu Ala Val Leu Thr Lys Gln Leu Leu His Cys Met Ala Cys Asn
180 185 190

Gln Leu Leu Gln Phe Arg Gly Ser Met Leu Ala Leu Ala Met Val Ser
195 200 205

Leu Glu Met Glu Lys Leu Ile Pro Asp Trp Leu Ser Leu Thr Ile Glu
210 215 220

Leu Leu Gln Lys Ala Gln Met Asp Ser Ser Gln Leu Ile His Cys Arg
225 230 235 240

Glu Leu Val Ala His His Leu Ser Thr Leu Gln Ser Ser Leu Pro Leu
245 250 255

Asn Ser Val Tyr Val Tyr Arg Pro Leu Lys His Thr Leu Val Thr Cys
260 265 270

Asp Lys Gly Val Phe Arg Leu His Pro Ser Ser Val Pro Gly Pro Asp

275 280 285

Phe Ser Lys Asp Asn Ser Lys Pro Glu Val Pro Val Arg Gly Thr Ala
290 295 300

Ala Phe Tyr His His Leu Pro Ala Ala Ser Gly Cys Lys Gln Thr Ser
305 310 315 320

Thr Lys Arg Lys Val Glu Glu Met Glu Val Asp Asp Phe Tyr Asp Gly
325 330 335

Ile Lys Arg Leu Tyr Asn Glu Asp Asn Val Ser Glu Asn Val Gly Ser
340 345 350

Val Cys Gly Thr Asp Leu Ser Arg Gln Glu Gly His Ala Ser Pro Cys
355 360 365

Pro Pro Leu Gln Pro Val Ser Val Met
370 375

<210> 2625
<211> 575
<212> PRT
<213> Homo sapiens

<400> 2625

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

Phe Pro Ala Pro Ala Glu Pro Gln Pro Gly Gly Ser Gln Cys Val Glu
20 25 30

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

Ser Gln Ile Cys Asp Gly Leu Arg Gly His Leu Met Thr Val Arg Ser
50 55 60

Ser Val Ala Ala Asp Val Ile Ser Leu Leu Leu Asn Gly Asp Gly Gly
65 70 75 80

Val Gly Arg Arg Arg Leu Trp Ile Gly Leu Gln Leu Pro Pro Gly Cys
85 90 95

Gly Asp Pro Lys Arg Leu Gly Pro Leu Arg Gly Phe Gln Trp Val Thr
100 105 110

Gly Asp Asn Asn Thr Ser Tyr Ser Arg Trp Ala Arg Leu Asp Leu Asn
115 120 125

Gly Ala Pro Leu Cys Gly Pro Leu Cys Val Ala Val Ser Ala Ala Glu
130 135 140

Ala Thr Val Pro Ser Glu Pro Ile Trp Glu Glu Gln Gln Cys Glu Val
145 150 155 160

Lys Ala Asp Gly Phe Leu Cys Glu Phe His Phe Pro Ala Thr Cys Arg
165 170 175

Pro Leu Ala Val Glu Pro Gly Ala Ala Ala Ala Ala Val Ser Ile Thr
180 185 190

Tyr Gly Thr Pro Phe Ala Ala Arg Gly Ala Asp Phe Gln Ala Leu Pro
195 200 205

Val Gly Ser Ser Ala Ala Val Ala Pro Leu Gly Leu Gln Leu Met Cys
210 215 220

Thr Ala Pro Pro Gly Ala Val Gln Gly His Trp Ala Arg Glu Ala Pro
225 230 235 240

Gly Ala Trp Asp Cys Ser Val Glu Asn Gly Gly Cys Glu His Ala Cys
245 250 255

Asn Ala Ile Pro Gly Ala Pro Arg Cys Gln Cys Pro Ala Gly Ala Ala
260 265 270

Leu Gln Ala Asp Gly Arg Ser Cys Thr Ala Ser Ala Thr Gln Ser Cys
275 280 285

Asn Asp Leu Cys Glu His Phe Cys Val Pro Asn Pro Asp Gln Pro Gly
290 295 300

Ser Tyr Ser Cys Met Cys Glu Thr Gly Tyr Arg Leu Ala Ala Asp Gln
305 310 315 320

His Arg Cys Glu Asp Val Asp Asp Cys Ile Leu Glu Pro Ser Pro Cys
325 330 335

Pro Gln Arg Cys Val Asn Thr Gln Gly Gly Phe Glu Cys His Cys Tyr
340 345 350

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Pro Asn Tyr Asp Leu Val Asp Gly Glu Cys Val Glu Pro Val Asp Pro
        355                 360                 365

Cys Phe Arg Ala Asn Cys Glu Tyr Gln Cys Gln Pro Leu Asn Gln Thr
    370                 375                 380

Ser Tyr Leu Cys Val Cys Ala Glu Gly Phe Ala Pro Ile Pro His Glu
385                 390                 395                 400

Pro His Arg Cys Gln Met Phe Cys Asn Gln Thr Ala Cys Pro Ala Asp
                405                 410                 415

Cys Asp Pro Asn Thr Gln Ala Ser Cys Glu Cys Pro Glu Gly Tyr Ile
            420                 425                 430

Leu Asp Asp Gly Phe Ile Cys Thr Asp Ile Asp Glu Cys Glu Asn Gly
        435                 440                 445

Gly Phe Cys Ser Gly Val Cys His Asn Leu Pro Gly Thr Phe Glu Cys
    450                 455                 460

Ile Cys Gly Pro Asp Ser Ala Leu Ala Arg His Ile Gly Thr Asp Cys
465                 470                 475                 480

Asp Ser Gly Lys Val Asp Gly Gly Asp Ser Gly Ser Gly Glu Pro Pro
                485                 490                 495

Pro Ser Pro Thr Pro Gly Ser Thr Leu Thr Pro Pro Ala Val Gly Leu
            500                 505                 510

Val His Ser Gly Leu Leu Ile Gly Ile Ser Ile Ala Ser Leu Cys Leu
        515                 520                 525

Val Val Ala Leu Leu Ala Leu Leu Cys His Leu Arg Lys Lys Gln Gly
    530                 535                 540

Ala Ala Arg Ala Lys Met Glu Tyr Lys Cys Ala Ala Pro Ser Lys Glu
545                 550                 555                 560

Val Val Leu Gln His Val Arg Thr Glu Arg Thr Pro Gln Arg Leu
                565                 570                 575
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<210> 2626
<211> 332
<212> PRT
<213> Homo sapiens

<400> 2626

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1               5                  10                  15

Tyr Ile Ala Val Val Phe Thr Cys Phe Ile Val Thr Thr Gly Leu Val
            20                  25                  30

Leu Gly Trp Phe Gly Trp Asp Val Pro Val Ile Leu Arg Asn Ser Glu
        35                  40                  45

Glu Thr Gln Phe Ser Thr Arg Val Phe Lys Lys Gln Met Arg Gln Val
    50                  55                  60

Lys Asn Pro Phe Gly Leu Glu Ile Thr Asn Pro Ser Ser Ala Ser Ile
65                  70                  75                  80

Thr Thr Gly Ile Thr Leu Thr Thr Asp Cys Leu Glu Asp Ser Leu Leu
                85                  90                  95

Thr Cys Tyr Trp Gly Cys Ser Val Gln Lys Leu Tyr Glu Ala Leu Gln
            100                 105                 110

Lys His Val Tyr Cys Phe Arg Ile Ser Thr Pro Gln Ala Leu Glu Asp
        115                 120                 125

Ala Leu Tyr Ser Glu Tyr Leu Tyr Gln Glu Gln Tyr Phe Ile Lys Lys
    130                 135                 140

Asp Ser Lys Glu Glu Ile Tyr Cys Gln Leu Pro Arg Asp Thr Lys Ile
145                 150                 155                 160

Glu Asp Phe Gly Thr Val Pro Arg Ser Arg Tyr Pro Leu Val Ala Leu
                165                 170                 175

Leu Thr Leu Ala Asp Glu Asp Asp Arg Glu Ile Tyr Asp Ile Ile Ser
            180                 185                 190

Met Val Ser Val Ile His Ile Pro Asp Arg Thr Tyr Lys Leu Ser Cys
        195                 200                 205

Arg Ile Leu Tyr Gln Tyr Leu Leu Leu Ala Gln Gly Gln Phe His Asp
    210                 215                 220

Leu Lys Gln Leu Phe Met Ser Ala Asn Asn Asn Phe Thr Pro Ser Asn
225                 230                 235                 240
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Asn Ser Ser Ser Glu Glu Lys Asn Thr Asp Arg Ser Leu Leu Glu Lys
                245                 250                 255

Val Gly Leu Ser Glu Ser Glu Val Glu Pro Ser Glu Glu Asn Ser Lys
            260                 265                 270

Asp Cys Val Val Cys Gln Asn Gly Thr Val Asn Trp Val Leu Leu Pro
        275                 280                 285

Cys Arg His Thr Cys Leu Cys Asp Gly Cys Val Lys Tyr Phe Gln Gln
    290                 295                 300

Cys Pro Met Cys Arg Gln Phe Val Gln Glu Ser Phe Ala Leu Cys Ser
305                 310                 315                 320

Gln Lys Glu Gln Asp Lys Asp Lys Pro Lys Thr Leu
                325                 330
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<211> 50
<212> DNA
<213> Homo sapiens

<400> 2627
agagcacttg cagagcctgg gacaacctcc ttattgaagg gaagagggac 50

<210> 2628
<211> 50
<212> DNA
<213> Homo sapiens

<400> 2628
taaggagtgt tggagatatg tgatttggct agtgctattt aaagacaccc 50

<210> 2629
<211> 50
<212> DNA
<213> Homo sapiens

<400> 2629
gccaagacaa taagctaggc tactgggtcc agctactact ttggtgggat 50

<210> 2630
<211> 50
<212> DNA
<213> Homo sapiens

<400> 2630
gtaaaggcta tacttgtctt gttcaccttg ggatgacgcc gcatgatatg 50

<210> 2631
<211> 50
<212> DNA
<213> Homo sapiens

<400> 2631
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<210> 2632
<211> 50
<212> DNA
<213> Homo sapiens

<400> 2632
ctttgcctaa accctatggc ctcctgtgca tctgtactca ccctgtacca 50

<210> 2633
<211> 50
<212> DNA
<213> Homo sapiens

<400> 2633
accttgggtt gagtaatgct cgtctgtgtg ttttagtttc atcacctgtt 50

<210> 2634
<211> 70
<212> DNA
<213> Homo sapiens

<400> 2634
atttatatta gtttagccaa aggataagtg tcctatgggg atggtccact gtcactgttt 60

ctctgctgtt 70

<210> 2635
<211> 50
<212> DNA
<213> Homo sapiens

<400> 2635
cccatgtaag caccccttca tttggcattc cccacttgag aattaccctt 50

<210> 2636
<211> 50
<212> DNA
<213> Homo sapiens

<400> 2636
tggaccgtaa tgaatgaatg tacacgccat aaacgccctt tgttcaagca 50

<210> 2637
<211> 50
<212> DNA
<213> Homo sapiens

<400> 2637
tttcaagaca gaaagtgacg cagagaacct ccccggccca gtctcgacgc 50

<210> 2638
<211> 50
<212> DNA
<213> Homo sapiens

<400> 2638
tgcactaaac agttgcccca aaagacatat cttgttttaa ggcccagacc 50

<210> 2639
<211> 50
<212> DNA
<213> Homo sapiens

<400> 2639
gggtaggcag cttgcaccca gttctccttt atctcaactt attttcctgg 50

<210> 2640
<211> 50
<212> DNA
<213> Homo sapiens

<400> 2640
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<210> 2641
<211> 50
<212> DNA
<213> Homo sapiens

<400> 2641
tgattttgca acttaggatg tttttgagtc ccatggttca ttttgattgt 50

<210> 2642
<211> 50
<212> DNA
<213> Homo sapiens

<400> 2642
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<210> 2643
<211> 50
<212> DNA
<213> Homo sapiens

<400> 2643
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<210> 2644
<211> 50
<212> DNA

<213> Homo sapiens

<400> 2644
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<210> 2645
<211> 50
<212> DNA
<213> Homo sapiens

<400> 2645
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<210> 2646
<211> 50
<212> DNA
<213> Homo sapiens

<400> 2646
acaaccaacc agtttctttt ctagccaatc atctctgaag agttgctgtt 50

<210> 2647
<211> 50
<212> DNA
<213> Homo sapiens

<400> 2647
cacacctgca cactcacggc tgaaatctcc ctaacccagg gggaccttag 50

<210> 2648
<211> 50
<212> DNA
<213> Homo sapiens

<400> 2648
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<210> 2649
<211> 50
<212> DNA
<213> Homo sapiens

<400> 2649
gggagtgttg tgactgaaat gcttgaaacc aaagcttcag ataaacttgc 50

<210> 2650
<211> 50
<212> DNA
<213> Homo sapiens

<400> 2650
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<210> 2651

<211> 50
<212> DNA
<213> Homo sapiens

<400> 2651
atccagcccc acccaatggc cttttgtgct tgtttcctat aacttcagta 50

<210> 2652
<211> 50
<212> DNA
<213> Homo sapiens

<400> 2652
tttacaagaa ttgtccatgt gcttccctag gctgagctgg cattggtctg 50

<210> 2653
<211> 50
<212> DNA
<213> Homo sapiens

<400> 2653
catggagact tgaggagggc ttgaggttgg tgaggttagg tgcgtgtttc 50

<210> 2654
<211> 50
<212> DNA
<213> Homo sapiens

<400> 2654
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<210> 2655
<211> 50
<212> DNA
<213> Homo sapiens

<400> 2655
acaagtttac atgataaaaa gaaatgtgat ttgtcttccc ttctttgcac 50

<210> 2656
<211> 50
<212> DNA
<213> Homo sapiens

<400> 2656
aaaaatacac atcacaccca tttaaaagtg atcttgagaa ccttttcaaa 50

<210> 2657
<211> 50
<212> DNA
<213> Homo sapiens

<400> 2657
tgtgtgttga tcccaagaca atgaaagttt gcactgtatg ctggacggca 50

<210> 2658
<211> 50
<212> DNA
<213> Homo sapiens

<400> 2658
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<210> 2659
<211> 50
<212> DNA
<213> Homo sapiens

<400> 2659
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<210> 2660
<211> 50
<212> DNA
<213> Homo sapiens

<400> 2660
gcctccaacc atgttccctt cttcttagca ccacaaataa tcaaaaccca 50

<210> 2661
<211> 50
<212> DNA
<213> Homo sapiens

<400> 2661
ggcagagaag gaggagtatg agcatcagaa gagggagctg gagcaaatct 50

<210> 2662
<211> 50
<212> DNA
<213> Homo sapiens

<400> 2662
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<210> 2663
<211> 50
<212> DNA
<213> Homo sapiens

<400> 2663
tgccattaag caggaatgtc atgttccagt tcattacaaa agaaaacaat 50

<210> 2664
<211> 50
<212> DNA
<213> Homo sapiens

<400> 2664

cctctcagga cgtgccgggt ttatcattgc tttgttattt gtaaggactg 50

<210> 2665
<211> 50
<212> DNA
<213> Homo sapiens

<400> 2665
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<210> 2666
<211> 50
<212> DNA
<213> Homo sapiens

<400> 2666
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<210> 2667
<211> 50
<212> DNA
<213> Homo sapiens

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<210> 2668
<211> 50
<212> DNA
<213> Homo sapiens

<400> 2668
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<210> 2669
<211> 50
<212> DNA
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<210> 2670
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<212> DNA
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<210> 2671
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<212> DNA
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<210> 2672
<211> 50
<212> DNA
<213> Homo sapiens

<400> 2672
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<210> 2673
<211> 50
<212> DNA
<213> Homo sapiens

<400> 2673
gagcacccag agggattttt cagtgggaag cattacactt tgctaaatca 50

<210> 2674
<211> 50
<212> DNA
<213> Homo sapiens

<400> 2674
acagctcaag taccctaatt tagttctttt ggactaatac aattcaggaa 50

<210> 2675
<211> 50
<212> DNA
<213> Homo sapiens

<400> 2675
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<210> 2676
<211> 50
<212> DNA
<213> Homo sapiens

<400> 2676
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<210> 2677
<211> 50
<212> DNA
<213> Homo sapiens

<400> 2677
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<210> 2678
<211> 50

<212> DNA
<213> Homo sapiens

<400> 2678
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<210> 2679
<211> 50
<212> DNA
<213> Homo sapiens

<400> 2679
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<210> 2680
<211> 50
<212> DNA
<213> Homo sapiens

<400> 2680
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<210> 2681
<211> 50
<212> DNA
<213> Homo sapiens

<400> 2681
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<210> 2682
<211> 50
<212> DNA
<213> Homo sapiens

<400> 2682
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<210> 2683
<211> 50
<212> DNA
<213> Homo sapiens

<400> 2683
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<210> 2684
<211> 50
<212> DNA
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<400> 2684
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<210> 2685
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<212> DNA
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<210> 2686
<211> 50
<212> DNA
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<400> 2686
tccagggacc aacattaaca caaccaatca acacatcatg ttacagaact 50

<210> 2687
<211> 50
<212> DNA
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<210> 2773

<211> 50
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cctgttggat acttctctgg aatatattct acaaagaaaa tgattggctt tgcattatgc 360

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ttcgttctgt tttatgatga ccccaaagac cacccatgta taagcatcag tgaaaaggaa 720

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gcagccatta atgtgactgg cctaattttc taccttatag ttgctacagc agaaattcag 1380

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tcagtacaga gggggctctg gaagtgtttg ttgactgaat aaacggaatt cagtgcgaaa 720

acaaaaaaat aggaaataaa agatctcgga aaatagcatt ttgttaaaac cttggggggt 780

aaaaccccgg ggagttttaa cggaaaaatt ccagggaaca caacttgggg gccaaa 836

<210> 2887
<211> 742
<212> DNA
<213> Homo sapiens

<400> 2887
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ttttggtggt ggcttatcca caaacagttt agttgtagaa taaaacttat gagtgacatc 180

tggaaagtaa ccatgctaag atggcaagca cactggaaac aattaggcca cttggctttc 240

ttttgctgta ttgttttata agcctacttt acctcccagt cttggaaaca agttttagtt 300

ttttattggt ttggagacta gagccaatag tataatgttc tcaaaggaaa cagacttgag 360

ttgttggatt agaggaacta acccaactta tatgattttg tttttggttt ttgtcgtgta 420

gttatggcac tgtcttattt ggaacatttg caactaggga taatacaaca tttttaactc 480

tcatttgaca acctactact aatcacagac cacaagggta atgaccaaat ttatgtggtt 540

tttgcactcc atagttgtct tagcccaatc tttctatact cttacgatta ctggggttaa 600

cgcttctgtg aggaccttct ggctcttgag ataccctaaa tatttacaga tacttagata 660

tcttgaagat agaataggat atcgagattg taccaaatag gaatatcagg agtatggtac 720

aaatgagcag atacctgttg aa 742

<210> 2888
<211> 440
<212> DNA
<213> Homo sapiens

<400> 2888
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agcctctgct ttatagctct tagcacacct ctcaaataag aaggcagtac tgggaaggct 180

ctgaacctgt ggcagaacca ctgatagctg tggagctatt ccaaggagtc tgggaatcag 240

ggggattatc aagatcattg ttagaataaa ttaatcttac tgtatatata gcagaagttt 300

tcaagcatat gtaaatgcta ctaataacca aataattaca ccttgttttt ctttaaactg 360

taactctcaa gtatgtctct acataatttt ttgatggtag tgtctgcatg ctcaaaaagc 420

ttgaaaacac tactggagaa 440

<210> 2889
<211> 524
<212> DNA
<213> Homo sapiens

<400> 2889
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atacagcatc agtgcttcct ataatgtcca ggttaggaga gaagcaaatg gagctttact 120

aaggaagaga aagtgatcaa taccagtgag aaaggtgaaa aaaaaaaaaa acaaacaaaa 180

acgaaaaaaa aacctaagca aattcagtga gaaaagaaaa agcagaactt agagtcctta 240

cccttcaatt taaggaagga gagttattgc ctagcagaat cttgaaataa aatttcctta 300

gaaagcccca gaaagttttg tgtgtattgc aagtccaaag gataaggaga acttctatat 360

gctttcttct tatttccact gggcaaagta ctgctccatc aagactcagc ccgccatgag 420

gctttccaat caactctcaa ccaccacaac agttagggct ttttcctcta tgttgcaaag 480

cactttctgc ataactcaga atgcaaaatg tactcattca tttg 524

<210> 2890
<211> 575
<212> DNA
<213> Homo sapiens

<400> 2890
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aaatgcggcc caaccctgcc ccacggaaac cggccatggc aacccctaaa taaaaagggg 180

tttttgaggc ggccggcccc cacccaaagg atgccccaa ttttttttg ccaggggga 240

atgtccttgg acacggggcc ccaaaattcc ccatgccggg ggtttgtact ttaaaagggc 300

ttcctaacct cctccgggtg ttcctaaggg ccatgctgga gctaaaactt gtaaaaaaag 360

gcccaggctt cccccaggtc cgagtaaatt ttcacagggg gggggaacca ccccctggcc 420

ttggggattt tccgttgact ccaaaacagt ttggccacgg ccagaaccac atgggggtaa 480

tgctcacact ttttaaggga atccacgctt tggggcctcc tgtggggcct tgcctggagg 540

aagatggcct cacaccaaag gataccggag ttggg 575

<210> 2891
<211> 467
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (428)..(428)
<223> n is a, c, g, t or u

<400> 2891
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atgcaagggt tcgaaattat cctttccctc acggacaact cgagctttct ccttattata 180

ctaccttccc taccggcatg accggaccgg tcacctgggg ggccacgcac atttctacag 240

gaaaactggc tcccttcttg ggggccgagg gcttcctgtg gaaaaggatg agtttggagc 300

ggtactccct cagccggtgc acgttgatct ggagggactc cgcggacttg ctcctgctcc 360

tgggatccac aaaaatgcgc taaggtccgg cccaccttct tgggaatgcc gcccaccctg 420

agctcctnca ggatgaatcc gcggccgact cgcaccttct tgggtac 467

<210> 2892
<211> 473
<212> DNA
<213> Homo sapiens

<400> 2892
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acaggtctgc agctataaaa atcatctcga aaacatgaga tttcagagat ccagttctca 120

gtgttacctt gaagatgaca atttatgaag aaacaggtga ttttaatccg aaattgccag 180

gaaacaaatt actcctcaaa agcccttgga aagtaataag atagctaggc agaaaaaaaa 240

agattctgca aaactaaact taatgtgtat tcatctagac ctgaattaaa aataaaattc 300

cactataaaa agaatttttc aaaatgttag gcccaagaat atggccatat tgttccatct 360

tgaagaaccc agttgattca gtttcattac tggcctcccc actcttctaa gtaagtccct 420

cactataaac atttacgaat tccatctcag cattagtact aaacaatatt cat 473

<210> 2893
<211> 546
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (280)..(280)
<223> n is a, c, g, t or u

<220>
<221> misc_feature
<222> (537)..(537)
<223> n is a, c, g, t or u

<400> 2893
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ttgcttaatg ggagaacttg caaatgagat ttaaaacatt gtaattttta taaggtaaca 120

gaagctagat ccctttcact gttcatctca agctattgat cttgtcagtg ttgtacagat 180

ctagaatggg ttgtcaggga taaggtcact gatctgatgg tgattgttga catctgctga 240

ctccacacaa caaccctagg ggaccggtgc tttgagcatn cttattttca gatggtttgc 300

ccacttcatg cagttaacag ctgttggtgt tgggcttcaa atccaggtct ttcggacatc 360

aaatcccagc ctcttaacaa ctcaccaagc agtgattact actccccaac ataggggcag 420

tatgtacaag tcatgttgaa ctaatacagt ttctttcttt gataggaata ctaattttgt 480

tgaacaagaa aatatgtact ggataagagt aaggcatttg acaaggcgtc ctgtganatc 540

tgtgaa 546

<210> 2894
<211> 1993
<212> DNA
<213> Homo sapiens

<400> 2894
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gcaagcacct gtgcacagca atgtgcgtgg gcatctgtga gaagaagaga atctgtgaag 120

tttgagcaag cggccttccc aagatgtacc gaatatctca actgatgtca acaccagtag 180

caagttcttc caggttggaa agagaatatg ctggagagct gtctcccacg tgcattttcc 240

caagtttcac ctgtgattcc ctggatggtt accattcttt tgaatgcggc tccatagatc 300

ccctgacagg ctcccactat acctgtcgcc gaagtcccag actcctcacc aatggctact 360
atatttggac tgaagacagc ttcctgtgcg acaaagatgg caacataact ctgaacccat 420
cccagaccag cgttatgtat aaggagaact tagttagtac ctccaaatct tggctgcatg 480
gaagtatctt tggtgacatc aactcttctc caagtgaaga caactggttg aaggggacca 540
ggaggttgga cacagaccat tgcaatggaa atgcagatga tttagactgt tcttctctga 600
ctgatgactg ggagtcaggg aagatgaatg cagagtctgt gatcacctcc tcttccagcc 660
acatcatatc tcagcctcct ggaggaaact cccatagctt gtctcttcag tcccagttga 720
cagcttctga acgtttccaa gagaatagtt cggatcattc agaaaccagg ttgttgcaag 780
aggtcttctt tcaggcaatc ctgcttgctg tgtgcttaat cacttctgca tgtgcaagat 840
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ctttaataga ataatgagag caagtttgtc taactaatac caacctgaca acttgaataa 1440
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gagtgacttg atattaggtg gtaaccgtag atgatggtta atatgaaaat ggacaggaaa 1560
gaagcatttt ctgaaagtta tattcttttg aaccacgttc taaaccaagt ttttaatctt 1620
cttggggctc gtaattacct ttcactttaa tgtcacttaa agatataaca cagaaaaatg 1680
ccttgagggc aaaatatagg caaaacacca atgcgctttc aaatgcatga aaatggtgca 1740
gttgtaccct tgagccttga ctcaagggct gtagatgttc cctttccacc ccccacactt 1800
ggtgcgtgtt cacaaagcaa atatggcctg taattcaaat ttgttctatg tgatactctc 1860
tgagtaaaaa ctcatacatg cagaaaattg tctttgctcg aaatgataat gccaaaatat 1920
aactttatat ataatttgca tttagtacat ttttggttaa aaaataaact aataaataag 1980
tgaagtcatc agc 1993

<210> 2895

<211> 521
<212> DNA
<213> Homo sapiens

<400> 2895
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aaagttgctc agatttatcc agacctcaca taagtttata gatttcaagt agccactgta 120

ttttattaca gaaaatacat tcttcaagag gaaaatgtta aggccatagc agctttcacc 180

ttagctatct aagcttgtat taggtcatca ttaaatagta tctgtatcat tcttatgtgt 240

tccgtaagtt atgccacaaa taccagacca agtacactca gtctagaaac aaaaaagtgg 300

gaaataaagg ttaaaacatt ctaataggtg taatgggctg atagatgact ttatattaca 360

aagctactta agacaattct acttttctag aatacaacgc attaatataa acatttgaaa 420

ttcagaagat ttggcctgtg gatgctttgt ttctcaatgc aattcttgtt aatatgttag 480

taagtaataa tttattaata ccaataataa aaaattaaca t 521

<210> 2896
<211> 1679
<212> DNA
<213> Homo sapiens

<400> 2896
gtttgttggc tgcggcagca ggtagcaaag tgacgccgag ggcctgagtg ctccagtagc 60

caccgcatct ggagaaccag cggttaccat ggaggggatc agtatataca cttcagataa 120

ctacaccgag gaaatgggct caggggacta tgactccatg aaggaaccct gtttccgtga 180

agaaaatgct aatttcaata aaatcttcct gcccaccatc tactccatca tcttcttaac 240

tggcattgtg ggcaatggat tggtcatcct ggtcatgggt taccagaaga aactgagaag 300

catgacggac aagtacaggc tgcacctgtc agtggccgac ctcctctttg tcatcacgct 360

tcccttctgg gcagttgatg ccgtggcaaa ctggtacttt gggaacttcc tatgcaaggc 420

agtccatgtc atctacacag tcaacctcta cagcagtgtc ctcatcctgg ccttcatcag 480

tctggaccgc tacctggcca tcgtccacgc caccaacagt cagaggccaa ggaagctgtt 540

ggctgaaaag gtggtctatg ttggcgtctg gatccctgcc ctcctgctga ctattcccga 600

cttcatcttt gccaacgtca gtgaggcaga tgacagatat atctgtgacc gcttctaccc 660

caatgacttg tgggtggttg tgttccagtt tcagcacatc atggttggcc ttatcctgcc 720

tggtattgtc atcctgtcct gctattgcat tatcatctcc aagctgtcac actccaaggg 780

ccaccagaag cgcaaggccc tcaagaccac agtcatcctc atcctggctt tcttcgcctg 840

ttggctgcct tactacattg ggatcagcat cgactccttc atcctcctgg aaatcatcaa 900

gcaagggtgt gagtttgaga acactgtgca caagtggatt tccatcaccg aggccctagc 960

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ctctgcccag cacgcactca cctctgtgag cagagggtcc agcctcaaga tcctctccaa 1080

aggaaagcga ggtggacatt catctgtttc cactgagtct gagtcttcaa gttttcactc 1140

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ttgtcttgtg tttctttagt ttttgtgaag tttaattgac ttatttatat aaatttttt 1320

tgtttcatat tgatgtgtgt ctaggcagga cctgtggcca agttcttagt tgctgtatgt 1380

ctcgtggtag gactgtagaa aagggaactg aacattccag agcgtgtagt gaatcacgta 1440

aagctagaaa tgatccccag ctgtttatgc atagataatc tctccattcc cgtggaacgt 1500

ttttcctgtt cttaagacgt gattttgctg tagaagatgg cacttataac caaagcccaa 1560

agtggtatag aaatgctggt ttttcagttt tcaggagtgg gttgatttca gcacctacag 1620

tgtacagtct tgtattaagt tgttaataaa agtacatgtt aaacttactt agtgttatg 1679

<210> 2897
<211> 450
<212> DNA
<213> Homo sapiens

<400> 2897
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ctgcaggaaa tgaagtgatt cagaactcac caattatgaa ctaaccttca atgccagagg 120

ctttaacagt ttctaataaa aattcagttc agatctcaag ttcagataag tctgaaaaaa 180

cacttcaagg tcatctgaac gaacatattc taccagtact ttatataatt gtatttacct 240

gttcctaaaa ctttccgtga aagaaatgtt gaattttctt cagaaatagt tttgagcaaa 300

atgtcaaaac aattctccca tgctcagtgt acttttgact atactctgaa aatatttctt 360

cttgttttcc tgcacttacc tgttagtgtg ctcacactcc tgtattatgg aacatgttca 420

gtaactcata cacatgtaac acagaagtct 450

<210> 2898
<211> 260
<212> DNA
<213> Homo sapiens

<400> 2898
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tccaagggtt ttctcatcca tgatctcatt tgatccttgc agcagtccta tgaggaaggc 120

agcacataca tcattagctc ccttttgcca aagaggaaac aaaaaacagg tgaaagggac 180

ttgtctaagg gcacccagct ctaagggaca gagcaaagta acaggtcatt tctttttttc 240

atttattttt agagacagag 260

<210> 2899
<211> 452
<212> DNA
<213> Homo sapiens

<400> 2899
ttttttttt ttttttttt ttttttttt ttttttttt tttggaaatt ggaaagggca 60

aattaattaa gtttttaaa gccatcaagt tacaaagggc tattaggggt cttaaaaaga 120

caaagagtat ccaataaaac aaaaagcaat tccagatggt tttaggtgga acaattttgg 180

gccagttata tctataggcc attcctaatt tacttagcaa actttatccc ggggattggc 240

aaattaaaaa aaaggaagaa ccaacctata ttttcttttc ggttttttgg aaacagagcc 300

tccactctgt catccaggct ggagtacagg ggggggatct cagctcaaca taccctcaac 360

ctttggggtt caaggaatct cgggcctaac cctcccaagc agttgggact acaggcatgc 420

accaccgggc tcggccaatt ttttgcattt tt 452

<210> 2900
<211> 511
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (500)..(500)
<223> n is a, c, g, t or u

<400> 2900
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gatgttttaa cagagtggac aggtaataaa cacgttcaac aaaggcagat gttcttggag 120

gttaaatccc actaatcaac acgattaact ttaagggtcc tgagactttc aatagcatgt 180

acctcatgga ctaaaaaaga ggaagagttt atgcttcaca attaatctcc agaacttgac 240

acatgtaatt cttatcacca aggctttaga ttgaaaagta atagaaaaca acagtaactg 300

ttctggtaca gtctagcatt tccaatgtgc ttctttttat tttaatgaaa aaaaaagata 360

cattatatca aacaaaactg ttgatggatc cacatctttg caggctcttt gcggaatggc 420

tcaccaaata cacatttcca tctttagatc attatactgc ttaaacagca agatatgcta 480

aagagatatg aatatgattn tgacctacca t 511

<210> 2901
<211> 541

<212> DNA
<213> Homo sapiens

<400> 2901
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ctgttaatca aagcagagat cagaacggat taactgtggc aacgtcgtat caggagcaca 120

aagagaagcc tgcctctttc agtttggtct tttctccagc aaaacagaaa tgcaatttag 180

tcaaacacat acagaggccc cactgtactg cctcactgat ggagggaaat acttgggtgc 240

aatcacacac agtgttagtg attggcaact gtccagtgct atttcgctaa aactggtaaa 300

aacagtttcc ttgggcaagc agctgattgg ctacttcata ctgtgctgag ttgggctcag 360

cttgtctgtc tctgggaggc cctaaggggc tcctcttttt cagctaggga taaggggaga 420

ctgtcaacca gtatcttagc gtgaactgtc aatcgctgag cccctgccaa ggactctctg 480

gaagtccctc aggtatgctg aaaatacctt atactgaaaa ggtagctctc gctgcatcca 540

c 541

<210> 2902
<211> 646
<212> DNA
<213> Homo sapiens

<400> 2902
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attgatgtga cttgccagaa tgtttgaaac accagtgacc aagggtcact atatctgccc 120

ccaaacaatt ccaccatgtt tacttatata gcactcacca aaccagaaga gaggctggga 180

tattctcagg ccactgcact gaacatcaat atgaaagaac catgaatgat gcgacaactg 240

agttgatttt ctacctcctc tgcccaccat gactttgcac cccaaattct ttcagtgtct 300

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caggatcatg tttaattatg taaaaaagct ctaaagtcag gtaatggttt tcatgtgctt 480

ctcttgagca gtctgaggag agaatagaaa cagaaacccc ttggggcctg agtagacgca 540

gctggccatg cacaggcaga ggctcttggt cagtgcagga agcagagtca cagccatcgc 600

cttggggtgg ggatgaaatg agatgacctg ttggctgtat gacagc 646

<210> 2903
<211> 557
<212> DNA
<213> Homo sapiens

<400> 2903
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accttgcaga gaataggcat tgaaatatta tttaaacaat caaaccaaag atgttcttct 120

atcttcagct gtcagtgatc taatgccctc atctctctta tcctcaggac ccagaatggt 180

atattccaca taaaagatgc tttgtttatc aaatgaatca aaaagcacgc ctgaggcatt 240

tatttttact cctttacttc tgtaggccag gtcaaggtgg gtctaattca cttttatcat 300

cagcacttaa gaaactggat ggaagaccac aacaccttgt tttttgcaaa aatttttccat 360

ctcctcaatc aggccaggaa gcatgtatct tctggacagg actttatctc tctactcagc 420

ttagtacact gccttatatt agtccatttg tcccatgttt tcatcactga ataaacttgt 480

taaatgactt ttggtctgga tctcacacct atattacttc atttccttct gtgagcactc 540

tataatgata acatcat 557

<210> 2904
<211> 488
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (239)..(239)
<223> n is a, c, g, t or u

<400> 2904
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tgcgcgtggg tcgcgaggtg acaggagccg gccctcgtcc ttaatggagc ggccagagct 120

gggtgggggc ggcccgggag ctcggggttc ccggcactac ctgaatgcag cccgaagcca 180

agttgtgcac gcgtttgtcc tataaaagcg aagtgagtgg attcccattt tggaatccnc 240

ggtgtctcca acctcgagtt ggagaaccat gttgagtcag ttccccggaa ccttacaaat 300

ggactccact tcccccgttc ccattctacc gttttttttta aaaaatgatt tttttgagtg 360

gcggttccag gattagtcaa atagcttctc ccgagaatgc tctttaaaag attgtcagac 420

acctttgggt taagtctcag tttttgcatg ggcccgaatt gcagtcctat gaatttctga 480

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<210> 2905
<211> 696
<212> DNA
<213> Homo sapiens

<400> 2905
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gtgactgtcc tgtctctcct catgctagta gctgccttct gctctccagc gctctcagca 180

ccaatgggct cagaccctcc caccgcctgc tgcttttctt acaccgcgag gaagcttcct 240

cgcaactttg tggtagatta ctatgagacc agcagcctct gctcccagcc agctgtggta 300

ttccaaacca aaagaagcaa gcaagtctgt gctgatccca gtgaatcctg ggtccaggag 360

tacgtgtatg acctggaact gaactgagct gctcagagac aggaagtctt cagggaaggt 420

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ggcaaatatt gcttcttgat tttttgtttt ccgtctatct aagcttgaat tttatgtgca 240

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<212> DNA
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gacacagccg ttcacccagc cacagatagt gacagggcac acatggcgac acccacatgt 180

acggagataa atctcccccа ccatgacatg ggtagacaga aaacacgccg cagtatactc 240

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aaatttttgtt catactattt tacattttta caaactcaaa tcactttggt tcatatattt 180

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acagatgaga atgttcgtaa agaaaaaaaa 2610

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<213> Homo sapiens

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<223> n is a, c, g, t or u

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tgtaaaagga tagtgtttgc atctagagga ctagagacat gcctgcacat ccctcacctt 180

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ttgtgtagta cctcggccgc gaccacgcta atcactagt 279

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<212> DNA
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<223> n is a, c, g, t or u

<220>
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<223> n is a, c, g, t or u

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<223> n is a, c, g, t or u

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ggcttgtggt caagcaaaaa ttcagccctg aaatcaggca catctgttcg ttggactaaa 1920

cccacaggtt agttcagtca aagcaggcaa ccccccttgtg ggcactgacc ctgccactgg 1980

ggtcatggcg gttgtggcag ctggggaggt ttggccccaa cagccctcct gtgcctgctt 2040

ccctgtgtgt cggggtcctc cagggagctg acccagaggt ggaggccacg gaggcagggt 2100

ctctggggac tgtcgggggg tacagaggga gaaggctctg caagagctcc ctggcaatac 2160

ccccttgtgt aattgctttg tgtgcgacag ggaggaagtt tcaataaagc aacaacaagc 2220

ttcaaggaat tc 2232

<210> 2920
<211> 1620
<212> DNA
<213> Homo sapiens

<400> 2920
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aaggaggtct ccaggacgga cttcagatca ctgtcaatgg gaccgttctc agctccagtg 180

gaaccaggtt tgctgtgaac tttcagactg gcttcagtgg aaatgacatt gccttccact 240

tcaaccctcg gtttgaagat ggagggtacg tggtgtgcaa cacgaggcag aacggaagct 300

gggggcccga ggagaggagg acacacatgc ctttccagaa ggggatgccc tttgacctct 360

gcttcctggt gcagagctca gatttcaagg tgatggtgaa cgggatcctc ttcgtgcagt 420

acttccaccg cgtgcccttc caccgtgtgg acaccatctt cgtcaatggc tctgtgcagc 480

tgtcctacat cagcttccag cctcccggcg tgtggcctgc caacccggct cccattaccc 540

agacagtcat ccacacagtg cagagcgccc ctggacagat gttctctact cccgccatcc 600

cacctatgat gtacccccac cccgcctatc cgatgccttt catcaccacc attctgggag 660

ggctgtaccc atccaagtcc atcctcctgt caggcactgt cctgcccagt gctcagaggt 720

tccacatcaa cctgtgctct gggaaccaca tcgccttcca cctgaacctc cgttttgatg 780

agaatgctgt ggtccgcaac acccagatcg acaactcctg ggggtctgag gagcgaagtc 840

tgccccgaaa aatgcccttc gtccgtggcc agagcttctc agtgtggatc ttgtgtggag 900

ctcactgcct caaggtggcc gtggatggtc agcacctgtt tgaatactac catcgcctga 960

ggaacctgcc caccatcaac agactggaag tgggggggcga catccagctg acccatgtgc 1020

agacataggc ggcttcctgg ccctggggcc gggggctggg gtgtggggca gtctgggtcc 1080

tctcatcatc cccacttccc aggcccagcc tttccaaccc tgcctgggat ctgggcttta 1140

atgcagaggc catgtccttg tctggtcctg cttctggcta cagccaccct ggaacggaga 1200

aggcagctga cggggattgc cttcctcagc cgcagcagca cctggggctc cagctgctgg 1260

aatcctacca tcccaggagg caggcacagc cagggagagg ggaggagtgg gcagtgaaga 1320

tgaagcccca tgctcagtcc cctcccatcc cccacgcagc tccaccccag tcccaagcca 1380

ccagctgtct gctcctggtg ggaggtggcc tcctcagccc ctcctctctg acctttaacc 1440

tcactctcac cttgcaccgt gcaccaaccc ttcacccctc ctggaaagca ggcctgatgg 1500

cttcccactg gcctccacca cctgaccaga gtgttctctt cagaggactg gctcctttcc 1560

cagtgtcctt aaaataaaga aatgaaaatg cttgttggca aaaaaaaaaa aaaaaaaaaa 1620

<210> 2921
<211> 916
<212> DNA
<213> Homo sapiens

<400> 2921
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ggctcgggtg gcagcgcgga ggacagcgtg ggctccagct ctgtcaccgt tgtcctgctg 180

ctgctgctgc tcctactgct ggccactggc ctagcactgg cctggcgccg cctcagccgt 240

gactcagggg gctactacca cccggcccgc ctaggtgccg cgctgtgggg ccgcacgcgg 300

cgcctgctct gggccagccc cccaggtcgc tggctgcagg cccgagctga gctggggtcc 360

acagacaatg accttgagcg acaggaggat gagcaggaca cagactatga ccacgtcgcg 420

gatggtggcc tgcaggctga ccctggggaa ggcgagcagc aatgtggaga ggcgtccagc 480

ccagagcagg tccccgtgcg ggctgaggaa gccagagaca gtgacacgga gggcgacctg 540

gtcctcggct ccccaggacc agcgagcgca gggggcagtg ctgaggccct gctgagtgac 600

ctgcacgcct ttgctggcag cgcagcctgg gatgacagcg ccagggcagc tgggggccag 660

ggcctccatg tcaccgcact gtagaggccg gtcttggtgt cccatccctg tcacagccgc 720

tcactccccg tgcctctgct tcccaagatg ccatggctgg actggacccc cagcccacat 780

gaccatgcct cagactgtca cccctaccag ttcccaagtc catgtgtacc ccgctcacca 840

cgggaacggc ccccccaac cacaggcatc aggcaaccat ttgaaataaa actccttcag 900

cctgtgaaaa aaaaaa 916

<210> 2922
<211> 1272
<212> DNA
<213> Homo sapiens

<400> 2922
gaattcggcc aaagaggcct atgcttctct gaagacttgc agcaaggctt gctgaggctc 60

acagaagata gccccagtgt tttggagtgg ttttgaatgt gattctgaga tcagactgac 120

tgagctggaa tcctggcttt atatcttacc agctacacaa ccttggagtc ttagaaattt 180

tttcttttca ataagcagtc atccttactt tccctcaaga tgacaaacag ttcgttcttc 240

tgcccagttt ataaagatct ggagccattc acgtattttt tttatttagt tttccttgtt 300

ggaattattg gaagttgttt tgcaacctgg gcttttatac agaagaatac gaatcacagg 360

tgtgtgagca tctacttaat taatttgctt acagccgatt tcctgcttac tctggcatta 420

ccagtgaaaa ttgttgttga cttgggtgtg gcaccttgga agctgaagat attccactgc 480

caagtaacag cctgcctcat ctatatcaat atgtatttat caattatctt cttagcattt 540

gtcagcattg accgctgtct tcagctgaca cacagctgca agatctaccg aatacaagaa 600

cccggatttg ccaaaatgat atcaaccgtt gtgtggctaa tggtccttct tataatggtg 660

ccaaatatga tgattcccat caaagacatc aaggaaaagt caaatgtggg ttgtatggag 720

tttaaaaagg aatttggaag aaattggcat ttgctgacaa atttcatatg tgtagcaata 780

tttttaaatt tctcagccat cattttaata tccaattgcc ttgtaattcg acagctctac 840

agaaacaaag ataatgaaaa ttacccaaat gtgaaaaagg ctctcatcaa catactttta 900

gtgaccacgg gctacatcat atgctttgtt ccttaccaca ttgtccgaat cccgtatacc 960

ctcagccaga cagaagtcat aactgattgc tcaaccagga tttcactctt caaagccaaa 1020

gaggctacac tgctcctggc tgtgtcgaac ctgtgctttg atcctatcct gtactatcac 1080

ctctcaaaag cattccgctc aaaggtcact gagacttttg cctcacctaa agagaccaag 1140

gctcagaaag aaaaattaag atgtgaaaat aatgcataaa agacaggatt ttttgtgcta 1200

ccaattctgg ccttactgga ccataaagtt aattatagct ttgaaagata aaaaaaaaaa 1260

aaaagcggcc gc 1272

<210> 2923
<211> 413
<212> DNA
<213> Homo sapiens

<400> 2923
ttttttttt tttttgtaga gggtcacatc aatccatagg aaaggaaacc tgcttcttct 60

cacaaaggga taacttttgt tttcctcatg agtcaacttg aaggataact ttaaaaaatt 120

ggtccatgca gcagagtgag actccgtctc aaaaaaaaaa aaaaaaaaaa aaaaaggtcc 180

atgcagaaga ctatcttttt ccaatttgta taagggaact atgtaagttc actgtagctc 240

tgggtatcct caacccacag atctggcagg cagcttgcag cccatcttca gaggagggcc 300

aagtgtccat tcagactcgg gtatttccac actagctgtc tttgagttcc atcaagtaga 360

tagagaactt ctgatccaag ggattttata gagattacaa ccccctcgtg ccg 413

<210> 2924
<211> 474
<212> DNA
<213> Homo sapiens

<400> 2924
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ggtccccagg ggatgctagg tggtgtctgg gggcatttgt gactgttatg actcagggat 120

gctcctggcg tggagtgggt ggaggccagg gatgctgatc agaaccttgc agtggccagg 180

acaaccccac cccagagaac gacccagccc tgaatgccaa gggggagaga ctctgcctta 240

attatttgga aaaatattgt atctgctccc tgttgacacc agacactaga aaaaattccc 300

gatggggtgg atggcagaaa ccaaggggggg ccccagctcc tgcgattctc ctcctctctc 360

cctccccact cagggtgtgg attacaatgt gtgcagcctc ctggaacctc aggaggacag 420

aggatcatga gacacagagt ttcttgggga tctgtggaat cccctaaccc ccgg 474

<210> 2925
<211> 199
<212> PRT
<213> Homo sapiens

<400> 2925

Met Ser Ser Glu Asn Cys Phe Val Ala Glu Asn Ser Ser Leu His Pro
1 5 10 15

```
Glu Ser Gly Gln Glu Asn Asp Ala Thr Ser Pro His Phe Ser Thr Arg
            20                  25                  30

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

Val Phe Ile Thr Ile Leu Ile Ile Ala Leu Ile Ala Leu Ser Val Gly
    50                  55                  60

Gln Tyr Asn Cys Pro Gly Gln Tyr Thr Phe Ser Met Pro Ser Asp Ser
65                  70                  75                  80

His Val Ser Ser Cys Ser Glu Asp Trp Val Gly Tyr Gln Arg Lys Cys
                85                  90                  95

Tyr Phe Ile Ser Thr Val Lys Arg Ser Trp Thr Ser Ala Gln Asn Ala
            100                 105                 110

Cys Ser Glu His Gly Ala Thr Leu Ala Val Ile Asp Ser Glu Lys Asp
        115                 120                 125

Met Asn Phe Leu Lys Arg Tyr Ala Gly Arg Glu Glu His Trp Val Gly
    130                 135                 140

Leu Lys Lys Glu Pro Gly His Pro Trp Lys Trp Ser Asn Gly Lys Glu
145                 150                 155                 160

Phe Asn Asn Trp Phe Asn Val Thr Gly Ser Asp Lys Cys Val Phe Leu
                165                 170                 175

Lys Asn Thr Glu Val Ser Ser Met Glu Cys Glu Lys Asn Leu Tyr Trp
            180                 185                 190

Ile Cys Asn Lys Pro Tyr Lys
        195
```

<210> 2926
<211> 326
<212> PRT
<213> Homo sapiens

<400> 2926

```
Met Asp Tyr Ser His Gln Thr Ser Leu Val Pro Cys Gly Gln Asp Lys
1               5                   10                  15

Tyr Ile Ser Lys Asn Glu Leu Leu Leu His Leu Lys Thr Tyr Asn Leu
            20                  25                  30
```

```
Tyr Tyr Glu Gly Gln Asn Leu Gln Leu Arg His Arg Glu Glu Glu Asp
        35                  40                  45

Glu Phe Ile Val Glu Gly Leu Leu Asn Ile Ser Trp Gly Leu Arg Arg
    50                  55                  60

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

Pro Ser Ser Ser Ser Trp His Ser Gly Cys Asn Leu Gly Ala Gln Gly
                85                  90                  95

Thr Thr Leu Lys Pro Leu Thr Val Pro Lys Val Gln Ile Ser Glu Val
            100                 105                 110

Asp Ala Pro Pro Glu Gly Asp Gln Met Pro Ser Ser Thr Asp Ser Arg
        115                 120                 125

Gly Leu Lys Pro Leu Gln Glu Asp Thr Pro Gln Leu Met Arg Thr Arg
    130                 135                 140

Ser Asp Val Gly Val Arg Arg Arg Gly Asn Val Arg Thr Pro Ser Asp
145                 150                 155                 160

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

Asn His Lys Thr Ser Val Phe Thr Pro Ala Tyr Gly Ser Val Thr Asn
            180                 185                 190

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

Leu Asn Lys Phe Lys Ile Glu Asn Ser Ala Glu Glu Phe Ala Leu Tyr
    210                 215                 220

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

Pro Leu Ile Ala Arg Ile Leu Gln Gly Pro Cys Glu Gln Ile Ser Lys
                245                 250                 255

Val Phe Leu Met Glu Lys Asp Gln Val Glu Glu Val Thr Tyr Asp Val
            260                 265                 270
```

```
Ala Gln Tyr Ile Lys Phe Glu Met Pro Val Leu Lys Ser Phe Ile Gln
        275                 280                 285

Lys Leu Gln Glu Glu Glu Asp Arg Glu Val Lys Lys Leu Met Arg Lys
    290                 295                 300

Tyr Thr Val Leu Arg Leu Met Ile Arg Gln Arg Leu Glu Glu Ile Ala
305                 310                 315                 320

Glu Thr Pro Ala Thr Ile
                325
```

<210> 2927
<211> 364
<212> PRT
<213> Homo sapiens

<400> 2927

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

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

Glu Gly Leu Cys Val Leu Val Pro Cys Thr Phe Phe His Pro Ile Pro
        35                  40                  45

Tyr Tyr Asp Lys Asn Ser Pro Val His Gly Tyr Trp Phe Arg Glu Gly
    50                  55                  60

Ala Ile Ile Ser Gly Asp Ser Pro Val Ala Thr Asn Lys Leu Asp Gln
65                  70                  75                  80

Glu Val Gln Glu Glu Thr Gln Gly Arg Phe Arg Leu Leu Gly Asp Pro
                85                  90                  95

Ser Arg Asn Asn Cys Ser Leu Ser Ile Val Asp Ala Arg Arg Arg Asp
            100                 105                 110

Asn Gly Ser Tyr Phe Phe Arg Met Glu Arg Gly Ser Thr Lys Tyr Ser
        115                 120                 125

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

Pro Lys Ile Leu Ile Pro Gly Thr Leu Glu Pro Gly His Ser Lys Asn
```

145 150 155 160

Leu Thr Cys Ser Val Ser Trp Ala Cys Glu Gln Gly Thr Pro Pro Ile
165 170 175

Phe Ser Trp Leu Ser Ala Ala Pro Thr Ser Leu Gly Pro Arg Thr Thr
180 185 190

His Ser Ser Val Leu Ile Ile Thr Pro Arg Pro Gln Asp His Gly Thr
195 200 205

Asn Leu Thr Cys Gln Val Lys Phe Ala Gly Ala Gly Val Thr Thr Glu
210 215 220

Arg Thr Ile Gln Leu Asn Val Thr Tyr Val Pro Gln Asn Pro Thr Thr
225 230 235 240

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

Leu Val His Gly Ala Ile Gly Gly Ala Gly Val Thr Ala Leu Leu Ala
260 265 270

Leu Cys Leu Cys Leu Ile Phe Phe Ile Val Lys Thr His Arg Arg Lys
275 280 285

Ala Ala Arg Thr Ala Val Gly Ser Asn Asp Thr His Pro Thr Thr Gly
290 295 300

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

Glu Thr Ser Ser Cys Ser Gly Ala Ala Pro Thr Val Glu Met Asp Glu
325 330 335

Glu Leu His Tyr Ala Ser Leu Asn Phe His Gly Met Asn Pro Ser Lys
340 345 350

Asp Thr Ser Thr Glu Tyr Ser Glu Val Arg Thr Gln
355 360

<210> 2928
<211> 326
<212> PRT
<213> Homo sapiens

<400> 2928

```
Met Asp Tyr Ser His Gln Thr Ser Leu Val Pro Cys Gly Gln Asp Lys
1               5                  10                  15

Tyr Ile Ser Lys Asn Glu Leu Leu Leu His Leu Lys Thr Tyr Asn Leu
            20                  25                  30

Tyr Tyr Glu Gly Gln Asn Leu Gln Leu Arg His Arg Glu Glu Glu Asp
        35                  40                  45

Glu Phe Ile Val Glu Gly Leu Leu Asn Ile Ser Trp Gly Leu Arg Arg
    50                  55                  60

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

Pro Ser Ser Ser Ser Trp His Ser Gly Cys Asn Leu Gly Ala Gln Gly
                85                  90                  95

Thr Thr Leu Lys Pro Leu Thr Val Pro Lys Val Gln Ile Ser Glu Val
            100                 105                 110

Asp Ala Pro Pro Glu Gly Asp Gln Met Pro Ser Ser Thr Asp Ser Arg
        115                 120                 125

Gly Leu Lys Pro Leu Gln Glu Asp Thr Pro Gln Leu Met Arg Thr Arg
    130                 135                 140

Ser Asp Val Gly Val Arg Arg Arg Gly Asn Val Arg Thr Pro Ser Asp
145                 150                 155                 160

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

Asn His Lys Thr Ser Val Phe Thr Pro Ala Tyr Gly Ser Val Thr Asn
            180                 185                 190

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

Leu Asn Lys Phe Lys Ile Glu Asn Ser Ala Glu Glu Phe Ala Leu Tyr
    210                 215                 220

Val Val His Thr Ser Gly Glu Lys Gln Lys Leu Lys Ala Thr Asp Tyr
225                 230                 235                 240
```

```
Pro Leu Ile Ala Arg Ile Leu Gln Gly Pro Cys Glu Gln Ile Ser Lys
                245                 250                 255

Val Phe Leu Met Glu Lys Asp Gln Val Glu Glu Val Thr Tyr Asp Val
            260                 265                 270

Ala Gln Tyr Ile Lys Phe Glu Met Pro Val Leu Lys Ser Phe Ile Gln
        275                 280                 285

Lys Leu Gln Glu Glu Glu Asp Arg Glu Val Lys Lys Leu Met Arg Lys
    290                 295                 300

Tyr Thr Val Leu Arg Leu Met Ile Arg Gln Arg Leu Glu Glu Ile Ala
305                 310                 315                 320

Glu Thr Pro Ala Thr Ile
                325
```

<210> 2929
<211> 1842
<212> PRT
<213> Homo sapiens

<400> 2929

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

Arg Lys Ala Asp Lys Glu Arg His Gly Val Ala Ile Tyr Asn Phe Gln
            20                  25                  30

Gly Ser Gly Ala Pro Gln Leu Ser Leu Gln Ile Gly Asp Val Val Arg
        35                  40                  45

Ile Gln Glu Thr Cys Gly Asp Trp Tyr Arg Gly Tyr Leu Ile Lys His
    50                  55                  60

Lys Met Leu Gln Gly Ile Phe Pro Lys Ser Phe Ile His Ile Lys Glu
65                  70                  75                  80

Val Thr Val Glu Lys Arg Arg Asn Thr Glu Asn Ile Ile Pro Ala Glu
                85                  90                  95

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

Ile Trp Lys Gln Leu Tyr Val Ala Ser Lys Lys Glu Arg Phe Leu Gln
        115                 120                 125
```

```
Val Gln Ser Met Met Tyr Asp Leu Met Glu Trp Arg Ser Gln Leu Leu
    130                 135                 140

Ser Gly Thr Leu Pro Lys Asp Glu Leu Lys Glu Leu Lys Gln Lys Val
145                 150                 155                 160

Thr Ser Lys Ile Asp Tyr Gly Asn Lys Ile Leu Glu Leu Asp Leu Ile
                165                 170                 175

Val Arg Asp Glu Asp Gly Asn Ile Leu Asp Pro Asp Asn Thr Ser Val
            180                 185                 190

Ile Ser Leu Phe His Ala His Glu Glu Ala Thr Asp Lys Ile Thr Glu
        195                 200                 205

Arg Ile Lys Glu Glu Met Ser Lys Asp Gln Pro Asp Tyr Ala Met Tyr
    210                 215                 220

Ser Arg Ile Ser Ser Ser Pro Thr His Ser Leu Tyr Val Phe Val Arg
225                 230                 235                 240

Asn Phe Val Cys Arg Ile Gly Glu Asp Ala Glu Leu Phe Met Ser Leu
                245                 250                 255

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

Trp Gly Ser Arg Gly Phe Pro Lys Glu Ile Glu Met Leu Asn Asn Leu
        275                 280                 285

Lys Val Val Phe Thr Asp Leu Gly Asn Lys Asp Leu Asn Arg Asp Lys
    290                 295                 300

Ile Tyr Leu Ile Cys Gln Ile Val Arg Val Gly Lys Met Asp Leu Lys
305                 310                 315                 320

Asp Thr Gly Ala Lys Lys Cys Thr Gln Gly Leu Arg Arg Pro Phe Gly
                325                 330                 335

Val Ala Val Met Asp Ile Thr Asp Ile Ile Lys Gly Lys Ala Glu Ser
            340                 345                 350

Asp Glu Glu Lys Gln His Phe Ile Pro Phe His Pro Val Thr Ala Glu
        355                 360                 365
```

```
Asn Asp Phe Leu His Ser Leu Leu Gly Lys Val Ile Ala Ser Lys Gly
    370                 375                 380

Asp Ser Gly Gly Gln Gly Leu Trp Val Thr Met Lys Met Leu Val Gly
385                 390                 395                 400

Asp Ile Ile Gln Ile Arg Lys Asp Tyr Pro His Leu Val Asp Arg Thr
                405                 410                 415

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

Asp Val Arg Asn Asp Ile Tyr Ile Thr Leu Leu Gln Gly Asp Phe Asp
        435                 440                 445

Lys Tyr Asn Lys Thr Thr Gln Arg Asn Val Glu Val Ile Met Cys Val
    450                 455                 460

Cys Ala Glu Asp Gly Lys Thr Leu Pro Asn Ala Ile Cys Val Gly Ala
465                 470                 475                 480

Gly Asp Lys Pro Met Asn Glu Tyr Arg Ser Val Val Tyr Tyr Gln Val
                485                 490                 495

Lys Gln Pro Arg Trp Met Glu Thr Val Lys Val Ala Val Pro Ile Glu
            500                 505                 510

Asp Met Gln Arg Ile His Leu Arg Phe Met Phe Arg His Arg Ser Ser
        515                 520                 525

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

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

Leu Val Val Leu Lys Gly Asp Ser Lys Lys Met Glu Asp Ala Ser Ala
                565                 570                 575

Tyr Leu Thr Leu Pro Ser Tyr Arg His His Val Glu Asn Lys Gly Ala
            580                 585                 590

Thr Leu Ser Arg Ser Ser Ser Ser Val Gly Gly Leu Ser Val Ser Ser
        595                 600                 605
```

```
Arg Asp Val Phe Ser Ile Ser Thr Leu Val Cys Ser Thr Lys Leu Thr
    610                 615                 620

Gln Asn Val Gly Leu Leu Gly Leu Leu Lys Trp Arg Met Lys Pro Gln
625                 630                 635                 640

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

Val Val Lys Phe Leu Gln Asp Thr Leu Asp Ala Leu Phe Asn Ile Met
            660                 665                 670

Met Glu His Ser Gln Ser Asp Glu Tyr Asp Ile Leu Val Phe Asp Ala
        675                 680                 685

Leu Ile Tyr Ile Ile Gly Leu Ile Ala Asp Arg Lys Phe Gln His Phe
    690                 695                 700

Asn Thr Val Leu Glu Ala Tyr Ile Gln Gln His Phe Ser Ala Thr Leu
705                 710                 715                 720

Ala Tyr Lys Lys Leu Met Thr Val Leu Lys Thr Tyr Leu Asp Thr Ser
                725                 730                 735

Ser Arg Gly Glu Gln Cys Glu Pro Ile Leu Arg Thr Leu Lys Ala Leu
            740                 745                 750

Glu Tyr Val Phe Lys Phe Ile Val Arg Ser Arg Thr Leu Phe Ser Gln
        755                 760                 765

Leu Tyr Glu Gly Lys Glu Gln Met Glu Phe Glu Glu Ser Met Arg Arg
    770                 775                 780

Leu Phe Glu Ser Ile Asn Asn Leu Met Lys Ser Gln Tyr Lys Thr Thr
785                 790                 795                 800

Ile Leu Leu Gln Val Ala Ala Leu Lys Tyr Ile Pro Ser Val Leu His
                805                 810                 815

Asp Val Glu Met Val Phe Asp Ala Lys Leu Leu Ser Gln Leu Leu Tyr
            820                 825                 830

Glu Phe Tyr Thr Cys Ile Pro Pro Val Lys Leu Gln Lys Gln Lys Val
        835                 840                 845

Gln Ser Met Asn Glu Ile Val Gln Ser Asn Leu Phe Lys Lys Gln Glu
```

```
    850                 855                 860

Cys Arg Asp Ile Leu Leu Pro Val Ile Thr Lys Glu Leu Lys Glu Leu
865                 870                 875                 880

Leu Glu Gln Lys Asp Asp Met Gln His Gln Val Leu Glu Arg Lys Tyr
                885                 890                 895

Cys Val Glu Leu Leu Asn Ser Ile Leu Glu Val Leu Ser Tyr Gln Asp
            900                 905                 910

Ala Ala Phe Thr Tyr His His Ile Gln Glu Ile Met Val Gln Leu Leu
        915                 920                 925

Arg Thr Val Asn Arg Thr Val Ile Thr Met Gly Arg Asp His Ile Leu
    930                 935                 940

Ile Ser His Phe Val Ala Cys Met Thr Ala Ile Leu Asn Gln Met Gly
945                 950                 955                 960

Asp Gln His Tyr Ser Phe Tyr Ile Glu Thr Phe Gln Thr Ser Ser Glu
                965                 970                 975

Leu Val Asp Phe Leu Met Glu Thr Phe Ile Met Phe Lys Asp Leu Ile
            980                 985                 990

Gly Lys Asn Val Tyr Pro Gly Asp  Trp Met Ala Met Ser  Met Val Gln
        995                 1000                1005

Asn Arg  Val Phe Leu Arg Ala  Ile Asn Lys Phe Ala  Glu Thr Met
    1010                1015                1020

Asn Gln  Lys Phe Leu Glu His  Thr Asn Phe Glu Phe  Gln Leu Trp
    1025                1030                1035

Asn Asn  Tyr Phe His Leu Ala  Val Ala Phe Ile Thr  Gln Asp Ser
    1040                1045                1050

Leu Gln  Leu Glu Gln Phe Ser  His Ala Lys Tyr Asn  Lys Ile Leu
    1055                1060                1065

Asn Lys  Tyr Gly Asp Met Arg  Arg Leu Ile Gly Phe  Ser Ile Arg
    1070                1075                1080

Asp Met  Trp Tyr Lys Leu Gly  Gln Asn Lys Ile Cys  Phe Ile Pro
    1085                1090                1095
```

```
Gly Met  Val Gly Pro Ile Leu  Glu Met Thr Leu Ile  Pro Glu Ala
    1100                 1105                 1110

Glu Leu  Arg Lys Ala Thr Ile  Pro Ile Phe Phe Asp  Met Met Leu
    1115                 1120                 1125

Cys Glu  Tyr Gln Arg Ser Gly  Asp Phe Lys Lys Phe  Glu Asn Glu
    1130                 1135                 1140

Ile Ile  Leu Lys Leu Asp His  Glu Val Glu Gly Gly  Arg Gly Asp
    1145                 1150                 1155

Glu Gln  Tyr Met Gln Leu Leu  Glu Ser Ile Leu Met  Glu Cys Ala
    1160                 1165                 1170

Ala Glu  His Pro Thr Ile Ala  Lys Ser Val Glu Asn  Phe Val Asn
    1175                 1180                 1185

Leu Val  Lys Gly Leu Leu Glu  Lys Leu Leu Asp Tyr  Arg Gly Val
    1190                 1195                 1200

Met Thr  Asp Glu Ser Lys Asp  Asn Arg Met Ser Cys  Thr Val Asn
    1205                 1210                 1215

Leu Leu  Asn Phe Tyr Lys Asp  Asn Asn Arg Glu Glu  Met Tyr Ile
    1220                 1225                 1230

Arg Tyr  Leu Tyr Lys Leu Arg  Asp Leu His Leu Asp  Cys Asp Asn
    1235                 1240                 1245

Tyr Thr  Glu Ala Ala Tyr Thr  Leu Leu Leu His Thr  Trp Leu Leu
    1250                 1255                 1260

Lys Trp  Ser Asp Glu Gln Cys  Ala Ser Gln Val Met  Gln Thr Gly
    1265                 1270                 1275

Gln Gln  His Pro Gln Thr His  Arg Gln Leu Lys Glu  Thr Leu Tyr
    1280                 1285                 1290

Glu Thr  Ile Ile Gly Tyr Phe  Asp Lys Gly Lys Met  Trp Glu Glu
    1295                 1300                 1305

Ala Ile  Ser Leu Cys Lys Glu  Leu Ala Glu Gln Tyr  Glu Met Glu
    1310                 1315                 1320
```

```
Ile Phe  Asp Tyr Glu Leu Leu  Ser Gln Asn Leu Ile  Gln Gln Ala
    1325                 1330                 1335

Lys Phe  Tyr Glu Ser Ile Met  Lys Ile Leu Arg Pro  Lys Pro Asp
    1340                 1345                 1350

Tyr Phe  Ala Val Gly Tyr Tyr  Gly Gln Gly Phe Pro  Ser Phe Leu
    1355                 1360                 1365

Arg Asn  Lys Val Phe Ile Tyr  Arg Gly Lys Glu Tyr  Glu Arg Arg
    1370                 1375                 1380

Glu Asp  Phe Gln Met Gln Leu  Met Thr Gln Phe Pro  Asn Ala Glu
    1385                 1390                 1395

Lys Met  Asn Thr Thr Ser Ala  Pro Gly Asp Asp Val  Lys Asn Ala
    1400                 1405                 1410

Pro Gly  Gln Tyr Ile Gln Cys  Phe Thr Val Gln Pro  Val Leu Asp
    1415                 1420                 1425

Glu His  Pro Arg Phe Lys Asn  Lys Pro Val Pro Asp  Gln Ile Ile
    1430                 1435                 1440

Asn Phe  Tyr Lys Ser Asn Tyr  Val Gln Arg Phe His  Tyr Ser Arg
    1445                 1450                 1455

Pro Val  Arg Arg Gly Thr Val  Asp Pro Glu Asn Glu  Phe Ala Ser
    1460                 1465                 1470

Met Trp  Ile Glu Arg Thr Ser  Phe Val Thr Ala Tyr  Lys Leu Pro
    1475                 1480                 1485

Gly Ile  Leu Arg Trp Phe Glu  Val Val His Met Ser  Gln Thr Thr
    1490                 1495                 1500

Ile Ser  Pro Leu Glu Asn Ala  Ile Glu Thr Met Ser  Thr Ala Asn
    1505                 1510                 1515

Glu Lys  Ile Leu Met Met Ile  Asn Gln Tyr Gln Ser  Asp Glu Thr
    1520                 1525                 1530

Leu Pro  Ile Asn Pro Leu Ser  Met Leu Leu Asn Gly  Ile Val Asp
    1535                 1540                 1545
```

```
Pro Ala  Val Met Gly Gly Phe  Ala Lys Tyr Glu Lys  Ala Phe Phe
    1550                 1555                 1560

Thr Glu  Glu Tyr Val Arg Asp  His Pro Glu Asp Gln  Asp Lys Leu
    1565                 1570                 1575

Thr His  Leu Lys Asp Leu Ile  Ala Trp Gln Ile Pro  Phe Leu Gly
    1580                 1585                 1590

Ala Gly  Ile Lys Ile His Glu  Lys Arg Val Ser Asp  Asn Leu Arg
    1595                 1600                 1605

Pro Phe  His Asp Arg Met Glu  Glu Cys Phe Lys Asn  Leu Lys Met
    1610                 1615                 1620

Lys Val  Glu Lys Glu Tyr Gly  Val Arg Glu Met Pro  Asp Phe Asp
    1625                 1630                 1635

Asp Arg  Arg Val Gly Arg Pro  Arg Ser Met Leu Arg  Ser Tyr Arg
    1640                 1645                 1650

Gln Met  Ser Ile Ile Ser Leu  Ala Ser Met Asn Ser  Asp Cys Ser
    1655                 1660                 1665

Thr Pro  Ser Lys Pro Thr Ser  Glu Ser Phe Asp Leu  Glu Leu Ala
    1670                 1675                 1680

Ser Pro  Lys Thr Pro Arg Val  Glu Gln Glu Glu Pro  Ile Ser Pro
    1685                 1690                 1695

Gly Ser  Thr Leu Pro Glu Val  Lys Leu Arg Arg Ser  Lys Lys Arg
    1700                 1705                 1710

Thr Lys  Arg Ser Ser Val Val  Phe Ala Asp Glu Lys  Ala Ala Ala
    1715                 1720                 1725

Glu Ser  Asp Leu Lys Arg Leu  Ser Arg Lys His Glu  Phe Met Ser
    1730                 1735                 1740

Asp Thr  Asn Leu Ser Glu His  Ala Ala Ile Pro Leu  Lys Ala Ser
    1745                 1750                 1755

Val Leu  Ser Gln Met Ser Phe  Ala Ser Gln Ser Met  Pro Thr Ile
    1760                 1765                 1770

Pro Ala  Leu Ala Leu Ser Val  Ala Gly Ile Pro Gly  Leu Asp Glu
```

1775 1780 1785

Ala Asn Thr Ser Pro Arg Leu Ser Gln Thr Phe Leu Gln Leu Ser
1790 1795 1800

Asp Gly Asp Lys Lys Thr Leu Thr Arg Lys Lys Val Asn Gln Phe
1805 1810 1815

Phe Lys Thr Met Leu Ala Ser Lys Ser Ala Glu Glu Gly Lys Gln
1820 1825 1830

Ile Pro Asp Ser Leu Ser Thr Asp Leu
1835 1840

<210> 2930
<211> 386
<212> PRT
<213> Homo sapiens

<400> 2930

Met Glu Glu Leu Asp Ala Leu Leu Glu Glu Leu Glu Arg Ser Thr Leu
1 5 10 15

Gln Asp Ser Asp Glu Tyr Ser Asn Pro Ala Pro Leu Pro Leu Asp Gln
20 25 30

His Ser Arg Lys Glu Thr Asn Leu Asp Glu Thr Ser Glu Ile Leu Ser
35 40 45

Ile Gln Asp Asn Thr Ser Pro Leu Pro Ala Gln Leu Val Tyr Thr Thr
50 55 60

Asn Ile Gln Glu Leu Asn Val Tyr Ser Glu Ala Gln Glu Pro Lys Glu
65 70 75 80

Ser Pro Pro Pro Ser Lys Thr Ser Ala Ala Ala Gln Leu Asp Glu Leu
85 90 95

Met Ala His Leu Thr Glu Met Gln Ala Lys Val Ala Val Arg Ala Asp
100 105 110

Ala Gly Lys Lys His Leu Pro Asp Lys Gln Asp His Lys Ala Ser Leu
115 120 125

Asp Ser Met Leu Gly Gly Leu Glu Gln Glu Leu Gln Asp Leu Gly Ile
130 135 140

```
Ala Thr Val Pro Lys Gly His Cys Ala Ser Cys Gln Lys Pro Ile Ala
145                 150                 155                 160

Gly Lys Val Ile His Ala Leu Gly Gln Ser Trp His Pro Glu His Phe
                165                 170                 175

Val Cys Thr His Cys Lys Glu Glu Ile Gly Ser Ser Pro Phe Phe Glu
            180                 185                 190

Arg Ser Gly Leu Ala Tyr Cys Pro Asn Asp Tyr His Gln Leu Phe Ser
        195                 200                 205

Pro Arg Cys Ala Tyr Cys Ala Ala Pro Ile Leu Asp Lys Val Leu Thr
    210                 215                 220

Ala Met Asn Gln Thr Trp His Pro Glu His Phe Phe Cys Ser His Cys
225                 230                 235                 240

Gly Glu Val Phe Gly Ala Glu Gly Phe His Glu Lys Asp Lys Lys Pro
                245                 250                 255

Tyr Cys Arg Lys Asp Phe Leu Ala Met Phe Ser Pro Lys Cys Gly Gly
            260                 265                 270

Cys Asn Arg Pro Val Leu Glu Asn Tyr Leu Ser Ala Met Asp Thr Val
        275                 280                 285

Trp His Pro Glu Cys Phe Val Cys Gly Asp Cys Phe Thr Ser Phe Ser
    290                 295                 300

Thr Gly Ser Phe Phe Glu Leu Asp Gly Arg Pro Phe Cys Glu Leu His
305                 310                 315                 320

Tyr His His Arg Arg Gly Thr Leu Cys His Gly Cys Gly Gln Pro Ile
                325                 330                 335

Thr Gly Arg Cys Ile Ser Ala Met Gly Tyr Lys Phe His Pro Glu His
            340                 345                 350

Phe Val Cys Ala Phe Cys Leu Thr Gln Leu Ser Lys Gly Ile Phe Arg
        355                 360                 365

Glu Gln Asn Asp Lys Thr Tyr Cys Gln Pro Cys Phe Asn Lys Leu Phe
    370                 375                 380
```

Pro Leu
385

<210> 2931
<211> 368
<212> PRT
<213> Homo sapiens

<400> 2931

Met Val Leu Glu Val Ser Asp His Gln Val Leu Asn Asp Ala Glu Val
1 5 10 15

Ala Ala Leu Leu Glu Asn Phe Ser Ser Ser Tyr Asp Tyr Gly Glu Asn
20 25 30

Glu Ser Asp Ser Cys Cys Thr Ser Pro Pro Cys Pro Gln Asp Phe Ser
35 40 45

Leu Asn Phe Asp Arg Ala Phe Leu Pro Ala Leu Tyr Ser Leu Leu Phe
50 55 60

Leu Leu Gly Leu Leu Gly Asn Gly Ala Val Ala Ala Val Leu Leu Ser
65 70 75 80

Arg Arg Thr Ala Leu Ser Ser Thr Asp Thr Phe Leu Leu His Leu Ala
85 90 95

Val Ala Asp Thr Leu Leu Val Leu Thr Leu Pro Leu Trp Ala Val Asp
100 105 110

Ala Ala Val Gln Trp Val Phe Gly Ser Gly Leu Cys Lys Val Ala Gly
115 120 125

Ala Leu Phe Asn Ile Asn Phe Tyr Ala Gly Ala Leu Leu Leu Ala Cys
130 135 140

Ile Ser Phe Asp Arg Tyr Leu Asn Ile Val His Ala Thr Gln Leu Tyr
145 150 155 160

Arg Arg Gly Pro Pro Ala Arg Val Thr Leu Thr Cys Leu Ala Val Trp
165 170 175

Gly Leu Cys Leu Leu Phe Ala Leu Pro Asp Phe Ile Phe Leu Ser Ala
180 185 190

His His Asp Glu Arg Leu Asn Ala Thr His Cys Gln Tyr Asn Phe Pro
195 200 205

```
Gln Val Gly Arg Thr Ala Leu Arg Val Leu Gln Leu Val Ala Gly Phe
    210                 215                 220

Leu Leu Pro Leu Leu Val Met Ala Tyr Cys Tyr Ala His Ile Leu Ala
225                 230                 235                 240

Val Leu Leu Val Ser Arg Gly Gln Arg Arg Leu Arg Ala Met Arg Leu
                245                 250                 255

Val Val Val Val Val Val Ala Phe Ala Leu Cys Trp Thr Pro Tyr His
            260                 265                 270

Leu Val Val Leu Val Asp Ile Leu Met Asp Leu Gly Ala Leu Ala Arg
        275                 280                 285

Asn Cys Gly Arg Glu Ser Arg Val Asp Val Ala Lys Ser Val Thr Ser
    290                 295                 300

Gly Leu Gly Tyr Met His Cys Cys Leu Asn Pro Leu Leu Tyr Ala Phe
305                 310                 315                 320

Val Gly Val Lys Phe Arg Glu Arg Met Trp Met Leu Leu Leu Arg Leu
                325                 330                 335

Gly Cys Pro Asn Gln Arg Gly Leu Gln Arg Gln Pro Ser Ser Ser Arg
            340                 345                 350

Arg Asp Ser Ser Trp Ser Glu Thr Ser Glu Ala Ser Tyr Ser Gly Leu
        355                 360                 365
```

<210> 2932
<211> 359
<212> PRT
<213> Homo sapiens

<400> 2932

```
Met Ala Glu Ala Ile Thr Tyr Ala Asp Leu Arg Phe Val Lys Ala Pro
1               5                   10                  15

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

Asp Asp Gly Glu Ile Thr Tyr Glu Asn Val Gln Val Pro Ala Val Leu
        35                  40                  45
```

```
Gly Val Pro Ser Ser Leu Ala Ser Ser Val Leu Gly Asp Lys Ala Ala
    50                  55                  60

Val Lys Ser Glu Gln Pro Thr Ala Ser Trp Arg Ala Val Thr Ser Pro
65                  70                  75                  80

Ala Val Gly Arg Ile Leu Pro Cys Arg Thr Thr Cys Leu Arg Tyr Leu
                85                  90                  95

Leu Leu Gly Leu Leu Leu Thr Cys Leu Leu Leu Gly Val Thr Ala Ile
            100                 105                 110

Cys Leu Gly Val Arg Tyr Leu Gln Val Ser Gln Gln Leu Gln Gln Thr
        115                 120                 125

Asn Arg Val Leu Glu Val Thr Asn Ser Ser Leu Arg Gln Gln Leu Arg
    130                 135                 140

Leu Lys Ile Thr Gln Leu Gly Gln Ser Ala Glu Asp Leu Gln Gly Ser
145                 150                 155                 160

Arg Arg Glu Leu Ala Gln Ser Gln Glu Ala Leu Gln Val Glu Gln Arg
                165                 170                 175

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

Gln Lys Thr Lys Glu Thr Leu Gln Ser Glu Glu Gln Gln Arg Arg Ala
        195                 200                 205

Leu Glu Gln Lys Leu Ser Asn Met Glu Asn Arg Leu Lys Pro Phe Phe
    210                 215                 220

Thr Cys Gly Ser Ala Asp Thr Cys Cys Pro Ser Gly Trp Ile Met His
225                 230                 235                 240

Gln Lys Ser Cys Phe Tyr Ile Ser Leu Thr Ser Lys Asn Trp Gln Glu
                245                 250                 255

Ser Gln Lys Gln Cys Glu Thr Leu Ser Ser Lys Leu Ala Thr Phe Ser
            260                 265                 270

Glu Ile Tyr Pro Gln Ser His Ser Tyr Tyr Phe Leu Asn Ser Leu Leu
        275                 280                 285

Pro Asn Gly Gly Ser Gly Asn Ser Tyr Trp Thr Gly Leu Ser Ser Asn
```

290 295 300

Lys Asp Trp Lys Leu Thr Asp Asp Thr Gln Arg Thr Arg Thr Tyr Ala
305 310 315 320

Gln Ser Ser Lys Cys Asn Lys Val His Lys Thr Trp Ser Trp Trp Thr
325 330 335

Leu Glu Ser Glu Ser Cys Arg Ser Ser Leu Pro Tyr Ile Cys Glu Met
340 345 350

Thr Ala Phe Arg Phe Pro Asp
355

<210> 2933
<211> 266
<212> PRT
<213> Homo sapiens

<400> 2933

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

Asn Tyr Ser His Thr Ala Asn Ile Leu Pro Asp Ile Glu Asn Glu Asp
20 25 30

Phe Ile Lys Asp Cys Val Arg Ile His Asn Lys Phe Arg Ser Glu Val
35 40 45

Lys Pro Thr Ala Ser Asp Met Leu Tyr Met Thr Trp Asp Pro Ala Leu
50 55 60

Ala Gln Ile Ala Lys Ala Trp Ala Ser Asn Cys Gln Phe Ser His Asn
65 70 75 80

Thr Arg Leu Lys Pro Pro His Lys Leu His Pro Asn Phe Thr Ser Leu
85 90 95

Gly Glu Asn Ile Trp Thr Gly Ser Val Pro Ile Phe Ser Val Ser Ser
100 105 110

Ala Ile Thr Asn Trp Tyr Asp Glu Ile Gln Asp Tyr Asp Phe Lys Thr
115 120 125

Arg Ile Cys Lys Lys Val Cys Gly His Tyr Thr Gln Val Val Trp Ala
130 135 140

```
Asp Ser Tyr Lys Val Gly Cys Ala Val Gln Phe Cys Pro Lys Val Ser
145                 150                 155                 160

Gly Phe Asp Ala Leu Ser Asn Gly Ala His Phe Ile Cys Asn Tyr Gly
                165                 170                 175

Pro Gly Gly Asn Tyr Pro Thr Trp Pro Tyr Lys Arg Gly Ala Thr Cys
            180                 185                 190

Ser Ala Cys Pro Asn Asn Asp Lys Cys Leu Asp Asn Leu Cys Val Asn
        195                 200                 205

Arg Gln Arg Asp Gln Val Lys Arg Tyr Tyr Ser Val Val Tyr Pro Gly
    210                 215                 220

Trp Pro Ile Tyr Pro Arg Asn Arg Tyr Thr Ser Leu Phe Leu Ile Val
225                 230                 235                 240

Asn Ser Val Ile Leu Ile Leu Ser Val Ile Ile Thr Ile Leu Val Gln
                245                 250                 255

Leu Lys Tyr Pro Asn Leu Val Leu Leu Asp
            260                 265
```

<210> 2934
<211> 1429
<212> PRT
<213> Homo sapiens

<400> 2934

```
Met Ala Gly Gly Ala Trp Gly Arg Leu Ala Cys Tyr Leu Glu Phe Leu
1               5                   10                  15

Lys Lys Glu Glu Leu Lys Glu Phe Gln Leu Leu Leu Ala Asn Lys Ala
            20                  25                  30

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

Ser Gly Met Glu Val Ala Ser Tyr Leu Val Ala Gln Tyr Gly Glu Gln
    50                  55                  60

Arg Ala Trp Asp Leu Ala Leu His Thr Trp Glu Gln Met Gly Leu Arg
65                  70                  75                  80

Ser Leu Cys Ala Gln Ala Gln Glu Gly Ala Gly His Ser Pro Ser Phe
```

```
                85                  90                  95

Pro Tyr Ser Pro Ser Glu Pro His Leu Gly Ser Pro Ser Gln Pro Thr
            100                 105                 110

Ser Thr Ala Val Leu Met Pro Trp Ile His Glu Leu Pro Ala Gly Cys
        115                 120                 125

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

Gly Arg Arg Trp Arg Glu Ile Ser Ala Ser Leu Leu Tyr Gln Ala Leu
145                 150                 155                 160

Pro Ser Ser Pro Asp His Glu Ser Pro Ser Gln Glu Ser Pro Asn Ala
                165                 170                 175

Pro Thr Ser Thr Ala Val Leu Gly Ser Trp Gly Ser Pro Pro Gln Pro
            180                 185                 190

Ser Leu Ala Pro Arg Glu Gln Glu Ala Pro Gly Thr Gln Trp Pro Leu
        195                 200                 205

Asp Glu Thr Ser Gly Ile Tyr Tyr Thr Glu Ile Arg Glu Arg Glu Arg
    210                 215                 220

Glu Lys Ser Glu Lys Gly Arg Pro Pro Trp Ala Ala Val Val Gly Thr
225                 230                 235                 240

Pro Pro Gln Ala His Thr Ser Leu Gln Pro His His His Pro Trp Glu
                245                 250                 255

Pro Ser Val Arg Glu Ser Leu Cys Ser Thr Trp Pro Trp Lys Asn Glu
            260                 265                 270

Asp Phe Asn Gln Lys Phe Thr Gln Leu Leu Leu Leu Gln Arg Pro His
        275                 280                 285

Pro Arg Ser Gln Asp Pro Leu Val Lys Arg Ser Trp Pro Asp Tyr Val
    290                 295                 300

Glu Glu Asn Arg Gly His Leu Ile Glu Ile Arg Asp Leu Phe Gly Pro
305                 310                 315                 320

Gly Leu Asp Thr Gln Glu Pro Arg Ile Val Ile Leu Gln Gly Ala Ala
                325                 330                 335
```

```
Gly Ile Gly Lys Ser Thr Leu Ala Arg Gln Val Lys Glu Ala Trp Gly
            340                 345                 350

Arg Gly Gln Leu Tyr Gly Asp Arg Phe Gln His Val Phe Tyr Phe Ser
        355                 360                 365

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

Gly Lys Asp Gly Thr Ala Thr Pro Ala Pro Ile Arg Gln Ile Leu Ser
385                 390                 395                 400

Arg Pro Glu Arg Leu Leu Phe Ile Leu Asp Gly Val Asp Glu Pro Gly
                405                 410                 415

Trp Val Leu Gln Glu Pro Ser Ser Glu Leu Cys Leu His Trp Ser Gln
            420                 425                 430

Pro Gln Pro Ala Asp Ala Leu Leu Gly Ser Leu Leu Gly Lys Thr Ile
        435                 440                 445

Leu Pro Glu Ala Ser Phe Leu Ile Thr Ala Arg Thr Thr Ala Leu Gln
    450                 455                 460

Asn Leu Ile Pro Ser Leu Glu Gln Ala Arg Trp Val Glu Val Leu Gly
465                 470                 475                 480

Phe Ser Glu Ser Ser Arg Lys Glu Tyr Phe Tyr Arg Tyr Phe Thr Asp
                485                 490                 495

Glu Arg Gln Ala Ile Arg Ala Phe Arg Leu Val Lys Ser Asn Lys Glu
            500                 505                 510

Leu Trp Ala Leu Cys Leu Val Pro Trp Val Ser Trp Leu Ala Cys Thr
        515                 520                 525

Cys Leu Met Gln Gln Met Lys Arg Lys Glu Lys Leu Thr Leu Thr Ser
    530                 535                 540

Lys Thr Thr Thr Thr Leu Cys Leu His Tyr Leu Ala Gln Ala Leu Gln
545                 550                 555                 560

Ala Gln Pro Leu Gly Pro Gln Leu Arg Asp Leu Cys Ser Leu Ala Ala
                565                 570                 575
```

```
Glu Gly Ile Trp Gln Lys Lys Thr Leu Phe Ser Pro Asp Asp Leu Arg
            580                 585                 590

Lys His Gly Leu Asp Gly Ala Ile Ile Ser Thr Phe Leu Lys Met Gly
        595                 600                 605

Ile Leu Gln Glu His Pro Ile Pro Leu Ser Tyr Ser Phe Ile His Leu
    610                 615                 620

Cys Phe Gln Glu Phe Phe Ala Ala Met Ser Tyr Val Leu Glu Asp Glu
625                 630                 635                 640

Lys Gly Arg Gly Lys His Ser Asn Cys Ile Ile Asp Leu Glu Lys Thr
                645                 650                 655

Leu Glu Ala Tyr Gly Ile His Gly Leu Phe Gly Ala Ser Thr Thr Arg
            660                 665                 670

Phe Leu Leu Gly Leu Leu Ser Asp Glu Gly Glu Arg Glu Met Glu Asn
        675                 680                 685

Ile Phe His Cys Arg Leu Ser Gln Gly Arg Asn Leu Met Gln Trp Val
    690                 695                 700

Pro Ser Leu Gln Leu Leu Leu Gln Pro His Ser Leu Glu Ser Leu His
705                 710                 715                 720

Cys Leu Tyr Glu Thr Arg Asn Lys Thr Phe Leu Thr Gln Val Met Ala
                725                 730                 735

His Phe Glu Glu Met Gly Met Cys Val Glu Thr Asp Met Glu Leu Leu
            740                 745                 750

Val Cys Thr Phe Cys Ile Lys Phe Ser Arg His Val Lys Lys Leu Gln
        755                 760                 765

Leu Ile Glu Gly Arg Gln His Arg Ser Thr Trp Ser Pro Thr Met Val
    770                 775                 780

Val Leu Phe Arg Trp Val Pro Val Thr Asp Ala Tyr Trp Gln Ile Leu
785                 790                 795                 800

Phe Ser Val Leu Lys Val Thr Arg Asn Leu Lys Glu Leu Asp Leu Ser
                805                 810                 815
```

```
Gly Asn Ser Leu Ser His Ser Ala Val Lys Ser Leu Cys Lys Thr Leu
            820                 825                 830

Arg Arg Pro Arg Cys Leu Leu Glu Thr Leu Arg Leu Ala Gly Cys Gly
        835                 840                 845

Leu Thr Ala Glu Asp Cys Lys Asp Leu Ala Phe Gly Leu Arg Ala Asn
    850                 855                 860

Gln Thr Leu Thr Glu Leu Asp Leu Ser Phe Asn Val Leu Thr Asp Ala
865                 870                 875                 880

Gly Ala Lys His Leu Cys Gln Arg Leu Arg Gln Pro Ser Cys Lys Leu
                885                 890                 895

Gln Arg Leu Gln Leu Val Ser Cys Gly Leu Thr Ser Asp Cys Cys Gln
            900                 905                 910

Asp Leu Ala Ser Val Leu Ser Ala Ser Pro Ser Leu Lys Glu Leu Asp
        915                 920                 925

Leu Gln Gln Asn Asn Leu Asp Asp Val Gly Val Arg Leu Leu Cys Glu
    930                 935                 940

Gly Leu Arg His Pro Ala Cys Lys Leu Ile Arg Leu Gly Leu Asp Gln
945                 950                 955                 960

Thr Thr Leu Ser Asp Glu Met Arg Gln Glu Leu Arg Ala Leu Glu Gln
                965                 970                 975

Glu Lys Pro Gln Leu Leu Ile Phe Ser Arg Arg Lys Pro Ser Val Met
            980                 985                 990

Thr Pro Thr Glu Gly Leu Asp Thr  Gly Glu Met Ser Asn  Ser Thr Ser
        995                 1000                1005

Ser Leu  Lys Arg Gln Arg Leu  Gly Ser Glu Arg Ala  Ala Ser His
    1010                1015                1020

Val Ala  Gln Ala Asn Leu Lys  Leu Leu Asp Val Ser  Lys Ile Phe
    1025                1030                1035

Pro Ile  Ala Glu Ile Ala Glu  Glu Ser Ser Pro Glu  Val Val Pro
    1040                1045                1050

Val Glu  Leu Leu Cys Val Pro  Ser Pro Ala Ser Gln  Gly Asp Leu
```

1055 1060 1065

His Thr Lys Pro Leu Gly Thr Asp Asp Asp Phe Trp Gly Pro Thr
1070 1075 1080

Gly Pro Val Ala Thr Glu Val Val Asp Lys Glu Lys Asn Leu Tyr
1085 1090 1095

Arg Val His Phe Pro Val Ala Gly Ser Tyr Arg Trp Pro Asn Thr
1100 1105 1110

Gly Leu Cys Phe Val Met Arg Glu Ala Val Thr Val Glu Ile Glu
1115 1120 1125

Phe Cys Val Trp Asp Gln Phe Leu Gly Glu Ile Asn Pro Gln His
1130 1135 1140

Ser Trp Met Val Ala Gly Pro Leu Leu Asp Ile Lys Ala Glu Pro
1145 1150 1155

Gly Ala Val Glu Ala Val His Leu Pro His Phe Val Ala Leu Gln
1160 1165 1170

Gly Gly His Val Asp Thr Ser Leu Phe Gln Met Ala His Phe Lys
1175 1180 1185

Glu Glu Gly Met Leu Leu Glu Lys Pro Ala Arg Val Glu Leu His
1190 1195 1200

His Ile Val Leu Glu Asn Pro Ser Phe Ser Pro Leu Gly Val Leu
1205 1210 1215

Leu Lys Met Ile His Asn Ala Leu Arg Phe Ile Pro Val Thr Ser
1220 1225 1230

Val Val Leu Leu Tyr His Arg Val His Pro Glu Glu Val Thr Phe
1235 1240 1245

His Leu Tyr Leu Ile Pro Ser Asp Cys Ser Ile Arg Lys Glu Leu
1250 1255 1260

Glu Leu Cys Tyr Arg Ser Pro Gly Glu Asp Gln Leu Phe Ser Glu
1265 1270 1275

Phe Tyr Val Gly His Leu Gly Ser Gly Ile Arg Leu Gln Val Lys
1280 1285 1290

```
Asp Lys  Lys Asp Glu Thr Leu  Val Trp Glu Ala Leu  Val Lys Pro
    1295                 1300                 1305

Gly Asp  Leu Met Pro Ala Thr  Thr Leu Ile Pro Pro  Ala Arg Ile
    1310                 1315                 1320

Ala Val  Pro Ser Pro Leu Asp  Ala Pro Gln Leu Leu  His Phe Val
    1325                 1330                 1335

Asp Gln  Tyr Arg Glu Gln Leu  Ile Ala Arg Val Thr  Ser Val Glu
    1340                 1345                 1350

Val Val  Leu Asp Lys Leu His  Gly Gln Val Leu Ser  Gln Glu Gln
    1355                 1360                 1365

Tyr Glu  Arg Val Leu Ala Glu  Asn Thr Arg Pro Ser  Gln Met Arg
    1370                 1375                 1380

Lys Leu  Phe Ser Leu Ser Gln  Ser Trp Asp Arg Lys  Cys Lys Asp
    1385                 1390                 1395

Gly Leu  Tyr Gln Ala Leu Lys  Glu Thr His Pro His  Leu Ile Met
    1400                 1405                 1410

Glu Leu  Trp Glu Lys Gly Ser  Lys Lys Gly Leu Leu  Pro Leu Ser
    1415                 1420                 1425

Ser
```

<210> 2935
<211> 352
<212> PRT
<213> Homo sapiens

<400> 2935

```
Met Glu Gly Ile Ser Ile Tyr Thr Ser Asp Asn Tyr Thr Glu Glu Met
1               5                  10                  15

Gly Ser Gly Asp Tyr Asp Ser Met Lys Glu Pro Cys Phe Arg Glu Glu
            20                  25                  30

Asn Ala Asn Phe Asn Lys Ile Phe Leu Pro Thr Ile Tyr Ser Ile Ile
        35                  40                  45
```

```
Phe Leu Thr Gly Ile Val Gly Asn Gly Leu Val Ile Leu Val Met Gly
    50                  55                  60

Tyr Gln Lys Lys Leu Arg Ser Met Thr Asp Lys Tyr Arg Leu His Leu
65                  70                  75                  80

Ser Val Ala Asp Leu Leu Phe Val Ile Thr Leu Pro Phe Trp Ala Val
                85                  90                  95

Asp Ala Val Ala Asn Trp Tyr Phe Gly Asn Phe Leu Cys Lys Ala Val
            100                 105                 110

His Val Ile Tyr Thr Val Asn Leu Tyr Ser Ser Val Leu Ile Leu Ala
        115                 120                 125

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

Gln Arg Pro Arg Lys Leu Leu Ala Glu Lys Val Val Tyr Val Gly Val
145                 150                 155                 160

Trp Ile Pro Ala Leu Leu Leu Thr Ile Pro Asp Phe Ile Phe Ala Asn
                165                 170                 175

Val Ser Glu Ala Asp Asp Arg Tyr Ile Cys Asp Arg Phe Tyr Pro Asn
            180                 185                 190

Asp Leu Trp Val Val Val Phe Gln Phe Gln His Ile Met Val Gly Leu
        195                 200                 205

Ile Leu Pro Gly Ile Val Ile Leu Ser Cys Tyr Cys Ile Ile Ile Ser
    210                 215                 220

Lys Leu Ser His Ser Lys Gly His Gln Lys Arg Lys Ala Leu Lys Thr
225                 230                 235                 240

Thr Val Ile Leu Ile Leu Ala Phe Phe Ala Cys Trp Leu Pro Tyr Tyr
                245                 250                 255

Ile Gly Ile Ser Ile Asp Ser Phe Ile Leu Leu Glu Ile Ile Lys Gln
            260                 265                 270

Gly Cys Glu Phe Glu Asn Thr Val His Lys Trp Ile Ser Ile Thr Glu
        275                 280                 285

Ala Leu Ala Phe Phe His Cys Cys Leu Asn Pro Ile Leu Tyr Ala Phe
```

290 295 300

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

Ser Arg Gly Ser Ser Leu Lys Ile Leu Ser Lys Gly Lys Arg Gly Gly
325 330 335

His Ser Ser Val Ser Thr Glu Ser Glu Ser Ser Ser Phe His Ser Ser
340 345 350

<210> 2936
<211> 248
<212> PRT
<213> Homo sapiens

<400> 2936

Met Leu Ser Thr Val Gly Ser Phe Leu Gln Asp Leu Gln Asn Glu Asp
1 5 10 15

Lys Gly Ile Lys Thr Ala Ala Ile Phe Thr Ala Asp Gly Asn Met Ile
20 25 30

Ser Ala Ser Thr Leu Met Asp Ile Leu Leu Met Asn Asp Phe Lys Leu
35 40 45

Val Ile Asn Lys Ile Ala Tyr Asp Val Gln Cys Pro Lys Arg Glu Lys
50 55 60

Pro Ser Asn Glu His Thr Ala Glu Met Glu His Met Lys Ser Leu Val
65 70 75 80

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

Glu His His Leu Leu Glu Lys Ile Asp His Leu Lys Glu Gln Leu Gln
100 105 110

Pro Leu Glu Gln Val Lys Ala Gly Ile Glu Ala His Ser Glu Ala Lys
115 120 125

Thr Ser Gly Leu Leu Trp Ala Gly Leu Ala Leu Leu Ser Ile Gln Gly
130 135 140

Gly Ala Leu Ala Trp Leu Thr Trp Trp Val Tyr Ser Trp Asp Ile Met
145 150 155 160

```
Glu Pro Val Thr Tyr Phe Ile Thr Phe Ala Asn Ser Met Val Phe Phe
                165                 170                 175

Ala Tyr Phe Ile Val Thr Arg Gln Asp Tyr Thr Tyr Ser Ala Val Lys
            180                 185                 190

Ser Arg Gln Phe Leu Gln Phe Phe His Lys Lys Ser Lys Gln Gln His
        195                 200                 205

Phe Asp Val Gln Gln Tyr Asn Lys Leu Lys Glu Asp Leu Ala Lys Ala
    210                 215                 220

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

Val Glu Glu Leu Asn Glu Lys Asn
                245
```

<210> 2937
<211> 790
<212> PRT
<213> Homo sapiens

<400> 2937

```
Met Ala Glu Gln Val Leu Pro Gln Ala Leu Tyr Leu Ser Asn Met Arg
1               5                   10                  15

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

Thr Asn Gly Ile Ile His His Phe Lys Thr Met His Arg Tyr Thr Leu
        35                  40                  45

Glu Met Phe Arg Thr Cys Gln Phe Cys Pro Gln Phe Arg Glu Ile Ile
    50                  55                  60

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

Lys Lys Leu Asn Trp Cys Arg Glu Val Arg Lys Leu Val Ala Leu Lys
                85                  90                  95

Thr Asn Gly Asp Gly Asn Cys Leu Met His Ala Thr Ser Gln Tyr Met
            100                 105                 110

Trp Gly Val Gln Asp Thr Asp Leu Val Leu Arg Lys Ala Leu Phe Ser
```

```
        115                 120                 125

Thr Leu Lys Glu Thr Asp Thr Arg Asn Phe Lys Phe Arg Trp Gln Leu
    130                 135                 140

Glu Ser Leu Lys Ser Gln Glu Phe Val Glu Thr Gly Leu Cys Tyr Asp
145                 150                 155                 160

Thr Arg Asn Trp Asn Asp Glu Trp Asp Asn Leu Ile Lys Met Ala Ser
                165                 170                 175

Thr Asp Thr Pro Met Ala Arg Ser Gly Leu Gln Tyr Asn Ser Leu Glu
            180                 185                 190

Glu Ile His Ile Phe Val Leu Cys Asn Ile Leu Arg Arg Pro Ile Ile
        195                 200                 205

Val Ile Ser Asp Lys Met Leu Arg Ser Leu Glu Ser Gly Ser Asn Phe
    210                 215                 220

Ala Pro Leu Lys Val Gly Gly Ile Tyr Leu Pro Leu His Trp Pro Ala
225                 230                 235                 240

Gln Glu Cys Tyr Arg Tyr Pro Ile Val Leu Gly Tyr Asp Ser His His
                245                 250                 255

Phe Val Pro Leu Val Thr Leu Lys Asp Ser Gly Pro Glu Ile Arg Ala
            260                 265                 270

Val Pro Leu Val Asn Arg Asp Arg Gly Arg Phe Glu Asp Leu Lys Val
        275                 280                 285

His Phe Leu Thr Asp Pro Glu Asn Glu Met Lys Glu Lys Leu Leu Lys
    290                 295                 300

Glu Tyr Leu Met Val Ile Glu Ile Pro Val Gln Gly Trp Asp His Gly
305                 310                 315                 320

Thr Thr His Leu Ile Asn Ala Ala Lys Leu Asp Glu Ala Asn Leu Pro
                325                 330                 335

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

Tyr Lys Lys Trp Gln Glu Asn Ser Glu Gln Gly Arg Arg Glu Gly His
        355                 360                 365
```

```
Ala Gln Asn Pro Met Glu Pro Ser Val Pro Gln Leu Ser Leu Met Asp
    370                 375                 380

Val Lys Cys Glu Thr Pro Asn Cys Pro Phe Phe Met Ser Val Asn Thr
385                 390                 395                 400

Gln Pro Leu Cys His Glu Cys Ser Glu Arg Arg Gln Lys Asn Gln Asn
                405                 410                 415

Lys Leu Pro Lys Leu Asn Ser Lys Pro Gly Pro Glu Gly Leu Pro Gly
            420                 425                 430

Met Ala Leu Gly Ala Ser Arg Gly Glu Ala Tyr Glu Pro Leu Ala Trp
        435                 440                 445

Asn Pro Glu Glu Ser Thr Gly Gly Pro His Ser Ala Pro Pro Thr Ala
    450                 455                 460

Pro Ser Pro Phe Leu Phe Ser Glu Thr Thr Ala Met Lys Cys Arg Ser
465                 470                 475                 480

Pro Gly Cys Pro Phe Thr Leu Asn Val Gln His Asn Gly Phe Cys Glu
                485                 490                 495

Arg Cys His Asn Ala Arg Gln Leu His Ala Ser His Ala Pro Asp His
            500                 505                 510

Thr Arg His Leu Asp Pro Gly Lys Cys Gln Ala Cys Leu Gln Asp Val
        515                 520                 525

Thr Arg Thr Phe Asn Gly Ile Cys Ser Thr Cys Phe Lys Arg Thr Thr
    530                 535                 540

Ala Glu Ala Ser Ser Ser Leu Ser Thr Ser Leu Pro Pro Ser Cys His
545                 550                 555                 560

Gln Arg Ser Lys Ser Asp Pro Ser Arg Leu Val Arg Ser Pro Ser Pro
                565                 570                 575

His Ser Cys His Arg Ala Gly Asn Asp Ala Pro Ala Gly Cys Leu Ser
            580                 585                 590

Gln Ala Ala Arg Thr Pro Gly Asp Arg Thr Gly Thr Ser Lys Cys Arg
        595                 600                 605
```

```
Lys Ala Gly Cys Val Tyr Phe Gly Thr Pro Glu Asn Lys Gly Phe Cys
    610                 615                 620

Thr Leu Cys Phe Ile Glu Tyr Arg Glu Asn Lys His Phe Ala Ala Ala
625                 630                 635                 640

Ser Gly Lys Val Ser Pro Thr Ala Ser Arg Phe Gln Asn Thr Ile Pro
                645                 650                 655

Cys Leu Gly Arg Glu Cys Gly Thr Leu Gly Ser Thr Met Phe Glu Gly
            660                 665                 670

Tyr Cys Gln Lys Cys Phe Ile Glu Ala Gln Asn Gln Arg Phe His Glu
        675                 680                 685

Ala Lys Arg Thr Glu Glu Gln Leu Arg Ser Ser Gln Arg Arg Asp Val
    690                 695                 700

Pro Arg Thr Thr Gln Ser Thr Ser Arg Pro Lys Cys Ala Arg Ala Ser
705                 710                 715                 720

Cys Lys Asn Ile Leu Ala Cys Arg Ser Glu Glu Leu Cys Met Glu Cys
                725                 730                 735

Gln His Pro Asn Gln Arg Met Gly Pro Gly Ala His Arg Gly Glu Pro
            740                 745                 750

Ala Pro Glu Asp Pro Pro Lys Gln Arg Cys Arg Ala Pro Ala Cys Asp
        755                 760                 765

His Phe Gly Asn Ala Lys Cys Asn Gly Tyr Cys Asn Glu Cys Phe Gln
    770                 775                 780

Phe Lys Gln Met Tyr Gly
785                 790


<210>  2938
<211>  206
<212>  PRT
<213>  Homo sapiens

<400>  2938

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

Gly Ala Leu Gly Ser Gly Gly Ser Ala Glu Asp Ser Val Gly Ser Ser
```

```
            20                  25                  30

Ser Val Thr Val Val Leu Leu Leu Leu Leu Leu Leu Ala Thr
        35                  40                  45

Gly Leu Ala Leu Ala Trp Arg Arg Leu Ser Arg Asp Ser Gly Gly Tyr
    50                  55                  60

Tyr His Pro Ala Arg Leu Gly Ala Ala Leu Trp Gly Arg Thr Arg Arg
65                  70                  75                  80

Leu Leu Trp Ala Ser Pro Pro Gly Arg Trp Leu Gln Ala Arg Ala Glu
                85                  90                  95

Leu Gly Ser Thr Asp Asn Asp Leu Glu Arg Gln Glu Asp Glu Gln Asp
            100                 105                 110

Thr Asp Tyr Asp His Val Ala Asp Gly Gly Leu Gln Ala Asp Pro Gly
        115                 120                 125

Glu Gly Glu Gln Gln Cys Gly Glu Ala Ser Ser Pro Glu Gln Val Pro
    130                 135                 140

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

Leu Gly Ser Pro Gly Pro Ala Ser Ala Gly Gly Ser Ala Glu Ala Leu
                165                 170                 175

Leu Ser Asp Leu His Ala Phe Ala Gly Ser Ala Ala Trp Asp Asp Ser
            180                 185                 190

Ala Arg Ala Ala Gly Gly Gln Gly Leu His Val Thr Ala Leu
        195                 200                 205


<210>  2939
<211>  718
<212>  PRT
<213>  Homo sapiens

<400>  2939

Met Ile Val Asp Lys Leu Leu Asp Asp Ser Arg Gly Gly Glu Gly Leu
1               5                   10                  15

Arg Asp Ala Ala Gly Gly Cys Gly Leu Met Thr Ser Pro Leu Asn Leu
            20                  25                  30
```

Ser Tyr Phe Tyr Gly Ala Ser Pro Pro Ala Ala Ala Pro Gly Ala Cys
35 40 45

Asp Ala Ser Cys Ser Val Leu Gly Pro Ser Ala Pro Gly Ser Pro Gly
50 55 60

Ser Asp Ser Ser Asp Phe Ser Ser Ala Ser Ser Val Ser Ser Cys Gly
65 70 75 80

Ala Val Glu Ser Arg Ser Arg Gly Gly Ala Arg Ala Glu Arg Gln Pro
85 90 95

Val Glu Pro His Met Gly Val Gly Arg Gln Gln Arg Gly Pro Phe Gln
100 105 110

Gly Val Arg Val Lys Asn Ser Val Lys Glu Leu Leu Leu His Ile Arg
115 120 125

Ser His Lys Gln Lys Ala Ser Gly Gln Ala Val Asp Asp Phe Lys Thr
130 135 140

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

Tyr Ser Gly Lys Arg Lys Gly Pro Asp Ser Leu Ser Asp Gly Pro Ala
165 170 175

Cys Lys Arg Pro Ala Leu Leu His Ser Gln Phe Leu Thr Pro Pro Gln
180 185 190

Thr Pro Thr Pro Gly Glu Ser Met Glu Asp Val His Leu Asn Glu Pro
195 200 205

Lys Gln Glu Ser Ser Ala Asp Leu Leu Gln Asn Ile Ile Asn Ile Lys
210 215 220

Asn Glu Cys Ser Pro Val Ser Leu Asn Thr Val Gln Val Ser Trp Leu
225 230 235 240

Asn Pro Val Val Val Pro Gln Ser Ser Pro Ala Glu Gln Cys Gln Asp
245 250 255

Phe His Gly Gly Gln Val Phe Ser Pro Pro Gln Lys Cys Gln Pro Phe
260 265 270

```
Gln Val Arg Gly Ser Gln Gln Met Ile Asp Gln Ala Ser Leu Tyr Gln
        275                 280                 285

Tyr Ser Pro Gln Asn Gln His Val Glu Gln Gln Pro His Tyr Thr His
    290                 295                 300

Lys Pro Thr Leu Glu Tyr Ser Pro Phe Pro Ile Pro Pro Gln Ser Pro
305                 310                 315                 320

Ala Tyr Glu Pro Asn Leu Phe Asp Gly Pro Glu Ser Gln Phe Cys Pro
                325                 330                 335

Asn Gln Ser Leu Val Ser Leu Leu Gly Asp Gln Arg Glu Ser Glu Asn
            340                 345                 350

Ile Ala Asn Pro Met Gln Thr Ser Ser Ser Val Gln Gln Gln Asn Asp
        355                 360                 365

Ala His Leu His Ser Phe Ser Met Met Pro Ser Ser Ala Cys Glu Ala
    370                 375                 380

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

Phe Ser Asn Met Gly Asn Pro Met Asn Thr Thr Gln Leu Gly Lys Ser
                405                 410                 415

Leu Phe Gln Trp Gln Val Glu Gln Glu Glu Ser Lys Leu Ala Asn Ile
            420                 425                 430

Ser Gln Asp Gln Phe Leu Ser Lys Asp Ala Asp Gly Asp Thr Phe Leu
        435                 440                 445

His Ile Ala Val Ala Gln Gly Arg Arg Ala Leu Ser Tyr Val Leu Ala
    450                 455                 460

Arg Lys Met Asn Ala Leu His Met Leu Asp Ile Lys Glu His Asn Gly
465                 470                 475                 480

Gln Ser Ala Phe Gln Val Ala Val Ala Ala Asn Gln His Leu Ile Val
                485                 490                 495

Gln Asp Leu Val Asn Ile Gly Ala Gln Val Asn Thr Thr Asp Cys Trp
            500                 505                 510

Gly Arg Thr Pro Leu His Val Cys Ala Glu Lys Gly His Ser Gln Val
```

515 520 525

Leu Gln Ala Ile Gln Lys Gly Ala Val Gly Ser Asn Gln Phe Val Asp
530 535 540

Leu Glu Ala Thr Asn Tyr Asp Gly Leu Thr Pro Leu His Cys Ala Val
545 550 555 560

Ile Ala His Asn Ala Val Val His Glu Leu Gln Arg Asn Gln Gln Pro
565 570 575

His Ser Pro Glu Val Gln Glu Leu Leu Leu Lys Asn Lys Ser Leu Val
580 585 590

Asp Thr Ile Lys Cys Leu Ile Gln Met Gly Ala Ala Val Glu Ala Lys
595 600 605

Asp Arg Lys Ser Gly Arg Thr Ala Leu His Leu Ala Ala Glu Glu Ala
610 615 620

Asn Leu Glu Leu Ile Arg Leu Phe Leu Glu Leu Pro Ser Cys Leu Ser
625 630 635 640

Phe Val Asn Ala Lys Ala Tyr Asn Gly Asn Thr Ala Leu His Val Ala
645 650 655

Ala Ser Leu Gln Tyr Arg Leu Thr Gln Leu Asp Ala Val Arg Leu Leu
660 665 670

Met Arg Lys Gly Ala Asp Pro Ser Thr Arg Asn Leu Glu Asn Glu Gln
675 680 685

Pro Val His Leu Val Pro Asp Gly Pro Val Gly Glu Gln Ile Arg Arg
690 695 700

Ile Leu Lys Gly Lys Ser Ile Gln Gln Arg Ala Pro Pro Tyr
705 710 715

<210> 2940
<211> 247
<212> PRT
<213> Homo sapiens

<400> 2940

Met Gln Pro Ile Leu Leu Leu Leu Ala Phe Leu Leu Leu Pro Arg Ala
1 5 10 15

```
Asp Ala Gly Glu Ile Ile Gly Gly His Glu Ala Lys Pro His Ser Arg
            20                  25                  30

Pro Tyr Met Ala Tyr Leu Met Ile Trp Asp Gln Lys Ser Leu Lys Arg
        35                  40                  45

Cys Gly Gly Phe Leu Ile Gln Asp Asp Phe Val Leu Thr Ala Ala His
    50                  55                  60

Cys Trp Gly Ser Ser Ile Asn Val Thr Leu Gly Ala His Asn Ile Lys
65                  70                  75                  80

Glu Gln Glu Pro Thr Gln Gln Phe Ile Pro Val Lys Arg Pro Ile Pro
                85                  90                  95

His Pro Ala Tyr Asn Pro Lys Asn Phe Ser Asn Asp Ile Met Leu Leu
            100                 105                 110

Gln Leu Glu Arg Lys Ala Lys Arg Thr Arg Ala Val Gln Pro Leu Arg
        115                 120                 125

Leu Pro Ser Asn Lys Ala Gln Val Lys Pro Gly Gln Thr Cys Ser Val
    130                 135                 140

Ala Gly Trp Gly Gln Thr Ala Pro Leu Gly Lys His Ser His Thr Leu
145                 150                 155                 160

Gln Glu Val Lys Met Thr Val Gln Glu Asp Arg Lys Cys Glu Ser Asp
                165                 170                 175

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

Glu Ile Lys Lys Thr Ser Phe Lys Gly Asp Ser Gly Gly Pro Leu Val
        195                 200                 205

Cys Asn Lys Val Ala Gln Gly Ile Val Ser Tyr Gly Arg Asn Asn Gly
    210                 215                 220

Met Pro Pro Arg Ala Cys Thr Lys Val Ser Ser Phe Val His Trp Ile
225                 230                 235                 240

Lys Lys Thr Met Lys Arg Tyr
                245
```

<210> 2941
<211> 191
<212> PRT
<213> Homo sapiens

<400> 2941

```
Met His Asp Ser Asn Asn Val Glu Lys Asp Ile Thr Pro Ser Glu Leu
1               5                  10                  15

Pro Ala Asn Pro Gly Cys Leu His Ser Lys Glu His Ser Ile Lys Ala
            20                  25                  30

Thr Leu Ile Trp Arg Leu Phe Phe Leu Ile Met Phe Leu Thr Ile Ile
        35                  40                  45

Val Cys Gly Met Val Ala Ala Leu Ser Ala Ile Arg Ala Asn Cys His
    50                  55                  60

Gln Glu Pro Ser Val Cys Leu Gln Ala Ala Cys Pro Glu Ser Trp Ile
65                  70                  75                  80

Gly Phe Gln Arg Lys Cys Phe Tyr Phe Ser Asp Asp Thr Lys Asn Trp
                85                  90                  95

Thr Ser Ser Gln Arg Phe Cys Asp Ser Gln Asp Ala Asp Leu Ala Gln
            100                 105                 110

Val Glu Ser Phe Gln Glu Leu Asn Phe Leu Leu Arg Tyr Lys Gly Pro
        115                 120                 125

Ser Asp His Trp Ile Gly Leu Ser Arg Glu Gln Gly Gln Pro Trp Lys
    130                 135                 140

Trp Ile Asn Gly Thr Glu Trp Thr Arg Gln Phe Pro Ile Leu Gly Ala
145                 150                 155                 160

Gly Glu Cys Ala Tyr Leu Asn Asp Lys Gly Ala Ser Ser Ala Arg His
                165                 170                 175

Tyr Thr Glu Arg Lys Trp Ile Cys Ser Lys Ser Asp Ile His Val
            180                 185                 190
```

<210> 2942
<211> 441
<212> PRT
<213> Homo sapiens

<400> 2942

```
Met Glu Ile Arg Leu Asp Thr Leu Ser Ala Ser Leu Gly Arg Ser Ser
1               5                  10                  15

Thr Leu Asn Asp Cys Asn Leu Glu Asp Lys Leu Ala Trp Tyr Glu Gly
            20                  25                  30

Glu Ala Tyr Met Trp His His Trp Lys Pro Phe Pro Glu Asn Pro Leu
        35                  40                  45

Trp Thr Cys Leu Asp Phe Gln Ile Ala Gln Val Gly Pro Trp Asp Tyr
    50                  55                  60

Cys Ser Ser Cys Ile Arg His Thr Arg Leu Lys Ser Ser Cys Ser Asp
65                  70                  75                  80

Met Asp Leu Leu His Ser Trp Arg Ser Ser Ser Phe Gly Asn Phe Asp
                85                  90                  95

Arg Phe Arg Asn Asn Ser Leu Ser Lys Pro Asp Asp Ser Thr Glu Ala
            100                 105                 110

His Glu Gly Asp Pro Thr Asn Gly Ser Gly Glu Gln Ser Lys Thr Ser
        115                 120                 125

Asn Asn Gly Gly Gly Leu Gly Lys Lys Met Arg Ala Ile Ser Trp Thr
    130                 135                 140

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

Lys Asp Glu Glu Asp Gly Glu Asn Ala His Pro Tyr Arg Asn Ser Asp
                165                 170                 175

Pro Val Ile Gly Thr His Thr Glu Lys Val Ser Leu Lys Ala Ser Asp
            180                 185                 190

Ser Met Asp Ser Leu Tyr Ser Gly Gln Ser Ser Ser Ser Gly Ile Thr
        195                 200                 205

Ser Cys Ser Asp Gly Thr Ser Asn Arg Asp Ser Phe Arg Leu Asp Asp
    210                 215                 220

Asp Gly Pro Tyr Ser Gly Pro Phe Cys Gly Arg Ala Arg Val His Thr
225                 230                 235                 240
```

```
Asp Phe Thr Pro Ser Pro Tyr Asp Thr Asp Ser Leu Lys Ile Lys Lys
                245                 250                 255

Gly Asp Ile Ile Asp Ile Ile Cys Lys Thr Pro Met Gly Met Trp Thr
            260                 265                 270

Gly Met Leu Asn Asn Lys Val Gly Asn Phe Lys Phe Ile Tyr Val Asp
        275                 280                 285

Val Ile Ser Glu Glu Glu Ala Ala Pro Lys Lys Ile Lys Ala Asn Arg
    290                 295                 300

Arg Ser Asn Ser Lys Lys Ser Lys Thr Leu Gln Glu Phe Leu Glu Arg
305                 310                 315                 320

Ile His Leu Gln Glu Tyr Thr Ser Thr Leu Leu Leu Asn Gly Tyr Glu
                325                 330                 335

Thr Leu Glu Asp Leu Lys Asp Ile Lys Glu Ser His Leu Ile Glu Leu
            340                 345                 350

Asn Ile Glu Asn Pro Asp Asp Arg Arg Arg Leu Leu Ser Ala Ala Glu
        355                 360                 365

Asn Phe Leu Glu Glu Glu Ile Ile Gln Glu Gln Glu Asn Glu Pro Glu
    370                 375                 380

Pro Leu Ser Leu Ser Ser Asp Ile Ser Leu Asn Lys Ser Gln Leu Asp
385                 390                 395                 400

Asp Cys Pro Arg Asp Ser Gly Cys Tyr Ile Ser Ser Gly Asn Ser Asp
                405                 410                 415

Asn Gly Lys Glu Asp Leu Glu Ser Glu Asn Leu Ser Asp Met Val His
            420                 425                 430

Lys Ile Ile Ile Thr Glu Pro Ser Asp
        435                 440

<210>  2943
<211>  564
<212>  PRT
<213>  Homo sapiens

<400>  2943

Met Lys Glu His Gly Gly Thr Phe Ser Ser Thr Gly Ile Ser Gly Gly
1               5                   10                  15
```

Ser Gly Asp Ser Ala Met Asp Ser Leu Gln Pro Leu Gln Pro Asn Tyr
20 25 30

Met Pro Val Cys Leu Phe Ala Glu Glu Ser Tyr Gln Lys Leu Ala Met
35 40 45

Glu Thr Leu Glu Glu Leu Asp Trp Cys Leu Asp Gln Leu Glu Thr Ile
50 55 60

Gln Thr Tyr Arg Ser Val Ser Glu Met Ala Ser Asn Lys Phe Lys Arg
65 70 75 80

Met Leu Asn Arg Glu Leu Thr His Leu Ser Glu Met Ser Arg Ser Gly
85 90 95

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

Asp Val Glu Ile Pro Ser Pro Thr Gln Lys Asp Arg Glu Lys Lys Lys
115 120 125

Lys Gln Gln Leu Met Thr Gln Ile Ser Gly Val Lys Lys Leu Met His
130 135 140

Ser Ser Ser Leu Asn Asn Thr Ser Ile Ser Arg Phe Gly Val Asn Thr
145 150 155 160

Glu Asn Glu Asp His Leu Ala Lys Glu Leu Glu Asp Leu Asn Lys Trp
165 170 175

Gly Leu Asn Ile Phe Asn Val Ala Gly Tyr Ser His Asn Arg Pro Leu
180 185 190

Thr Cys Ile Met Tyr Ala Ile Phe Gln Glu Arg Asp Leu Leu Lys Thr
195 200 205

Phe Arg Ile Ser Ser Asp Thr Phe Ile Thr Tyr Met Met Thr Leu Glu
210 215 220

Asp His Tyr His Ser Asp Val Ala Tyr His Asn Ser Leu His Ala Ala
225 230 235 240

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

```
Ala Val Phe Thr Asp Leu Glu Ile Leu Ala Ala Ile Phe Ala Ala Ala
            260                 265                 270

Ile His Asp Val Asp His Pro Gly Val Ser Asn Gln Phe Leu Ile Asn
        275                 280                 285

Thr Asn Ser Glu Leu Ala Leu Met Tyr Asn Asp Glu Ser Val Leu Glu
    290                 295                 300

Asn His His Leu Ala Val Gly Phe Lys Leu Leu Gln Glu Glu His Cys
305                 310                 315                 320

Asp Ile Phe Met Asn Leu Thr Lys Lys Gln Arg Gln Thr Leu Arg Lys
                325                 330                 335

Met Val Ile Asp Met Val Leu Ala Thr Asp Met Ser Lys His Met Ser
            340                 345                 350

Leu Leu Ala Asp Leu Lys Thr Met Val Glu Thr Lys Lys Val Thr Ser
        355                 360                 365

Ser Gly Val Leu Leu Leu Asp Asn Tyr Thr Asp Arg Ile Gln Val Leu
    370                 375                 380

Arg Asn Met Val His Cys Ala Asp Leu Ser Asn Pro Thr Lys Ser Leu
385                 390                 395                 400

Glu Leu Tyr Arg Gln Trp Thr Asp Arg Ile Met Glu Glu Phe Phe Gln
                405                 410                 415

Gln Gly Asp Lys Glu Arg Glu Arg Gly Met Glu Ile Ser Pro Met Cys
            420                 425                 430

Asp Lys His Thr Ala Ser Val Glu Lys Ser Gln Val Gly Phe Ile Asp
        435                 440                 445

Tyr Ile Val His Pro Leu Trp Glu Thr Trp Ala Asp Leu Val Gln Pro
    450                 455                 460

Asp Ala Gln Asp Ile Leu Asp Thr Leu Glu Asp Asn Arg Asn Trp Tyr
465                 470                 475                 480

Gln Ser Met Ile Pro Gln Ser Pro Ser Pro Pro Leu Asp Glu Gln Asn
                485                 490                 495
```

```
Arg Asp Cys Gln Gly Leu Met Glu Lys Phe Gln Phe Glu Leu Thr Leu
            500                 505                 510

Asp Glu Glu Asp Ser Glu Gly Pro Glu Lys Glu Gly Glu Gly His Ser
        515                 520                 525

Tyr Phe Ser Ser Thr Lys Thr Leu Cys Val Ile Asp Pro Glu Asn Arg
    530                 535                 540

Asp Ser Leu Gly Glu Thr Asp Ile Asp Ile Ala Thr Glu Asp Lys Ser
545                 550                 555                 560

Pro Val Asp Thr
```

<210> 2944
<211> 91
<212> PRT
<213> Homo sapiens

<400> 2944

```
Met Lys Val Ser Ala Ala Ala Leu Ala Val Ile Leu Ile Ala Thr Ala
1               5                   10                  15

Leu Cys Ala Pro Ala Ser Ala Ser Pro Tyr Ser Ser Asp Thr Thr Pro
            20                  25                  30

Cys Cys Phe Ala Tyr Ile Ala Arg Pro Leu Pro Arg Ala His Ile Lys
        35                  40                  45

Glu Tyr Phe Tyr Thr Ser Gly Lys Cys Ser Asn Pro Ala Val Val Phe
    50                  55                  60

Val Thr Arg Lys Asn Arg Gln Val Cys Ala Asn Pro Glu Lys Lys Trp
65                  70                  75                  80

Val Arg Glu Tyr Ile Asn Ser Leu Glu Met Ser
                85                  90
```

<210> 2945
<211> 461
<212> PRT
<213> Homo sapiens

<400> 2945

```
Met Ala Pro Val Ala Val Trp Ala Ala Leu Ala Val Gly Leu Glu Leu
1               5                   10                  15
```

```
Trp Ala Ala Ala His Ala Leu Pro Ala Gln Val Ala Phe Thr Pro Tyr
            20                  25                  30

Ala Pro Glu Pro Gly Ser Thr Cys Arg Leu Arg Glu Tyr Tyr Asp Gln
        35                  40                  45

Thr Ala Gln Met Cys Cys Ser Lys Cys Ser Pro Gly Gln His Ala Lys
    50                  55                  60

Val Phe Cys Thr Lys Thr Ser Asp Thr Val Cys Asp Ser Cys Glu Asp
65                  70                  75                  80

Ser Thr Tyr Thr Gln Leu Trp Asn Trp Val Pro Glu Cys Leu Ser Cys
                85                  90                  95

Gly Ser Arg Cys Ser Ser Asp Gln Val Glu Thr Gln Ala Cys Thr Arg
            100                 105                 110

Glu Gln Asn Arg Ile Cys Thr Cys Arg Pro Gly Trp Tyr Cys Ala Leu
        115                 120                 125

Ser Lys Gln Glu Gly Cys Arg Leu Cys Ala Pro Leu Arg Lys Cys Arg
    130                 135                 140

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

Cys Lys Pro Cys Ala Pro Gly Thr Phe Ser Asn Thr Thr Ser Ser Thr
                165                 170                 175

Asp Ile Cys Arg Pro His Gln Ile Cys Asn Val Val Ala Ile Pro Gly
            180                 185                 190

Asn Ala Ser Met Asp Ala Val Cys Thr Ser Thr Ser Pro Thr Arg Ser
        195                 200                 205

Met Ala Pro Gly Ala Val His Leu Pro Gln Pro Val Ser Thr Arg Ser
    210                 215                 220

Gln His Thr Gln Pro Thr Pro Glu Pro Ser Thr Ala Pro Ser Thr Ser
225                 230                 235                 240

Phe Leu Leu Pro Met Gly Pro Ser Pro Pro Ala Glu Gly Ser Thr Gly
                245                 250                 255
```

Asp Phe Ala Leu Pro Val Gly Leu Ile Val Gly Val Thr Ala Leu Gly
260 265 270

Leu Leu Ile Ile Gly Val Val Asn Cys Val Ile Met Thr Gln Val Lys
275 280 285

Lys Lys Pro Leu Cys Leu Gln Arg Glu Ala Lys Val Pro His Leu Pro
290 295 300

Ala Asp Lys Ala Arg Gly Thr Gln Gly Pro Glu Gln Gln His Leu Leu
305 310 315 320

Ile Thr Ala Pro Ser Ser Ser Ser Ser Ser Leu Glu Ser Ser Ala Ser
325 330 335

Ala Leu Asp Arg Arg Ala Pro Thr Arg Asn Gln Pro Gln Ala Pro Gly
340 345 350

Val Glu Ala Ser Gly Ala Gly Glu Ala Arg Ala Ser Thr Gly Ser Ser
355 360 365

Asp Ser Ser Pro Gly Gly His Gly Thr Gln Val Asn Val Thr Cys Ile
370 375 380

Val Asn Val Cys Ser Ser Ser Asp His Ser Ser Gln Cys Ser Ser Gln
385 390 395 400

Ala Ser Ser Thr Met Gly Asp Thr Asp Ser Ser Pro Ser Glu Ser Pro
405 410 415

Lys Asp Glu Gln Val Pro Phe Ser Lys Glu Glu Cys Ala Phe Arg Ser
420 425 430

Gln Leu Glu Thr Pro Glu Thr Leu Leu Gly Ser Thr Glu Glu Lys Pro
435 440 445

Leu Pro Leu Gly Val Pro Asp Ala Gly Met Lys Pro Ser
450 455 460

<210> 2946
<211> 823
<212> PRT
<213> Homo sapiens

<400> 2946

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

```
Leu Ile Thr Pro Glu Ala Asp His Val Glu Ala Ala Ile Leu Glu Glu
            20                  25                  30

Asp Glu Gly Leu Glu Ile Glu Glu Pro Ser Gly Leu Gly Leu Met Val
        35                  40                  45

Gly Gly Pro Asp Pro Asp Leu Leu Thr Cys Gly Gln Cys Gln Met Asn
    50                  55                  60

Phe Pro Leu Gly Asp Ile Leu Val Phe Ile Glu His Lys Arg Lys Gln
65                  70                  75                  80

Cys Gly Gly Ser Leu Gly Ala Cys Tyr Asp Lys Ala Leu Asp Lys Asp
                85                  90                  95

Ser Pro Pro Pro Ser Ser Arg Ser Glu Leu Arg Lys Val Ser Glu Pro
            100                 105                 110

Val Glu Ile Gly Ile Gln Val Thr Pro Asp Glu Asp Asp His Leu Leu
        115                 120                 125

Ser Pro Thr Lys Gly Ile Cys Pro Lys Gln Glu Asn Ile Ala Gly Lys
    130                 135                 140

Asp Glu Pro Ser Ser Tyr Ile Cys Thr Thr Cys Lys Gln Pro Phe Asn
145                 150                 155                 160

Ser Ala Trp Phe Leu Leu Gln His Ala Gln Asn Thr His Gly Phe Arg
                165                 170                 175

Ile Tyr Leu Glu Pro Gly Pro Ala Ser Ser Ser Leu Thr Pro Arg Leu
            180                 185                 190

Thr Ile Pro Pro Pro Leu Gly Pro Glu Ala Val Ala Gln Ser Pro Leu
        195                 200                 205

Met Asn Phe Leu Gly Asp Ser Asn Pro Phe Asn Leu Leu Arg Met Thr
    210                 215                 220

Gly Pro Ile Leu Arg Asp His Pro Gly Phe Gly Glu Gly Arg Leu Pro
225                 230                 235                 240

Gly Thr Pro Pro Leu Phe Ser Pro Pro Pro Arg His His Leu Asp Pro
                245                 250                 255
```

His Arg Leu Ser Ala Glu Glu Met Gly Leu Val Ala Gln His Pro Ser
260 265 270

Ala Phe Asp Arg Val Met Arg Leu Asn Pro Met Ala Ile Asp Ser Pro
275 280 285

Ala Met Asp Phe Ser Arg Arg Leu Arg Glu Leu Ala Gly Asn Ser Ser
290 295 300

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

Leu Asn Pro Phe Gln Pro Ser Pro Lys Ser Pro Phe Leu Ser Thr Pro
325 330 335

Pro Leu Pro Pro Met Pro Pro Gly Gly Thr Pro Pro Pro Gln Pro Pro
340 345 350

Ala Lys Ser Lys Ser Cys Glu Phe Cys Gly Lys Thr Phe Lys Phe Gln
355 360 365

Ser Asn Leu Ile Val His Arg Arg Ser His Thr Gly Glu Lys Pro Tyr
370 375 380

Lys Cys Gln Leu Cys Asp His Ala Cys Ser Gln Ala Ser Lys Leu Lys
385 390 395 400

Arg His Met Lys Thr His Met His Lys Ala Gly Ser Leu Ala Gly Arg
405 410 415

Ser Asp Asp Gly Leu Ser Ala Ala Ser Ser Pro Glu Pro Gly Thr Ser
420 425 430

Glu Leu Ala Gly Glu Gly Leu Lys Ala Ala Asp Gly Asp Phe Arg His
435 440 445

His Glu Ser Asp Pro Ser Leu Gly His Glu Pro Glu Glu Glu Asp Glu
450 455 460

Glu Glu Glu Glu Glu Glu Glu Glu Leu Leu Leu Glu Asn Glu Ser Arg
465 470 475 480

Pro Glu Ser Ser Phe Ser Met Asp Ser Glu Leu Ser Arg Asn Arg Glu
485 490 495

```
Asn Gly Gly Gly Gly Val Pro Gly Val Pro Gly Ala Gly Gly Gly Ala
            500                 505                 510

Ala Lys Ala Leu Ala Asp Glu Lys Ala Leu Val Leu Gly Lys Val Met
        515                 520                 525

Glu Asn Val Gly Leu Gly Ala Leu Pro Gln Tyr Gly Glu Leu Leu Ala
    530                 535                 540

Asp Lys Gln Lys Arg Gly Ala Phe Leu Lys Arg Ala Ala Gly Gly Gly
545                 550                 555                 560

Asp Ala Gly Asp Asp Asp Asp Ala Gly Gly Cys Gly Asp Ala Gly Ala
                565                 570                 575

Gly Gly Ala Val Asn Gly Arg Gly Gly Gly Phe Ala Pro Gly Thr Glu
            580                 585                 590

Pro Phe Pro Gly Leu Phe Pro Arg Lys Pro Ala Pro Leu Pro Ser Pro
        595                 600                 605

Gly Leu Asn Ser Ala Ala Lys Arg Ile Lys Val Glu Lys Asp Leu Glu
    610                 615                 620

Leu Pro Pro Ala Ala Leu Ile Pro Ser Glu Asn Val Tyr Ser Gln Trp
625                 630                 635                 640

Leu Val Gly Tyr Ala Ala Ser Arg His Phe Met Lys Asp Pro Phe Leu
                645                 650                 655

Gly Phe Thr Asp Ala Arg Gln Ser Pro Phe Ala Thr Ser Ser Glu His
            660                 665                 670

Ser Ser Glu Asn Gly Ser Leu Arg Phe Ser Thr Pro Pro Gly Asp Leu
        675                 680                 685

Leu Asp Gly Gly Leu Ser Gly Arg Ser Gly Thr Ala Ser Gly Gly Ser
    690                 695                 700

Thr Pro His Leu Gly Gly Pro Gly Pro Gly Arg Pro Ser Ser Lys Glu
705                 710                 715                 720

Gly Arg Arg Ser Asp Thr Cys Glu Tyr Cys Gly Lys Val Phe Lys Asn
                725                 730                 735

Cys Ser Asn Leu Thr Val His Arg Arg Ser His Thr Gly Glu Arg Pro
```

740 745 750

Tyr Lys Cys Glu Leu Cys Asn Tyr Ala Cys Ala Gln Ser Ser Lys Leu
755 760 765

Thr Arg His Met Lys Thr His Gly Gln Ile Gly Lys Glu Val Tyr Arg
770 775 780

Cys Asp Ile Cys Gln Met Pro Phe Ser Val Tyr Ser Thr Leu Glu Lys
785 790 795 800

His Met Lys Lys Trp His Gly Glu His Leu Leu Thr Asn Asp Val Lys
805 810 815

Ile Glu Gln Ala Glu Arg Ser
820

<210> 2947
<211> 441
<212> PRT
<213> Homo sapiens

<400> 2947

Met Val Pro Pro Lys Leu His Val Leu Phe Cys Leu Cys Gly Cys Leu
1 5 10 15

Ala Val Val Tyr Pro Phe Asp Trp Gln Tyr Ile Asn Pro Val Ala His
20 25 30

Met Lys Ser Ser Ala Trp Val Asn Lys Ile Gln Val Leu Met Ala Ala
35 40 45

Ala Ser Phe Gly Gln Thr Lys Ile Pro Arg Gly Asn Gly Pro Tyr Ser
50 55 60

Val Gly Cys Thr Asp Leu Met Phe Asp His Thr Asn Lys Gly Thr Phe
65 70 75 80

Leu Arg Leu Tyr Tyr Pro Ser Gln Asp Asn Asp Arg Leu Asp Thr Leu
85 90 95

Trp Ile Pro Asn Lys Glu Tyr Phe Trp Gly Leu Ser Lys Phe Leu Gly
100 105 110

Thr His Trp Leu Met Gly Asn Ile Leu Arg Leu Leu Phe Gly Ser Met
115 120 125

```
Thr Thr Pro Ala Asn Trp Asn Ser Pro Leu Arg Pro Gly Glu Lys Tyr
    130                 135                 140

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

Ser Ala Ile Gly Ile Asp Leu Ala Ser His Gly Phe Ile Val Ala Ala
                165                 170                 175

Val Glu His Arg Asp Arg Ser Ala Ser Ala Thr Tyr Tyr Phe Lys Asp
            180                 185                 190

Gln Ser Ala Ala Glu Ile Gly Asp Lys Ser Trp Leu Tyr Leu Arg Thr
        195                 200                 205

Leu Lys Gln Glu Glu Glu Thr His Ile Arg Asn Glu Gln Val Arg Gln
    210                 215                 220

Arg Ala Lys Glu Cys Ser Gln Ala Leu Ser Leu Ile Leu Asp Ile Asp
225                 230                 235                 240

His Gly Lys Pro Val Lys Asn Ala Leu Asp Leu Lys Phe Asp Met Glu
                245                 250                 255

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

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

Phe Arg Cys Gly Ile Ala Leu Asp Ala Trp Met Phe Pro Leu Gly Asp
    290                 295                 300

Glu Val Tyr Ser Arg Ile Pro Gln Pro Leu Phe Phe Ile Asn Ser Glu
305                 310                 315                 320

Tyr Phe Gln Tyr Pro Ala Asn Ile Ile Lys Met Lys Lys Cys Tyr Ser
                325                 330                 335

Pro Asp Lys Glu Arg Lys Met Ile Thr Ile Arg Gly Ser Val His Gln
            340                 345                 350

Asn Phe Ala Asp Phe Thr Phe Ala Thr Gly Lys Ile Ile Gly His Met
        355                 360                 365
```

Leu Lys Leu Lys Gly Asp Ile Asp Ser Asn Val Ala Ile Asp Leu Ser
370 375 380

Asn Lys Ala Ser Leu Ala Phe Leu Gln Lys His Leu Gly Leu His Lys
385 390 395 400

Asp Phe Asp Gln Trp Asp Cys Leu Ile Glu Gly Asp Asp Glu Asn Leu
405 410 415

Ile Pro Gly Thr Asn Ile Asn Thr Thr Asn Gln His Ile Met Leu Gln
420 425 430

Asn Ser Ser Gly Ile Glu Lys Tyr Asn
435 440

<210> 2948
<211> 1044
<212> PRT
<213> Homo sapiens

<400> 2948

Met Pro Pro Gly Val Asp Cys Pro Met Glu Phe Trp Thr Lys Glu Glu
1 5 10 15

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

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

Leu Trp His Arg Ala Gln Tyr Glu Pro Leu Phe His Met Leu Ser Gly
50 55 60

Pro Glu Ala Tyr Val Phe Thr Cys Ile Asn Gln Thr Ala Glu Gln Gln
65 70 75 80

Glu Leu Glu Asp Glu Gln Arg Arg Leu Cys Asp Val Gln Pro Phe Leu
85 90 95

Pro Val Leu Arg Leu Val Ala Arg Glu Gly Asp Arg Val Lys Lys Leu
100 105 110

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

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

Gln Phe Cys Glu Glu Ala Ala Ala Arg Arg Gln Gln Leu Gly Trp Glu
145 150 155 160

Ala Trp Leu Gln Tyr Ser Phe Pro Leu Gln Leu Glu Pro Ser Ala Gln
165 170 175

Thr Trp Gly Pro Gly Thr Leu Arg Leu Pro Asn Arg Ala Leu Leu Val
180 185 190

Asn Val Lys Phe Glu Gly Ser Glu Glu Ser Phe Thr Phe Gln Val Ser
195 200 205

Thr Lys Asp Val Pro Leu Ala Leu Met Ala Cys Ala Leu Arg Lys Lys
210 215 220

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

Leu Gln Val Asn Gly Arg His Glu Tyr Leu Tyr Gly Asn Tyr Pro Leu
245 250 255

Cys Gln Phe Gln Tyr Ile Cys Ser Cys Leu His Ser Gly Leu Thr Pro
260 265 270

His Leu Thr Met Val His Ser Ser Ser Ile Leu Ala Met Arg Asp Glu
275 280 285

Gln Ser Asn Pro Ala Pro Gln Val Gln Lys Pro Arg Ala Lys Pro Pro
290 295 300

Pro Ile Pro Ala Lys Lys Pro Ser Ser Val Ser Leu Trp Ser Leu Glu
305 310 315 320

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

Glu Arg Met Lys Leu Val Val Gln Ala Gly Leu Phe His Gly Asn Glu
340 345 350

Met Leu Cys Lys Thr Val Ser Ser Ser Glu Val Ser Val Cys Ser Glu
355 360 365

Pro Val Trp Lys Gln Arg Leu Glu Phe Asp Ile Asn Ile Cys Asp Leu
370 375 380

```
Pro Arg Met Ala Arg Leu Cys Phe Ala Leu Tyr Ala Val Ile Glu Lys
385                 390                 395                 400

Ala Lys Lys Ala Arg Ser Thr Lys Lys Lys Ser Lys Lys Ala Asp Cys
                405                 410                 415

Pro Ile Ala Trp Ala Asn Leu Met Leu Phe Asp Tyr Lys Asp Gln Leu
            420                 425                 430

Lys Thr Gly Glu Arg Cys Leu Tyr Met Trp Pro Ser Val Pro Asp Glu
        435                 440                 445

Lys Gly Glu Leu Leu Asn Pro Thr Gly Thr Val Arg Ser Asn Pro Asn
    450                 455                 460

Thr Asp Ser Ala Ala Ala Leu Leu Ile Cys Leu Pro Glu Val Ala Pro
465                 470                 475                 480

His Pro Val Tyr Tyr Pro Ala Leu Glu Lys Ile Leu Glu Leu Gly Arg
                485                 490                 495

His Ser Glu Cys Val His Val Thr Glu Glu Glu Gln Leu Gln Leu Arg
            500                 505                 510

Glu Ile Leu Glu Arg Arg Gly Ser Gly Glu Leu Tyr Glu His Glu Lys
        515                 520                 525

Asp Leu Val Trp Lys Leu Arg His Glu Val Gln Glu His Phe Pro Glu
    530                 535                 540

Ala Leu Ala Arg Leu Leu Leu Val Thr Lys Trp Asn Lys His Glu Asp
545                 550                 555                 560

Val Ala Gln Met Leu Tyr Leu Leu Cys Ser Trp Pro Glu Leu Pro Val
                565                 570                 575

Leu Ser Ala Leu Glu Leu Leu Asp Phe Ser Phe Pro Asp Cys His Val
            580                 585                 590

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

Phe Gln Tyr Leu Leu Gln Leu Val Gln Val Leu Lys Tyr Glu Ser Tyr
    610                 615                 620
```

Leu Asp Cys Glu Leu Thr Lys Phe Leu Leu Asp Arg Ala Leu Ala Asn
625 630 635 640

Arg Lys Ile Gly His Phe Leu Phe Trp His Leu Arg Ser Glu Met His
645 650 655

Val Pro Ser Val Ala Leu Arg Phe Gly Leu Ile Leu Glu Ala Tyr Cys
660 665 670

Arg Gly Ser Thr His His Met Lys Val Leu Met Lys Gln Gly Glu Ala
675 680 685

Leu Ser Lys Leu Lys Ala Leu Asn Asp Phe Val Lys Leu Ser Ser Gln
690 695 700

Lys Thr Pro Lys Pro Gln Thr Lys Glu Leu Met His Leu Cys Met Arg
705 710 715 720

Gln Glu Ala Tyr Leu Glu Ala Leu Ser His Leu Gln Ser Pro Leu Asp
725 730 735

Pro Ser Thr Leu Leu Ala Glu Val Cys Val Glu Gln Cys Thr Phe Met
740 745 750

Asp Ser Lys Met Lys Pro Leu Trp Ile Met Tyr Ser Asn Glu Glu Ala
755 760 765

Gly Ser Gly Gly Ser Val Gly Ile Ile Phe Lys Asn Gly Asp Asp Leu
770 775 780

Arg Gln Asp Met Leu Thr Leu Gln Met Ile Gln Leu Met Asp Val Leu
785 790 795 800

Trp Lys Gln Glu Gly Leu Asp Leu Arg Met Thr Pro Tyr Gly Cys Leu
805 810 815

Pro Thr Gly Asp Arg Thr Gly Leu Ile Glu Val Val Leu Arg Ser Asp
820 825 830

Thr Ile Ala Asn Ile Gln Leu Asn Lys Ser Asn Met Ala Ala Thr Ala
835 840 845

Ala Phe Asn Lys Asp Ala Leu Leu Asn Trp Leu Lys Ser Lys Asn Pro
850 855 860

Gly Glu Ala Leu Asp Arg Ala Ile Glu Glu Phe Thr Leu Ser Cys Ala

865 870 875 880

Gly Tyr Cys Val Ala Thr Tyr Val Leu Gly Ile Gly Asp Arg His Ser
885 890 895

Asp Asn Ile Met Ile Arg Glu Ser Gly Gln Leu Phe His Ile Asp Phe
900 905 910

Gly His Phe Leu Gly Asn Phe Lys Thr Lys Phe Gly Ile Asn Arg Glu
915 920 925

Arg Val Pro Phe Ile Leu Thr Tyr Asp Phe Val His Val Ile Gln Gln
930 935 940

Gly Lys Thr Asn Asn Ser Glu Lys Phe Glu Arg Phe Arg Gly Tyr Cys
945 950 955 960

Glu Arg Ala Tyr Thr Ile Leu Arg Arg His Gly Leu Leu Phe Leu His
965 970 975

Leu Phe Ala Leu Met Arg Ala Ala Gly Leu Pro Glu Leu Ser Cys Ser
980 985 990

Lys Asp Ile Gln Tyr Leu Lys Asp Ser Leu Ala Leu Gly Lys Thr Glu
995 1000 1005

Glu Glu Ala Leu Lys His Phe Arg Val Lys Phe Asn Glu Ala Leu
1010 1015 1020

Arg Glu Ser Trp Lys Thr Lys Val Asn Trp Leu Ala His Asn Val
1025 1030 1035

Ser Lys Asp Asn Arg Gln
1040

<210> 2949
<211> 167
<212> PRT
<213> Homo sapiens

<400> 2949

Met Glu His Ile His Asp Ser Asp Gly Ser Ser Ser Ser Ser His Gln
1 5 10 15

Ser Leu Lys Ser Thr Ala Lys Trp Ala Ala Ser Leu Glu Asn Leu Leu
20 25 30

```
Glu Asp Pro Glu Gly Val Lys Arg Phe Arg Glu Phe Leu Lys Lys Glu
        35                  40                  45

Phe Ser Glu Glu Asn Val Leu Phe Trp Leu Ala Cys Glu Asp Phe Lys
    50                  55                  60

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

Met Thr Phe Leu Ser Ser Lys Ala Ser Ser Gln Val Asn Val Glu Gly
                85                  90                  95

Gln Ser Arg Leu Asn Glu Lys Ile Leu Glu Glu Pro His Pro Leu Met
            100                 105                 110

Phe Gln Lys Leu Gln Asp Gln Ile Phe Asn Leu Met Lys Tyr Asp Ser
        115                 120                 125

Tyr Ser Arg Phe Leu Lys Ser Asp Leu Phe Leu Lys His Lys Arg Thr
    130                 135                 140

Glu Glu Glu Glu Glu Asp Leu Pro Asp Ala Gln Thr Ala Ala Lys Arg
145                 150                 155                 160

Ala Ser Arg Ile Tyr Asn Thr
                165
```

<210> 2950
<211> 263
<212> PRT
<213> Homo sapiens

<400> 2950

```
Met Val Lys Ile Ala Phe Asn Thr Pro Thr Ala Val Gln Lys Glu Glu
1               5                   10                  15

Ala Arg Gln Asp Val Glu Ala Leu Leu Ser Arg Thr Val Arg Thr Gln
            20                  25                  30

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

Ser Ser Gly Arg Cys Met Leu Thr Leu Leu Gly Leu Ser Phe Ile Leu
    50                  55                  60

Ala Gly Leu Ile Val Gly Gly Ala Cys Ile Tyr Lys Tyr Phe Met Pro
```

65 70 75 80

Lys Ser Thr Ile Tyr Arg Gly Glu Met Cys Phe Phe Asp Ser Glu Asp
85 90 95

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

Glu Glu Ala Asp Ile Arg Glu Asp Asp Asn Ile Ala Ile Ile Asp Val
115 120 125

Pro Val Pro Ser Phe Ser Asp Ser Asp Pro Ala Ala Ile Ile His Asp
130 135 140

Phe Glu Lys Gly Met Thr Ala Tyr Leu Asp Leu Leu Leu Gly Asn Cys
145 150 155 160

Tyr Leu Met Pro Leu Asn Thr Ser Ile Val Met Pro Pro Lys Asn Leu
165 170 175

Val Glu Leu Phe Gly Lys Leu Ala Ser Gly Arg Tyr Leu Pro Gln Thr
180 185 190

Tyr Val Val Arg Glu Asp Leu Val Ala Val Glu Glu Ile Arg Asp Val
195 200 205

Ser Asn Leu Gly Ile Phe Ile Tyr Gln Leu Cys Asn Asn Arg Lys Ser
210 215 220

Phe Arg Leu Arg Arg Arg Asp Leu Leu Leu Gly Phe Asn Lys Arg Ala
225 230 235 240

Ile Asp Lys Cys Trp Lys Ile Arg His Phe Pro Asn Glu Phe Ile Val
245 250 255

Glu Thr Lys Ile Cys Gln Glu
260

<210> 2951
<211> 201
<212> PRT
<213> Homo sapiens

<400> 2951

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

```
Arg Trp Leu Gln Ser Phe Val Asp Gly Leu Phe Cys Thr Gly Gly Leu
            20                  25                  30

Leu Arg Gln Arg Thr Cys Lys Phe Ala Gly Ala Ala Ser Gln Ala Pro
        35                  40                  45

His Ala Pro Ala Phe Leu Arg Ala Arg Gly Glu Pro Gln Asp Pro Leu
    50                  55                  60

Ser His Pro Arg Val Pro Ala Val Ser Ala Asn Cys Arg Met Trp Lys
65                  70                  75                  80

His Leu Pro Val His Ser Ser Pro Thr Pro Arg Leu Thr Pro Leu Trp
                85                  90                  95

Lys Leu Gln Ala Arg Trp Leu Leu Pro Gln Leu Val Tyr Leu Gln Gly
            100                 105                 110

Trp Gly Ser Tyr Ser Leu Leu Arg Pro Ala Ala Leu Ile Ser Met Val
        115                 120                 125

Leu Leu Ala Arg Glu Phe Leu Tyr Pro Ala Lys Met Ser Val Ser Glu
    130                 135                 140

Val Cys Ser Ser Gly Leu Ser Ser Pro Leu Leu Glu Gln His Lys Thr
145                 150                 155                 160

Asn Leu Ile Phe Tyr Ala Ser Gly Asp Ile Cys Ser Ala Asn Gly Lys
                165                 170                 175

Ser Gly Phe Asn Gln Pro Leu Pro Phe Leu Lys Thr Phe Cys Ser Thr
            180                 185                 190

His Arg Ile Leu Ser Cys Thr Tyr Leu
        195                 200


<210>  2952
<211>  492
<212>  PRT
<213>  Homo sapiens

<400>  2952

Met Ser Asp Tyr Glu Asn Asp Asp Glu Cys Trp Ser Val Leu Glu Gly
1               5                   10                  15

Phe Arg Val Thr Leu Thr Ser Val Ile Asp Pro Ser Arg Ile Thr Pro
```

20 25 30

Tyr Leu Arg Gln Cys Lys Val Leu Asn Pro Asp Asp Glu Glu Gln Val
35 40 45

Leu Ser Asp Pro Asn Leu Val Ile Arg Lys Arg Lys Val Gly Val Leu
50 55 60

Leu Asp Ile Leu Gln Arg Thr Gly His Lys Gly Tyr Val Ala Phe Leu
65 70 75 80

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

Lys Glu Pro Ala Arg Val Phe Ser Met Ile Ile Asp Ala Ser Gly Glu
100 105 110

Ser Gly Leu Thr Gln Leu Leu Met Thr Glu Val Met Lys Leu Gln Lys
115 120 125

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

Lys Glu Leu Arg Val Lys Asp Ser Leu Leu Arg Lys His Gln Glu Arg
145 150 155 160

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

Arg Cys Lys Glu Glu Asn Tyr Asp Leu Ala Met Arg Leu Ala His Gln
180 185 190

Ser Glu Glu Lys Gly Ala Ala Leu Met Arg Asn Arg Asp Leu Gln Leu
195 200 205

Glu Ile Asp Gln Leu Lys His Ser Leu Met Lys Ala Glu Asp Asp Cys
210 215 220

Lys Val Glu Arg Lys His Thr Leu Lys Leu Arg His Ala Met Glu Gln
225 230 235 240

Arg Pro Ser Gln Glu Leu Leu Trp Glu Leu Gln Gln Glu Lys Ala Leu
245 250 255

Leu Gln Ala Arg Val Gln Glu Leu Glu Ala Ser Val Gln Glu Gly Lys
260 265 270

Leu Asp Arg Ser Ser Pro Tyr Ile Gln Val Leu Glu Glu Asp Trp Arg
275 280 285

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

Arg Lys Asp Leu Arg Gln Gly Glu Ala Arg Arg Leu Arg Cys Met Glu
305 310 315 320

Glu Lys Glu Met Phe Glu Leu Gln Cys Leu Ala Leu Arg Lys Asp Ser
325 330 335

Lys Met Tyr Lys Asp Arg Ile Glu Ala Ile Leu Leu Gln Met Glu Glu
340 345 350

Val Ala Ile Glu Arg Asp Gln Ala Ile Ala Thr Arg Glu Glu Leu His
355 360 365

Ala Gln His Ala Arg Gly Leu Gln Glu Lys Asp Ala Leu Arg Lys Gln
370 375 380

Val Arg Glu Leu Gly Glu Lys Ala Asp Glu Leu Gln Leu Gln Val Phe
385 390 395 400

Gln Cys Glu Ala Gln Leu Leu Ala Val Glu Gly Arg Leu Arg Arg Gln
405 410 415

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

Arg Arg Ser Gln Glu Leu Ser Leu Pro Gln Asp Leu Glu Asp Thr Gln
435 440 445

Leu Ser Asp Lys Gly Cys Leu Ala Gly Gly Gly Ser Pro Lys Gln Pro
450 455 460

Phe Ala Ala Leu His Gln Glu Gln Val Leu Arg Asn Pro His Asp Ala
465 470 475 480

Gly Pro Ala Gly Leu Pro Gly Ile Gly Ala Val Cys
485 490

<210> 2953
<211> 92
<212> PRT

<213> Homo sapiens

<400> 2953

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

Phe Cys Ser Pro Ala Leu Ser Ala Pro Met Gly Ser Asp Pro Pro Thr
20 25 30

Ala Cys Cys Phe Ser Tyr Thr Ala Arg Lys Leu Pro Arg Asn Phe Val
35 40 45

Val Asp Tyr Tyr Glu Thr Ser Ser Leu Cys Ser Gln Pro Ala Val Val
50 55 60

Phe Gln Thr Lys Arg Ser Lys Gln Val Cys Ala Asp Pro Ser Glu Ser
65 70 75 80

Trp Val Gln Glu Tyr Val Tyr Asp Leu Glu Leu Asn
85 90

<210> 2954
<211> 266
<212> PRT
<213> Homo sapiens

<400> 2954

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

Val Thr Leu Met Val Leu Ser Ser Pro Leu Ala Leu Ala Gly Asp Thr
20 25 30

Arg Pro Arg Phe Leu Trp Gln Leu Lys Phe Glu Cys His Phe Phe Asn
35 40 45

Gly Thr Glu Arg Val Arg Leu Leu Glu Arg Cys Ile Tyr Asn Gln Glu
50 55 60

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

Glu Leu Gly Arg Pro Asp Ala Glu Tyr Trp Asn Ser Gln Lys Asp Leu
85 90 95

Leu Glu Gln Arg Arg Ala Ala Val Asp Thr Tyr Cys Arg His Asn Tyr
100 105 110

```
Gly Val Gly Glu Ser Phe Thr Val Gln Arg Arg Val Glu Pro Lys Val
        115                 120                 125

Thr Val Tyr Pro Ser Lys Thr Gln Pro Leu Gln His His Asn Leu Leu
    130                 135                 140

Val Cys Ser Val Ser Gly Phe Tyr Pro Gly Ser Ile Glu Val Arg Trp
145                 150                 155                 160

Phe Arg Asn Gly Gln Glu Glu Lys Ala Gly Val Val Ser Thr Gly Leu
                165                 170                 175

Ile Gln Asn Gly Asp Trp Thr Phe Gln Thr Leu Val Met Leu Glu Thr
            180                 185                 190

Val Pro Arg Ser Gly Glu Val Tyr Thr Cys Gln Val Glu His Pro Ser
        195                 200                 205

Val Thr Ser Pro Leu Thr Val Glu Trp Arg Ala Arg Ser Glu Ser Ala
    210                 215                 220

Gln Ser Lys Met Leu Ser Gly Val Gly Gly Phe Val Leu Gly Leu Leu
225                 230                 235                 240

Phe Leu Gly Ala Gly Leu Phe Ile Tyr Phe Arg Asn Gln Lys Gly His
                245                 250                 255

Ser Gly Leu Gln Pro Thr Gly Phe Leu Ser
            260                 265


<210>  2955
<211>  359
<212>  PRT
<213>  Homo sapiens

<400>  2955

Met Ala Glu Ala Ile Thr Tyr Ala Asp Leu Arg Phe Val Lys Ala Pro
1               5                   10                  15

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

Asp Asp Gly Glu Ile Thr Tyr Glu Asn Val Gln Val Pro Ala Val Leu
        35                  40                  45
```

```
Gly Val Pro Ser Ser Leu Ala Ser Ser Val Leu Gly Asp Lys Ala Ala
    50                  55                  60

Val Lys Ser Glu Gln Pro Thr Ala Ser Trp Arg Ala Val Thr Ser Pro
65                  70                  75                  80

Ala Val Gly Arg Ile Leu Pro Cys Arg Thr Thr Cys Leu Arg Tyr Leu
                85                  90                  95

Leu Leu Gly Leu Leu Leu Thr Cys Leu Leu Leu Gly Val Thr Ala Ile
            100                 105                 110

Cys Leu Gly Val Arg Tyr Leu Gln Val Ser Gln Gln Leu Gln Gln Thr
        115                 120                 125

Asn Arg Val Leu Glu Val Thr Asn Ser Ser Leu Arg Gln Gln Leu Arg
    130                 135                 140

Leu Lys Ile Thr Gln Leu Gly Gln Ser Ala Glu Asp Leu Gln Gly Ser
145                 150                 155                 160

Arg Arg Glu Leu Ala Gln Ser Gln Glu Ala Leu Gln Val Glu Gln Arg
                165                 170                 175

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

Gln Lys Thr Lys Glu Thr Leu Gln Ser Glu Glu Gln Gln Arg Arg Ala
        195                 200                 205

Leu Glu Gln Lys Leu Ser Asn Met Glu Asn Arg Leu Lys Pro Phe Phe
    210                 215                 220

Thr Cys Gly Ser Ala Asp Thr Cys Cys Pro Ser Gly Trp Ile Met His
225                 230                 235                 240

Gln Lys Ser Cys Phe Tyr Ile Ser Leu Thr Ser Lys Asn Trp Gln Glu
                245                 250                 255

Ser Gln Lys Gln Cys Glu Thr Leu Ser Ser Lys Leu Ala Thr Phe Ser
            260                 265                 270

Glu Ile Tyr Pro Gln Ser His Ser Tyr Tyr Phe Leu Asn Ser Leu Leu
        275                 280                 285

Pro Asn Gly Gly Ser Gly Asn Ser Tyr Trp Thr Gly Leu Ser Ser Asn
```

290 295 300

Lys Asp Trp Lys Leu Thr Asp Asp Thr Gln Arg Thr Arg Thr Tyr Ala
305 310 315 320

Gln Ser Ser Lys Cys Asn Lys Val His Lys Thr Trp Ser Trp Trp Thr
325 330 335

Leu Glu Ser Glu Ser Cys Arg Ser Ser Leu Pro Tyr Ile Cys Glu Met
340 345 350

Thr Ala Phe Arg Phe Pro Asp
355

<210> 2956
<211> 643
<212> PRT
<213> Homo sapiens

<400> 2956

Met Gln Ala Pro Arg Glu Leu Ala Val Gly Ile Asp Leu Gly Thr Thr
1 5 10 15

Tyr Ser Cys Val Gly Val Phe Gln Gln Gly Arg Val Glu Ile Leu Ala
20 25 30

Asn Asp Gln Gly Asn Arg Thr Thr Pro Ser Tyr Val Ala Phe Thr Asp
35 40 45

Thr Glu Arg Leu Val Gly Asp Ala Ala Lys Ser Gln Ala Ala Leu Asn
50 55 60

Pro His Asn Thr Val Phe Asp Ala Lys Arg Leu Ile Gly Arg Lys Phe
65 70 75 80

Ala Asp Thr Thr Val Gln Ser Asp Met Lys His Trp Pro Phe Arg Val
85 90 95

Val Ser Glu Gly Gly Lys Pro Lys Val Pro Val Ser Tyr Arg Gly Glu
100 105 110

Asp Lys Thr Phe Tyr Pro Glu Glu Ile Ser Ser Met Val Leu Ser Lys
115 120 125

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

```
Val Ile Thr Val Pro Ala Tyr Phe Asn Asp Ser Gln Arg Gln Ala Thr
145                 150                 155                 160

Lys Asp Ala Gly Ala Ile Ala Gly Leu Asn Val Leu Arg Ile Ile Asn
                165                 170                 175

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

Gly Glu Arg Asn Val Leu Ile Phe Asp Leu Gly Gly Gly Thr Phe Asp
        195                 200                 205

Val Ser Val Leu Ser Ile Asp Ala Gly Val Phe Glu Val Lys Ala Thr
    210                 215                 220

Ala Gly Asp Thr His Leu Gly Gly Glu Asp Phe Asp Asn Arg Leu Val
225                 230                 235                 240

Asn His Phe Met Glu Glu Phe Arg Arg Lys His Gly Lys Asp Leu Ser
                245                 250                 255

Gly Asn Lys Arg Ala Leu Gly Arg Leu Arg Thr Ala Cys Glu Arg Ala
            260                 265                 270

Lys Arg Thr Leu Ser Ser Ser Thr Gln Ala Thr Leu Glu Ile Asp Ser
        275                 280                 285

Leu Phe Glu Gly Val Asp Phe Tyr Thr Ser Ile Thr Arg Ala Arg Phe
    290                 295                 300

Glu Glu Leu Cys Ser Asp Leu Phe Arg Ser Thr Leu Glu Pro Val Glu
305                 310                 315                 320

Lys Ala Leu Arg Asp Ala Lys Leu Asp Lys Ala Gln Ile His Asp Val
                325                 330                 335

Val Leu Val Gly Gly Ser Thr Arg Ile Pro Lys Val Gln Lys Leu Leu
            340                 345                 350

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

Glu Ala Val Ala Tyr Gly Ala Ala Val Gln Ala Ala Val Leu Met Gly
    370                 375                 380
```

Asp Lys Cys Glu Lys Val Gln Asp Leu Leu Leu Leu Asp Val Ala Pro
385 390 395 400

Leu Ser Leu Gly Leu Glu Thr Ala Gly Gly Val Met Thr Thr Leu Ile
405 410 415

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

Tyr Ser Asp Asn Gln Pro Gly Val Phe Ile Gln Val Tyr Glu Gly Glu
435 440 445

Arg Ala Met Thr Lys Asp Asn Asn Leu Leu Gly Arg Phe Glu Leu Ser
450 455 460

Gly Ile Pro Pro Ala Pro Arg Gly Val Pro Gln Ile Glu Val Thr Phe
465 470 475 480

Asp Ile Asp Ala Asn Gly Ile Leu Ser Val Thr Ala Thr Asp Arg Ser
485 490 495

Thr Gly Lys Ala Asn Lys Ile Thr Ile Thr Asn Asp Lys Gly Arg Leu
500 505 510

Ser Lys Glu Glu Val Glu Arg Met Val His Glu Ala Glu Gln Tyr Lys
515 520 525

Ala Glu Asp Glu Ala Gln Arg Asp Arg Val Ala Ala Lys Asn Ser Leu
530 535 540

Glu Ala His Val Phe His Val Lys Gly Ser Leu Gln Glu Glu Ser Leu
545 550 555 560

Arg Asp Lys Ile Pro Glu Glu Asp Arg Arg Lys Met Gln Asp Lys Cys
565 570 575

Arg Glu Val Leu Ala Trp Leu Glu His Asn Gln Leu Ala Glu Lys Glu
580 585 590

Glu Tyr Glu His Gln Lys Arg Glu Leu Glu Gln Ile Cys Arg Pro Ile
595 600 605

Phe Ser Arg Leu Tyr Gly Gly Pro Gly Val Pro Gly Gly Ser Ser Cys
610 615 620

Gly Thr Gln Ala Arg Gln Gly Asp Pro Ser Thr Gly Pro Ile Ile Glu

625 630 635 640

Glu Val Asp

<210> 2957
<211> 565
<212> PRT
<213> Homo sapiens

<400> 2957

Met Ala Glu Gly Lys Ala Gly Gly Ala Ala Gly Leu Phe Ala Lys Gln
1 5 10 15

Val Gln Lys Lys Phe Ser Arg Ala Gln Glu Lys Val Leu Gln Lys Leu
20 25 30

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

Asn Phe Tyr Gln Gln Gln Ala Glu Gly His Lys Leu Tyr Lys Asp Leu
50 55 60

Lys Asn Phe Leu Ser Ala Val Lys Val Met His Glu Ser Ser Lys Arg
65 70 75 80

Val Ser Glu Thr Leu Gln Glu Ile Tyr Ser Ser Glu Trp Asp Gly His
85 90 95

Glu Glu Leu Lys Ala Ile Val Trp Asn Asn Asp Leu Leu Trp Glu Asp
100 105 110

Tyr Glu Glu Lys Leu Ala Asp Gln Ala Val Arg Thr Met Glu Ile Tyr
115 120 125

Val Ala Gln Phe Ser Glu Ile Lys Glu Arg Ile Ala Lys Arg Gly Arg
130 135 140

Lys Leu Val Asp Tyr Asp Ser Ala Arg His His Leu Glu Ala Val Gln
145 150 155 160

Asn Ala Lys Lys Lys Asp Glu Ala Lys Thr Ala Lys Ala Glu Glu Glu
165 170 175

Phe Asn Lys Ala Gln Thr Val Phe Glu Asp Leu Asn Gln Glu Leu Leu
180 185 190

```
Glu Glu Leu Pro Ile Leu Tyr Asn Ser Arg Ile Gly Cys Tyr Val Thr
        195                 200                 205

Ile Phe Gln Asn Ile Ser Asn Leu Arg Asp Val Phe Tyr Arg Glu Met
    210                 215                 220

Ser Lys Leu Asn His Asn Leu Tyr Glu Val Met Ser Lys Leu Glu Lys
225                 230                 235                 240

Gln His Ser Asn Lys Val Phe Val Val Lys Gly Leu Ser Ser Ser Ser
                245                 250                 255

Arg Arg Ser Leu Val Ile Ser Pro Pro Val Arg Thr Ala Thr Val Ser
            260                 265                 270

Ser Pro Leu Thr Ser Pro Thr Ser Pro Ser Thr Leu Ser Leu Lys Ser
        275                 280                 285

Glu Ser Glu Ser Val Ser Ala Thr Glu Asp Leu Ala Pro Asp Ala Ala
    290                 295                 300

Gln Gly Glu Asp Asn Ser Glu Ile Lys Glu Leu Leu Glu Glu Glu Glu
305                 310                 315                 320

Ile Glu Lys Glu Gly Ser Glu Ala Ser Ser Ser Glu Glu Asp Glu Pro
                325                 330                 335

Leu Pro Ala Cys Asn Gly Pro Ala Gln Ala Gln Pro Ser Pro Thr Thr
            340                 345                 350

Glu Arg Ala Lys Ser Gln Glu Glu Val Leu Pro Ser Ser Thr Thr Pro
        355                 360                 365

Ser Pro Gly Gly Ala Leu Ser Pro Ser Gly Gln Pro Ser Ser Ser Ala
    370                 375                 380

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

Pro Lys Lys Arg Ala Ser Ile Gln Arg Thr Ser Ala Pro Pro Ser Arg
                405                 410                 415

Pro Pro Pro Pro Arg Ala Thr Ala Ser Pro Arg Pro Ser Ser Gly Asn
            420                 425                 430
```

```
Ile Pro Ser Ser Pro Thr Ala Ser Gly Gly Gly Ser Pro Thr Ser Pro
        435                 440                 445

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

Val Ser Pro Asn Pro Glu Pro Pro Glu Lys Pro Val Arg Thr Pro Glu
465                 470                 475                 480

Ala Lys Glu Asn Glu Asn Ile His Asn Gln Asn Pro Glu Glu Leu Cys
                485                 490                 495

Thr Ser Pro Thr Leu Met Thr Ser Gln Val Ala Ser Glu Pro Gly Glu
            500                 505                 510

Ala Lys Lys Met Glu Asp Lys Glu Lys Asp Asn Lys Leu Ile Ser Ala
        515                 520                 525

Asp Ser Ser Glu Gly Gln Asp Gln Leu Gln Val Ser Met Val Pro Glu
    530                 535                 540

Asn Asn Asn Leu Thr Ala Pro Glu Pro Gln Glu Glu Val Ser Thr Ser
545                 550                 555                 560

Glu Asn Pro Gln Leu
                565
```

<210> 2958
<211> 349
<212> PRT
<213> Homo sapiens

<400> 2958

```
Met Glu Thr Pro Pro Val Asn Thr Ile Gly Glu Lys Asp Thr Ser Gln
1               5                   10                  15

Pro Gln Gln Glu Trp Glu Lys Asn Leu Arg Glu Asn Leu Asp Ser Val
            20                  25                  30

Ile Gln Ile Arg Gln Gln Pro Arg Asp Pro Pro Thr Glu Thr Leu Glu
        35                  40                  45

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

Gly Ala Glu Lys Leu Val Ala Glu Leu Glu Gly Asp Ser His Lys Ser
65                  70                  75                  80
```

```
His Gly Ser Thr Ser Gln Met Pro Glu Ala Leu Gln Ala Ser Asp Leu
                85                  90                  95

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

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

Leu Gly Phe Pro Phe Gly Ser Gly Pro Pro Glu Gly Trp Thr Glu Leu
    130                 135                 140

Thr Met Gly Val Gly Pro Trp Arg Glu Glu Thr Trp Gly Glu Leu Ile
145                 150                 155                 160

Glu Lys Cys Leu Glu Ser Met Cys Gln Gly Glu Glu Ala Glu Leu Gln
                165                 170                 175

Leu Pro Gly His Ser Gly Pro Pro Val Arg Leu Thr Leu Ala Ser Phe
            180                 185                 190

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

Leu Ala Arg Glu Glu Arg Ala Arg Gly Thr Glu Leu Phe Arg Ala Gly
    210                 215                 220

Asn Pro Glu Gly Ala Ala Arg Cys Tyr Gly Arg Ala Leu Arg Leu Leu
225                 230                 235                 240

Leu Thr Leu Pro Pro Pro Gly Pro Pro Glu Arg Thr Val Leu His Ala
                245                 250                 255

Asn Leu Ala Ala Cys Gln Leu Leu Leu Gly Gln Pro Gln Leu Ala Ala
            260                 265                 270

Gln Ser Cys Asp Arg Val Leu Glu Arg Glu Pro Gly His Leu Lys Ala
        275                 280                 285

Leu Tyr Arg Arg Gly Val Ala Gln Ala Ala Leu Gly Asn Leu Glu Lys
    290                 295                 300

Ala Thr Ala Asp Leu Lys Lys Val Leu Ala Ile Asp Pro Lys Asn Arg
305                 310                 315                 320
```

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

Asp Ala Gly Leu Ala Gln Gly Leu Arg Lys Met Phe Gly
            340                 345

<210>  2959
<211>  620
<212>  PRT
<213>  Homo sapiens

<400>  2959

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

Gln Lys Arg Arg Thr Ser Pro Ser Asn Phe Lys Val Arg Phe Phe Val
            20                  25                  30

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

Arg Thr Leu Lys Gly Ser Ile Glu Leu Ser Arg Ile Lys Cys Val Glu
    50                  55                  60

Ile Val Lys Ser Asp Ile Ser Ile Pro Cys His Tyr Lys Tyr Pro Phe
65                  70                  75                  80

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

Glu Ser Arg Gln Arg Trp Val Leu Ala Leu Lys Glu Glu Thr Arg Asn
            100                 105                 110

Asn Asn Ser Leu Val Pro Lys Tyr His Pro Asn Phe Trp Met Asp Gly
        115                 120                 125

Lys Trp Arg Cys Cys Ser Gln Leu Glu Lys Leu Ala Thr Gly Cys Ala
    130                 135                 140

Gln Tyr Asp Pro Thr Lys Asn Ala Ser Lys Lys Pro Leu Pro Pro Thr
145                 150                 155                 160

Pro Glu Asp Asn Arg Arg Pro Leu Trp Glu Pro Glu Glu Thr Val Val
                165                 170                 175

Ile Ala Leu Tyr Asp Tyr Gln Thr Asn Asp Pro Gln Glu Leu Ala Leu
```

```
            180                 185                 190

Arg Arg Asn Glu Glu Tyr Cys Leu Leu Asp Ser Ser Glu Ile His Trp
        195                 200                 205

Trp Arg Val Gln Asp Arg Asn Gly His Glu Gly Tyr Val Pro Ser Ser
    210                 215                 220

Tyr Leu Val Glu Lys Ser Pro Asn Asn Leu Glu Thr Tyr Glu Trp Tyr
225                 230                 235                 240

Asn Lys Ser Ile Ser Arg Asp Lys Ala Glu Lys Leu Leu Leu Asp Thr
                245                 250                 255

Gly Lys Glu Gly Ala Phe Met Val Arg Asp Ser Arg Thr Ala Gly Thr
            260                 265                 270

Tyr Thr Val Ser Val Phe Thr Lys Ala Val Val Ser Glu Asn Asn Pro
        275                 280                 285

Cys Ile Lys His Tyr His Ile Lys Glu Thr Asn Asp Asn Pro Lys Arg
    290                 295                 300

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

Asn Tyr His Gln His Asn Gly Gly Gly Leu Val Thr Arg Leu Arg Tyr
                325                 330                 335

Pro Val Cys Phe Gly Arg Gln Lys Ala Pro Val Thr Ala Gly Leu Arg
            340                 345                 350

Tyr Gly Lys Trp Val Ile Asp Pro Ser Glu Leu Thr Phe Val Gln Glu
        355                 360                 365

Ile Gly Ser Gly Gln Phe Gly Leu Val His Leu Gly Tyr Trp Leu Asn
    370                 375                 380

Lys Asp Lys Val Ala Ile Lys Thr Ile Arg Glu Gly Ala Met Ser Glu
385                 390                 395                 400

Glu Asp Phe Ile Glu Glu Ala Glu Val Met Met Lys Leu Ser His Pro
                405                 410                 415

Lys Leu Val Gln Leu Tyr Gly Val Cys Leu Glu Gln Ala Pro Ile Cys
            420                 425                 430
```

```
Leu Val Phe Glu Phe Met Glu His Gly Cys Leu Ser Asp Tyr Leu Arg
        435                 440                 445

Thr Gln Arg Gly Leu Phe Ala Ala Glu Thr Leu Leu Gly Met Cys Leu
    450                 455                 460

Asp Val Cys Glu Gly Met Ala Tyr Leu Glu Glu Ala Cys Val Ile His
465                 470                 475                 480

Arg Asp Leu Ala Ala Arg Asn Cys Leu Val Gly Glu Asn Gln Val Ile
                485                 490                 495

Lys Val Ser Asp Phe Gly Met Thr Arg Phe Val Leu Asp Asp Gln Tyr
            500                 505                 510

Thr Ser Ser Thr Gly Thr Lys Phe Pro Val Lys Trp Ala Ser Pro Glu
        515                 520                 525

Val Phe Ser Phe Ser Arg Tyr Ser Ser Lys Ser Asp Val Trp Ser Phe
    530                 535                 540

Gly Val Leu Met Trp Glu Val Phe Ser Glu Gly Lys Ile Pro Tyr Glu
545                 550                 555                 560

Asn Arg Ser Asn Ser Glu Val Val Glu Asp Ile Ser Thr Gly Phe Arg
                565                 570                 575

Leu Tyr Lys Pro Arg Leu Ala Ser Thr His Val Tyr Gln Ile Met Asn
            580                 585                 590

His Cys Trp Lys Glu Arg Pro Glu Asp Arg Pro Ala Phe Ser Arg Leu
        595                 600                 605

Leu Arg Gln Leu Ala Glu Ile Ala Glu Ser Gly Leu
    610                 615                 620
```

<210> 2960
<211> 262
<212> PRT
<213> Homo sapiens

<400> 2960

```
Met Asp Pro Arg Leu Ser Thr Val Arg Gln Thr Cys Cys Cys Phe Asn
1               5                   10                  15
```

```
Val Arg Ile Ala Thr Thr Ala Leu Ala Ile Tyr His Val Ile Met Ser
            20                  25                  30

Val Leu Leu Phe Ile Glu His Ser Val Glu Val Ala His Gly Lys Ala
        35                  40                  45

Ser Cys Lys Leu Ser Gln Met Gly Tyr Leu Arg Ile Ala Asp Leu Ile
    50                  55                  60

Ser Ser Phe Leu Leu Ile Thr Met Leu Phe Ile Ile Ser Leu Ser Leu
65                  70                  75                  80

Leu Ile Gly Val Val Lys Asn Arg Glu Lys Tyr Leu Leu Pro Phe Leu
                85                  90                  95

Ser Leu Gln Ile Met Asp Tyr Leu Leu Cys Leu Leu Thr Leu Leu Gly
            100                 105                 110

Ser Tyr Ile Glu Leu Pro Ala Tyr Leu Lys Leu Ala Ser Arg Ser Arg
        115                 120                 125

Ala Ser Ser Ser Lys Phe Pro Leu Met Thr Leu Gln Leu Leu Asp Phe
    130                 135                 140

Cys Leu Ser Ile Leu Thr Leu Cys Ser Ser Tyr Met Glu Val Pro Thr
145                 150                 155                 160

Tyr Leu Asn Phe Lys Ser Met Asn His Met Asn Tyr Leu Pro Ser Gln
                165                 170                 175

Glu Asp Met Pro His Asn Gln Phe Ile Lys Met Met Ile Ile Phe Ser
            180                 185                 190

Ile Ala Phe Ile Thr Val Leu Ile Phe Lys Val Tyr Met Phe Lys Cys
        195                 200                 205

Val Trp Arg Cys Tyr Arg Leu Ile Lys Cys Met Asn Ser Val Glu Glu
    210                 215                 220

Lys Arg Asn Ser Lys Met Leu Gln Lys Val Val Leu Pro Ser Tyr Glu
225                 230                 235                 240

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

Pro Pro Tyr Ser Glu Val
```

260

<210> 2961
<211> 467
<212> PRT
<213> Homo sapiens

<400> 2961

Met Gln Met Asp Asn Arg Leu Pro Pro Lys Lys Val Pro Gly Phe Cys
1 5 10 15

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

Ile Thr Ala Gln Arg Ala Cys Leu Asn Leu Thr Met Val Val Met Val
35 40 45

Asn Ser Thr Asp Pro His Gly Leu Pro Asn Thr Ser Thr Lys Lys Leu
50 55 60

Leu Asp Asn Ile Lys Asn Pro Met Tyr Asn Trp Ser Pro Asp Ile Gln
65 70 75 80

Gly Ile Ile Leu Ser Ser Thr Ser Tyr Gly Val Ile Ile Ile Gln Val
85 90 95

Pro Val Gly Tyr Phe Ser Gly Ile Tyr Ser Thr Lys Lys Met Ile Gly
100 105 110

Phe Ala Leu Cys Leu Ser Ser Val Leu Ser Leu Leu Ile Pro Pro Ala
115 120 125

Ala Gly Ile Gly Val Ala Trp Val Val Val Cys Arg Ala Val Gln Gly
130 135 140

Ala Ala Gln Gly Ile Val Ala Thr Ala Gln Phe Glu Ile Tyr Val Lys
145 150 155 160

Trp Ala Pro Pro Leu Glu Arg Gly Arg Leu Thr Ser Met Ser Thr Ser
165 170 175

Gly Phe Leu Leu Gly Pro Phe Ile Val Leu Leu Val Thr Gly Val Ile
180 185 190

Cys Glu Ser Leu Gly Trp Pro Met Val Phe Tyr Ile Phe Gly Ala Cys
195 200 205

Gly Cys Ala Val Cys Leu Leu Trp Phe Val Leu Phe Tyr Asp Asp Pro
210 215 220

Lys Asp His Pro Cys Ile Ser Ile Ser Glu Lys Glu Tyr Ile Thr Ser
225 230 235 240

Ser Leu Val Gln Gln Val Ser Ser Ser Arg Gln Ser Leu Pro Ile Lys
245 250 255

Ala Ile Leu Lys Ser Leu Pro Val Trp Ala Ile Ser Ile Gly Ser Phe
260 265 270

Thr Phe Phe Trp Ser His Asn Ile Met Thr Leu Tyr Thr Pro Met Phe
275 280 285

Ile Asn Ser Met Leu His Val Asn Ile Lys Glu Asn Gly Phe Leu Ser
290 295 300

Ser Leu Pro Tyr Leu Phe Ala Trp Ile Cys Gly Asn Leu Ala Gly Gln
305 310 315 320

Leu Ser Asp Phe Phe Leu Thr Arg Asn Ile Leu Ser Val Ile Ala Val
325 330 335

Arg Lys Leu Phe Thr Ala Ala Gly Phe Leu Leu Pro Ala Ile Phe Gly
340 345 350

Val Cys Leu Pro Tyr Leu Ser Ser Thr Phe Tyr Ser Ile Val Ile Phe
355 360 365

Leu Ile Leu Ala Gly Ala Thr Gly Ser Phe Cys Leu Gly Gly Val Phe
370 375 380

Ile Asn Gly Leu Asp Ile Ala Pro Arg Tyr Phe Gly Phe Ile Lys Ala
385 390 395 400

Cys Ser Thr Leu Thr Gly Met Ile Gly Gly Leu Ile Ala Ser Thr Leu
405 410 415

Thr Gly Leu Ile Leu Lys Gln Asp Pro Glu Ser Ala Trp Phe Lys Thr
420 425 430

Phe Ile Leu Met Ala Ala Ile Asn Val Thr Gly Leu Ile Phe Tyr Leu
435 440 445

Ile Val Ala Thr Ala Glu Ile Gln Asp Trp Ala Lys Glu Lys Gln His
450 455 460

Thr Arg Leu
465

<210> 2962
<211> 444
<212> PRT
<213> Homo sapiens

<400> 2962

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

Gly Cys Leu Ala Ala Val Phe Val Thr Gln Glu Glu Ala His Gly Val
20 25 30

Leu His Arg Arg Arg Arg Ala Asn Ala Phe Leu Glu Glu Leu Arg Pro
35 40 45

Gly Ser Leu Glu Arg Glu Cys Lys Glu Glu Gln Cys Ser Phe Glu Glu
50 55 60

Ala Arg Glu Ile Phe Lys Asp Ala Glu Arg Thr Lys Leu Phe Trp Ile
65 70 75 80

Ser Tyr Ser Asp Gly Asp Gln Cys Ala Ser Ser Pro Cys Gln Asn Gly
85 90 95

Gly Ser Cys Lys Asp Gln Leu Gln Ser Tyr Ile Cys Phe Cys Leu Pro
100 105 110

Ala Phe Glu Gly Arg Asn Cys Glu Thr His Lys Asp Asp Gln Leu Ile
115 120 125

Cys Val Asn Glu Asn Gly Gly Cys Glu Gln Tyr Cys Ser Asp His Thr
130 135 140

Gly Thr Lys Arg Ser Cys Arg Cys His Glu Gly Tyr Ser Leu Leu Ala
145 150 155 160

Asp Gly Val Ser Cys Thr Pro Thr Val Glu Tyr Pro Cys Gly Lys Ile
165 170 175

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

```
Gly Gly Lys Val Cys Pro Lys Gly Glu Cys Pro Trp Gln Val Leu Leu
        195                 200                 205

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

Trp Val Val Ser Ala Ala His Cys Phe Asp Lys Ile Lys Asn Trp Arg
225                 230                 235                 240

Asn Leu Ile Ala Val Leu Gly Glu His Asp Leu Ser Glu His Asp Gly
                245                 250                 255

Asp Glu Gln Ser Arg Arg Val Ala Gln Val Ile Ile Pro Ser Thr Tyr
            260                 265                 270

Val Pro Gly Thr Thr Asn His Asp Ile Ala Leu Leu Arg Leu His Gln
        275                 280                 285

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

Thr Phe Ser Glu Arg Thr Leu Ala Phe Val Arg Phe Ser Leu Val Ser
305                 310                 315                 320

Gly Trp Gly Gln Leu Leu Asp Arg Gly Ala Thr Ala Leu Glu Leu Met
                325                 330                 335

Val Leu Asn Val Pro Arg Leu Met Thr Gln Asp Cys Leu Gln Gln Ser
            340                 345                 350

Arg Lys Val Gly Asp Ser Pro Asn Ile Thr Glu Tyr Met Phe Cys Ala
        355                 360                 365

Gly Tyr Ser Asp Gly Ser Lys Asp Ser Cys Lys Gly Asp Ser Gly Gly
    370                 375                 380

Pro His Ala Thr His Tyr Arg Gly Thr Trp Tyr Leu Thr Gly Ile Val
385                 390                 395                 400

Ser Trp Gly Gln Gly Cys Ala Thr Val Gly His Phe Gly Val Tyr Thr
                405                 410                 415

Arg Val Ser Gln Tyr Ile Glu Trp Leu Gln Lys Leu Met Arg Ser Glu
            420                 425                 430
```

Pro Arg Pro Gly Val Leu Leu Arg Ala Pro Phe Pro
435 440

<210> 2963
<211> 272
<212> PRT
<213> Homo sapiens

<400> 2963

Arg Cys Lys Pro Ile Ser Gly His Asn Ser Leu Phe Trp Tyr Arg Gln
1 5 10 15

Thr Met Met Arg Gly Leu Glu Leu Leu Ile Tyr Phe Asn Asn Asn Val
20 25 30

Pro Ile Asp Asp Ser Gly Met Pro Glu Asp Arg Phe Ser Ala Lys Met
35 40 45

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

Asp Ser Ala Val Tyr Phe Cys Ala Ser Ser Phe Ser Thr Cys Ser Ala
65 70 75 80

Asn Tyr Gly Tyr Thr Phe Gly Ser Gly Thr Arg Leu Thr Val Val Glu
85 90 95

Asp Leu Asn Lys Val Phe Pro Pro Glu Val Ala Val Phe Glu Pro Ser
100 105 110

Glu Ala Glu Ile Ser His Thr Gln Lys Ala Thr Leu Val Cys Leu Ala
115 120 125

Thr Gly Phe Phe Pro Asp His Val Glu Leu Ser Trp Trp Val Asn Gly
130 135 140

Lys Glu Val His Ser Gly Val Ser Thr Asp Pro Gln Pro Leu Lys Glu
145 150 155 160

Gln Pro Ala Leu Asn Asp Ser Arg Tyr Cys Leu Ser Ser Arg Leu Arg
165 170 175

Val Ser Ala Thr Phe Trp Gln Asn Pro Arg Asn His Phe Arg Cys Gln
180 185 190

Val Gln Phe Tyr Gly Leu Ser Glu Asn Asp Glu Trp Thr Gln Asp Arg

195 200 205

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

Asp Cys Gly Phe Thr Ser Val Ser Tyr Gln Gln Gly Val Leu Ser Ala
225 230 235 240

Thr Ile Leu Tyr Glu Ile Leu Leu Gly Lys Ala Thr Leu Tyr Ala Val
245 250 255

Leu Val Ser Ala Leu Val Leu Met Ala Met Val Lys Arg Lys Asp Phe
260 265 270

<210> 2964
<211> 276
<212> PRT
<213> Homo sapiens

<400> 2964

Met Tyr Arg Ile Ser Gln Leu Met Ser Thr Pro Val Ala Ser Ser Ser
1 5 10 15

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

Pro Ser Phe Thr Cys Asp Ser Leu Asp Gly Tyr His Ser Phe Glu Cys
35 40 45

Gly Ser Ile Asp Pro Leu Thr Gly Ser His Tyr Thr Cys Arg Arg Ser
50 55 60

Pro Arg Leu Leu Thr Asn Gly Tyr Tyr Ile Trp Thr Glu Asp Ser Phe
65 70 75 80

Leu Cys Asp Lys Asp Gly Asn Ile Thr Leu Asn Pro Ser Gln Thr Ser
85 90 95

Val Met Tyr Lys Glu Asn Leu Val Ser Thr Ser Lys Ser Trp Leu His
100 105 110

Gly Ser Ile Phe Gly Asp Ile Asn Ser Ser Pro Ser Glu Asp Asn Trp
115 120 125

Leu Lys Gly Thr Arg Arg Leu Asp Thr Asp His Cys Asn Gly Asn Ala
130 135 140

```
Asp Asp Leu Asp Cys Ser Ser Leu Thr Asp Asp Trp Glu Ser Gly Lys
145                 150                 155                 160

Met Asn Ala Glu Ser Val Ile Thr Ser Ser Ser Ser His Ile Ile Ser
                165                 170                 175

Gln Pro Pro Gly Gly Asn Ser His Ser Leu Ser Leu Gln Ser Gln Leu
            180                 185                 190

Thr Ala Ser Glu Arg Phe Gln Glu Asn Ser Ser Asp His Ser Glu Thr
        195                 200                 205

Arg Leu Leu Gln Glu Val Phe Phe Gln Ala Ile Leu Leu Ala Val Cys
    210                 215                 220

Leu Ile Thr Ser Ala Cys Ala Arg Trp Phe Met Gly Glu Ile Leu Ala
225                 230                 235                 240

Ser Val Phe Thr Cys Ser Leu Met Ile Thr Val Ala Tyr Val Lys Ser
                245                 250                 255

Leu Phe Leu Ser Leu Ala Ser Tyr Phe Lys Thr Thr Ala Cys Ala Arg
            260                 265                 270

Phe Val Lys Ile
        275
```

<210> 2965
<211> 133
<212> PRT
<213> Homo sapiens

<400> 2965

```
Met Val Leu Gln Thr Gln Val Phe Ile Ser Leu Leu Leu Trp Ile Ser
1               5                   10                  15

Gly Ala Tyr Gly Asp Ile Val Met Thr Gln Ser Pro Asp Ser Leu Ala
            20                  25                  30

Val Ser Leu Gly Glu Arg Ala Thr Ile Asn Cys Lys Ser Ser Gln Ser
        35                  40                  45

Val Leu Tyr Ser Ser Asn Asn Lys Asn Tyr Leu Ala Trp Tyr Gln Gln
    50                  55                  60

Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg
```

65 70 75 80

Glu Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
85 90 95

Phe Thr Leu Thr Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr
100 105 110

Tyr Cys Gln Gln Tyr Asp Thr Ile Pro Thr Phe Gly Gly Gly Thr Lys
115 120 125

Val Glu Ile Lys Arg
130

<210> 2966
<211> 369
<212> PRT
<213> Homo sapiens

<400> 2966

Met Leu Lys Pro Ser Leu Pro Phe Thr Ser Leu Leu Phe Leu Gln Leu
1 5 10 15

Pro Leu Leu Gly Val Gly Leu Asn Thr Thr Ile Leu Thr Pro Asn Gly
20 25 30

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

Ser Leu Ser Val Ser Thr Leu Pro Leu Pro Glu Val Gln Cys Phe Val
50 55 60

Phe Asn Val Glu Tyr Met Asn Cys Thr Trp Asn Ser Ser Ser Glu Pro
65 70 75 80

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

Asp Lys Val Gln Lys Cys Ser His Tyr Leu Phe Ser Glu Glu Ile Thr
100 105 110

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

Val Val Gln Leu Gln Asp Pro Arg Glu Pro Arg Arg Gln Ala Thr Gln
130 135 140

Met Leu Lys Leu Gln Asn Leu Val Ile Pro Trp Ala Pro Glu Asn Leu
145 150 155 160

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

Arg Phe Leu Asn His Cys Leu Glu His Leu Val Gln Tyr Arg Thr Asp
180 185 190

Trp Asp His Ser Trp Thr Glu Gln Ser Val Asp Tyr Arg His Lys Phe
195 200 205

Ser Leu Pro Ser Val Asp Gly Gln Lys Arg Tyr Thr Phe Arg Val Arg
210 215 220

Ser Arg Phe Asn Pro Leu Cys Gly Ser Ala Gln His Trp Ser Glu Trp
225 230 235 240

Ser His Pro Ile His Trp Gly Ser Asn Thr Ser Lys Glu Asn Pro Phe
245 250 255

Leu Phe Ala Leu Glu Ala Val Val Ile Ser Val Gly Ser Met Gly Leu
260 265 270

Ile Ile Ser Leu Leu Cys Val Tyr Phe Trp Leu Glu Arg Thr Met Pro
275 280 285

Arg Ile Pro Thr Leu Lys Asn Leu Glu Asp Leu Val Thr Glu Tyr His
290 295 300

Gly Asn Phe Ser Ala Trp Ser Gly Val Ser Lys Gly Leu Ala Glu Ser
305 310 315 320

Leu Gln Pro Asp Tyr Ser Glu Arg Leu Cys Leu Val Ser Glu Ile Pro
325 330 335

Pro Lys Gly Gly Ala Leu Gly Glu Gly Pro Gly Ala Ser Pro Cys Asn
340 345 350

Gln His Ser Pro Tyr Trp Ala Pro Pro Cys Tyr Thr Leu Lys Pro Glu
355 360 365

Thr

<210> 2967
<211> 323
<212> PRT
<213> Homo sapiens

<400> 2967

```
Met Ala Phe Ser Gly Ser Gln Ala Pro Tyr Leu Ser Pro Ala Val Pro
1               5                  10                  15

Phe Ser Gly Thr Ile Gln Gly Gly Leu Gln Asp Gly Leu Gln Ile Thr
            20                  25                  30

Val Asn Gly Thr Val Leu Ser Ser Ser Gly Thr Arg Phe Ala Val Asn
        35                  40                  45

Phe Gln Thr Gly Phe Ser Gly Asn Asp Ile Ala Phe His Phe Asn Pro
    50                  55                  60

Arg Phe Glu Asp Gly Gly Tyr Val Val Cys Asn Thr Arg Gln Asn Gly
65                  70                  75                  80

Ser Trp Gly Pro Glu Glu Arg Arg Thr His Met Pro Phe Gln Lys Gly
                85                  90                  95

Met Pro Phe Asp Leu Cys Phe Leu Val Gln Ser Ser Asp Phe Lys Val
            100                 105                 110

Met Val Asn Gly Ile Leu Phe Val Gln Tyr Phe His Arg Val Pro Phe
        115                 120                 125

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

Ile Ser Phe Gln Pro Pro Gly Val Trp Pro Ala Asn Pro Ala Pro Ile
145                 150                 155                 160

Thr Gln Thr Val Ile His Thr Val Gln Ser Ala Pro Gly Gln Met Phe
                165                 170                 175

Ser Thr Pro Ala Ile Pro Pro Met Met Tyr Pro His Pro Ala Tyr Pro
            180                 185                 190

Met Pro Phe Ile Thr Thr Ile Leu Gly Gly Leu Tyr Pro Ser Lys Ser
        195                 200                 205

Ile Leu Leu Ser Gly Thr Val Leu Pro Ser Ala Gln Arg Phe His Ile
    210                 215                 220
```

Asn Leu Cys Ser Gly Asn His Ile Ala Phe His Leu Asn Leu Arg Phe
225 230 235 240

Asp Glu Asn Ala Val Val Arg Asn Thr Gln Ile Asp Asn Ser Trp Gly
245 250 255

Ser Glu Glu Arg Ser Leu Pro Arg Lys Met Pro Phe Val Arg Gly Gln
260 265 270

Ser Phe Ser Val Trp Ile Leu Cys Gly Ala His Cys Leu Lys Val Ala
275 280 285

Val Asp Gly Gln His Leu Phe Glu Tyr Tyr His Arg Leu Arg Asn Leu
290 295 300

Pro Thr Ile Asn Arg Leu Glu Val Gly Gly Asp Ile Gln Leu Thr His
305 310 315 320

Val Gln Thr

<210> 2968
<211> 1866
<212> PRT
<213> Homo sapiens

<400> 2968

Met Asp Pro Val Gly Leu Gln Leu Gly Asn Lys Asn Leu Trp Ser Cys
1 5 10 15

Leu Val Arg Leu Leu Thr Lys Asp Pro Glu Trp Leu Asn Ala Lys Met
20 25 30

Lys Phe Phe Leu Pro Asn Thr Asp Leu Asp Ser Arg Asn Glu Thr Leu
35 40 45

Asp Pro Glu Gln Arg Val Ile Leu Gln Leu Asn Lys Leu His Val Gln
50 55 60

Gly Ser Asp Thr Trp Gln Ser Phe Ile His Cys Val Cys Met Gln Leu
65 70 75 80

Glu Val Pro Leu Asp Leu Glu Val Leu Leu Leu Ser Thr Phe Gly Tyr
85 90 95

```
Asp Asp Gly Phe Thr Ser Gln Leu Gly Ala Glu Gly Lys Ser Gln Pro
            100                 105                 110

Glu Ser Gln Leu His His Gly Leu Lys Arg Pro His Gln Ser Cys Gly
        115                 120                 125

Ser Ser Pro Arg Arg Lys Gln Cys Lys Lys Gln Gln Leu Glu Leu Ala
    130                 135                 140

Lys Lys Tyr Leu Gln Leu Leu Arg Thr Ser Ala Gln Gln Arg Tyr Arg
145                 150                 155                 160

Ser Gln Ile Pro Gly Ser Gly Gln Pro His Ala Phe His Gln Val Tyr
                165                 170                 175

Val Pro Pro Ile Leu Arg Arg Ala Thr Ala Ser Leu Asp Thr Pro Glu
            180                 185                 190

Gly Ala Ile Met Gly Asp Val Lys Val Glu Asp Gly Ala Asp Val Ser
        195                 200                 205

Ile Ser Asp Leu Phe Asn Thr Arg Val Asn Lys Gly Pro Arg Val Thr
    210                 215                 220

Val Leu Leu Gly Lys Ala Gly Met Gly Lys Thr Thr Leu Ala His Arg
225                 230                 235                 240

Leu Cys Gln Lys Trp Ala Glu Gly His Leu Asn Cys Phe Gln Ala Leu
                245                 250                 255

Phe Leu Phe Glu Phe Arg Gln Leu Asn Leu Ile Thr Arg Phe Leu Thr
            260                 265                 270

Pro Ser Glu Leu Leu Phe Asp Leu Tyr Leu Ser Pro Glu Ser Asp His
        275                 280                 285

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

Ile Phe Asp Gly Leu Asp Glu Ala Leu Gln Pro Met Gly Pro Asp Gly
305                 310                 315                 320

Pro Gly Pro Val Leu Thr Leu Phe Ser His Leu Cys Asn Gly Thr Leu
                325                 330                 335

Leu Pro Gly Cys Arg Val Met Ala Thr Ser Arg Pro Gly Lys Leu Pro
```

```
            340                 345                 350

Ala Cys Leu Pro Ala Glu Ala Ala Met Val His Met Leu Gly Phe Asp
        355                 360                 365

Gly Pro Arg Val Glu Glu Tyr Val Asn His Phe Phe Ser Ala Gln Pro
    370                 375                 380

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

Ser Leu Cys Ala Val Pro Ala Leu Cys Gln Val Ala Cys Leu Cys Leu
                405                 410                 415

His His Leu Leu Pro Asp His Ala Pro Gly Gln Ser Val Ala Leu Leu
            420                 425                 430

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

Pro Gly His Leu Pro Thr Ser Ser Leu Leu Asp Leu Gly Glu Val Ala
    450                 455                 460

Leu Arg Gly Leu Glu Thr Gly Lys Val Ile Phe Tyr Ala Lys Asp Ile
465                 470                 475                 480

Ala Pro Pro Leu Ile Ala Phe Gly Ala Thr His Ser Leu Leu Thr Ser
                485                 490                 495

Phe Cys Val Cys Thr Gly Pro Gly His Gln Gln Thr Gly Tyr Ala Phe
            500                 505                 510

Thr His Leu Ser Leu Gln Glu Phe Leu Ala Ala Leu His Leu Met Ala
        515                 520                 525

Ser Pro Lys Val Asn Lys Asp Thr Leu Thr Gln Tyr Val Thr Leu His
    530                 535                 540

Ser Arg Trp Val Gln Arg Thr Lys Ala Arg Leu Gly Leu Ser Asp His
545                 550                 555                 560

Leu Pro Thr Phe Leu Ala Gly Leu Ala Ser Cys Thr Cys Arg Pro Phe
                565                 570                 575

Leu Ser His Leu Ala Gln Gly Asn Glu Asp Cys Val Gly Ala Lys Gln
            580                 585                 590
```

Ala Ala Val Val Gln Val Leu Lys Lys Leu Ala Thr Arg Lys Leu Thr
595 600 605

Gly Pro Lys Val Val Glu Leu Cys His Cys Val Asp Glu Thr Gln Glu
610 615 620

Pro Glu Leu Ala Ser Leu Thr Ala Gln Ser Leu Pro Tyr Gln Leu Pro
625 630 635 640

Phe His Asn Phe Pro Leu Thr Cys Thr Asp Leu Ala Thr Leu Thr Asn
645 650 655

Ile Leu Glu His Arg Glu Ala Pro Ile His Leu Asp Phe Asp Gly Cys
660 665 670

Pro Leu Glu Pro His Cys Pro Glu Ala Leu Val Gly Cys Gly Gln Ile
675 680 685

Glu Asn Leu Ser Phe Lys Ser Arg Lys Cys Gly Asp Ala Phe Ala Glu
690 695 700

Ala Leu Ser Arg Ser Leu Pro Thr Met Gly Arg Leu Gln Met Leu Gly
705 710 715 720

Leu Ala Gly Ser Lys Ile Thr Ala Arg Gly Ile Ser His Leu Val Lys
725 730 735

Ala Leu Pro Leu Cys Pro Gln Leu Lys Glu Val Ser Phe Arg Asp Asn
740 745 750

Gln Leu Ser Asp Gln Val Val Leu Asn Ile Val Glu Val Leu Pro His
755 760 765

Leu Pro Arg Leu Arg Lys Leu Asp Leu Ser Ser Asn Ser Ile Cys Val
770 775 780

Ser Thr Leu Leu Cys Leu Ala Arg Val Ala Val Thr Cys Pro Thr Val
785 790 795 800

Arg Met Leu Gln Ala Arg Glu Arg Thr Ile Ile Phe Leu Leu Ser Pro
805 810 815

Pro Thr Glu Thr Thr Ala Glu Leu Gln Arg Ala Pro Asp Leu Gln Glu
820 825 830

Ser Asp Gly Gln Arg Lys Gly Ala Gln Ser Arg Ser Leu Thr Leu Arg
835 840 845

Leu Gln Lys Cys Gln Leu Gln Val His Asp Ala Glu Ala Leu Ile Ala
850 855 860

Leu Leu Gln Glu Gly Pro His Leu Glu Glu Val Asp Leu Ser Gly Asn
865 870 875 880

Gln Leu Glu Asp Glu Gly Cys Arg Leu Met Ala Glu Ala Ala Ser Gln
885 890 895

Leu His Ile Ala Arg Lys Leu Asp Leu Ser Asp Asn Gly Leu Ser Val
900 905 910

Ala Gly Val His Cys Val Leu Arg Ala Val Ser Ala Cys Trp Thr Leu
915 920 925

Ala Glu Leu His Ile Ser Leu Gln His Lys Thr Val Ile Phe Met Phe
930 935 940

Ala Gln Glu Pro Glu Glu Gln Lys Gly Pro Gln Glu Arg Ala Ala Phe
945 950 955 960

Leu Asp Ser Leu Met Leu Gln Met Pro Ser Glu Leu Pro Leu Ser Ser
965 970 975

Arg Arg Met Arg Leu Thr His Cys Gly Leu Gln Glu Lys His Leu Glu
980 985 990

Gln Leu Cys Lys Ala Leu Gly Gly Ser Cys His Leu Gly His Leu His
995 1000 1005

Leu Asp Phe Ser Gly Asn Ala Leu Gly Asp Glu Gly Ala Ala Arg
1010 1015 1020

Leu Ala Gln Leu Leu Pro Gly Leu Gly Ala Leu Gln Ser Leu Asn
1025 1030 1035

Leu Ser Glu Asn Gly Leu Ser Leu Asp Ala Val Leu Gly Leu Val
1040 1045 1050

Arg Cys Phe Ser Thr Leu Gln Trp Leu Phe Arg Leu Asp Ile Ser
1055 1060 1065

```
Phe Glu  Ser Gln His Ile Leu  Leu Arg Gly Asp Lys  Thr Ser Arg
    1070                 1075                 1080

Asp Met  Trp Ala Thr Gly Ser  Leu Pro Asp Phe Pro  Ala Ala Ala
    1085                 1090                 1095

Lys Phe  Leu Gly Phe Arg Gln  Arg Cys Ile Pro Arg  Ser Leu Cys
    1100                 1105                 1110

Leu Ser  Glu Cys Pro Leu Glu  Pro Pro Ser Leu Thr  Arg Leu Cys
    1115                 1120                 1125

Ala Thr  Leu Lys Asp Cys Pro  Gly Pro Leu Glu Leu  Gln Leu Ser
    1130                 1135                 1140

Cys Glu  Phe Leu Ser Asp Gln  Ser Leu Glu Thr Leu  Leu Asp Cys
    1145                 1150                 1155

Leu Pro  Gln Leu Pro Gln Leu  Ser Leu Leu Gln Leu  Ser Gln Thr
    1160                 1165                 1170

Gly Leu  Ser Pro Lys Ser Pro  Phe Leu Leu Ala Asn  Thr Leu Ser
    1175                 1180                 1185

Leu Cys  Pro Arg Val Lys Lys  Val Asp Leu Arg Ser  Leu His His
    1190                 1195                 1200

Ala Thr  Leu His Phe Arg Ser  Asn Glu Glu Glu Glu  Gly Val Cys
    1205                 1210                 1215

Cys Gly  Arg Phe Thr Gly Cys  Ser Leu Ser Gln Glu  His Val Glu
    1220                 1225                 1230

Ser Leu  Cys Trp Leu Leu Ser  Lys Cys Lys Asp Leu  Ser Gln Val
    1235                 1240                 1245

Asp Leu  Ser Ala Asn Leu Leu  Gly Asp Ser Gly Leu  Arg Cys Leu
    1250                 1255                 1260

Leu Glu  Cys Leu Pro Gln Val  Pro Ile Ser Gly Leu  Leu Asp Leu
    1265                 1270                 1275

Ser His  Asn Ser Ile Ser Gln  Glu Ser Ala Leu Tyr  Leu Leu Glu
    1280                 1285                 1290

Thr Leu  Pro Ser Cys Pro Arg  Val Arg Glu Ala Ser  Val Asn Leu
```

1295 1300 1305

Gly Ser Glu Gln Ser Phe Arg Ile His Phe Ser Arg Glu Asp Gln
1310 1315 1320

Ala Gly Lys Thr Leu Arg Leu Ser Glu Cys Ser Phe Arg Pro Glu
1325 1330 1335

His Val Ser Arg Leu Ala Thr Gly Leu Ser Lys Ser Leu Gln Leu
1340 1345 1350

Thr Glu Leu Thr Leu Thr Gln Cys Cys Leu Gly Gln Lys Gln Leu
1355 1360 1365

Ala Ile Leu Leu Ser Leu Val Gly Arg Pro Ala Gly Leu Phe Ser
1370 1375 1380

Leu Arg Val Gln Glu Pro Trp Ala Asp Arg Ala Arg Val Leu Ser
1385 1390 1395

Leu Leu Glu Val Cys Ala Gln Ala Ser Gly Ser Val Thr Glu Ile
1400 1405 1410

Ser Ile Ser Glu Thr Gln Gln Gln Leu Cys Val Gln Leu Glu Phe
1415 1420 1425

Pro Arg Gln Glu Glu Asn Pro Glu Ala Val Ala Leu Arg Leu Ala
1430 1435 1440

His Cys Asp Leu Gly Ala His His Ser Leu Leu Val Gly Gln Leu
1445 1450 1455

Met Glu Thr Cys Ala Arg Leu Gln Gln Leu Ser Leu Ser Gln Val
1460 1465 1470

Asn Leu Cys Glu Asp Asp Asp Ala Ser Ser Leu Leu Leu Gln Ser
1475 1480 1485

Leu Leu Leu Ser Leu Ser Glu Leu Lys Thr Phe Arg Leu Thr Ser
1490 1495 1500

Ser Cys Val Ser Thr Glu Gly Leu Ala His Leu Ala Ser Gly Leu
1505 1510 1515

Gly His Cys His His Leu Glu Glu Leu Asp Leu Ser Asn Asn Gln
1520 1525 1530

```
Phe Asp  Glu Glu Gly Thr Lys  Ala Leu Met Arg Ala  Leu Glu Gly
    1535                 1540                 1545

Lys Trp  Met Leu Lys Arg Leu  Asp Leu Ser His Leu  Leu Leu Asn
    1550                 1555                 1560

Ser Ser  Thr Leu Ala Leu Leu  Thr His Arg Leu Ser  Gln Met Thr
    1565                 1570                 1575

Cys Leu  Gln Ser Leu Arg Leu  Asn Arg Asn Ser Ile  Gly Asp Val
    1580                 1585                 1590

Gly Cys  Cys His Leu Ser Glu  Ala Leu Arg Ala Ala  Thr Ser Leu
    1595                 1600                 1605

Glu Glu  Leu Asp Leu Ser His  Asn Gln Ile Gly Asp  Ala Gly Val
    1610                 1615                 1620

Gln His  Leu Ala Thr Ile Leu  Pro Gly Leu Pro Glu  Leu Arg Lys
    1625                 1630                 1635

Ile Asp  Leu Ser Gly Asn Ser  Ile Ser Ser Ala Gly  Gly Val Gln
    1640                 1645                 1650

Leu Ala  Glu Ser Leu Val Leu  Cys Arg Arg Leu Glu  Glu Leu Met
    1655                 1660                 1665

Leu Gly  Cys Asn Ala Leu Gly  Asp Pro Thr Ala Leu  Gly Leu Ala
    1670                 1675                 1680

Gln Glu  Leu Pro Gln His Leu  Arg Val Leu His Leu  Pro Phe Ser
    1685                 1690                 1695

His Leu  Gly Pro Gly Gly Ala  Leu Ser Leu Ala Gln  Ala Leu Asp
    1700                 1705                 1710

Gly Ser  Pro His Leu Glu Glu  Ile Ser Leu Ala Glu  Asn Asn Leu
    1715                 1720                 1725

Ala Gly  Gly Val Leu Arg Phe  Cys Met Glu Leu Pro  Leu Leu Arg
    1730                 1735                 1740

Gln Ile  Asp Leu Val Ser Cys  Lys Ile Asp Asn Gln  Thr Ala Lys
    1745                 1750                 1755
```

```
Leu Leu  Thr Ser Ser Phe Thr  Ser Cys Pro Ala Leu  Glu Val Ile
    1760                 1765                 1770

Leu Leu  Ser Trp Asn Leu Leu  Gly Asp Glu Ala Ala  Ala Glu Leu
    1775                 1780                 1785

Ala Gln  Val Leu Pro Lys Met  Gly Arg Leu Lys Arg  Val Asp Leu
    1790                 1795                 1800

Glu Lys  Asn Gln Ile Thr Ala  Leu Gly Ala Trp Leu  Leu Ala Glu
    1805                 1810                 1815

Gly Leu  Ala Gln Gly Ser Ser  Ile Gln Val Ile Arg  Leu Trp Asn
    1820                 1825                 1830

Asn Pro  Ile Pro Cys Asp Met  Ala Gln His Leu Lys  Ser Gln Glu
    1835                 1840                 1845

Pro Arg  Leu Asp Phe Ala Phe  Phe Asp Asn Gln Pro  Gln Ala Pro
    1850                 1855                 1860

Trp Gly  Thr
    1865
```

<210> 2969
<211> 547
<212> PRT
<213> Homo sapiens

<400> 2969

```
Met Ala Thr Met Val Pro Ser Val Leu Trp Pro Arg Ala Cys Trp Thr
1               5                  10                  15

Leu Leu Val Cys Cys Leu Leu Thr Pro Gly Val Gln Gly Gln Glu Phe
            20                  25                  30

Leu Leu Arg Val Glu Pro Gln Asn Pro Val Leu Ser Ala Gly Gly Ser
        35                  40                  45

Leu Phe Val Asn Cys Ser Thr Asp Cys Pro Ser Ser Glu Lys Ile Ala
    50                  55                  60

Leu Glu Thr Ser Leu Ser Lys Glu Leu Val Ala Ser Gly Met Gly Trp
65                  70                  75                  80

Ala Ala Phe Asn Leu Ser Asn Val Thr Gly Asn Ser Arg Ile Leu Cys
```

85 90 95

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

Val Tyr Gly Leu Pro Glu Arg Val Glu Leu Ala Pro Leu Pro Pro Trp
115 120 125

Gln Pro Val Gly Gln Asn Phe Thr Leu Arg Cys Gln Val Glu Gly Gly
130 135 140

Ser Pro Arg Thr Ser Leu Thr Val Val Leu Leu Arg Trp Glu Glu Glu
145 150 155 160

Leu Ser Arg Gln Pro Ala Val Glu Glu Pro Ala Glu Val Thr Ala Thr
165 170 175

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

Glu Leu Asp Met Gln Pro Gln Gly Leu Gly Leu Phe Val Asn Thr Ser
195 200 205

Ala Pro Arg Gln Leu Arg Thr Phe Val Leu Pro Val Thr Pro Pro Arg
210 215 220

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

Cys Thr Leu Asp Gly Leu Phe Pro Ala Ser Glu Ala Gln Val Tyr Leu
245 250 255

Ala Leu Gly Asp Gln Met Leu Asn Ala Thr Val Met Asn His Gly Asp
260 265 270

Thr Leu Thr Ala Thr Ala Thr Ala Thr Ala Arg Ala Asp Gln Glu Gly
275 280 285

Ala Arg Glu Ile Val Cys Asn Val Thr Leu Gly Gly Glu Arg Arg Glu
290 295 300

Ala Arg Glu Asn Leu Thr Val Phe Ser Phe Leu Gly Pro Ile Val Asn
305 310 315 320

Leu Ser Glu Pro Thr Ala His Glu Gly Ser Thr Val Thr Val Ser Cys
325 330 335

```
Met Ala Gly Ala Arg Val Gln Val Thr Leu Asp Gly Val Pro Ala Ala
            340                 345                 350

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

Asp Gly Arg Ser Phe Phe Cys Ser Ala Thr Leu Glu Val Asp Gly Glu
    370                 375                 380

Phe Leu His Arg Asn Ser Ser Val Gln Leu Arg Val Leu Tyr Gly Pro
385                 390                 395                 400

Lys Ile Asp Arg Ala Thr Cys Pro Gln His Leu Lys Trp Lys Asp Lys
                405                 410                 415

Thr Arg His Val Leu Gln Cys Gln Ala Arg Gly Asn Pro Tyr Pro Glu
            420                 425                 430

Leu Arg Cys Leu Lys Glu Gly Ser Ser Arg Glu Val Pro Val Gly Ile
        435                 440                 445

Pro Phe Phe Val Asn Val Thr His Asn Gly Thr Tyr Gln Cys Gln Ala
    450                 455                 460

Ser Ser Ser Arg Gly Lys Tyr Thr Leu Val Val Val Met Asp Ile Glu
465                 470                 475                 480

Ala Gly Ser Ser His Phe Val Pro Val Phe Val Ala Val Leu Leu Thr
                485                 490                 495

Leu Gly Val Val Thr Ile Val Leu Ala Leu Met Tyr Val Phe Arg Glu
            500                 505                 510

His Gln Arg Ser Gly Ser Tyr His Val Arg Glu Glu Ser Thr Tyr Leu
        515                 520                 525

Pro Leu Thr Ser Met Gln Pro Thr Glu Ala Met Gly Glu Glu Pro Ser
    530                 535                 540

Arg Ala Glu
545
```

<210> 2970
<211> 260
<212> PRT

<213> Homo sapiens

<400> 2970

Met Arg Pro Glu Asp Arg Met Phe His Ile Arg Ala Val Ile Leu Arg
1 5 10 15

Ala Leu Ser Leu Ala Phe Leu Leu Ser Leu Arg Gly Ala Gly Ala Ile
20 25 30

Lys Ala Asp His Val Ser Thr Tyr Ala Ala Phe Val Gln Thr His Arg
35 40 45

Pro Thr Gly Glu Phe Met Phe Glu Phe Asp Glu Asp Glu Met Phe Tyr
50 55 60

Val Asp Leu Asp Lys Lys Glu Thr Val Trp His Leu Glu Glu Phe Gly
65 70 75 80

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

Leu Asn Asn Asn Leu Asn Thr Leu Ile Gln Arg Ser Asn His Thr Gln
100 105 110

Ala Thr Asn Asp Pro Pro Glu Val Thr Val Phe Pro Lys Glu Pro Val
115 120 125

Glu Leu Gly Gln Pro Asn Thr Leu Ile Cys His Ile Asp Lys Phe Phe
130 135 140

Pro Pro Val Leu Asn Val Thr Trp Leu Cys Asn Gly Glu Leu Val Thr
145 150 155 160

Glu Gly Val Ala Glu Ser Leu Phe Leu Pro Arg Thr Asp Tyr Ser Phe
165 170 175

His Lys Phe His Tyr Leu Thr Phe Val Pro Ser Ala Glu Asp Phe Tyr
180 185 190

Asp Cys Arg Val Glu His Trp Gly Leu Asp Gln Pro Leu Leu Lys His
195 200 205

Trp Glu Ala Gln Glu Pro Ile Gln Met Pro Glu Thr Thr Glu Thr Val
210 215 220

Leu Cys Ala Leu Gly Leu Val Leu Gly Leu Val Gly Ile Ile Val Gly

225 230 235 240

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

Gln Gly Thr Leu
260

<210> 2971
<211> 495
<212> PRT
<213> Homo sapiens

<400> 2971

Met Pro Met Gly Ser Leu Gln Pro Leu Ala Thr Leu Tyr Leu Leu Gly
1 5 10 15

Met Leu Val Ala Ser Cys Leu Gly Arg Leu Ser Trp Tyr Asp Pro Asp
20 25 30

Phe Gln Ala Arg Leu Thr Arg Ser Asn Ser Lys Cys Gln Gly Gln Leu
35 40 45

Glu Val Tyr Leu Lys Asp Gly Trp His Met Val Cys Ser Gln Ser Trp
50 55 60

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

Cys Gln Arg Leu Asn Cys Gly Val Pro Leu Ser Leu Gly Pro Phe Leu
85 90 95

Val Thr Tyr Thr Pro Gln Ser Ser Ile Ile Cys Tyr Gly Gln Leu Gly
100 105 110

Ser Phe Ser Asn Cys Ser His Ser Arg Asn Asp Met Cys His Ser Leu
115 120 125

Gly Leu Thr Cys Leu Glu Pro Gln Lys Thr Thr Pro Pro Thr Thr Arg
130 135 140

Pro Pro Pro Thr Thr Thr Pro Glu Pro Thr Ala Pro Pro Arg Leu Gln
145 150 155 160

Leu Val Ala Gln Ser Gly Gly Gln His Cys Ala Gly Val Val Glu Phe
165 170 175

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

Thr Gln Asp Leu Glu Asn Phe Leu Cys Asn Asn Leu Gln Cys Gly Ser
195 200 205

Phe Leu Lys His Leu Pro Glu Thr Glu Ala Gly Arg Ala Gln Asp Pro
210 215 220

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

Asn Ser Ser Cys Thr Ser Leu Glu His Cys Phe Arg Lys Ile Lys Pro
245 250 255

Gln Lys Ser Gly Arg Val Leu Ala Leu Leu Cys Ser Gly Phe Gln Pro
260 265 270

Lys Val Gln Ser Arg Leu Val Gly Gly Ser Ser Ile Cys Glu Gly Thr
275 280 285

Val Glu Val Arg Gln Gly Ala Gln Trp Ala Ala Leu Cys Asp Ser Ser
290 295 300

Ser Ala Arg Ser Ser Leu Arg Trp Glu Glu Val Cys Arg Glu Gln Gln
305 310 315 320

Cys Gly Ser Val Asn Ser Tyr Arg Val Leu Asp Ala Gly Asp Pro Thr
325 330 335

Ser Arg Gly Leu Phe Cys Pro His Gln Lys Leu Ser Gln Cys His Glu
340 345 350

Leu Trp Glu Arg Asn Ser Tyr Cys Lys Lys Val Phe Val Thr Cys Gln
355 360 365

Asp Pro Asn Pro Ala Gly Leu Ala Ala Gly Thr Val Ala Ser Ile Ile
370 375 380

Leu Ala Leu Val Leu Leu Val Val Leu Leu Val Val Cys Gly Pro Leu
385 390 395 400

Ala Tyr Lys Lys Leu Val Lys Lys Phe Arg Gln Lys Lys Gln Arg Gln
405 410 415

```
Trp Ile Gly Pro Thr Gly Met Asn Gln Asn Met Ser Phe His Arg Asn
            420                 425                 430

His Thr Ala Thr Val Arg Ser His Ala Glu Asn Pro Thr Ala Ser His
        435                 440                 445

Val Asp Asn Glu Tyr Ser Gln Pro Pro Arg Asn Ser Arg Leu Ser Ala
    450                 455                 460

Tyr Pro Ala Leu Glu Gly Val Leu His Arg Ser Ser Met Gln Pro Asp
465                 470                 475                 480

Asn Ser Ser Asp Ser Asp Tyr Asp Leu His Gly Ala Gln Arg Leu
                485                 490                 495
```

<210> 2972
<211> 130
<212> PRT
<213> Homo sapiens

<400> 2972

```
Lys Val Phe Glu Arg Cys Glu Leu Ala Arg Thr Leu Lys Arg Leu Gly
1               5                   10                  15

Met Asp Gly Tyr Arg Gly Ile Ser Leu Ala Asn Trp Met Cys Leu Ala
            20                  25                  30

Lys Trp Glu Ser Gly Tyr Asn Thr Arg Ala Thr Asn Tyr Asn Ala Gly
        35                  40                  45

Asp Arg Ser Thr Asp Tyr Gly Ile Phe Gln Ile Asn Ser Arg Tyr Trp
    50                  55                  60

Cys Asn Asp Gly Lys Thr Pro Gly Ala Val Asn Ala Cys His Leu Ser
65                  70                  75                  80

Cys Ser Ala Leu Leu Gln Asp Asn Ile Ala Asp Ala Val Ala Cys Ala
                85                  90                  95

Lys Arg Val Val Arg Asp Pro Gln Gly Ile Arg Ala Trp Val Ala Trp
            100                 105                 110

Arg Asn Arg Cys Gln Asn Arg Asp Val Arg Gln Tyr Val Gln Gly Cys
        115                 120                 125

Gly Val
    130
```

<210> 2973
<211> 491
<212> PRT
<213> Homo sapiens

<400> 2973

Met Asn Pro Ala Ala Glu Ala Glu Phe Asn Ile Leu Leu Ala Thr Asp
1 5 10 15

Ser Tyr Lys Val Thr His Tyr Lys Gln Tyr Pro Pro Asn Thr Ser Lys
20 25 30

Val Tyr Ser Tyr Phe Glu Cys Arg Glu Lys Lys Thr Glu Asn Ser Lys
35 40 45

Leu Arg Lys Val Lys Tyr Glu Glu Thr Val Phe Tyr Gly Leu Gln Tyr
50 55 60

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

Gln Glu Ala Lys Asp Val Tyr Lys Glu His Phe Gln Asp Asp Val Phe
85 90 95

Asn Glu Lys Gly Trp Asn Tyr Ile Leu Glu Lys Tyr Asp Gly His Leu
100 105 110

Pro Ile Glu Ile Lys Ala Val Pro Glu Gly Phe Val Ile Pro Arg Gly
115 120 125

Asn Val Leu Phe Thr Val Glu Asn Thr Asp Pro Glu Cys Tyr Trp Leu
130 135 140

Thr Asn Trp Ile Glu Thr Ile Leu Val Gln Ser Trp Tyr Pro Ile Thr
145 150 155 160

Val Ala Thr Asn Ser Arg Glu Gln Lys Lys Ile Leu Ala Lys Tyr Leu
165 170 175

Leu Glu Thr Ser Gly Asn Leu Asp Gly Leu Glu Tyr Lys Leu His Asp
180 185 190

Phe Gly Tyr Arg Gly Val Ser Ser Gln Glu Thr Ala Gly Ile Gly Ala
195 200 205

```
Ser Ala His Leu Val Asn Phe Lys Gly Thr Asp Thr Val Ala Gly Leu
    210                 215                 220

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

Ser Val Pro Ala Ala Glu His Ser Thr Ile Thr Ala Trp Gly Lys Asp
                245                 250                 255

His Glu Lys Asp Ala Phe Glu His Ile Val Thr Gln Phe Ser Ser Val
            260                 265                 270

Pro Val Ser Val Val Ser Asp Ser Tyr Asp Ile Tyr Asn Ala Cys Glu
        275                 280                 285

Lys Ile Trp Gly Glu Asp Leu Arg His Leu Ile Val Ser Arg Ser Thr
    290                 295                 300

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

Val Leu Lys Val Leu Glu Ile Leu Gly Lys Lys Phe Pro Val Thr Glu
                325                 330                 335

Asn Ser Lys Gly Tyr Lys Leu Leu Pro Pro Tyr Leu Arg Val Ile Gln
            340                 345                 350

Gly Asp Gly Val Asp Ile Asn Thr Leu Gln Glu Ile Val Glu Gly Met
        355                 360                 365

Lys Gln Lys Met Trp Ser Ile Glu Asn Ile Ala Phe Gly Ser Gly Gly
    370                 375                 380

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

Cys Ser Tyr Val Val Thr Asn Gly Leu Gly Ile Asn Val Phe Lys Asp
                405                 410                 415

Pro Val Ala Asp Pro Asn Lys Arg Ser Lys Lys Gly Arg Leu Ser Leu
            420                 425                 430

His Arg Thr Pro Ala Gly Asn Phe Val Thr Leu Glu Glu Gly Lys Gly
        435                 440                 445

Asp Leu Glu Glu Tyr Gly Gln Asp Leu Leu His Thr Val Phe Lys Asn
```

450 455 460

Gly Lys Val Thr Lys Ser Tyr Ser Phe Asp Glu Ile Arg Lys Asn Ala
465 470 475 480

Gln Leu Asn Ile Glu Leu Glu Ala Ala His His
485 490

<210> 2974
<211> 862
<212> PRT
<213> Homo sapiens

<400> 2974

Met Glu Arg Ala Glu Ser Ser Ser Thr Glu Pro Ala Lys Ala Ile Lys
1 5 10 15

Pro Ile Asp Arg Lys Ser Val His Gln Ile Cys Ser Gly Gln Val Val
20 25 30

Leu Ser Leu Ser Thr Ala Val Lys Glu Leu Val Glu Asn Ser Leu Asp
35 40 45

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

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

Glu Gly Leu Thr Leu Lys His His Thr Ser Lys Ile Gln Glu Phe Ala
85 90 95

Asp Leu Thr Gln Val Glu Thr Phe Gly Phe Arg Gly Glu Ala Leu Ser
100 105 110

Ser Leu Cys Ala Leu Ser Asp Val Thr Ile Ser Thr Cys His Ala Ser
115 120 125

Ala Lys Val Gly Thr Arg Leu Met Phe Asp His Asn Gly Lys Ile Ile
130 135 140

Gln Lys Thr Pro Tyr Pro Arg Pro Arg Gly Thr Thr Val Ser Val Gln
145 150 155 160

Gln Leu Phe Ser Thr Leu Pro Val Arg His Lys Glu Phe Gln Arg Asn
165 170 175

Ile Lys Lys Glu Tyr Ala Lys Met Val Gln Val Leu His Ala Tyr Cys
180 185 190

Ile Ile Ser Ala Gly Ile Arg Val Ser Cys Thr Asn Gln Leu Gly Gln
195 200 205

Gly Lys Arg Gln Pro Val Val Cys Thr Gly Gly Ser Pro Ser Ile Lys
210 215 220

Glu Asn Ile Gly Ser Val Phe Gly Gln Lys Gln Leu Gln Ser Leu Ile
225 230 235 240

Pro Phe Val Gln Leu Pro Pro Ser Asp Ser Val Cys Glu Glu Tyr Gly
245 250 255

Leu Ser Cys Ser Asp Ala Leu His Asn Leu Phe Tyr Ile Ser Gly Phe
260 265 270

Ile Ser Gln Cys Thr His Gly Val Gly Arg Ser Ser Thr Asp Arg Gln
275 280 285

Phe Phe Phe Ile Asn Arg Arg Pro Cys Asp Pro Ala Lys Val Cys Arg
290 295 300

Leu Val Asn Glu Val Tyr His Met Tyr Asn Arg His Gln Tyr Pro Phe
305 310 315 320

Val Val Leu Asn Ile Ser Val Asp Ser Glu Cys Val Asp Ile Asn Val
325 330 335

Thr Pro Asp Lys Arg Gln Ile Leu Leu Gln Glu Glu Lys Leu Leu Leu
340 345 350

Ala Val Leu Lys Thr Ser Leu Ile Gly Met Phe Asp Ser Asp Val Asn
355 360 365

Lys Leu Asn Val Ser Gln Gln Pro Leu Leu Asp Val Glu Gly Asn Leu
370 375 380

Ile Lys Met His Ala Ala Asp Leu Glu Lys Pro Met Val Glu Lys Gln
385 390 395 400

Asp Gln Ser Pro Ser Leu Arg Thr Gly Glu Glu Lys Lys Asp Val Ser
405 410 415

```
Ile Ser Arg Leu Arg Glu Ala Phe Ser Leu Arg His Thr Thr Glu Asn
            420                 425                 430

Lys Pro His Ser Pro Lys Thr Pro Glu Pro Arg Arg Ser Pro Leu Gly
        435                 440                 445

Gln Lys Arg Gly Met Leu Ser Ser Ser Thr Ser Gly Ala Ile Ser Asp
    450                 455                 460

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

Pro Ser Asp Pro Thr Asp Arg Ala Glu Val Glu Lys Asp Ser Gly His
                485                 490                 495

Gly Ser Thr Ser Val Asp Ser Glu Gly Phe Ser Ile Pro Asp Thr Gly
            500                 505                 510

Ser His Cys Ser Ser Glu Tyr Ala Ala Ser Ser Pro Gly Asp Arg Gly
        515                 520                 525

Ser Gln Glu His Val Asp Ser Gln Glu Lys Ala Pro Glu Thr Asp Asp
    530                 535                 540

Ser Phe Ser Asp Val Asp Cys His Ser Asn Gln Glu Asp Thr Gly Cys
545                 550                 555                 560

Lys Phe Arg Val Leu Pro Gln Pro Thr Asn Leu Ala Thr Pro Asn Thr
                565                 570                 575

Lys Arg Phe Lys Lys Glu Glu Ile Leu Ser Ser Ser Asp Ile Cys Gln
            580                 585                 590

Lys Leu Val Asn Thr Gln Asp Met Ser Ala Ser Gln Val Asp Val Ala
        595                 600                 605

Val Lys Ile Asn Lys Lys Val Val Pro Leu Asp Phe Ser Met Ser Ser
    610                 615                 620

Leu Ala Lys Arg Ile Lys Gln Leu His His Glu Ala Gln Gln Ser Glu
625                 630                 635                 640

Gly Glu Gln Asn Tyr Arg Lys Phe Arg Ala Lys Ile Cys Pro Gly Glu
                645                 650                 655

Asn Gln Ala Ala Glu Asp Glu Leu Arg Lys Glu Ile Ser Lys Thr Met
```

660 665 670

Phe Ala Glu Met Glu Ile Ile Gly Gln Phe Asn Leu Gly Phe Ile Ile
675 680 685

Thr Lys Leu Asn Glu Asp Ile Phe Ile Val Asp Gln His Ala Thr Asp
690 695 700

Glu Lys Tyr Asn Phe Glu Met Leu Gln Gln His Thr Val Leu Gln Gly
705 710 715 720

Gln Arg Leu Ile Ala Pro Gln Thr Leu Asn Leu Thr Ala Val Asn Glu
725 730 735

Ala Val Leu Ile Glu Asn Leu Glu Ile Phe Arg Lys Asn Gly Phe Asp
740 745 750

Phe Val Ile Asp Glu Asn Ala Pro Val Thr Glu Arg Ala Lys Leu Ile
755 760 765

Ser Leu Pro Thr Ser Lys Asn Trp Thr Phe Gly Pro Gln Asp Val Asp
770 775 780

Glu Leu Ile Phe Met Leu Ser Asp Ser Pro Gly Val Met Cys Arg Pro
785 790 795 800

Ser Arg Val Lys Gln Met Phe Ala Ser Arg Ala Cys Arg Lys Ser Val
805 810 815

Met Ile Gly Thr Ala Leu Asn Thr Ser Glu Met Lys Lys Leu Ile Thr
820 825 830

His Met Gly Glu Met Asp His Pro Trp Asn Cys Pro His Gly Arg Pro
835 840 845

Thr Met Arg His Ile Ala Asn Leu Gly Val Ile Ser Gln Asn
850 855 860

<210> 2975
<211> 1256
<212> PRT
<213> Homo sapiens

<400> 2975

Met Tyr Leu Trp Leu Lys Leu Leu Ala Phe Gly Phe Ala Phe Leu Asp
1 5 10 15

Thr Glu Val Phe Val Thr Gly Gln Ser Pro Thr Pro Ser Pro Thr Gly
20 25 30

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

Pro Thr His Thr Thr Ala Phe Ser Pro Ala Ser Thr Phe Glu Arg Glu
50 55 60

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

Thr Gln Val Ser Pro Asp Ser Leu Asp Asn Ala Ser Ala Phe Asn Thr
85 90 95

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

Ser Gln Thr Pro Ser Ala Gly Thr Asp Thr Gln Thr Phe Ser Gly Ser
115 120 125

Ala Ala Asn Ala Lys Leu Asn Pro Thr Pro Gly Ser Asn Ala Ile Ser
130 135 140

Asp Ala Tyr Leu Asn Ala Ser Glu Thr Thr Thr Leu Ser Pro Ser Gly
145 150 155 160

Ser Ala Val Ile Ser Thr Thr Thr Ile Ala Thr Thr Pro Ser Lys Pro
165 170 175

Thr Cys Asp Glu Lys Tyr Ala Asn Ile Thr Val Asp Tyr Leu Tyr Asn
180 185 190

Lys Glu Thr Lys Leu Phe Thr Ala Lys Leu Asn Val Asn Glu Asn Val
195 200 205

Glu Cys Gly Asn Asn Thr Cys Thr Asn Asn Glu Val His Asn Leu Thr
210 215 220

Glu Cys Lys Asn Ala Ser Val Ser Ile Ser His Asn Ser Cys Thr Ala
225 230 235 240

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

Gln Leu His Asp Cys Thr Gln Val Glu Lys Ala Asp Thr Thr Ile Cys
260 265 270

Leu Lys Trp Lys Asn Ile Glu Thr Phe Thr Cys Asp Thr Gln Asn Ile
275 280 285

Thr Tyr Arg Phe Gln Cys Gly Asn Met Ile Phe Asp Asn Lys Glu Ile
290 295 300

Lys Leu Glu Asn Leu Glu Pro Glu His Glu Tyr Lys Cys Asp Ser Glu
305 310 315 320

Ile Leu Tyr Asn Asn His Lys Phe Thr Asn Ala Ser Lys Ile Ile Lys
325 330 335

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

Glu Ala Ala His Gln Gly Val Ile Thr Trp Asn Pro Pro Gln Arg Ser
355 360 365

Phe His Asn Phe Thr Leu Cys Tyr Ile Lys Glu Thr Glu Lys Asp Cys
370 375 380

Leu Asn Leu Asp Lys Asn Leu Ile Lys Tyr Asp Leu Gln Asn Leu Lys
385 390 395 400

Pro Tyr Thr Lys Tyr Val Leu Ser Leu His Ala Tyr Ile Ile Ala Lys
405 410 415

Val Gln Arg Asn Gly Ser Ala Ala Met Cys His Phe Thr Thr Lys Ser
420 425 430

Ala Pro Pro Ser Gln Val Trp Asn Met Thr Val Ser Met Thr Ser Asp
435 440 445

Asn Ser Met His Val Lys Cys Arg Pro Pro Arg Asp Arg Asn Gly Pro
450 455 460

His Glu Arg Tyr His Leu Glu Val Glu Ala Gly Asn Thr Leu Val Arg
465 470 475 480

Asn Glu Ser His Lys Asn Cys Asp Phe Arg Val Lys Asp Leu Gln Tyr
485 490 495

Ser Thr Asp Tyr Thr Phe Lys Ala Tyr Phe His Asn Gly Asp Tyr Pro

```
            500                 505                 510

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

Leu Ile Ala Phe Leu Ala Phe Leu Ile Ile Val Thr Ser Ile Ala Leu
    530                 535                 540

Leu Val Val Leu Tyr Lys Ile Tyr Asp Leu His Lys Lys Arg Ser Cys
545                 550                 555                 560

Asn Leu Asp Glu Gln Gln Glu Leu Val Glu Arg Asp Asp Glu Lys Gln
                565                 570                 575

Leu Met Asn Val Glu Pro Ile His Ala Asp Ile Leu Leu Glu Thr Tyr
            580                 585                 590

Lys Arg Lys Ile Ala Asp Glu Gly Arg Leu Phe Leu Ala Glu Phe Gln
        595                 600                 605

Ser Ile Pro Arg Val Phe Ser Lys Phe Pro Ile Lys Glu Ala Arg Lys
    610                 615                 620

Pro Phe Asn Gln Asn Lys Asn Arg Tyr Val Asp Ile Leu Pro Tyr Asp
625                 630                 635                 640

Tyr Asn Arg Val Glu Leu Ser Glu Ile Asn Gly Asp Ala Gly Ser Asn
                645                 650                 655

Tyr Ile Asn Ala Ser Tyr Ile Asp Gly Phe Lys Glu Pro Arg Lys Tyr
            660                 665                 670

Ile Ala Ala Gln Gly Pro Arg Asp Glu Thr Val Asp Asp Phe Trp Arg
        675                 680                 685

Met Ile Trp Glu Gln Lys Ala Thr Val Ile Val Met Val Thr Arg Cys
    690                 695                 700

Glu Glu Gly Asn Arg Asn Lys Cys Ala Glu Tyr Trp Pro Ser Met Glu
705                 710                 715                 720

Glu Gly Thr Arg Ala Phe Gly Asp Val Val Val Lys Ile Asn Gln His
                725                 730                 735

Lys Arg Cys Pro Asp Tyr Ile Ile Gln Lys Leu Asn Ile Val Asn Lys
            740                 745                 750
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Lys Glu Lys Ala Thr Gly Arg Glu Val Thr His Ile Gln Phe Thr Ser
755 760 765

Trp Pro Asp His Gly Val Pro Glu Asp Pro His Leu Leu Leu Lys Leu
770 775 780

Arg Arg Arg Val Asn Ala Phe Ser Asn Phe Phe Ser Gly Pro Ile Val
785 790 795 800

Val His Cys Ser Ala Gly Val Gly Arg Thr Gly Thr Tyr Ile Gly Ile
805 810 815

Asp Ala Met Leu Glu Gly Leu Glu Ala Glu Asn Lys Val Asp Val Tyr
820 825 830

Gly Tyr Val Val Lys Leu Arg Arg Gln Arg Cys Leu Met Val Gln Val
835 840 845

Glu Ala Gln Tyr Ile Leu Ile His Gln Ala Leu Val Glu Tyr Asn Gln
850 855 860

Phe Gly Glu Thr Glu Val Asn Leu Ser Glu Leu His Pro Tyr Leu His
865 870 875 880

Asn Met Lys Lys Arg Asp Pro Pro Ser Glu Pro Ser Pro Leu Glu Ala
885 890 895

Glu Phe Gln Arg Leu Pro Ser Tyr Arg Ser Trp Arg Thr Gln His Ile
900 905 910

Gly Asn Gln Glu Glu Asn Lys Ser Lys Asn Arg Asn Ser Asn Val Ile
915 920 925

Pro Tyr Asp Tyr Asn Arg Val Pro Leu Lys His Glu Leu Glu Met Ser
930 935 940

Lys Glu Ser Glu His Asp Ser Asp Glu Ser Ser Asp Asp Asp Ser Asp
945 950 955 960

Ser Glu Glu Pro Ser Lys Tyr Ile Asn Ala Ser Phe Ile Met Ser Tyr
965 970 975

Trp Lys Pro Glu Val Met Ile Ala Ala Gln Gly Pro Leu Lys Glu Thr
980 985 990

Ile Gly Asp Phe Trp Gln Met Ile Phe Gln Arg Lys Val Lys Val Ile
995 1000 1005

Val Met Leu Thr Glu Leu Lys His Gly Asp Gln Glu Ile Cys Ala
1010 1015 1020

Gln Tyr Trp Gly Glu Gly Lys Gln Thr Tyr Gly Asp Ile Glu Val
1025 1030 1035

Asp Leu Lys Asp Thr Asp Lys Ser Ser Thr Tyr Thr Leu Arg Val
1040 1045 1050

Phe Glu Leu Arg His Ser Lys Arg Lys Asp Ser Arg Thr Val Tyr
1055 1060 1065

Gln Tyr Gln Tyr Thr Asn Trp Ser Val Glu Gln Leu Pro Ala Glu
1070 1075 1080

Pro Lys Glu Leu Ile Ser Met Ile Gln Val Val Lys Gln Lys Leu
1085 1090 1095

Pro Gln Lys Asn Ser Ser Glu Gly Asn Lys His His Lys Ser Thr
1100 1105 1110

Pro Leu Leu Ile His Cys Arg Asp Gly Ser Gln Gln Thr Gly Ile
1115 1120 1125

Phe Cys Ala Leu Leu Asn Leu Leu Glu Ser Ala Glu Thr Glu Glu
1130 1135 1140

Val Val Asp Ile Phe Gln Val Val Lys Ala Leu Arg Lys Ala Arg
1145 1150 1155

Pro Gly Met Val Ser Thr Phe Glu Gln Tyr Gln Phe Leu Tyr Asp
1160 1165 1170

Val Ile Ala Ser Thr Tyr Pro Ala Gln Asn Gly Gln Val Lys Lys
1175 1180 1185

Asn Asn His Gln Glu Asp Lys Ile Glu Phe Asp Asn Glu Val Asp
1190 1195 1200

Lys Val Lys Gln Asp Ala Asn Cys Val Asn Pro Leu Gly Ala Pro
1205 1210 1215

Glu Lys Leu Pro Glu Ala Lys Glu Gln Ala Glu Gly Ser Glu Pro
1220 1225 1230

Thr Ser Gly Thr Glu Gly Pro Glu His Ser Val Asn Gly Pro Ala
1235 1240 1245

Ser Pro Ala Leu Asn Gln Gly Ser
1250 1255

<210> 2976
<211> 319
<212> PRT
<213> Homo sapiens

<400> 2976

Met Lys Met Ala Ser Ser Leu Ala Phe Leu Leu Leu Asn Phe His Val
1 5 10 15

Ser Leu Leu Leu Val Gln Leu Leu Thr Pro Cys Ser Ala Gln Phe Ser
20 25 30

Val Leu Gly Pro Ser Gly Pro Ile Leu Ala Met Val Gly Glu Asp Ala
35 40 45

Asp Leu Pro Cys His Leu Phe Pro Thr Met Ser Ala Glu Thr Met Glu
50 55 60

Leu Lys Trp Val Ser Ser Ser Leu Arg Gln Val Val Asn Val Tyr Ala
65 70 75 80

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

Thr Ser Ile Leu Arg Asp Gly Ile Thr Ala Gly Lys Ala Ala Leu Arg
100 105 110

Ile His Asn Val Thr Ala Ser Asp Ser Gly Lys Tyr Leu Cys Tyr Phe
115 120 125

Gln Asp Gly Asp Phe Tyr Glu Lys Ala Leu Val Glu Leu Lys Val Ala
130 135 140

Ala Leu Gly Ser Asn Leu His Val Glu Val Lys Gly Tyr Glu Asp Gly
145 150 155 160

Gly Ile His Leu Glu Cys Arg Ser Thr Gly Trp Tyr Pro Gln Pro Gln
165 170 175

Ile Gln Trp Ser Asn Ala Lys Gly Glu Asn Ile Pro Ala Val Glu Ala
180 185 190

Pro Val Val Ala Asp Gly Val Gly Leu Tyr Glu Val Ala Ala Ser Val
195 200 205

Ile Met Arg Gly Gly Ser Gly Glu Gly Val Ser Cys Ile Ile Arg Asn
210 215 220

Ser Leu Leu Gly Leu Glu Lys Thr Ala Ser Ile Ser Ile Ala Asp Pro
225 230 235 240

Phe Phe Arg Ser Ala Gln Pro Trp Ile Ala Ala Leu Ala Gly Thr Leu
245 250 255

Pro Ile Leu Leu Leu Leu Leu Ala Gly Ala Ser Tyr Phe Leu Trp Arg
260 265 270

Gln Gln Lys Glu Ile Thr Ala Leu Ser Ser Glu Ile Glu Ser Glu Gln
275 280 285

Glu Met Lys Glu Met Gly Tyr Ala Ala Thr Glu Arg Glu Ile Ser Leu
290 295 300

Arg Glu Ser Leu Gln Glu Glu Leu Lys Arg Lys Lys Ser Ser Thr
305 310 315

<210> 2977
<211> 240
<212> PRT
<213> Homo sapiens

<400> 2977

Met Leu Leu Gln Ser Gln Thr Met Gly Val Ser His Ser Phe Thr Pro
1 5 10 15

Lys Gly Ile Thr Ile Pro Gln Arg Glu Lys Pro Gly His Met Tyr Gln
20 25 30

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

Gly Thr Val Gln Ile Leu Cys Cys Leu Leu Ile Ser Ser Leu Gly Ala
50 55 60

```
Ile Leu Val Phe Ala Pro Tyr Pro Ser His Phe Asn Pro Ala Ile Ser
65                  70                  75                  80

Thr Thr Leu Met Ser Gly Tyr Pro Phe Leu Gly Ala Leu Cys Phe Gly
                85                  90                  95

Ile Thr Gly Ser Leu Ser Ile Ile Ser Gly Lys Gln Ser Thr Lys Pro
            100                 105                 110

Phe Asp Leu Ser Ser Leu Thr Ser Asn Ala Val Ser Ser Val Thr Ala
        115                 120                 125

Gly Ala Gly Leu Phe Leu Leu Ala Asp Ser Met Val Ala Leu Arg Thr
    130                 135                 140

Ala Ser Gln His Cys Gly Ser Glu Met Asp Tyr Leu Ser Ser Leu Pro
145                 150                 155                 160

Tyr Ser Glu Tyr Tyr Tyr Pro Ile Tyr Glu Ile Lys Asp Cys Leu Leu
                165                 170                 175

Thr Ser Val Ser Leu Thr Gly Val Leu Val Val Met Leu Ile Phe Thr
            180                 185                 190

Val Leu Glu Leu Leu Leu Ala Ala Tyr Ser Ser Val Phe Trp Trp Lys
        195                 200                 205

Gln Leu Tyr Ser Asn Asn Pro Gly Ser Ser Phe Ser Ser Thr Gln Ser
    210                 215                 220

Gln Asp His Ile Gln Gln Val Lys Lys Ser Ser Ser Arg Ser Trp Ile
225                 230                 235                 240
```

<210> 2978
<211> 266
<212> PRT
<213> Homo sapiens

<400> 2978

```
Met Val Cys Leu Lys Leu Pro Gly Gly Ser Ser Leu Ala Ala Leu Thr
1               5                   10                  15

Val Thr Leu Met Val Leu Ser Ser Arg Leu Ala Phe Ala Gly Asp Thr
            20                  25                  30

Arg Pro Arg Phe Leu Glu Leu Arg Lys Ser Glu Cys His Phe Phe Asn
        35                  40                  45
```

```
Gly Thr Glu Arg Val Arg Tyr Leu Asp Arg Tyr Phe His Asn Gln Glu
 50                  55                  60

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

Glu Leu Gly Arg Pro Val Ala Glu Ser Trp Asn Ser Gln Lys Asp Leu
                85                  90                  95

Leu Glu Gln Lys Arg Gly Arg Val Asp Asn Tyr Cys Arg His Asn Tyr
            100                 105                 110

Gly Val Gly Glu Ser Phe Thr Val Gln Arg Arg Val His Pro Gln Val
        115                 120                 125

Thr Val Tyr Pro Ala Lys Thr Gln Pro Leu Gln His His Asn Leu Leu
    130                 135                 140

Val Cys Ser Val Ser Gly Phe Tyr Pro Gly Ser Ile Glu Val Arg Trp
145                 150                 155                 160

Phe Arg Asn Gly Gln Glu Glu Lys Ala Gly Val Val Ser Thr Gly Leu
                165                 170                 175

Ile Gln Asn Gly Asp Trp Thr Phe Gln Thr Leu Val Met Leu Glu Thr
            180                 185                 190

Val Pro Arg Ser Gly Glu Val Tyr Thr Cys Gln Val Glu His Pro Ser
        195                 200                 205

Val Thr Ser Ala Leu Thr Val Glu Trp Arg Ala Arg Ser Glu Ser Ala
    210                 215                 220

Gln Ser Lys Met Leu Ser Gly Val Gly Gly Phe Val Leu Gly Leu Leu
225                 230                 235                 240

Phe Leu Gly Ala Gly Leu Phe Ile Tyr Phe Arg Asn Gln Lys Gly His
                245                 250                 255

Ser Gly Leu Gln Pro Thr Gly Phe Leu Ser
            260                 265
```

<210> 2979
<211> 325
<212> PRT

<213> Homo sapiens

<400> 2979

Met Pro Ile Thr Arg Met Arg Met Arg Pro Trp Leu Glu Met Gln Ile
1 5 10 15

Asn Ser Asn Gln Ile Pro Gly Leu Ile Trp Ile Asn Lys Glu Glu Met
20 25 30

Ile Phe Gln Ile Pro Trp Lys His Ala Ala Lys His Gly Trp Asp Ile
35 40 45

Asn Lys Asp Ala Cys Leu Phe Arg Ser Trp Ala Ile His Thr Gly Arg
50 55 60

Tyr Lys Ala Gly Glu Lys Glu Pro Asp Pro Lys Thr Trp Lys Ala Asn
65 70 75 80

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

Gln Ser Arg Asn Lys Gly Ser Ser Ala Val Arg Val Tyr Arg Met Leu
100 105 110

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

Arg Asp Ala Lys Ser Lys Ala Lys Arg Lys Ser Cys Gly Asp Ser Ser
130 135 140

Pro Asp Thr Phe Ser Asp Gly Leu Ser Ser Ser Thr Leu Pro Asp Asp
145 150 155 160

His Ser Ser Tyr Thr Val Pro Gly Tyr Met Gln Asp Leu Glu Val Glu
165 170 175

Gln Ala Leu Thr Pro Ala Leu Ser Pro Cys Ala Val Ser Ser Thr Leu
180 185 190

Pro Asp Trp His Ile Pro Val Glu Val Val Pro Asp Ser Thr Ser Asp
195 200 205

Leu Tyr Asn Phe Gln Val Ser Pro Met Pro Ser Thr Ser Glu Ala Thr
210 215 220

Thr Asp Glu Asp Glu Glu Gly Lys Leu Pro Glu Asp Ile Met Lys Leu

225 230 235 240

Leu Glu Gln Ser Glu Trp Gln Pro Thr Asn Val Asp Gly Lys Gly Tyr
245 250 255

Leu Leu Asn Glu Pro Gly Val Gln Pro Thr Ser Val Tyr Gly Asp Phe
260 265 270

Ser Cys Lys Glu Glu Pro Glu Ile Asp Ser Pro Gly Gly Asp Ile Gly
275 280 285

Leu Ser Leu Gln Arg Val Phe Thr Asp Leu Lys Asn Met Asp Ala Thr
290 295 300

Trp Leu Asp Ser Leu Leu Thr Pro Val Arg Leu Pro Ser Ile Gln Ala
305 310 315 320

Ile Pro Cys Ala Pro
325

<210> 2980
<211> 132
<212> PRT
<213> Homo sapiens

<400> 2980

Met Glu Phe Asp Leu Asn Gly Asn Gly Asp Ile Gly Glu Lys Arg Val
1 5 10 15

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

Pro Thr Cys Ser Ile Pro His Asp Leu Gly Gly Gly Pro Pro Thr Thr
35 40 45

Val Gly Gly Arg Arg Met Gly Met Arg Lys Trp Glu Arg Arg Glu Arg
50 55 60

Val Ser Pro Pro Ser Pro His Pro His Pro Leu Pro Pro Asp Ile Met
65 70 75 80

Ser Leu Lys Arg Met Leu Glu Lys Leu Gly Val Pro Lys Thr His Leu
85 90 95

Glu Leu Lys Lys Leu Ile Gly Glu Val Ser Ser Gly Ser Gly Glu Thr
100 105 110

```
Phe Ser Tyr Pro Asp Phe Leu Arg Met Met Leu Gly Lys Arg Ser Ala
        115                 120                 125

Ile Leu Lys Met
    130
```

<210> 2981
<211> 319
<212> PRT
<213> Homo sapiens

<400> 2981

```
Met Thr Asn Ser Ser Phe Phe Cys Pro Val Tyr Lys Asp Leu Glu Pro
1               5                   10                  15

Phe Thr Tyr Phe Phe Tyr Leu Val Phe Leu Val Gly Ile Ile Gly Ser
            20                  25                  30

Cys Phe Ala Thr Trp Ala Phe Ile Gln Lys Asn Thr Asn His Arg Cys
        35                  40                  45

Val Ser Ile Tyr Leu Ile Asn Leu Leu Thr Ala Asp Phe Leu Leu Thr
    50                  55                  60

Leu Ala Leu Pro Val Lys Ile Val Val Asp Leu Gly Val Ala Pro Trp
65                  70                  75                  80

Lys Leu Lys Ile Phe His Cys Gln Val Thr Ala Cys Leu Ile Tyr Ile
                85                  90                  95

Asn Met Tyr Leu Ser Ile Ile Phe Leu Ala Phe Val Ser Ile Asp Arg
            100                 105                 110

Cys Leu Gln Leu Thr His Ser Cys Lys Ile Tyr Arg Ile Gln Glu Pro
        115                 120                 125

Gly Phe Ala Lys Met Ile Ser Thr Val Val Trp Leu Met Val Leu Leu
    130                 135                 140

Ile Met Val Pro Asn Met Met Ile Pro Ile Lys Asp Ile Lys Glu Lys
145                 150                 155                 160

Ser Asn Val Gly Cys Met Glu Phe Lys Lys Glu Phe Gly Arg Asn Trp
                165                 170                 175

His Leu Leu Thr Asn Phe Ile Cys Val Ala Ile Phe Leu Asn Phe Ser
```

180 185 190

Ala Ile Ile Leu Ile Ser Asn Cys Leu Val Ile Arg Gln Leu Tyr Arg
195 200 205

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

Ile Leu Leu Val Thr Thr Gly Tyr Ile Ile Cys Phe Val Pro Tyr His
225 230 235 240

Ile Val Arg Ile Pro Tyr Thr Leu Ser Gln Thr Glu Val Ile Thr Asp
245 250 255

Cys Ser Thr Arg Ile Ser Leu Phe Lys Ala Lys Glu Ala Thr Leu Leu
260 265 270

Leu Ala Val Ser Asn Leu Cys Phe Asp Pro Ile Leu Tyr Tyr His Leu
275 280 285

Ser Lys Ala Phe Arg Ser Lys Val Thr Glu Thr Phe Ala Ser Pro Lys
290 295 300

Glu Thr Lys Ala Gln Lys Glu Lys Leu Arg Cys Glu Asn Asn Ala
305 310 315

<210> 2982
<211> 334
<212> PRT
<213> Homo sapiens

<400> 2982

Met Leu Thr Lys Pro Leu Gln Gly Pro Pro Ala Pro Pro Gly Thr Pro
1 5 10 15

Thr Pro Pro Pro Gly Gly Lys Asp Arg Glu Ala Phe Glu Ala Glu Tyr
20 25 30

Arg Leu Gly Pro Leu Leu Gly Lys Gly Gly Phe Gly Thr Val Phe Ala
35 40 45

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

Arg Asn Arg Val Leu Gly Trp Ser Pro Leu Ser Asp Ser Val Thr Cys
65 70 75 80

```
Pro Leu Glu Val Ala Leu Leu Trp Lys Val Gly Ala Gly Gly Gly His
                85                  90                  95

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

Met Leu Val Leu Glu Arg Pro Leu Pro Ala Gln Asp Leu Phe Asp Tyr
        115                 120                 125

Ile Thr Glu Lys Gly Pro Leu Gly Glu Gly Pro Ser Arg Cys Phe Phe
    130                 135                 140

Gly Gln Val Val Ala Ala Ile Gln His Cys His Ser Arg Gly Val Val
145                 150                 155                 160

His Arg Asp Ile Lys Asp Glu Asn Ile Leu Ile Asp Leu Arg Arg Gly
                165                 170                 175

Cys Ala Lys Leu Ile Asp Phe Gly Ser Gly Ala Leu Leu His Asp Glu
            180                 185                 190

Pro Tyr Thr Asp Phe Asp Gly Thr Arg Val Tyr Ser Pro Pro Glu Trp
        195                 200                 205

Ile Ser Arg His Gln Tyr His Ala Leu Pro Ala Thr Val Trp Ser Leu
    210                 215                 220

Gly Ile Leu Leu Tyr Asp Met Val Cys Gly Asp Ile Pro Phe Glu Arg
225                 230                 235                 240

Asp Gln Glu Ile Leu Glu Ala Glu Leu His Phe Pro Ala His Val Ser
                245                 250                 255

Pro Asp Cys Cys Ala Leu Ile Arg Arg Cys Leu Ala Pro Lys Pro Ser
            260                 265                 270

Ser Arg Pro Ser Leu Glu Glu Ile Leu Leu Asp Pro Trp Met Gln Thr
        275                 280                 285

Pro Ala Glu Asp Val Thr Pro Gln Pro Leu Gln Arg Arg Pro Cys Pro
    290                 295                 300

Phe Gly Leu Val Leu Ala Thr Leu Ser Leu Ala Trp Pro Gly Leu Ala
305                 310                 315                 320
```

```
Pro Asn Gly Gln Lys Ser His Pro Met Ala Met Ser Gln Gly
                325                 330


<210>  2983
<211>  158
<212>  PRT
<213>  Homo sapiens

<400>  2983

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

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

Ala Arg Tyr Gln Trp Val Arg Cys Asn Pro Asp Ser Asn Ser Ala Asn
        35                  40                  45

Cys Leu Glu Glu Lys Gly Pro Met Phe Glu Leu Leu Pro Gly Glu Ser
    50                  55                  60

Asn Lys Ile Pro Arg Leu Arg Thr Asp Leu Phe Pro Lys Thr Arg Ile
65                  70                  75                  80

Gln Asp Leu Asn Arg Ile Phe Pro Leu Ser Glu Asp Tyr Ser Gly Ser
                85                  90                  95

Gly Phe Gly Ser Gly Ser Gly Ser Gly Ser Gly Ser Gly Ser Gly Phe
            100                 105                 110

Leu Thr Glu Met Glu Gln Asp Tyr Gln Leu Val Asp Glu Ser Asp Ala
        115                 120                 125

Phe His Asp Asn Leu Arg Ser Leu Asp Arg Asn Leu Pro Ser Asp Ser
    130                 135                 140

Gln Asp Leu Gly Gln His Gly Leu Glu Glu Asp Phe Met Leu
145                 150                 155


<210>  2984
<211>  1019
<212>  PRT
<213>  Homo sapiens

<400>  2984

Ala Asp Pro Glu Ser Pro Ile Leu Asp Leu Asp Leu His Leu Pro Leu
1               5                   10                  15
```

```
Leu Cys Phe Arg Pro Glu Lys Val Leu Gln Ile Leu Thr Cys Ile Leu
            20                  25                  30

Thr Glu Gln Arg Ile Val Phe Phe Ser Ser Asp Trp Ala Leu Leu Thr
        35                  40                  45

Leu Val Thr Glu Cys Phe Met Ala Tyr Leu Tyr Pro Leu Gln Trp Gln
    50                  55                  60

His Pro Phe Val Pro Ile Leu Ser Asp Gln Met Leu Asp Phe Val Met
65                  70                  75                  80

Ala Pro Thr Ser Phe Leu Met Gly Cys His Leu Asp His Phe Glu Glu
                85                  90                  95

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

Ser Ile Thr Tyr Ser Lys Ser Thr Asp Asp Asn Val Asp Ile Pro Asp
        115                 120                 125

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

Gln Leu His His Glu Leu His Ala Ala His Leu Leu Ser Ser Thr Asp
145                 150                 155                 160

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

Cys Gln Ile Gln Gln Thr Thr Leu Gln Leu Leu Val Ser Ile Phe Arg
            180                 185                 190

Asp Val Lys Asn His Leu Asn Tyr Glu His Arg Val Phe Asn Ser Glu
        195                 200                 205

Glu Phe Leu Lys Thr Arg Ala Pro Gly Asp His Gln Phe Tyr Lys Gln
    210                 215                 220

Val Leu Asp Thr Tyr Met Phe His Ser Phe Leu Lys Ala Arg Leu Asn
225                 230                 235                 240

Arg Arg Met Asp Ala Phe Ala Gln Met Asp Leu Asp Thr Gln Ser Glu
                245                 250                 255
```

```
Glu Asp Arg Ile Asn Gly Met Leu Leu Ser Pro Arg Arg Pro Thr Val
            260                 265                 270

Glu Lys Arg Ala Ser Arg Lys Ser Ser His Leu His Val Thr His Arg
        275                 280                 285

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

Leu Ala Pro Arg Asn Ser Ser Leu Arg Leu Thr Asp Thr Ala Gly Cys
305                 310                 315                 320

Arg Gly Ser Ser Ala Val Leu Asn Val Thr Pro Lys Ser Pro Tyr Thr
                325                 330                 335

Phe Lys Ile Pro Glu Ile His Phe Pro Leu Glu Ser Lys Cys Val Gln
            340                 345                 350

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

Leu Ala Pro Asp Asn Ser Leu Leu Leu Ala Arg Tyr Leu Tyr Leu Arg
    370                 375                 380

Gly Leu Val Tyr Leu Met Gln Gly Gln Leu Leu Asn Ala Leu Leu Asp
385                 390                 395                 400

Phe Gln Asn Leu Tyr Lys Thr Asp Ile Arg Ile Phe Pro Thr Asp Leu
                405                 410                 415

Val Lys Arg Thr Val Glu Ser Met Ser Ala Pro Glu Trp Glu Gly Ala
            420                 425                 430

Glu Gln Ala Pro Glu Leu Met Arg Leu Ile Ser Glu Ile Leu Asp Lys
        435                 440                 445

Pro His Glu Ala Ser Lys Leu Asp Asp His Val Lys Lys Phe Lys Leu
    450                 455                 460

Pro Lys Lys His Met Gln Leu Gly Asp Phe Met Lys Arg Val Gln Glu
465                 470                 475                 480

Ser Gly Ile Val Lys Asp Ala Ser Ile Ile His Arg Leu Phe Glu Ala
                485                 490                 495

Leu Thr Val Gly Gln Glu Lys Gln Ile Asp Pro Glu Thr Phe Lys Asp
```

500 505 510

Phe Tyr Asn Cys Trp Lys Glu Thr Glu Ala Glu Ala Gln Glu Val Ser
515 520 525

Leu Pro Trp Leu Val Met Glu His Leu Asp Lys Asn Glu Cys Val Cys
530 535 540

Lys Leu Ser Ser Ser Val Lys Thr Asn Leu Gly Val Gly Lys Ile Ala
545 550 555 560

Met Thr Gln Lys Arg Leu Phe Leu Leu Thr Glu Gly Arg Pro Gly Tyr
565 570 575

Leu Glu Ile Ser Thr Phe Arg Asn Ile Glu Glu Val Arg Arg Thr Thr
580 585 590

Thr Thr Phe Leu Leu Arg Arg Ile Pro Thr Leu Lys Ile Arg Val Ala
595 600 605

Ser Lys Lys Glu Val Phe Glu Ala Asn Leu Lys Thr Glu Cys Asp Leu
610 615 620

Trp His Leu Met Val Lys Glu Met Trp Ala Gly Lys Lys Leu Ala Asp
625 630 635 640

Asp His Lys Asp Pro His Tyr Val Gln Gln Ala Leu Thr Asn Val Leu
645 650 655

Leu Met Asp Ala Val Val Gly Thr Leu Gln Ser Pro Gly Ala Ile Tyr
660 665 670

Ala Ala Ser Lys Leu Ser Tyr Phe Asp Lys Met Ser Asn Glu Met Pro
675 680 685

Met Thr Leu Pro Glu Thr Thr Leu Glu Thr Leu Lys His Lys Ile Asn
690 695 700

Pro Ser Ala Gly Glu Ala Phe Pro Gln Ala Val Asp Val Leu Leu Tyr
705 710 715 720

Thr Pro Gly His Leu Asp Pro Ala Glu Lys Val Glu Asp Ala His Pro
725 730 735

Lys Leu Trp Cys Ala Leu Ser Glu Gly Lys Val Thr Val Phe Asn Ala
740 745 750

Ser Ser Trp Thr Ile His Gln His Ser Phe Lys Val Gly Thr Ala Lys
755 760 765

Val Asn Cys Met Val Met Ala Asp Gln Asn Gln Val Trp Val Gly Ser
770 775 780

Glu Asp Ser Val Ile Tyr Ile Ile Asn Val His Ser Met Ser Cys Asn
785 790 795 800

Lys Gln Leu Thr Ala His Cys Ser Ser Val Thr Asp Leu Ile Val Gln
805 810 815

Asp Gly Gln Glu Ala Pro Ser Asn Val Tyr Ser Cys Ser Met Asp Gly
820 825 830

Met Val Leu Val Trp Asn Val Ser Thr Leu Gln Val Thr Ser Arg Phe
835 840 845

Gln Leu Pro Arg Gly Gly Leu Thr Ser Ile Arg Leu His Gly Gly Arg
850 855 860

Leu Trp Cys Cys Thr Gly Asn Ser Ile Met Val Met Lys Met Asn Gly
865 870 875 880

Ser Leu His Gln Glu Leu Lys Ile Glu Glu Asn Phe Lys Asp Thr Ser
885 890 895

Thr Ser Phe Leu Ala Phe Gln Leu Leu Pro Glu Glu Glu Gln Leu Trp
900 905 910

Ala Ala Cys Ala Gly Arg Ser Glu Val Tyr Ile Trp Ser Leu Lys Asp
915 920 925

Leu Ala Gln Pro Pro Gln Arg Val Pro Leu Glu Asp Cys Ser Glu Ile
930 935 940

Asn Cys Met Ile Arg Val Lys Lys Gln Val Trp Val Gly Ser Arg Gly
945 950 955 960

Leu Gly Gln Gly Thr Pro Lys Gly Lys Ile Tyr Val Ile Asp Ala Glu
965 970 975

Arg Lys Thr Val Glu Lys Glu Leu Val Ala His Met Asp Thr Val Arg
980 985 990

```
Thr Leu Cys Ser Ala Glu Asp Arg  Tyr Val Leu Ser Gly  Ser Gly Arg
        995                 1000                1005

Glu Glu  Gly Lys Val Ala Ile  Trp Lys Gly Glu
    1010                1015
```

<210> 2985
<211> 783
<212> PRT
<213> Homo sapiens

<400> 2985

```
Met Ala Lys Tyr Asn Thr Gly Gly Asn Pro Thr Glu Asp Val Ser Val
1               5                  10                  15

Asn Ser Arg Pro Phe Arg Val Thr Gly Pro Asn Ser Ser Ser Gly Ile
            20                  25                  30

Gln Ala Arg Lys Asn Leu Phe Asn Asn Gln Gly Asn Ala Ser Pro Pro
        35                  40                  45

Ala Gly Pro Ser Asn Val Pro Lys Phe Gly Ser Pro Lys Pro Pro Val
    50                  55                  60

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

Pro Phe Leu Lys Pro Thr Gly Ala Gly Gln Arg Phe Gly Thr Pro Ala
                85                  90                  95

Ser Leu Thr Thr Arg Asp Pro Glu Ala Lys Val Gly Phe Leu Lys Pro
            100                 105                 110

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

Phe Pro Trp Pro Pro Gly Asn Lys Pro Ser Leu His Ser Val Asn Gln
    130                 135                 140

Asp His Asp Leu Lys Pro Leu Gly Pro Lys Ser Gly Pro Thr Pro Pro
145                 150                 155                 160

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

Lys Gly Lys Phe Met Ser Ala Ser Gln Asp Leu Glu Pro Lys Pro Leu
```

180 185 190

Phe Pro Lys Pro Ala Phe Gly Gln Lys Pro Pro Leu Ser Thr Glu Asn
195 200 205

Ser His Glu Asp Glu Ser Pro Met Lys Asn Val Ser Ser Ser Lys Gly
210 215 220

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

Ala Arg Glu Asp Ser Glu Asn Lys Asp His Ala Gly Glu Ile Ser Ser
245 250 255

Leu Pro Phe Pro Gly Val Val Leu Lys Pro Ala Ala Ser Arg Gly Gly
260 265 270

Leu Gly Leu Ser Lys Asn Gly Glu Glu Lys Lys Glu Asp Arg Lys Ile
275 280 285

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

Ala Ser Gly Thr Pro Pro Ala Arg Phe Pro Lys Ala Pro Ser Lys Leu
305 310 315 320

Thr Val Gly Gly Pro Trp Gly Gln Ser Gln Glu Lys Glu Lys Gly Asp
325 330 335

Lys Asn Ser Ala Thr Pro Lys Gln Lys Pro Leu Pro Pro Leu Phe Thr
340 345 350

Leu Gly Pro Pro Pro Pro Lys Pro Asn Arg Pro Pro Asn Val Asp Leu
355 360 365

Thr Lys Phe His Lys Thr Ser Ser Gly Asn Ser Thr Ser Lys Gly Gln
370 375 380

Thr Ser Tyr Ser Thr Thr Ser Leu Pro Pro Pro Pro Pro Ser His Pro
385 390 395 400

Ala Ser Gln Pro Pro Leu Pro Ala Ser His Pro Ser Gln Pro Pro Val
405 410 415

Pro Ser Leu Pro Pro Arg Asn Ile Lys Pro Pro Phe Asp Leu Lys Ser
420 425 430

Pro Val Asn Glu Asp Asn Gln Asp Gly Val Thr His Ser Asp Gly Ala
435 440 445

Gly Asn Leu Asp Glu Glu Gln Asp Ser Glu Gly Glu Thr Tyr Glu Asp
450 455 460

Ile Glu Ala Ser Lys Glu Arg Glu Lys Lys Arg Glu Lys Glu Glu Lys
465 470 475 480

Lys Arg Leu Glu Leu Glu Lys Lys Glu Gln Lys Glu Lys Glu Lys Lys
485 490 495

Glu Gln Glu Ile Lys Lys Lys Phe Lys Leu Thr Gly Pro Ile Gln Val
500 505 510

Ile His Leu Ala Lys Ala Cys Cys Asp Val Lys Gly Gly Lys Asn Glu
515 520 525

Leu Ser Phe Lys Gln Gly Glu Gln Ile Glu Ile Ile Arg Ile Thr Asp
530 535 540

Asn Pro Glu Gly Lys Trp Leu Gly Arg Thr Ala Arg Gly Ser Tyr Gly
545 550 555 560

Tyr Ile Lys Thr Thr Ala Val Glu Ile Asp Tyr Asp Ser Leu Lys Leu
565 570 575

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

Glu Val Tyr Asp Asp Val Ala Glu Gln Asp Asp Ile Ser Ser His Ser
595 600 605

Gln Ser Gly Ser Gly Gly Ile Phe Pro Pro Pro Pro Asp Asp Asp Ile
610 615 620

Tyr Asp Gly Ile Glu Glu Glu Asp Ala Asp Asp Gly Phe Pro Ala Pro
625 630 635 640

Pro Lys Gln Leu Asp Met Gly Asp Glu Val Tyr Asp Asp Val Asp Thr
645 650 655

Ser Asp Phe Pro Val Ser Ser Ala Glu Met Ser Gln Gly Thr Asn Phe
660 665 670

Gly Lys Ala Lys Thr Glu Glu Lys Asp Leu Lys Lys Leu Lys Lys Gln
675 680 685

Glu Lys Glu Glu Lys Asp Phe Arg Lys Lys Phe Lys Tyr Asp Gly Glu
690 695 700

Ile Arg Val Leu Tyr Ser Thr Lys Val Thr Thr Ser Ile Thr Ser Lys
705 710 715 720

Lys Trp Gly Thr Arg Asp Leu Gln Val Lys Pro Gly Glu Ser Leu Glu
725 730 735

Val Ile Gln Thr Thr Asp Asp Thr Lys Val Leu Cys Arg Asn Glu Glu
740 745 750

Gly Lys Tyr Gly Tyr Val Leu Arg Ser Tyr Leu Ala Asp Asn Asp Gly
755 760 765

Glu Ile Tyr Asp Asp Ile Ala Asp Gly Cys Ile Tyr Asp Asn Asp
770 775 780

<210> 2986
<211> 266
<212> PRT
<213> Homo sapiens

<400> 2986

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

Val Thr Leu Met Val Leu Ser Ser Arg Leu Ala Phe Ala Gly Asp Thr
20 25 30

Arg Pro Arg Phe Leu Glu Leu Arg Lys Ser Glu Cys His Phe Phe Asn
35 40 45

Gly Thr Glu Arg Val Arg Tyr Leu Asp Arg Tyr Phe His Asn Gln Glu
50 55 60

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

Glu Leu Gly Arg Pro Val Ala Glu Ser Trp Asn Ser Gln Lys Asp Leu
85 90 95

Leu Glu Gln Lys Arg Gly Arg Val Asp Asn Tyr Cys Arg His Asn Tyr

100 105 110

Gly Val Gly Glu Ser Phe Thr Val Gln Arg Arg Val His Pro Gln Val
115 120 125

Thr Val Tyr Pro Ala Lys Thr Gln Pro Leu Gln His His Asn Leu Leu
130 135 140

Val Cys Ser Val Ser Gly Phe Tyr Pro Gly Ser Ile Glu Val Arg Trp
145 150 155 160

Phe Arg Asn Gly Gln Glu Glu Lys Ala Gly Val Val Ser Thr Gly Leu
165 170 175

Ile Gln Asn Gly Asp Trp Thr Phe Gln Thr Leu Val Met Leu Glu Thr
180 185 190

Val Pro Arg Ser Gly Glu Val Tyr Thr Cys Gln Val Glu His Pro Ser
195 200 205

Val Thr Ser Ala Leu Thr Val Glu Trp Arg Ala Arg Ser Glu Ser Ala
210 215 220

Gln Ser Lys Met Leu Ser Gly Val Gly Gly Phe Val Leu Gly Leu Leu
225 230 235 240

Phe Leu Gly Ala Gly Leu Phe Ile Tyr Phe Arg Asn Gln Lys Gly His
245 250 255

Ser Gly Leu Gln Pro Thr Gly Phe Leu Ser
260 265

<210> 2987
<211> 363
<212> PRT
<213> Homo sapiens

<400> 2987

Met Glu Val Lys Lys Lys Lys His Asp Lys Gln Glu Gln Lys Gly Ser
1 5 10 15

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

Arg Ala Ile Val Lys Glu Lys Met Val Ser Asn Thr Lys Ser Val Asp
35 40 45

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

Tyr Leu Gln Arg Gln Lys His Lys Glu Ala Pro Ser Asn Lys Ala Ser
65 70 75 80

Lys Lys Ile Cys Val Lys Asn Val Pro Cys Asp Ser Glu His Met Arg
85 90 95

Pro Ser Lys Leu Ala Val Gln Val Glu Ser Cys Gly Lys Ser Asn Glu
100 105 110

Lys His Ser Ser Gly Val Gln Thr Ser Lys Glu Ser Leu Asn Gly Leu
115 120 125

Thr Ser His Gly Lys Asn Leu Lys Ile His His Ser Gln Glu Ser Lys
130 135 140

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

Pro Asp Lys Ile Trp Ile Asp Lys Thr Lys Leu Asp Lys Leu Thr Asn
165 170 175

Ile Ser Asn Glu Ala Gln Phe Ser Gln Met Pro Pro Gln Val Lys Asp
180 185 190

Gln Lys Lys Leu Tyr Leu Asn Arg Val Gly Phe Lys Cys Thr Glu Arg
195 200 205

Glu Ser Ile Ser Leu Thr Lys Leu Glu Ser Ser Pro Arg Lys Leu His
210 215 220

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

Gly Asn Thr Glu Lys Ser Asn Met Leu Glu Phe Lys Leu Cys Pro Asp
245 250 255

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

Pro His Pro Arg Lys Glu Gln Ala Pro Leu Gln Val Ser Gly Ile Lys
275 280 285

Ser Thr Lys Glu Asp Trp Leu Lys Phe Val Ala Thr Lys Lys Arg Thr
290 295 300

Gln Lys Asp Ser Gln Glu Arg Asp Asn Val Asn Ser Arg Leu Ser Lys
305 310 315 320

Arg Ser Phe Ser Ala Asp Gly Phe Glu Met Leu Gln Asn Pro Val Lys
325 330 335

Asp Ser Lys Glu Met Phe Gln Thr Tyr Lys Gln Met Tyr Leu Glu Lys
340 345 350

Arg Ser Arg Ser Leu Gly Ser Ser Pro Val Lys
355 360

<210> 2988
<211> 836
<212> PRT
<213> Homo sapiens

<400> 2988

Met Ala Arg Leu Gly Asn Cys Ser Leu Thr Trp Ala Ala Leu Ile Ile
1 5 10 15

Leu Leu Leu Pro Gly Ser Leu Glu Glu Cys Gly His Ile Ser Val Ser
20 25 30

Ala Pro Ile Val His Leu Gly Asp Pro Ile Thr Ala Ser Cys Ile Ile
35 40 45

Lys Gln Asn Cys Ser His Leu Asp Pro Glu Pro Gln Ile Leu Trp Arg
50 55 60

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

Gly Thr Gln Glu Ser Ile Ile Thr Leu Pro His Leu Asn His Thr Gln
85 90 95

Ala Phe Leu Ser Cys Cys Leu Asn Trp Gly Asn Ser Leu Gln Ile Leu
100 105 110

Asp Gln Val Glu Leu Arg Ala Gly Tyr Pro Pro Ala Ile Pro His Asn
115 120 125

Leu Ser Cys Leu Met Asn Leu Thr Thr Ser Ser Leu Ile Cys Gln Trp
130 135 140

```
Glu Pro Gly Pro Glu Thr His Leu Pro Thr Ser Phe Thr Leu Lys Ser
145                 150                 155                 160

Phe Lys Ser Arg Gly Asn Cys Gln Thr Gln Gly Asp Ser Ile Leu Asp
                165                 170                 175

Cys Val Pro Lys Asp Gly Gln Ser His Cys Cys Ile Pro Arg Lys His
            180                 185                 190

Leu Leu Leu Tyr Gln Asn Met Gly Ile Trp Val Gln Ala Glu Asn Ala
        195                 200                 205

Leu Gly Thr Ser Met Ser Pro Gln Leu Cys Leu Asp Pro Met Asp Val
    210                 215                 220

Val Lys Leu Glu Pro Pro Met Leu Arg Thr Met Asp Pro Ser Pro Glu
225                 230                 235                 240

Ala Ala Pro Pro Gln Ala Gly Cys Leu Gln Leu Cys Trp Glu Pro Trp
                245                 250                 255

Gln Pro Gly Leu His Ile Asn Gln Lys Cys Glu Leu Arg His Lys Pro
            260                 265                 270

Gln Arg Gly Glu Ala Ser Trp Ala Leu Val Gly Pro Leu Pro Leu Glu
        275                 280                 285

Ala Leu Gln Tyr Glu Leu Cys Gly Leu Leu Pro Ala Thr Ala Tyr Thr
    290                 295                 300

Leu Gln Ile Arg Cys Ile Arg Trp Pro Leu Pro Gly His Trp Ser Asp
305                 310                 315                 320

Trp Ser Pro Ser Leu Glu Leu Arg Thr Thr Glu Arg Ala Pro Thr Val
                325                 330                 335

Arg Leu Asp Thr Trp Trp Arg Gln Arg Gln Leu Asp Pro Arg Thr Val
            340                 345                 350

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

Gln Gly Tyr Val Val Ser Trp Arg Pro Ser Gly Gln Ala Gly Ala Ile
    370                 375                 380
```

```
Leu Pro Leu Cys Asn Thr Thr Glu Leu Ser Cys Thr Phe His Leu Pro
385                 390                 395                 400

Ser Glu Ala Gln Glu Val Ala Leu Val Ala Tyr Asn Ser Ala Gly Thr
                405                 410                 415

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

Thr Arg Leu His Ala Met Ala Arg Asp Pro His Ser Leu Trp Val Gly
        435                 440                 445

Trp Glu Pro Pro Asn Pro Trp Pro Gln Gly Tyr Val Ile Glu Trp Gly
    450                 455                 460

Leu Gly Pro Pro Ser Ala Ser Asn Ser Asn Lys Thr Trp Arg Met Glu
465                 470                 475                 480

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

Phe Gln Leu Tyr Glu Ile Ile Val Thr Pro Leu Tyr Gln Asp Thr Met
            500                 505                 510

Gly Pro Ser Gln His Val Tyr Ala Tyr Ser Gln Glu Met Ala Pro Ser
        515                 520                 525

His Ala Pro Glu Leu His Leu Lys His Ile Gly Lys Thr Trp Ala Gln
    530                 535                 540

Leu Glu Trp Val Pro Glu Pro Pro Glu Leu Gly Lys Ser Pro Leu Thr
545                 550                 555                 560

His Tyr Thr Ile Phe Trp Thr Asn Ala Gln Asn Gln Ser Phe Ser Ala
                565                 570                 575

Ile Leu Asn Ala Ser Ser Arg Gly Phe Val Leu His Gly Leu Glu Pro
            580                 585                 590

Ala Ser Leu Tyr His Ile His Leu Met Ala Ala Ser Gln Ala Gly Ala
        595                 600                 605

Thr Asn Ser Thr Val Leu Thr Leu Met Thr Leu Thr Pro Glu Gly Ser
    610                 615                 620
```

Glu Leu His Ile Ile Leu Gly Leu Phe Gly Leu Leu Leu Leu Leu Thr
625 630 635 640

Cys Leu Cys Gly Thr Ala Trp Leu Cys Cys Ser Pro Asn Arg Lys Asn
645 650 655

Pro Leu Trp Pro Ser Val Pro Asp Pro Ala His Ser Ser Leu Gly Ser
660 665 670

Trp Val Pro Thr Ile Met Glu Glu Asp Ala Phe Gln Leu Pro Gly Leu
675 680 685

Gly Thr Pro Pro Ile Thr Lys Leu Thr Val Leu Glu Glu Asp Glu Lys
690 695 700

Lys Pro Val Pro Trp Glu Ser His Asn Ser Ser Glu Thr Cys Gly Leu
705 710 715 720

Pro Thr Leu Val Gln Thr Tyr Val Leu Gln Gly Asp Pro Arg Ala Val
725 730 735

Ser Thr Gln Pro Gln Ser Gln Ser Gly Thr Ser Asp Gln Val Leu Tyr
740 745 750

Gly Gln Leu Leu Gly Ser Pro Thr Ser Pro Gly Pro Gly His Tyr Leu
755 760 765

Arg Cys Asp Ser Thr Gln Pro Leu Leu Ala Gly Leu Thr Pro Ser Pro
770 775 780

Lys Ser Tyr Glu Asn Leu Trp Phe Gln Ala Ser Pro Leu Gly Thr Leu
785 790 795 800

Val Thr Pro Ala Pro Ser Gln Glu Asp Asp Cys Val Phe Gly Pro Leu
805 810 815

Leu Asn Phe Pro Leu Leu Gln Gly Ile Arg Val His Gly Met Glu Ala
820 825 830

Leu Gly Ser Phe
835

<210> 2989
<211> 276
<212> PRT
<213> Homo sapiens

<400> 2989

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

Pro Asn Pro Glu Gly Leu Asp Ser Asp Phe Leu Ala Val Leu Ser Asp
            20                  25                  30

Tyr Pro Ser Pro Asp Ile Ser Pro Pro Ile Phe Arg Arg Gly Glu Lys
        35                  40                  45

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

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

Tyr His Gly Trp Leu Phe Glu Gly Leu Gly Arg Asp Lys Ala Glu Glu
                85                  90                  95

Leu Leu Gln Leu Pro Asp Thr Lys Val Gly Ser Phe Met Ile Arg Glu
            100                 105                 110

Ser Glu Thr Lys Lys Gly Phe Tyr Ser Leu Ser Val Arg His Arg Gln
        115                 120                 125

Val Lys His Tyr Arg Ile Phe Arg Leu Pro Asn Asn Trp Tyr Tyr Ile
    130                 135                 140

Ser Pro Arg Leu Thr Phe Gln Cys Leu Glu Asp Leu Val Asn His Tyr
145                 150                 155                 160

Ser Glu Val Ala Asp Gly Leu Cys Cys Val Leu Thr Thr Pro Cys Leu
                165                 170                 175

Thr Gln Ser Thr Ala Ala Pro Ala Val Arg Ala Ser Ser Ser Pro Val
            180                 185                 190

Thr Leu Arg Gln Lys Thr Val Asp Trp Arg Arg Val Ser Arg Leu Gln
        195                 200                 205

Glu Asp Pro Glu Gly Thr Glu Asn Pro Leu Gly Val Asp Glu Ser Leu
    210                 215                 220

Phe Ser Tyr Gly Leu Arg Glu Ser Ile Ala Ser Tyr Leu Ser Leu Thr
225                 230                 235                 240
```

```
Ser Glu Asp Asn Thr Ser Phe Asp Arg Lys Lys Lys Ser Ile Ser Leu
                245                 250                 255

Met Tyr Gly Gly Ser Lys Arg Lys Ser Ser Phe Phe Ser Ser Pro Pro
            260                 265                 270

Tyr Phe Glu Asp
        275
```

<210> 2990
<211> 359
<212> PRT
<213> Homo sapiens

<400> 2990

```
Met Ala Pro Asn Gly Thr Ala Ser Ser Phe Cys Leu Asp Ser Thr Ala
1               5                   10                  15

Cys Lys Ile Thr Ile Thr Val Val Leu Ala Val Leu Ile Leu Ile Thr
            20                  25                  30

Val Ala Gly Asn Val Val Val Cys Leu Ala Val Gly Leu Asn Arg Arg
        35                  40                  45

Leu Arg Asn Leu Thr Asn Cys Phe Ile Val Ser Leu Ala Ile Thr Asp
    50                  55                  60

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

Ser Cys Lys Trp Ser Phe Gly Lys Val Phe Cys Asn Ile Tyr Thr Ser
                85                  90                  95

Leu Asp Val Met Leu Cys Thr Ala Ser Ile Leu Asn Leu Phe Met Ile
            100                 105                 110

Ser Leu Asp Arg Tyr Cys Ala Val Met Asp Pro Leu Arg Tyr Pro Val
        115                 120                 125

Leu Val Thr Pro Val Arg Val Ala Ile Ser Leu Val Leu Ile Trp Val
    130                 135                 140

Ile Ser Ile Thr Leu Ser Phe Leu Ser Ile His Leu Gly Trp Asn Ser
145                 150                 155                 160

Arg Asn Glu Thr Ser Lys Gly Asn His Thr Thr Ser Lys Cys Lys Val
```

165 170 175

Gln Val Asn Glu Val Tyr Gly Leu Val Asp Gly Leu Val Thr Phe Tyr
180 185 190

Leu Pro Leu Leu Ile Met Cys Ile Thr Tyr Tyr Arg Ile Phe Lys Val
195 200 205

Ala Arg Asp Gln Ala Lys Arg Ile Asn His Ile Ser Ser Trp Lys Ala
210 215 220

Ala Thr Ile Arg Glu His Lys Ala Thr Val Thr Leu Ala Ala Val Met
225 230 235 240

Gly Ala Phe Ile Ile Cys Trp Phe Pro Tyr Phe Thr Ala Phe Val Tyr
245 250 255

Arg Gly Leu Arg Gly Asp Asp Ala Ile Asn Glu Val Leu Glu Ala Ile
260 265 270

Val Leu Trp Leu Gly Tyr Ala Asn Ser Ala Leu Asn Pro Ile Leu Tyr
275 280 285

Ala Ala Leu Asn Arg Asp Phe Arg Thr Gly Tyr Gln Gln Leu Phe Cys
290 295 300

Cys Arg Leu Ala Asn Arg Asn Ser His Lys Thr Ser Leu Arg Ser Asn
305 310 315 320

Ala Ser Gln Leu Ser Arg Thr Gln Ser Arg Glu Pro Arg Gln Gln Glu
325 330 335

Glu Lys Pro Leu Lys Leu Gln Val Trp Ser Gly Thr Glu Val Thr Ala
340 345 350

Pro Gln Gly Ala Thr Asp Arg
355

<210> 2991
<211> 505
<212> PRT
<213> Homo sapiens

<400> 2991

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

```
Ser Lys Thr Glu Thr Ser Ala Ser Pro His Cys Pro Val Tyr Val Pro
            20                  25                  30

Asp Pro Thr Ser Thr Ile Lys Pro Gly Pro Asn Ser His Asn Ser Asn
        35                  40                  45

Thr Pro Gly Ile Arg Glu Ala Gly Ser Glu Asp Ile Ile Val Val Ala
    50                  55                  60

Leu Tyr Asp Tyr Glu Ala Ile His His Glu Asp Leu Ser Phe Gln Lys
65                  70                  75                  80

Gly Asp Gln Met Val Val Leu Glu Glu Ser Gly Glu Trp Trp Lys Ala
                85                  90                  95

Arg Ser Leu Ala Thr Arg Lys Glu Gly Tyr Ile Pro Ser Asn Tyr Val
            100                 105                 110

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

Ser Arg Lys Asp Ala Glu Arg Gln Leu Leu Ala Pro Gly Asn Met Leu
    130                 135                 140

Gly Ser Phe Met Ile Arg Asp Ser Glu Thr Thr Lys Gly Ser Tyr Ser
145                 150                 155                 160

Leu Ser Val Arg Asp Tyr Asp Pro Arg Gln Gly Asp Thr Val Lys His
                165                 170                 175

Tyr Lys Ile Arg Thr Leu Asp Asn Gly Gly Phe Tyr Ile Ser Pro Arg
            180                 185                 190

Ser Thr Phe Ser Thr Leu Gln Glu Leu Val Asp His Tyr Lys Lys Gly
        195                 200                 205

Asn Asp Gly Leu Cys Gln Lys Leu Ser Val Pro Cys Met Ser Ser Lys
    210                 215                 220

Pro Gln Lys Pro Trp Glu Lys Asp Ala Trp Glu Ile Pro Arg Glu Ser
225                 230                 235                 240

Leu Lys Leu Glu Lys Lys Leu Gly Ala Gly Gln Phe Gly Glu Val Trp
                245                 250                 255
```

```
Met Ala Thr Tyr Asn Lys His Thr Lys Val Ala Val Lys Thr Met Lys
            260                 265                 270

Pro Gly Ser Met Ser Val Glu Ala Phe Leu Ala Glu Ala Asn Val Met
        275                 280                 285

Lys Thr Leu Gln His Asp Lys Leu Val Lys Leu His Ala Val Val Thr
    290                 295                 300

Lys Glu Pro Ile Tyr Ile Ile Thr Glu Phe Met Ala Lys Gly Ser Leu
305                 310                 315                 320

Leu Asp Phe Leu Lys Ser Asp Glu Gly Ser Lys Gln Pro Leu Pro Lys
                325                 330                 335

Leu Ile Asp Phe Ser Ala Gln Ile Ala Glu Gly Met Ala Phe Ile Glu
            340                 345                 350

Gln Arg Asn Tyr Ile His Arg Asp Leu Arg Ala Ala Asn Ile Leu Val
        355                 360                 365

Ser Ala Ser Leu Val Cys Lys Ile Ala Asp Phe Gly Leu Ala Arg Val
    370                 375                 380

Ile Glu Asp Asn Glu Tyr Thr Ala Arg Glu Gly Ala Lys Phe Pro Ile
385                 390                 395                 400

Lys Trp Thr Ala Pro Glu Ala Ile Asn Phe Gly Ser Phe Thr Ile Lys
                405                 410                 415

Ser Asp Val Trp Ser Phe Gly Ile Leu Leu Met Glu Ile Val Thr Tyr
            420                 425                 430

Gly Arg Ile Pro Tyr Pro Gly Met Ser Asn Pro Glu Val Ile Arg Ala
        435                 440                 445

Leu Glu Arg Gly Tyr Arg Met Pro Arg Pro Glu Asn Cys Pro Glu Glu
    450                 455                 460

Leu Tyr Asn Ile Met Met Arg Cys Trp Lys Asn Arg Pro Glu Glu Arg
465                 470                 475                 480

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

Thr Glu Ser Gln Tyr Gln Gln Gln Pro
```

500 505

<210> 2992
<211> 1333
<212> PRT
<213> Homo sapiens

<400> 2992

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

Glu Lys Asn Ala Asp Pro Glu Thr Thr Leu Leu Ala Tyr Leu Arg Arg
20 25 30

Lys Leu Gly Leu Ser Gly Thr Lys Leu Gly Cys Gly Glu Gly Gly Cys
35 40 45

Gly Ala Cys Thr Val Met Leu Ser Lys Tyr Asp Arg Leu Gln Asn Lys
50 55 60

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

His His Val Ala Val Thr Thr Val Glu Gly Ile Gly Ser Thr Lys Thr
85 90 95

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

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

Arg Asn Gln Pro Glu Pro Thr Met Glu Glu Ile Glu Asn Ala Phe Gln
130 135 140

Gly Asn Leu Cys Arg Cys Thr Gly Tyr Arg Pro Ile Leu Gln Gly Phe
145 150 155 160

Arg Thr Phe Ala Arg Asp Gly Gly Cys Cys Gly Gly Asp Gly Asn Asn
165 170 175

Pro Asn Cys Cys Met Asn Gln Lys Lys Asp His Ser Val Ser His Ser
180 185 190

Pro Ser Leu Phe Lys Pro Glu Glu Phe Thr Pro Leu Asp Pro Thr Gln
195 200 205

```
Glu Pro Ile Phe Pro Pro Glu Leu Leu Arg Leu Lys Asp Thr Pro Arg
    210                 215                 220

Lys Gln Leu Arg Phe Glu Arg Glu Arg Val Thr Trp Ile Gln Ala Ser
225                 230                 235                 240

Thr Leu Lys Glu Leu Leu Asp Leu Lys Ala Gln His Pro Asp Ala Lys
                245                 250                 255

Leu Val Val Gly Asn Thr Glu Ile Gly Ile Glu Met Lys Phe Lys Asn
            260                 265                 270

Met Leu Phe Pro Met Ile Val Cys Pro Ala Trp Ile Pro Glu Leu Asn
        275                 280                 285

Ser Val Glu His Gly Pro Asp Gly Ile Ser Phe Gly Ala Ala Cys Pro
    290                 295                 300

Leu Ser Ile Val Glu Lys Thr Leu Val Asp Ala Val Ala Lys Leu Pro
305                 310                 315                 320

Ala Gln Lys Thr Glu Val Phe Arg Gly Val Leu Glu Gln Leu Arg Trp
                325                 330                 335

Phe Ala Gly Lys Gln Val Lys Ser Val Ala Ser Val Gly Gly Asn Ile
            340                 345                 350

Ile Thr Ala Ser Pro Ile Ser Asp Leu Asn Pro Val Phe Met Ala Ser
        355                 360                 365

Gly Ala Lys Leu Thr Leu Val Ser Arg Gly Thr Arg Arg Thr Val Gln
    370                 375                 380

Met Asp His Thr Phe Phe Pro Gly Tyr Arg Lys Thr Leu Leu Ser Pro
385                 390                 395                 400

Glu Glu Ile Leu Leu Ser Ile Glu Ile Pro Tyr Ser Arg Glu Gly Glu
                405                 410                 415

Tyr Phe Ser Ala Phe Lys Gln Ala Ser Arg Arg Glu Asp Asp Ile Ala
            420                 425                 430

Lys Val Thr Ser Gly Met Arg Val Leu Phe Lys Pro Gly Thr Thr Glu
        435                 440                 445
```

```
Val Gln Glu Leu Ala Leu Cys Tyr Gly Gly Met Ala Asn Arg Thr Ile
    450                 455                 460

Ser Ala Leu Lys Thr Thr Gln Arg Gln Leu Ser Lys Leu Trp Lys Glu
465                 470                 475                 480

Glu Leu Leu Gln Asp Val Cys Ala Gly Leu Ala Glu Glu Leu His Leu
                485                 490                 495

Pro Pro Asp Ala Pro Gly Gly Met Val Asp Phe Arg Cys Thr Leu Thr
            500                 505                 510

Leu Ser Phe Phe Phe Lys Phe Tyr Leu Thr Val Leu Gln Lys Leu Gly
        515                 520                 525

Gln Glu Asn Leu Glu Asp Lys Cys Gly Lys Leu Asp Pro Thr Phe Ala
    530                 535                 540

Ser Ala Thr Leu Leu Phe Gln Lys Asp Pro Pro Ala Asp Val Gln Leu
545                 550                 555                 560

Phe Gln Glu Val Pro Lys Gly Gln Ser Glu Glu Asp Met Val Gly Arg
                565                 570                 575

Pro Leu Pro His Leu Ala Ala Asp Met Gln Ala Ser Gly Glu Ala Val
            580                 585                 590

Tyr Cys Asp Asp Ile Pro Arg Tyr Glu Asn Glu Leu Ser Leu Arg Leu
        595                 600                 605

Val Thr Ser Thr Arg Ala His Ala Lys Ile Lys Ser Ile Asp Thr Ser
    610                 615                 620

Glu Ala Lys Lys Val Pro Gly Phe Val Cys Phe Ile Ser Ala Asp Asp
625                 630                 635                 640

Val Pro Gly Ser Asn Ile Thr Gly Ile Cys Asn Asp Glu Thr Val Phe
                645                 650                 655

Ala Lys Asp Lys Val Thr Cys Val Gly His Ile Ile Gly Ala Val Val
            660                 665                 670

Ala Asp Thr Pro Glu His Thr Gln Arg Ala Ala Gln Gly Val Lys Ile
        675                 680                 685

Thr Tyr Glu Glu Leu Pro Ala Ile Ile Thr Ile Glu Asp Ala Ile Lys
```

690 695 700

Asn Asn Ser Phe Tyr Gly Pro Glu Leu Lys Ile Glu Lys Gly Asp Leu
705 710 715 720

Lys Lys Gly Phe Ser Glu Ala Asp Asn Val Val Ser Gly Glu Ile Tyr
725 730 735

Ile Gly Gly Gln Glu His Phe Tyr Leu Glu Thr His Cys Thr Ile Ala
740 745 750

Val Pro Lys Gly Glu Ala Gly Glu Met Glu Leu Phe Val Ser Thr Gln
755 760 765

Asn Thr Met Lys Thr Gln Ser Phe Val Ala Lys Met Leu Gly Val Pro
770 775 780

Ala Asn Arg Ile Val Val Arg Val Lys Arg Met Gly Gly Gly Phe Gly
785 790 795 800

Gly Lys Glu Thr Arg Ser Thr Val Val Ser Thr Ala Val Ala Leu Ala
805 810 815

Ala Tyr Lys Thr Gly Arg Pro Val Arg Cys Met Leu Asp Arg Asp Glu
820 825 830

Asp Met Leu Ile Thr Gly Gly Arg His Pro Phe Leu Ala Arg Tyr Lys
835 840 845

Val Gly Phe Met Lys Thr Gly Thr Val Val Ala Leu Glu Val Asp His
850 855 860

Phe Ser Asn Val Gly Asn Thr Gln Asp Leu Ser Gln Ser Ile Met Glu
865 870 875 880

Arg Ala Leu Phe His Met Asp Asn Cys Tyr Lys Ile Pro Asn Ile Arg
885 890 895

Gly Thr Gly Arg Leu Cys Lys Thr Asn Leu Pro Ser Asn Thr Ala Phe
900 905 910

Arg Gly Phe Gly Gly Pro Gln Gly Met Leu Ile Ala Glu Cys Trp Met
915 920 925

Ser Glu Val Ala Val Thr Cys Gly Met Pro Ala Glu Glu Val Arg Arg
930 935 940

Lys Asn Leu Tyr Lys Glu Gly Asp Leu Thr His Phe Asn Gln Lys Leu
945 950 955 960

Glu Gly Phe Thr Leu Pro Arg Cys Trp Glu Glu Cys Leu Ala Ser Ser
965 970 975

Gln Tyr His Ala Arg Lys Ser Glu Val Asp Lys Phe Asn Lys Glu Asn
980 985 990

Cys Trp Lys Lys Arg Gly Leu Cys Ile Ile Pro Thr Lys Phe Gly Ile
995 1000 1005

Ser Phe Thr Val Pro Phe Leu Asn Gln Ala Gly Ala Leu Leu His
1010 1015 1020

Val Tyr Thr Asp Gly Ser Val Leu Leu Thr His Gly Gly Thr Glu
1025 1030 1035

Met Gly Gln Gly Leu His Thr Lys Met Val Gln Val Ala Ser Arg
1040 1045 1050

Ala Leu Lys Ile Pro Thr Ser Lys Ile Tyr Ile Ser Glu Thr Ser
1055 1060 1065

Thr Asn Thr Val Pro Asn Thr Ser Pro Thr Ala Ala Ser Val Ser
1070 1075 1080

Ala Asp Leu Asn Gly Gln Ala Val Tyr Ala Ala Cys Gln Thr Ile
1085 1090 1095

Leu Lys Arg Leu Glu Pro Tyr Lys Lys Lys Asn Pro Ser Gly Ser
1100 1105 1110

Trp Glu Asp Trp Val Thr Ala Ala Tyr Met Asp Thr Val Ser Leu
1115 1120 1125

Ser Ala Thr Gly Phe Tyr Arg Thr Pro Asn Leu Gly Tyr Ser Phe
1130 1135 1140

Glu Thr Asn Ser Gly Asn Arg Phe His Tyr Phe Ser Tyr Gly Val
1145 1150 1155

Ala Cys Ser Glu Val Glu Ile Asp Cys Leu Thr Gly Asp His Lys
1160 1165 1170

```
Asn Leu  Arg Thr Asp Ile Val  Met Asp Val Gly Ser  Ser Leu Asn
    1175                 1180                 1185

Pro Ala  Ile Asp Ile Gly Gln  Val Glu Gly Ala Phe  Val Gln Gly
    1190                 1195                 1200

Leu Gly  Leu Phe Thr Leu Glu  Glu Leu His Tyr Ser  Pro Glu Gly
    1205                 1210                 1215

Ser Leu  His Thr Arg Gly Pro  Ser Thr Tyr Lys Ile  Pro Ala Phe
    1220                 1225                 1230

Gly Ser  Ile Pro Ile Glu Phe  Arg Val Ser Leu Leu  Arg Asp Cys
    1235                 1240                 1245

Pro Asn  Lys Lys Ala Ile Tyr  Ala Ser Lys Ala Val  Gly Glu Pro
    1250                 1255                 1260

Pro Leu  Phe Leu Ala Ala Ser  Ile Phe Phe Ala Ile  Lys Asp Ala
    1265                 1270                 1275

Ile Arg  Ala Ala Arg Ala Gln  His Thr Gly Asn Asn  Val Lys Glu
    1280                 1285                 1290

Leu Phe  Arg Leu Asp Ser Pro  Ala Thr Pro Glu Lys  Ile Arg Asn
    1295                 1300                 1305

Ala Cys  Val Asp Lys Phe Thr  Thr Leu Cys Val Thr  Gly Val Pro
    1310                 1315                 1320

Glu Asn  Cys Lys Pro Trp Ser  Val Arg Val
    1325                 1330
```

<210> 2993
<211> 415
<212> PRT
<213> Homo sapiens

<400> 2993

```
Met Glu Gly Lys Ala Ile Ala Thr Ser Leu Gly Gly Asp Arg Val Leu
1               5                  10                  15

Ile Phe Pro Cys Ser Pro Arg Ser Ser Phe Val Phe Thr Ser Arg Leu
            20                  25                  30

Ser Ser Leu Pro Leu Lys Arg Ala Ser Ile Gly Gly Ala Val Ser Cys
```

```
        35                  40                  45

Ser Gly Val Asn Gly Leu Thr Arg Trp Asn Ser Ile Val Ser Thr Arg
    50                  55                  60

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

Asp Phe Pro His Glu Asn Gln Gln Gly Asn Pro Gly Leu Gly Lys Phe
                85                  90                  95

Lys Glu Tyr Gln Glu Trp Asp Ser Trp Thr Ala Lys Phe Ser Gly Gly
            100                 105                 110

Ala Asn Ile Pro Phe Leu Met Leu Gln Leu Pro Gln Ile Ile Leu Asn
        115                 120                 125

Thr Gln Asn Leu Leu Ala Gly Asn Asn Thr Ala Leu Ser Ala Val Pro
    130                 135                 140

Trp Leu Gly Met Leu Thr Gly Leu Leu Gly Asn Leu Ser Leu Leu Ser
145                 150                 155                 160

Tyr Phe Ala Lys Lys Arg Glu Lys Glu Ala Ala Val Val Gln Thr Leu
                165                 170                 175

Gly Val Val Ser Thr His Ile Val Leu Ala Gln Leu Thr Met Ala Glu
            180                 185                 190

Ala Met Pro Ile Gln Tyr Phe Val Ala Thr Ser Ala Val Val Thr Ile
        195                 200                 205

Gly Leu Ile Val Asn Cys Leu Tyr Tyr Phe Gly Lys Leu Ser Lys Thr
    210                 215                 220

Val Trp Gln Leu Trp Glu Asp Val Ile Thr Ile Gly Gly Leu Ser Val
225                 230                 235                 240

Leu Pro Gln Ile Met Trp Ser Thr Phe Val Pro Leu Val Pro Asn Ser
                245                 250                 255

Ile Leu Pro Gly Thr Thr Ala Phe Gly Ile Ala Val Ala Ala Ile Ile
            260                 265                 270

Met Ala Arg Thr Gly Lys Leu Ser Glu Lys Gly Val Arg Phe Val Gly
        275                 280                 285
```

Ser Leu Ser Gly Trp Thr Ala Thr Leu Met Phe Met Trp Met Pro Val
290 295 300

Ser Gln Met Trp Thr Asn Phe Leu Asn Pro Asp Asn Ile Lys Gly Leu
305 310 315 320

Ser Ser Ile Thr Met Leu Leu Ser Met Met Gly Asn Gly Leu Met Ile
325 330 335

Pro Arg Ala Leu Phe Ile Arg Asp Leu Met Trp Leu Thr Gly Ser Leu
340 345 350

Trp Ala Thr Leu Phe Tyr Gly Tyr Gly Asn Ile Leu Cys Leu Tyr Leu
355 360 365

Val Asn Cys Thr Ser Gln Ser Phe Phe Val Ala Ala Thr Ile Gly Leu
370 375 380

Ile Ser Trp Ile Gly Leu Ala Leu Trp Arg Asp Ala Val Ala Tyr Gly
385 390 395 400

His Asn Ser Pro Phe Arg Ser Leu Lys Glu Leu Val Phe Gly Pro
405 410 415

<210> 2994
<211> 363
<212> PRT
<213> Homo sapiens

<400> 2994

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

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

Arg Arg Gly Ile Ala Leu Pro Ala Asn Thr Ala Glu Gly Leu Leu Asn
35 40 45

Val Ile Gly Met Asp Lys Pro Leu Thr Leu Pro Asp Phe Leu Ala Lys
50 55 60

Phe Asp Tyr Tyr Met Pro Ala Ile Ala Gly Cys Arg Glu Ala Ile Lys
65 70 75 80

```
Arg Ile Ala Tyr Glu Phe Val Glu Met Lys Ala Lys Glu Gly Val Val
                85                  90                  95

Tyr Val Glu Val Arg Tyr Ser Pro His Leu Leu Ala Asn Ser Lys Val
            100                 105                 110

Glu Pro Ile Pro Trp Asn Gln Ala Glu Gly Asp Leu Thr Pro Asp Glu
        115                 120                 125

Val Val Ala Leu Val Gly Gln Gly Leu Gln Glu Gly Glu Arg Asp Phe
    130                 135                 140

Gly Val Lys Ala Arg Ser Ile Leu Cys Cys Met Arg His Gln Pro Asn
145                 150                 155                 160

Trp Ser Pro Lys Val Val Glu Leu Cys Lys Asn Tyr Gln Gln Gln Thr
                165                 170                 175

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

Leu Leu Pro Gly His Val Gln Ala Tyr Gln Glu Ala Val Lys Ser Gly
        195                 200                 205

Ile His Arg Thr Val His Ala Gly Glu Val Gly Ser Ala Glu Val Val
    210                 215                 220

Lys Glu Ala Val Asp Ile Leu Lys Thr Glu Arg Leu Gly His Gly Tyr
225                 230                 235                 240

His Thr Leu Glu Asp Gln Ala Leu Tyr Asn Arg Leu Arg Gln Glu Asn
                245                 250                 255

Met His Phe Glu Ile Cys Pro Trp Ser Ser Tyr Leu Thr Gly Ala Trp
            260                 265                 270

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

Asn Tyr Ser Leu Asn Thr Asp Asp Pro Leu Ile Phe Lys Ser Thr Leu
    290                 295                 300

Asp Thr Asp Tyr Gln Met Thr Lys Arg Asp Met Gly Phe Thr Glu Glu
305                 310                 315                 320

Glu Phe Lys Arg Leu Asn Ile Asn Ala Ala Lys Ser Ser Phe Leu Pro
```

325 330 335

Glu Asp Glu Lys Arg Glu Leu Leu Asp Leu Leu Tyr Lys Ala Tyr Gly
340 345 350

Met Pro Pro Ser Ala Ser Ala Gly Gln Asn Leu
355 360

<210> 2995
<211> 691
<212> PRT
<213> Homo sapiens

<400> 2995

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

Phe Ser Lys Lys Lys Lys Lys Lys Lys Lys Asn Asn Met Ala Ala Lys
20 25 30

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

Met Leu Leu Asp Val Leu Tyr Arg Trp Asp Val Ser Ser Phe Phe Gln
50 55 60

Gln Ile Gln Arg Ser Ser Leu Ser Asn Asn Pro Leu Phe Gln Tyr Lys
65 70 75 80

Tyr Leu Ala Leu Asn Met His Tyr Val Gly Tyr Ile Leu Ser Val Val
85 90 95

Leu Leu Thr Leu Pro Arg Gln His Leu Val Gln Leu Tyr Leu Tyr Phe
100 105 110

Leu Thr Ala Leu Leu Leu Tyr Ala Gly His Gln Ile Ser Arg Asp Tyr
115 120 125

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

Pro Leu Ser Met Asn Arg Phe Thr Thr Ala Leu Ile Gly Gln Leu Val
145 150 155 160

Val Cys Thr Leu Cys Ser Cys Val Met Lys Thr Lys Gln Ile Trp Leu
165 170 175

Phe Ser Ala His Met Leu Pro Leu Leu Ala Arg Leu Cys Leu Val Pro
180 185 190

Leu Glu Thr Ile Val Ile Ile Asn Lys Phe Ala Met Ile Phe Thr Gly
195 200 205

Leu Glu Val Leu Tyr Phe Leu Gly Ser Asn Leu Leu Val Pro Tyr Asn
210 215 220

Leu Ala Lys Ser Ala Tyr Arg Glu Leu Val Gln Val Val Glu Val Tyr
225 230 235 240

Gly Leu Leu Ala Leu Gly Met Ser Leu Trp Asn Gln Leu Val Val Pro
245 250 255

Val Leu Phe Met Val Phe Trp Leu Val Leu Phe Ala Leu Gln Ile Tyr
260 265 270

Ser Tyr Phe Ser Thr Arg Asp Gln Pro Ala Ser Arg Glu Arg Leu Leu
275 280 285

Phe Leu Phe Leu Thr Ser Ile Ala Glu Cys Cys Ser Thr Pro Tyr Ser
290 295 300

Leu Leu Gly Leu Val Phe Thr Val Ser Phe Val Ala Leu Gly Val Leu
305 310 315 320

Thr Leu Cys Lys Phe Tyr Leu Gln Gly Tyr Arg Ala Phe Met Asn Asp
325 330 335

Pro Ala Met Asn Arg Gly Met Thr Glu Gly Val Thr Leu Leu Ile Leu
340 345 350

Ala Val Gln Thr Gly Leu Ile Glu Leu Gln Val Val His Arg Ala Phe
355 360 365

Leu Leu Ser Ile Ile Leu Phe Ile Val Val Ala Ser Ile Leu Gln Ser
370 375 380

Met Leu Glu Ile Ala Asp Pro Ile Val Leu Ala Leu Gly Ala Ser Arg
385 390 395 400

Asp Lys Ser Leu Trp Lys His Phe Arg Ala Val Ser Leu Cys Leu Phe
405 410 415

Leu Leu Val Phe Pro Ala Tyr Met Ala Tyr Met Ile Cys Gln Phe Phe
420 425 430

His Met Asp Phe Trp Leu Leu Ile Ile Ile Ser Ser Ser Ile Leu Thr
435 440 445

Ser Leu Gln Val Leu Gly Thr Leu Phe Ile Tyr Val Leu Phe Met Val
450 455 460

Glu Glu Phe Arg Lys Glu Pro Val Glu Asn Met Asp Asp Val Ile Tyr
465 470 475 480

Tyr Val Asn Gly Thr Tyr Arg Leu Leu Glu Phe Leu Val Ala Leu Cys
485 490 495

Val Val Ala Tyr Gly Val Ser Glu Thr Ile Phe Gly Glu Trp Thr Val
500 505 510

Met Gly Ser Met Ile Ile Phe Ile His Ser Tyr Tyr Asn Val Trp Leu
515 520 525

Arg Ala Gln Leu Gly Trp Lys Ser Phe Leu Leu Arg Arg Asp Ala Val
530 535 540

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

His Asn Asp Ile Cys Ala Ile Cys Tyr Gln Asp Met Lys Ser Ala Val
565 570 575

Ile Thr Pro Cys Ser His Phe Phe His Ala Gly Cys Leu Lys Lys Trp
580 585 590

Leu Tyr Val Gln Glu Thr Cys Pro Leu Cys His Cys His Leu Lys Asn
595 600 605

Ser Ser Gln Leu Pro Gly Leu Gly Thr Glu Pro Val Leu Gln Pro His
610 615 620

Ala Gly Ala Glu Gln Asn Val Met Phe Gln Glu Gly Thr Glu Pro Pro
625 630 635 640

Gly Gln Glu His Thr Pro Gly Thr Arg Ile Gln Glu Gly Ser Arg Asp
645 650 655

Asn Asn Glu Tyr Ile Ala Arg Arg Pro Asp Asn Gln Glu Gly Ala Phe

660 665 670

Asp Pro Lys Glu Tyr Pro His Ser Ala Lys Asp Glu Ala His Pro Val
675 680 685

Glu Ser Ala
690

<210> 2996
<211> 390
<212> PRT
<213> Homo sapiens

<400> 2996

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

Pro Glu Pro Pro Arg Tyr Leu Gln Ser Leu Ser Gly Pro Glu Leu Pro
20 25 30

Pro Pro Pro Pro Asp Arg Ser Ser Arg Leu Cys Val Pro Ala Pro Leu
35 40 45

Ser Thr Ala Pro Gly Ala Arg Glu Gly Arg Ser Ala Arg Arg Ala Ala
50 55 60

Arg Gly Asn Leu Glu Pro Pro Pro Arg Ala Ser Arg Pro Ala Arg Pro
65 70 75 80

Leu Arg Pro Gly Leu Gln Gln Arg Leu Arg Arg Arg Pro Gly Ala Pro
85 90 95

Arg Pro Arg Asp Val Arg Ser Ile Phe Glu Gln Pro Gln Asp Pro Arg
100 105 110

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

Pro Gly Gly Pro Gly Trp Cys Asp Leu Cys Gly Arg Glu Val Leu Arg
130 135 140

Gln Ala Leu Arg Cys Thr Asn Cys Lys Phe Thr Cys His Pro Glu Cys
145 150 155 160

Arg Ser Leu Ile Gln Leu Asp Cys Ser Gln Gln Glu Gly Leu Ser Arg
165 170 175

```
Asp Arg Pro Ser Pro Glu Ser Thr Leu Thr Val Thr Phe Ser Gln Asn
            180                 185                 190

Val Cys Lys Pro Val Glu Glu Thr Gln Arg Pro Pro Thr Leu Gln Glu
        195                 200                 205

Ile Lys Gln Lys Ile Asp Ser Tyr Asn Thr Arg Glu Lys Asn Cys Leu
    210                 215                 220

Gly Met Lys Leu Ser Glu Asp Gly Thr Tyr Thr Gly Phe Ile Lys Val
225                 230                 235                 240

His Leu Lys Leu Arg Arg Pro Val Thr Val Pro Ala Gly Ile Arg Pro
                245                 250                 255

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

Asp Lys Arg Thr Ser Phe Tyr Leu Pro Leu Asp Ala Ile Lys Gln Leu
        275                 280                 285

His Ile Ser Ser Thr Thr Thr Val Ser Glu Val Ile Gln Gly Leu Leu
    290                 295                 300

Lys Lys Phe Met Val Val Asp Asn Pro Gln Lys Phe Ala Leu Phe Lys
305                 310                 315                 320

Arg Ile His Lys Asp Gly Gln Val Leu Phe Gln Lys Leu Ser Ile Ala
                325                 330                 335

Asp Arg Pro Leu Tyr Leu Arg Leu Leu Ala Gly Pro Asp Thr Glu Val
            340                 345                 350

Leu Ser Phe Val Leu Lys Glu Asn Glu Thr Gly Glu Val Glu Trp Asp
        355                 360                 365

Ala Phe Ser Ile Pro Glu Leu Gln Asn Phe Leu Ser Ser Trp Cys Ile
    370                 375                 380

Gln Ile Tyr Leu Tyr Tyr
385                 390
```

<210> 2997
<211> 297
<212> PRT
<213> Homo sapiens

<400> 2997

```
Met Thr Thr Pro Arg Asn Ser Val Asn Gly Thr Phe Pro Ala Glu Pro
1               5                  10                  15

Met Lys Gly Pro Ile Ala Met Gln Ser Gly Pro Lys Pro Leu Phe Arg
            20                  25                  30

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

Ser Lys Thr Leu Gly Ala Val Gln Ile Met Asn Gly Leu Phe His Ile
    50                  55                  60

Ala Leu Gly Gly Leu Leu Met Ile Pro Ala Gly Ile Tyr Ala Pro Ile
65                  70                  75                  80

Cys Val Thr Val Trp Tyr Pro Leu Trp Gly Gly Ile Met Tyr Ile Ile
                85                  90                  95

Ser Gly Ser Leu Leu Ala Ala Thr Glu Lys Asn Ser Arg Lys Cys Leu
            100                 105                 110

Val Lys Gly Lys Met Ile Met Asn Ser Leu Ser Leu Phe Ala Ala Ile
        115                 120                 125

Ser Gly Met Ile Leu Ser Ile Met Asp Ile Leu Asn Ile Lys Ile Ser
    130                 135                 140

His Phe Leu Lys Met Glu Ser Leu Asn Phe Ile Arg Ala His Thr Pro
145                 150                 155                 160

Tyr Ile Asn Ile Tyr Asn Cys Glu Pro Ala Asn Pro Ser Glu Lys Asn
                165                 170                 175

Ser Pro Ser Thr Gln Tyr Cys Tyr Ser Ile Gln Ser Leu Phe Leu Gly
            180                 185                 190

Ile Leu Ser Val Met Leu Ile Phe Ala Phe Phe Gln Glu Leu Val Ile
        195                 200                 205

Ala Gly Ile Val Glu Asn Glu Trp Lys Arg Thr Cys Ser Arg Pro Lys
    210                 215                 220

Ser Asn Ile Val Leu Leu Ser Ala Glu Glu Lys Lys Glu Gln Thr Ile
225                 230                 235                 240
```

```
Glu Ile Lys Glu Glu Val Val Gly Leu Thr Glu Thr Ser Ser Gln Pro
               245                 250                 255

Lys Asn Glu Glu Asp Ile Glu Ile Ile Pro Ile Gln Glu Glu Glu Glu
            260                 265                 270

Glu Glu Thr Glu Thr Asn Phe Pro Glu Pro Pro Gln Asp Gln Glu Ser
        275                 280                 285

Ser Pro Ile Glu Asn Asp Ser Ser Pro
    290                 295
```

<210> 2998
<211> 261
<212> PRT
<213> Homo sapiens

<400> 2998

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

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

Arg Asp Ser Pro Glu Asp Phe Val Tyr Gln Phe Lys Gly Met Cys Tyr
        35                  40                  45

Phe Thr Asn Gly Thr Glu Arg Val Arg Leu Val Ser Arg Ser Ile Tyr
    50                  55                  60

Asn Arg Glu Glu Ile Val Arg Phe Asp Ser Asp Val Gly Glu Phe Arg
65                  70                  75                  80

Ala Val Thr Leu Leu Gly Leu Pro Ala Ala Glu Tyr Trp Asn Ser Gln
                85                  90                  95

Lys Asp Ile Leu Glu Arg Lys Arg Ala Ala Val Asp Arg Val Cys Arg
            100                 105                 110

His Asn Tyr Gln Leu Glu Leu Arg Thr Thr Leu Gln Arg Arg Val Glu
        115                 120                 125

Pro Thr Val Thr Ile Ser Pro Ser Arg Thr Glu Ala Leu Asn His His
    130                 135                 140
```

Asn Leu Leu Val Cys Ser Val Thr Asp Phe Tyr Pro Ala Gln Ile Lys
145 150 155 160

Val Arg Trp Phe Arg Asn Asp Gln Glu Glu Thr Ala Gly Val Val Ser
165 170 175

Thr Pro Leu Ile Arg Asn Gly Asp Trp Thr Phe Gln Ile Leu Val Met
180 185 190

Leu Glu Met Thr Pro Gln Arg Gly Asp Val Tyr Thr Cys His Val Glu
195 200 205

His Pro Ser Leu Gln Ser Pro Ile Thr Val Glu Trp Arg Ala Gln Ser
210 215 220

Glu Ser Ala Gln Ser Lys Met Leu Ser Gly Ile Gly Gly Phe Val Leu
225 230 235 240

Gly Leu Ile Phe Leu Gly Leu Gly Leu Ile Ile His His Arg Ser Gln
245 250 255

Lys Gly Leu Leu His
260

<210> 2999
<211> 258
<212> PRT
<213> Homo sapiens

<400> 2999

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

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

Pro Glu Asn Tyr Leu Phe Gln Gly Arg Gln Glu Cys Tyr Ala Phe Asn
35 40 45

Gly Thr Gln Arg Phe Leu Glu Arg Tyr Ile Tyr Asn Arg Glu Glu Phe
50 55 60

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

Gly Arg Pro Ala Ala Glu Tyr Trp Asn Ser Gln Lys Asp Ile Leu Glu
85 90 95

Glu Lys Arg Ala Val Pro Asp Arg Met Cys Arg His Asn Tyr Glu Leu
100 105 110

Gly Gly Pro Met Thr Leu Gln Arg Arg Val Gln Pro Arg Val Asn Val
115 120 125

Ser Pro Ser Lys Lys Gly Pro Leu Gln His His Asn Leu Leu Val Cys
130 135 140

His Val Thr Asp Phe Tyr Pro Gly Ser Ile Gln Val Arg Trp Phe Leu
145 150 155 160

Asn Gly Gln Glu Glu Thr Ala Gly Val Val Ser Thr Asn Leu Ile Arg
165 170 175

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

Gln Gln Gly Asp Val Tyr Thr Cys Gln Val Glu His Thr Ser Leu Asp
195 200 205

Ser Pro Val Thr Val Glu Trp Lys Ala Gln Ser Asp Ser Ala Arg Ser
210 215 220

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

Gly Val Gly Ile Phe Met His Arg Arg Ser Lys Lys Val Gln Arg Gly
245 250 255

Ser Ala

<210> 3000
<211> 175
<212> PRT
<213> Homo sapiens

<400> 3000

Met Thr Asp Cys Glu Phe Gly Tyr Ile Tyr Arg Leu Ala Gln Asp Tyr
1 5 10 15

Leu Gln Cys Val Leu Gln Ile Pro Gln Pro Gly Ser Gly Pro Ser Lys
20 25 30

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Thr Ser Arg Val Leu Gln Asn Val Ala Phe Ser Val Gln Lys Glu Val
        35                  40                  45

Glu Lys Asn Leu Lys Ser Cys Leu Asp Asn Val Asn Val Val Ser Val
    50                  55                  60

Asp Thr Ala Arg Thr Leu Phe Asn Gln Val Met Glu Lys Glu Phe Glu
65                  70                  75                  80

Asp Gly Ile Ile Asn Trp Gly Arg Ile Val Thr Ile Phe Ala Phe Glu
                85                  90                  95

Gly Ile Leu Ile Lys Lys Leu Leu Arg Gln Gln Ile Ala Pro Asp Val
            100                 105                 110

Asp Thr Tyr Lys Glu Ile Ser Tyr Phe Val Ala Glu Phe Ile Met Asn
        115                 120                 125

Asn Thr Gly Glu Trp Ile Arg Gln Asn Gly Gly Trp Glu Asn Gly Phe
    130                 135                 140

Val Lys Lys Phe Glu Pro Lys Ser Gly Trp Met Thr Phe Leu Glu Val
145                 150                 155                 160

Thr Gly Lys Ile Cys Glu Met Leu Ser Leu Leu Lys Gln Tyr Cys
                165                 170                 175
```

<210> 3001
<211> 825
<212> PRT
<213> Homo sapiens

<400> 3001

```
Met Gly Trp Leu Cys Ser Gly Leu Leu Phe Pro Val Ser Cys Leu Val
1               5                   10                  15

Leu Leu Gln Val Ala Ser Ser Gly Asn Met Lys Val Leu Gln Glu Pro
            20                  25                  30

Thr Cys Val Ser Asp Tyr Met Ser Ile Ser Thr Cys Glu Trp Lys Met
        35                  40                  45

Asn Gly Pro Thr Asn Cys Ser Thr Glu Leu Arg Leu Leu Tyr Gln Leu
    50                  55                  60

Val Phe Leu Leu Ser Glu Ala His Thr Cys Ile Pro Glu Asn Asn Gly
65                  70                  75                  80
```

Gly Ala Gly Cys Val Cys His Leu Leu Met Asp Asp Val Val Ser Ala
85 90 95

Asp Asn Tyr Thr Leu Asp Leu Trp Ala Gly Gln Gln Leu Leu Trp Lys
100 105 110

Gly Ser Phe Lys Pro Ser Glu His Val Lys Pro Arg Ala Pro Gly Asn
115 120 125

Leu Thr Val His Thr Asn Val Ser Asp Thr Leu Leu Leu Thr Trp Ser
130 135 140

Asn Pro Tyr Pro Pro Asp Asn Tyr Leu Tyr Asn His Leu Thr Tyr Ala
145 150 155 160

Val Asn Ile Trp Ser Glu Asn Asp Pro Ala Asp Phe Arg Ile Tyr Asn
165 170 175

Val Thr Tyr Leu Glu Pro Ser Leu Arg Ile Ala Ala Ser Thr Leu Lys
180 185 190

Ser Gly Ile Ser Tyr Arg Ala Arg Val Arg Ala Trp Ala Gln Cys Tyr
195 200 205

Asn Thr Thr Trp Ser Glu Trp Ser Pro Ser Thr Lys Trp His Asn Ser
210 215 220

Tyr Arg Glu Pro Phe Glu Gln His Leu Leu Leu Gly Val Ser Val Ser
225 230 235 240

Cys Ile Val Ile Leu Ala Val Cys Leu Leu Cys Tyr Val Ser Ile Thr
245 250 255

Lys Ile Lys Lys Glu Trp Trp Asp Gln Ile Pro Asn Pro Ala Arg Ser
260 265 270

Arg Leu Val Ala Ile Ile Ile Gln Asp Ala Gln Gly Ser Gln Trp Glu
275 280 285

Lys Arg Ser Arg Gly Gln Glu Pro Ala Lys Cys Pro His Trp Lys Asn
290 295 300

Cys Leu Thr Lys Leu Leu Pro Cys Phe Leu Glu His Asn Met Lys Arg
305 310 315 320

```
Asp Glu Asp Pro His Lys Ala Ala Lys Glu Met Pro Phe Gln Gly Ser
                325                 330                 335

Gly Lys Ser Ala Trp Cys Pro Val Glu Ile Ser Lys Thr Val Leu Trp
            340                 345                 350

Pro Glu Ser Ile Ser Val Val Arg Cys Val Glu Leu Phe Glu Ala Pro
        355                 360                 365

Val Glu Cys Glu Glu Glu Glu Glu Val Glu Glu Glu Lys Gly Ser Phe
    370                 375                 380

Cys Ala Ser Pro Glu Ser Ser Arg Asp Asp Phe Gln Glu Gly Arg Glu
385                 390                 395                 400

Gly Ile Val Ala Arg Leu Thr Glu Ser Leu Phe Leu Asp Leu Leu Gly
                405                 410                 415

Glu Glu Asn Gly Gly Phe Cys Gln Gln Asp Met Gly Glu Ser Cys Leu
            420                 425                 430

Leu Pro Pro Ser Gly Ser Thr Ser Ala His Met Pro Trp Asp Glu Phe
        435                 440                 445

Pro Ser Ala Gly Pro Lys Glu Ala Pro Pro Trp Gly Lys Glu Gln Pro
    450                 455                 460

Leu His Leu Glu Pro Ser Pro Pro Ala Ser Pro Thr Gln Ser Pro Asp
465                 470                 475                 480

Asn Leu Thr Cys Thr Glu Thr Pro Leu Val Ile Ala Gly Asn Pro Ala
                485                 490                 495

Tyr Arg Ser Phe Ser Asn Ser Leu Ser Gln Ser Pro Cys Pro Arg Glu
            500                 505                 510

Leu Gly Pro Asp Pro Leu Leu Ala Arg His Leu Glu Glu Val Glu Pro
        515                 520                 525

Glu Met Pro Cys Val Pro Gln Leu Ser Glu Pro Thr Thr Val Pro Gln
    530                 535                 540

Pro Glu Pro Glu Thr Trp Glu Gln Ile Leu Arg Arg Asn Val Leu Gln
545                 550                 555                 560
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His Gly Ala Ala Ala Ala Pro Val Ser Ala Pro Thr Ser Gly Tyr Gln
                565                 570                 575

Glu Phe Val His Ala Val Glu Gln Gly Gly Thr Gln Ala Ser Ala Val
            580                 585                 590

Val Gly Leu Gly Pro Pro Gly Glu Ala Gly Tyr Lys Ala Phe Ser Ser
        595                 600                 605

Leu Leu Ala Ser Ser Ala Val Ser Pro Glu Lys Cys Gly Phe Gly Ala
    610                 615                 620

Ser Ser Gly Glu Glu Gly Tyr Lys Pro Phe Gln Asp Leu Ile Pro Gly
625                 630                 635                 640

Cys Pro Gly Asp Pro Ala Pro Val Pro Val Pro Leu Phe Thr Phe Gly
                645                 650                 655

Leu Asp Arg Glu Pro Pro Arg Ser Pro Gln Ser Ser His Leu Pro Ser
            660                 665                 670

Ser Ser Pro Glu His Leu Gly Leu Glu Pro Gly Glu Lys Val Glu Asp
        675                 680                 685

Met Pro Lys Pro Pro Leu Pro Gln Glu Gln Ala Thr Asp Pro Leu Val
    690                 695                 700

Asp Ser Leu Gly Ser Gly Ile Val Tyr Ser Ala Leu Thr Cys His Leu
705                 710                 715                 720

Cys Gly His Leu Lys Gln Cys His Gly Gln Glu Asp Gly Gly Gln Thr
                725                 730                 735

Pro Val Met Ala Ser Pro Cys Cys Gly Cys Cys Cys Gly Asp Arg Ser
            740                 745                 750

Ser Pro Pro Thr Thr Pro Leu Arg Ala Pro Asp Pro Ser Pro Gly Gly
        755                 760                 765

Val Pro Leu Glu Ala Ser Leu Cys Pro Ala Ser Leu Ala Pro Ser Gly
    770                 775                 780

Ile Ser Glu Lys Ser Lys Ser Ser Ser Ser Phe His Pro Ala Pro Gly
785                 790                 795                 800

Asn Ala Gln Ser Ser Ser Gln Thr Pro Lys Ile Val Asn Phe Val Ser
```

805 810 815

Val Gly Pro Thr Tyr Met Arg Val Ser
820 825

<210> 3002
<211> 285
<212> PRT
<213> Homo sapiens

<400> 3002

Met Asp Asp Ser Thr Glu Arg Glu Gln Ser Arg Leu Thr Ser Cys Leu
1 5 10 15

Lys Lys Arg Glu Glu Met Lys Leu Lys Glu Cys Val Ser Ile Leu Pro
20 25 30

Arg Lys Glu Ser Pro Ser Val Arg Ser Ser Lys Asp Gly Lys Leu Leu
35 40 45

Ala Ala Thr Leu Leu Leu Ala Leu Leu Ser Cys Cys Leu Thr Val Val
50 55 60

Ser Phe Tyr Gln Val Ala Ala Leu Gln Gly Asp Leu Ala Ser Leu Arg
65 70 75 80

Ala Glu Leu Gln Gly His His Ala Glu Lys Leu Pro Ala Gly Ala Gly
85 90 95

Ala Pro Lys Ala Gly Leu Glu Glu Ala Pro Ala Val Thr Ala Gly Leu
100 105 110

Lys Ile Phe Glu Pro Pro Ala Pro Gly Glu Gly Asn Ser Ser Gln Asn
115 120 125

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

Asp Cys Leu Gln Leu Ile Ala Asp Ser Glu Thr Pro Thr Ile Gln Lys
145 150 155 160

Gly Ser Tyr Thr Phe Val Pro Trp Leu Leu Ser Phe Lys Arg Gly Ser
165 170 175

Ala Leu Glu Glu Lys Glu Asn Lys Ile Leu Val Lys Glu Thr Gly Tyr
180 185 190

Phe Phe Ile Tyr Gly Gln Val Leu Tyr Thr Asp Lys Thr Tyr Ala Met
195 200 205

Gly His Leu Ile Gln Arg Lys Lys Val His Val Phe Gly Asp Glu Leu
210 215 220

Ser Leu Val Thr Leu Phe Arg Cys Ile Gln Asn Met Pro Glu Thr Leu
225 230 235 240

Pro Asn Asn Ser Cys Tyr Ser Ala Gly Ile Ala Lys Leu Glu Glu Gly
245 250 255

Asp Glu Leu Gln Leu Ala Ile Pro Arg Glu Asn Ala Gln Ile Ser Leu
260 265 270

Asp Gly Asp Val Thr Phe Phe Gly Ala Leu Lys Leu Leu
275 280 285

<210> 3003
<211> 444
<212> PRT
<213> Homo sapiens

<400> 3003

Met Ala Val Thr Thr Arg Leu Thr Arg Leu His Glu Lys Ile Leu Gln
1 5 10 15

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

His Gly Phe Arg Asn Gly Val Leu Leu Asp Arg Cys Cys Asn Gln Gly
35 40 45

Pro Thr Leu Thr Val Ile Tyr Ser Glu Asp His Ile Ile Gly Ala Tyr
50 55 60

Ala Glu Glu Ser Tyr Gln Glu Gly Lys Tyr Ala Ser Ile Ile Leu Phe
65 70 75 80

Ala Leu Gln Asp Thr Lys Ile Ser Glu Trp Lys Leu Gly Leu Cys Thr
85 90 95

Pro Glu Thr Leu Phe Cys Cys Asp Val Thr Lys Tyr Asn Ser Pro Thr
100 105 110

Asn Phe Gln Ile Asp Gly Arg Asn Arg Lys Val Ile Met Asp Leu Lys

115 120 125

Thr Met Glu Asn Leu Gly Leu Ala Gln Asn Cys Thr Ile Ser Ile Gln
130 135 140

Asp Tyr Glu Val Phe Arg Cys Glu Asp Ser Leu Asp Glu Arg Lys Ile
145 150 155 160

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

Tyr Glu Pro Tyr Gly Ser Leu Val Gln Gln Ile Arg Ile Leu Leu Leu
180 185 190

Gly Pro Ile Gly Ala Gly Lys Ser Ser Phe Phe Asn Ser Val Arg Ser
195 200 205

Val Phe Gln Gly His Val Thr His Gln Ala Leu Val Gly Thr Asn Thr
210 215 220

Thr Gly Ile Ser Glu Lys Tyr Arg Thr Tyr Ser Ile Arg Asp Gly Lys
225 230 235 240

Asp Gly Lys Tyr Leu Pro Phe Ile Leu Cys Asp Ser Leu Gly Leu Ser
245 250 255

Glu Lys Glu Gly Gly Leu Cys Arg Asp Asp Ile Phe Tyr Ile Leu Asn
260 265 270

Gly Asn Ile Arg Asp Arg Tyr Gln Phe Asn Pro Met Glu Ser Ile Lys
275 280 285

Leu Asn His His Asp Tyr Ile Asp Ser Pro Ser Leu Lys Asp Arg Ile
290 295 300

His Cys Val Ala Phe Val Phe Asp Ala Ser Ser Ile Gln Tyr Phe Ser
305 310 315 320

Ser Gln Met Ile Val Lys Ile Lys Arg Ile Arg Arg Glu Leu Val Asn
325 330 335

Ala Gly Val Val His Val Ala Leu Leu Thr His Val Asp Ser Met Asp
340 345 350

Leu Ile Thr Lys Gly Asp Leu Ile Glu Ile Glu Arg Cys Glu Pro Val
355 360 365

Arg Ser Lys Leu Glu Glu Val Gln Arg Lys Leu Gly Phe Ala Leu Ser
370 375 380

Asp Ile Ser Val Val Ser Asn Tyr Ser Ser Glu Trp Glu Leu Asp Pro
385 390 395 400

Val Lys Asp Val Leu Ile Leu Ser Ala Leu Arg Arg Met Leu Trp Ala
405 410 415

Ala Asp Asp Phe Leu Glu Asp Leu Pro Phe Glu Gln Ile Gly Asn Leu
420 425 430

Arg Glu Glu Ile Ile Asn Cys Ala Gln Gly Lys Lys
435 440

<210> 3004
<211> 432
<212> PRT
<213> Homo sapiens

<400> 3004

Met Gly Pro Ala Gly Ser Leu Leu Gly Ser Gly Gln Met Gln Ile Thr
1 5 10 15

Leu Trp Gly Ser Leu Ala Ala Val Ala Ile Phe Phe Val Ile Thr Phe
20 25 30

Leu Ile Phe Pro Cys Ser Ser Cys Asp Arg Glu Lys Lys Pro Arg Gln
35 40 45

His Ser Gly Asp His Glu Asn Leu Met Asn Val Pro Ser Asp Lys Glu
50 55 60

Met Phe Ser Arg Ser Val Thr Ser Leu Ala Thr Asp Ala Pro Ala Ser
65 70 75 80

Ser Glu Gln Asn Gly Ala Leu Thr Asn Gly Asp Ile Leu Ser Glu Asp
85 90 95

Ser Thr Leu Thr Cys Met Gln His Tyr Glu Glu Val Gln Thr Ser Ala
100 105 110

Ser Asp Leu Leu Asp Ser Gln Asp Ser Thr Gly Lys Pro Lys Cys His
115 120 125

Gln Ser Arg Glu Leu Pro Arg Ile Pro Pro Glu Ser Ala Val Asp Thr
130 135 140

Met Leu Thr Ala Arg Ser Val Asp Gly Asp Gln Gly Leu Gly Met Glu
145 150 155 160

Gly Pro Tyr Glu Val Leu Lys Asp Ser Ser Ser Gln Glu Asn Met Val
165 170 175

Glu Asp Cys Leu Tyr Glu Thr Val Lys Glu Ile Lys Glu Val Ala Ala
180 185 190

Ala Ala His Leu Glu Lys Gly His Ser Gly Lys Ala Lys Ser Thr Ser
195 200 205

Ala Ser Lys Glu Leu Pro Gly Pro Gln Thr Glu Gly Lys Ala Glu Phe
210 215 220

Ala Glu Tyr Ala Ser Val Asp Arg Asn Lys Lys Cys Arg Gln Ser Val
225 230 235 240

Asn Val Glu Ser Ile Leu Gly Asn Ser Cys Asp Pro Glu Glu Glu Ala
245 250 255

Pro Pro Pro Val Pro Val Lys Leu Leu Asp Glu Asn Glu Asn Leu Gln
260 265 270

Glu Lys Glu Gly Gly Glu Ala Glu Glu Ser Ala Thr Asp Thr Thr Ser
275 280 285

Glu Thr Asn Lys Arg Phe Ser Ser Leu Ser Tyr Lys Ser Arg Glu Glu
290 295 300

Asp Pro Thr Leu Thr Glu Glu Glu Ile Ser Ala Met Tyr Ser Ser Val
305 310 315 320

Asn Lys Pro Gly Gln Leu Val Asn Lys Ser Gly Gln Ser Leu Thr Val
325 330 335

Pro Glu Ser Thr Tyr Thr Ser Ile Gln Gly Asp Pro Gln Arg Ser Pro
340 345 350

Ser Ser Cys Asn Asp Leu Tyr Ala Thr Val Lys Asp Phe Glu Lys Thr
355 360 365

Pro Asn Ser Thr Leu Pro Pro Ala Gly Arg Pro Ser Glu Glu Pro Glu

370 375 380

Pro Asp Tyr Glu Ala Ile Gln Thr Leu Asn Arg Glu Glu Glu Lys Ala
385 390 395 400

Thr Leu Gly Thr Asn Gly His His Gly Leu Val Pro Lys Glu Asn Asp
405 410 415

Tyr Glu Ser Ile Ser Asp Leu Gln Gln Gly Arg Asp Ile Thr Arg Leu
420 425 430

<210> 3005
<211> 501
<212> PRT
<213> Homo sapiens

<400> 3005

Met Ile Ile Ser His Phe Pro Lys Cys Val Ala Val Phe Ala Leu Leu
1 5 10 15

Ala Leu Ser Val Gly Ala Leu Asp Thr Phe Ile Ala Ala Val Tyr Glu
20 25 30

His Ala Val Ile Leu Pro Asn Arg Thr Glu Thr Pro Val Ser Lys Glu
35 40 45

Glu Ala Leu Leu Leu Met Asn Lys Asn Ile Asp Val Leu Glu Lys Ala
50 55 60

Val Lys Leu Ala Ala Lys Gln Gly Ala His Ile Ile Val Thr Pro Glu
65 70 75 80

Asp Gly Ile Tyr Gly Trp Ile Phe Thr Arg Glu Ser Ile Tyr Pro Tyr
85 90 95

Leu Glu Asp Ile Pro Asp Pro Gly Val Asn Trp Ile Pro Cys Arg Asp
100 105 110

Pro Trp Arg Phe Gly Asn Thr Pro Val Gln Gln Arg Leu Ser Cys Leu
115 120 125

Ala Lys Asp Asn Ser Ile Tyr Val Val Ala Asn Ile Gly Asp Lys Lys
130 135 140

Pro Cys Asn Ala Ser Asp Ser Gln Cys Pro Pro Asp Gly Arg Tyr Gln
145 150 155 160

Tyr Asn Thr Asp Val Val Phe Asp Ser Gln Gly Lys Leu Leu Ala Arg
165 170 175

Tyr His Lys Tyr Asn Leu Phe Ala Pro Glu Ile Gln Phe Asp Phe Pro
180 185 190

Lys Asp Ser Glu Leu Val Thr Phe Asp Thr Pro Phe Gly Lys Phe Gly
195 200 205

Ile Phe Thr Cys Phe Asp Ile Phe Ser His Asp Pro Ala Ala Val Val
210 215 220

Val Asp Glu Val Ser Ile Asp Ser Ile Leu Tyr Pro Thr Ala Trp Tyr
225 230 235 240

Asn Thr Leu Pro Leu Leu Ser Ala Val Pro Phe His Ser Ala Trp Ala
245 250 255

Lys Ala Met Gly Val Asn Leu Leu Ala Ala Asn Thr His Asn Thr Ser
260 265 270

Met His Met Thr Gly Ser Gly Ile Tyr Ala Pro Glu Ala Val Lys Val
275 280 285

Tyr His Tyr Asp Met Glu Thr Glu Ser Gly Gln Leu Leu Leu Ser Glu
290 295 300

Leu Lys Ser Arg Pro Arg Arg Glu Pro Thr Tyr Pro Ala Ala Val Asp
305 310 315 320

Trp His Ala Tyr Ala Ser Ser Val Lys Pro Phe Ser Ser Glu Gln Ser
325 330 335

Asp Phe Leu Gly Met Ile Tyr Phe Asp Glu Phe Thr Phe Thr Lys Leu
340 345 350

Lys Arg Asn Thr Gly Asn Tyr Thr Ala Cys Gln Lys Asp Leu Cys Cys
355 360 365

His Leu Thr Tyr Lys Met Ser Glu Lys Arg Thr Asp Glu Ile Tyr Ala
370 375 380

Leu Gly Ala Phe Asp Gly Leu His Thr Val Glu Gly Gln Tyr Tyr Leu
385 390 395 400

```
Gln Ile Cys Ala Leu Leu Lys Cys Gln Thr Thr Asp Leu Glu Thr Cys
                405                 410                 415

Gly Glu Pro Val Gly Ser Ala Phe Thr Lys Phe Glu Asp Phe Ser Leu
            420                 425                 430

Ser Gly Thr Phe Gly Thr Arg Tyr Val Phe Pro Gln Ile Ile Leu Ser
        435                 440                 445

Gly Ser Gln Leu Ala Pro Glu Arg His Tyr Glu Ile Ser Arg Asp Gly
    450                 455                 460

Arg Leu Arg Ser Arg Ser Gly Ala Pro Leu Pro Val Leu Val Met Ala
465                 470                 475                 480

Leu Tyr Gly Arg Val Phe Glu Lys Asp Pro Pro Arg Leu Gly Gln Gly
                485                 490                 495

Ser Gly Lys Phe Gln
            500
```

<210> 3006
<211> 329
<212> PRT
<213> Homo sapiens

<400> 3006

```
Met Trp Gly Leu Lys Val Leu Leu Leu Pro Val Val Ser Phe Ala Leu
1               5                   10                  15

Tyr Pro Glu Glu Ile Leu Asp Thr His Trp Glu Leu Trp Lys Lys Thr
            20                  25                  30

His Arg Lys Gln Tyr Asn Asn Lys Val Asp Glu Ile Ser Arg Arg Leu
        35                  40                  45

Ile Trp Glu Lys Asn Leu Lys Tyr Ile Ser Ile His Asn Leu Glu Ala
    50                  55                  60

Ser Leu Gly Val His Thr Tyr Glu Leu Ala Met Asn His Leu Gly Asp
65                  70                  75                  80

Met Thr Ser Glu Glu Val Val Gln Lys Met Thr Gly Leu Lys Val Pro
                85                  90                  95

Leu Ser His Ser Arg Ser Asn Asp Thr Leu Tyr Ile Pro Glu Trp Glu
            100                 105                 110
```

```
Gly Arg Ala Pro Asp Ser Val Asp Tyr Arg Lys Lys Gly Tyr Val Thr
        115                 120                 125

Pro Val Lys Asn Gln Gly Gln Cys Gly Ser Cys Trp Ala Phe Ser Ser
    130                 135                 140

Val Gly Ala Leu Glu Gly Gln Leu Lys Lys Lys Thr Gly Lys Leu Leu
145                 150                 155                 160

Asn Leu Ser Pro Gln Asn Leu Val Asp Cys Val Ser Glu Asn Asp Gly
                165                 170                 175

Cys Gly Gly Gly Tyr Met Thr Asn Ala Phe Gln Tyr Val Gln Lys Asn
            180                 185                 190

Arg Gly Ile Asp Ser Glu Asp Ala Tyr Pro Tyr Val Gly Gln Glu Glu
        195                 200                 205

Ser Cys Met Tyr Asn Pro Thr Gly Lys Ala Ala Lys Cys Arg Gly Tyr
    210                 215                 220

Arg Glu Ile Pro Glu Gly Asn Glu Lys Ala Leu Lys Arg Ala Val Ala
225                 230                 235                 240

Arg Val Gly Pro Val Ser Val Ala Ile Asp Ala Ser Leu Thr Ser Phe
                245                 250                 255

Gln Phe Tyr Ser Lys Gly Val Tyr Tyr Asp Glu Ser Cys Asn Ser Asp
            260                 265                 270

Asn Leu Asn His Ala Val Leu Ala Val Gly Tyr Gly Ile Gln Lys Gly
        275                 280                 285

Asn Lys His Trp Ile Ile Lys Asn Ser Trp Gly Glu Asn Trp Gly Asn
    290                 295                 300

Lys Gly Tyr Ile Leu Met Ala Arg Asn Lys Asn Asn Ala Cys Gly Ile
305                 310                 315                 320

Ala Asn Leu Ala Ser Phe Pro Lys Met
                325
```

<210> 3007
<211> 1170
<212> PRT

<213> Homo sapiens

<400> 3007

Met Lys Asp Ser Cys Ile Thr Val Met Ala Met Ala Leu Leu Ser Gly
1 5 10 15

Phe Phe Phe Phe Ala Pro Ala Ser Ser Tyr Asn Leu Asp Val Arg Gly
20 25 30

Ala Arg Ser Phe Ser Pro Pro Arg Ala Gly Arg His Phe Gly Tyr Arg
35 40 45

Val Leu Gln Val Gly Asn Gly Val Ile Val Gly Ala Pro Gly Glu Gly
50 55 60

Asn Ser Thr Gly Ser Leu Tyr Gln Cys Gln Ser Gly Thr Gly His Cys
65 70 75 80

Leu Pro Val Thr Leu Arg Gly Ser Asn Tyr Thr Ser Lys Tyr Leu Gly
85 90 95

Met Thr Leu Ala Thr Asp Pro Thr Asp Gly Ser Ile Leu Ala Cys Asp
100 105 110

Pro Gly Leu Ser Arg Thr Cys Asp Gln Asn Thr Tyr Leu Ser Gly Leu
115 120 125

Cys Tyr Leu Phe Arg Gln Asn Leu Gln Gly Pro Met Leu Gln Gly Arg
130 135 140

Pro Gly Phe Gln Glu Cys Ile Lys Gly Asn Val Asp Leu Val Phe Leu
145 150 155 160

Phe Asp Gly Ser Met Ser Leu Gln Pro Asp Glu Phe Gln Lys Ile Leu
165 170 175

Asp Phe Met Lys Asp Val Met Lys Lys Leu Ser Asn Thr Ser Tyr Gln
180 185 190

Phe Ala Ala Val Gln Phe Ser Thr Ser Tyr Lys Thr Glu Phe Asp Phe
195 200 205

Ser Asp Tyr Val Lys Trp Lys Asp Pro Asp Ala Leu Leu Lys His Val
210 215 220

Lys His Met Leu Leu Leu Thr Asn Thr Phe Gly Ala Ile Asn Tyr Val

225 230 235 240

Ala Thr Glu Val Phe Arg Glu Glu Leu Gly Ala Arg Pro Asp Ala Thr
245 250 255

Lys Val Leu Ile Ile Ile Thr Asp Gly Glu Ala Thr Asp Ser Gly Asn
260 265 270

Ile Asp Ala Ala Lys Asp Ile Ile Arg Tyr Ile Ile Gly Ile Gly Lys
275 280 285

His Phe Gln Thr Lys Glu Ser Gln Glu Thr Leu His Lys Phe Ala Ser
290 295 300

Lys Pro Ala Ser Glu Phe Val Lys Ile Leu Asp Thr Phe Glu Lys Leu
305 310 315 320

Lys Asp Leu Phe Thr Glu Leu Gln Lys Lys Ile Tyr Val Ile Glu Gly
325 330 335

Thr Ser Lys Gln Asp Leu Thr Ser Phe Asn Met Glu Leu Ser Ser Ser
340 345 350

Gly Ile Ser Ala Asp Leu Ser Arg Gly His Ala Val Val Gly Ala Val
355 360 365

Gly Ala Lys Asp Trp Ala Gly Gly Phe Leu Asp Leu Lys Ala Asp Leu
370 375 380

Gln Asp Asp Thr Phe Ile Gly Asn Glu Pro Leu Thr Pro Glu Val Arg
385 390 395 400

Ala Gly Tyr Leu Gly Tyr Thr Val Thr Trp Leu Pro Ser Arg Gln Lys
405 410 415

Thr Ser Leu Leu Ala Ser Gly Ala Pro Arg Tyr Gln His Met Gly Arg
420 425 430

Val Leu Leu Phe Gln Glu Pro Gln Gly Gly Gly His Trp Ser Gln Val
435 440 445

Gln Thr Ile His Gly Thr Gln Ile Gly Ser Tyr Phe Gly Gly Glu Leu
450 455 460

Cys Gly Val Asp Val Asp Gln Asp Gly Glu Thr Glu Leu Leu Leu Ile
465 470 475 480

Gly Ala Pro Leu Phe Tyr Gly Glu Gln Arg Gly Gly Arg Val Phe Ile
485 490 495

Tyr Gln Arg Arg Gln Leu Gly Phe Glu Glu Val Ser Glu Leu Gln Gly
500 505 510

Asp Pro Gly Tyr Pro Leu Gly Arg Phe Gly Glu Ala Ile Thr Ala Leu
515 520 525

Thr Asp Ile Asn Gly Asp Gly Leu Val Asp Val Ala Val Gly Ala Pro
530 535 540

Leu Glu Glu Gln Gly Ala Val Tyr Ile Phe Asn Gly Arg His Gly Gly
545 550 555 560

Leu Ser Pro Gln Pro Ser Gln Arg Ile Glu Gly Thr Gln Val Leu Ser
565 570 575

Gly Ile Gln Trp Phe Gly Arg Ser Ile His Gly Val Lys Asp Leu Glu
580 585 590

Gly Asp Gly Leu Ala Asp Val Ala Val Gly Ala Glu Ser Gln Met Ile
595 600 605

Val Leu Ser Ser Arg Pro Val Val Asp Met Val Thr Leu Met Ser Phe
610 615 620

Ser Pro Ala Glu Ile Pro Val His Glu Val Glu Cys Ser Tyr Ser Thr
625 630 635 640

Ser Asn Lys Met Lys Glu Gly Val Asn Ile Thr Ile Cys Phe Gln Ile
645 650 655

Lys Ser Leu Tyr Pro Gln Phe Gln Gly Arg Leu Val Ala Asn Leu Thr
660 665 670

Tyr Thr Leu Gln Leu Asp Gly His Arg Thr Arg Arg Arg Gly Leu Phe
675 680 685

Pro Gly Gly Arg His Glu Leu Arg Arg Asn Ile Ala Val Thr Thr Ser
690 695 700

Met Ser Cys Thr Asp Phe Ser Phe His Phe Pro Val Cys Val Gln Asp
705 710 715 720

Leu Ile Ser Pro Ile Asn Val Ser Leu Asn Phe Ser Leu Trp Glu Glu
725 730 735

Glu Gly Thr Pro Arg Asp Gln Arg Ala Gln Gly Lys Asp Ile Pro Pro
740 745 750

Ile Leu Arg Pro Ser Leu His Ser Glu Thr Trp Glu Ile Pro Phe Glu
755 760 765

Lys Asn Cys Gly Glu Asp Lys Lys Cys Glu Ala Asn Leu Arg Val Ser
770 775 780

Phe Ser Pro Ala Arg Ser Arg Ala Leu Arg Leu Thr Ala Phe Ala Ser
785 790 795 800

Leu Ser Val Glu Leu Ser Leu Ser Asn Leu Glu Glu Asp Ala Tyr Trp
805 810 815

Val Gln Leu Asp Leu His Phe Pro Pro Gly Leu Ser Phe Arg Lys Val
820 825 830

Glu Met Leu Lys Pro His Ser Gln Ile Pro Val Ser Cys Glu Glu Leu
835 840 845

Pro Glu Glu Ser Arg Leu Leu Ser Arg Ala Leu Ser Cys Asn Val Ser
850 855 860

Ser Pro Ile Phe Lys Ala Gly His Ser Val Ala Leu Gln Met Met Phe
865 870 875 880

Asn Thr Leu Val Asn Ser Ser Trp Gly Asp Ser Val Glu Leu His Ala
885 890 895

Asn Val Thr Cys Asn Asn Glu Asp Ser Asp Leu Leu Glu Asp Asn Ser
900 905 910

Ala Thr Thr Ile Ile Pro Ile Leu Tyr Pro Ile Asn Ile Leu Ile Gln
915 920 925

Asp Gln Glu Asp Ser Thr Leu Tyr Val Ser Phe Thr Pro Lys Gly Pro
930 935 940

Lys Ile His Gln Val Lys His Met Tyr Gln Val Arg Ile Gln Pro Ser
945 950 955 960

```
Ile His Asp His Asn Ile Pro Thr Leu Glu Ala Val Val Gly Val Pro
                965                 970                 975

Gln Pro Pro Ser Glu Gly Pro Ile Thr His Gln Trp Ser Val Gln Met
            980                 985                 990

Glu Pro Pro Val Pro Cys His Tyr  Glu Asp Leu Glu Arg  Leu Pro Asp
        995                1000                1005

Ala Ala  Glu Pro Cys Leu Pro  Gly Ala Leu Phe Arg  Cys Pro Val
    1010                1015                1020

Val Phe  Arg Gln Glu Ile Leu  Val Gln Val Ile Gly  Thr Leu Glu
    1025                1030                1035

Leu Val  Gly Glu Ile Glu Ala  Ser Ser Met Phe Ser  Leu Cys Ser
    1040                1045                1050

Ser Leu  Ser Ile Ser Phe Asn  Ser Ser Lys His Phe  His Leu Tyr
    1055                1060                1065

Gly Ser  Asn Ala Ser Leu Ala  Gln Val Val Met Lys  Val Asp Val
    1070                1075                1080

Val Tyr  Glu Lys Gln Met Leu  Tyr Leu Tyr Val Leu  Ser Gly Ile
    1085                1090                1095

Gly Gly  Leu Leu Leu Leu Leu  Leu Ile Phe Ile Val  Leu Tyr Lys
    1100                1105                1110

Val Gly  Phe Phe Lys Arg Asn  Leu Lys Glu Lys Met  Glu Ala Gly
    1115                1120                1125

Arg Gly  Val Pro Asn Gly Ile  Pro Ala Glu Asp Ser  Glu Gln Leu
    1130                1135                1140

Ala Ser  Gly Gln Glu Ala Gly  Asp Pro Gly Cys Leu  Lys Pro Leu
    1145                1150                1155

His Glu  Lys Asp Ser Glu Ser  Gly Gly Gly Lys Asp
    1160                1165                1170
```

<210> 3008
<211> 502
<212> PRT
<213> Homo sapiens

<400> 3008

Met Ala Thr Asn Pro Gln Pro Gln Pro Pro Pro Pro Ala Pro Pro Pro
1 5 10 15

Pro Pro Pro Gln Pro Gln Pro Gln Pro Pro Pro Pro Pro Pro Gly Pro
20 25 30

Gly Ala Gly Pro Gly Ala Gly Gly Ala Gly Gly Ala Gly Ala Gly Ala
35 40 45

Gly Asp Pro Gln Leu Val Ala Met Ile Val Asn His Leu Lys Ser Gln
50 55 60

Gly Leu Phe Asp Gln Phe Arg Arg Asp Cys Leu Ala Asp Val Asp Thr
65 70 75 80

Lys Pro Ala Tyr Gln Asn Leu Arg Gln Arg Val Asp Asn Phe Val Ala
85 90 95

Asn His Leu Ala Thr His Thr Trp Ser Pro His Leu Asn Lys Asn Gln
100 105 110

Leu Arg Asn Asn Ile Arg Gln Gln Val Leu Lys Ser Gly Met Leu Glu
115 120 125

Ser Gly Ile Asp Arg Ile Ile Ser Gln Val Val Asp Pro Lys Ile Asn
130 135 140

His Thr Phe Arg Pro Gln Val Glu Lys Ala Val His Glu Phe Leu Ala
145 150 155 160

Thr Leu Asn His Lys Glu Glu Gly Ser Gly Asn Thr Ala Pro Asp Asp
165 170 175

Glu Lys Pro Asp Thr Ser Leu Ile Thr Gln Gly Val Pro Thr Pro Gly
180 185 190

Pro Ser Ala Asn Val Ala Asn Asp Ala Met Ser Ile Leu Glu Thr Ile
195 200 205

Thr Ser Leu Asn Gln Glu Ala Ser Ala Ala Arg Ala Ser Thr Glu Thr
210 215 220

Ser Asn Ala Lys Thr Ser Glu Arg Ala Ser Lys Lys Leu Pro Ser Gln
225 230 235 240

```
Pro Thr Thr Asp Thr Ser Thr Asp Lys Glu Arg Thr Ser Glu Asp Met
                245                 250                 255

Ala Asp Lys Glu Lys Ser Thr Ala Asp Ser Gly Gly Glu Gly Leu Glu
            260                 265                 270

Thr Ala Pro Lys Ser Glu Glu Phe Ser Asp Leu Pro Cys Pro Val Glu
        275                 280                 285

Glu Ile Lys Asn Tyr Thr Lys Glu His Asn Asn Leu Ile Leu Leu Asn
    290                 295                 300

Lys Asp Val Gln Gln Glu Ser Ser Glu Gln Lys Asn Lys Ser Thr Asp
305                 310                 315                 320

Lys Gly Glu Lys Lys Pro Asp Ser Asn Glu Lys Gly Glu Arg Lys Lys
                325                 330                 335

Glu Lys Lys Glu Lys Thr Glu Lys Lys Phe Asp His Ser Lys Lys Ser
            340                 345                 350

Glu Asp Thr Gln Lys Val Lys Asp Glu Lys Gln Ala Lys Glu Lys Glu
        355                 360                 365

Val Glu Ser Leu Lys Leu Pro Ser Glu Lys Asn Ser Asn Lys Ala Lys
    370                 375                 380

Thr Val Glu Gly Thr Lys Glu Asp Phe Ser Leu Ile Asp Ser Asp Val
385                 390                 395                 400

Asp Gly Leu Thr Asp Ile Thr Val Ser Ser Val His Thr Ser Asp Leu
                405                 410                 415

Ser Ser Phe Glu Glu Asp Thr Glu Glu Glu Val Val Thr Ser Asp Ser
            420                 425                 430

Met Glu Glu Gly Glu Ile Thr Ser Asp Asp Glu Glu Lys Asn Lys Gln
        435                 440                 445

Asn Lys Thr Lys Thr Gln Thr Ser Asp Ser Ser Glu Gly Lys Thr Lys
    450                 455                 460

Ser Val Arg His Ala Tyr Val His Lys Pro Tyr Leu Tyr Ser Lys Tyr
465                 470                 475                 480
```

Tyr Ser Asp Ser Asp Asp Glu Leu Thr Val Glu Gln Arg Arg Gln Ser
485 490 495

Ile Gly Ile Leu Trp Phe
500

<210> 3009
<211> 61
<212> PRT
<213> Homo sapiens

<400> 3009

Met Lys Arg Phe Leu Phe Leu Leu Leu Thr Ile Ser Leu Leu Val Met
1 5 10 15

Val Gln Ile Gln Thr Gly Leu Ser Gly Gln Asn Asp Thr Ser Gln Thr
20 25 30

Ser Ser Pro Ser Ala Ser Ser Ser Met Ser Gly Gly Ile Phe Leu Phe
35 40 45

Phe Val Ala Asn Ala Ile Ile His Leu Phe Cys Phe Ser
50 55 60

<210> 3010
<211> 352
<212> PRT
<213> Homo sapiens

<400> 3010

Met Glu Gly Ile Ser Ile Tyr Thr Ser Asp Asn Tyr Thr Glu Glu Met
1 5 10 15

Gly Ser Gly Asp Tyr Asp Ser Met Lys Glu Pro Cys Phe Arg Glu Glu
20 25 30

Asn Ala Asn Phe Asn Lys Ile Phe Leu Pro Thr Ile Tyr Ser Ile Ile
35 40 45

Phe Leu Thr Gly Ile Val Gly Asn Gly Leu Val Ile Leu Val Met Gly
50 55 60

Tyr Gln Lys Lys Leu Arg Ser Met Thr Asp Lys Tyr Arg Leu His Leu
65 70 75 80

Ser Val Ala Asp Leu Leu Phe Val Ile Thr Leu Pro Phe Trp Ala Val
85 90 95

```
Asp Ala Val Ala Asn Trp Tyr Phe Gly Asn Phe Leu Cys Lys Ala Val
            100                 105                 110

His Val Ile Tyr Thr Val Asn Leu Tyr Ser Ser Val Leu Ile Leu Ala
        115                 120                 125

Phe Ile Ser Leu Asp Arg Tyr Leu Ala Ile Val His Ala Thr Asn Ser
    130                 135                 140

Gln Arg Pro Arg Lys Leu Leu Ala Glu Lys Val Val Tyr Val Gly Val
145                 150                 155                 160

Trp Ile Pro Ala Leu Leu Leu Thr Ile Pro Asp Phe Ile Phe Ala Asn
                165                 170                 175

Val Ser Glu Ala Asp Asp Arg Tyr Ile Cys Asp Arg Phe Tyr Pro Asn
            180                 185                 190

Asp Leu Trp Val Val Val Phe Gln Phe Gln His Ile Met Val Gly Leu
        195                 200                 205

Ile Leu Pro Gly Ile Val Ile Leu Ser Cys Tyr Cys Ile Ile Ile Ser
    210                 215                 220

Lys Leu Ser His Ser Lys Gly His Gln Lys Arg Lys Ala Leu Lys Thr
225                 230                 235                 240

Thr Val Ile Leu Ile Leu Ala Phe Phe Ala Cys Trp Leu Pro Tyr Tyr
                245                 250                 255

Ile Gly Ile Ser Ile Asp Ser Phe Ile Leu Leu Glu Ile Ile Lys Gln
            260                 265                 270

Gly Cys Glu Phe Glu Asn Thr Val His Lys Trp Ile Ser Ile Thr Glu
        275                 280                 285

Ala Leu Ala Phe Phe His Cys Cys Leu Asn Pro Ile Leu Tyr Ala Phe
    290                 295                 300

Leu Gly Ala Lys Phe Lys Thr Ser Ala Gln His Ala Leu Thr Ser Val
305                 310                 315                 320

Ser Arg Gly Ser Ser Leu Lys Ile Leu Ser Lys Gly Lys Arg Gly Gly
                325                 330                 335
```

```
His Ser Ser Val Ser Thr Glu Ser Glu Ser Ser Ser Phe His Ser Ser
            340                 345                 350


<210>  3011
<211>  94
<212>  PRT
<213>  Homo sapiens

<400>  3011

Met Ala Pro Leu Lys Met Leu Ala Leu Val Thr Leu Leu Leu Gly Ala
1               5                  10                  15


Ser Leu Gln His Ile His Ala Ala Arg Gly Thr Asn Val Gly Arg Glu
            20                  25                  30


Cys Cys Leu Glu Tyr Phe Lys Gly Ala Ile Pro Leu Arg Lys Leu Lys
        35                  40                  45


Thr Trp Tyr Gln Thr Ser Glu Asp Cys Ser Arg Asp Ala Ile Val Phe
    50                  55                  60


Val Thr Val Gln Gly Arg Ala Ile Cys Ser Asp Pro Asn Asn Lys Arg
65                  70                  75                  80


Val Lys Asn Ala Val Lys Tyr Leu Gln Ser Leu Glu Arg Ser
                85                  90


<210>  3012
<211>  748
<212>  PRT
<213>  Homo sapiens

<400>  3012

Met Ser Gln Trp Asn Gln Val Gln Gln Leu Glu Ile Lys Phe Leu Glu
1               5                  10                  15


Gln Val Asp Gln Phe Tyr Asp Asp Asn Phe Pro Met Glu Ile Arg His
            20                  25                  30


Leu Leu Ala Gln Trp Ile Glu Asn Gln Asp Trp Glu Ala Ala Ser Asn
        35                  40                  45


Asn Glu Thr Met Ala Thr Ile Leu Leu Gln Asn Leu Leu Ile Gln Leu
    50                  55                  60


Asp Glu Gln Leu Gly Arg Val Ser Lys Glu Lys Asn Leu Leu Leu Ile
65                  70                  75                  80
```

```
His Asn Leu Lys Arg Ile Arg Lys Val Leu Gln Gly Lys Phe His Gly
                85                  90                  95

Asn Pro Met His Val Ala Val Val Ile Ser Asn Cys Leu Arg Glu Glu
            100                 105                 110

Arg Arg Ile Leu Ala Ala Ala Asn Met Pro Val Gln Gly Pro Leu Glu
        115                 120                 125

Lys Ser Leu Gln Ser Ser Ser Val Ser Glu Arg Gln Arg Asn Val Glu
    130                 135                 140

His Lys Val Ala Ala Ile Lys Asn Ser Val Gln Met Thr Glu Gln Asp
145                 150                 155                 160

Thr Lys Tyr Leu Glu Asp Leu Gln Asp Glu Phe Asp Tyr Arg Tyr Lys
                165                 170                 175

Thr Ile Gln Thr Met Asp Gln Ser Asp Lys Asn Ser Ala Met Val Asn
            180                 185                 190

Gln Glu Val Leu Thr Leu Gln Glu Met Leu Asn Ser Leu Asp Phe Lys
        195                 200                 205

Arg Lys Glu Ala Leu Ser Lys Met Thr Gln Ile Ile His Glu Thr Asp
    210                 215                 220

Leu Leu Met Asn Thr Met Leu Ile Glu Glu Leu Gln Asp Trp Lys Arg
225                 230                 235                 240

Arg Gln Gln Ile Ala Cys Ile Gly Gly Pro Leu His Asn Gly Leu Asp
                245                 250                 255

Gln Leu Gln Asn Cys Phe Thr Leu Leu Ala Glu Ser Leu Phe Gln Leu
            260                 265                 270

Arg Arg Gln Leu Glu Lys Leu Glu Glu Gln Ser Thr Lys Met Thr Tyr
        275                 280                 285

Glu Gly Asp Pro Ile Pro Met Gln Arg Thr His Met Leu Glu Arg Val
    290                 295                 300

Thr Phe Leu Ile Tyr Asn Leu Phe Lys Asn Ser Phe Val Val Glu Arg
305                 310                 315                 320
```

```
Gln Pro Cys Met Pro Thr His Pro Gln Arg Pro Leu Val Leu Lys Thr
                325                 330                 335

Leu Ile Gln Phe Thr Val Lys Leu Arg Leu Leu Ile Lys Leu Pro Glu
            340                 345                 350

Leu Asn Tyr Gln Val Lys Val Lys Ala Ser Ile Asp Lys Asn Val Ser
        355                 360                 365

Thr Leu Ser Asn Arg Arg Phe Val Leu Cys Gly Thr Asn Val Lys Ala
    370                 375                 380

Met Ser Ile Glu Glu Ser Ser Asn Gly Ser Leu Ser Val Glu Phe Arg
385                 390                 395                 400

His Leu Gln Pro Lys Glu Met Lys Ser Ser Ala Gly Gly Lys Gly Asn
                405                 410                 415

Glu Gly Cys His Met Val Thr Glu Glu Leu His Ser Ile Thr Phe Glu
            420                 425                 430

Thr Gln Ile Cys Leu Tyr Gly Leu Thr Ile Asp Leu Glu Thr Ser Ser
        435                 440                 445

Leu Pro Val Val Met Ile Ser Asn Val Ser Gln Leu Pro Asn Ala Trp
    450                 455                 460

Ala Ser Ile Ile Trp Tyr Asn Val Ser Thr Asn Asp Ser Gln Asn Leu
465                 470                 475                 480

Val Phe Phe Asn Asn Pro Pro Pro Ala Thr Leu Ser Gln Leu Leu Glu
                485                 490                 495

Val Met Ser Trp Gln Phe Ser Ser Tyr Val Gly Arg Gly Leu Asn Ser
            500                 505                 510

Asp Gln Leu His Met Leu Ala Glu Lys Leu Thr Val Gln Ser Ser Tyr
        515                 520                 525

Ser Asp Gly His Leu Thr Trp Ala Lys Phe Cys Lys Glu His Leu Pro
    530                 535                 540

Gly Lys Ser Phe Thr Phe Trp Thr Trp Leu Glu Ala Ile Leu Asp Leu
545                 550                 555                 560

Ile Lys Lys His Ile Leu Pro Leu Trp Ile Asp Gly Tyr Val Met Gly
```

565 570 575

Phe Val Ser Lys Glu Lys Glu Arg Leu Leu Leu Lys Asp Lys Met Pro
580 585 590

Gly Thr Phe Leu Leu Arg Phe Ser Glu Ser His Leu Gly Gly Ile Thr
595 600 605

Phe Thr Trp Val Asp His Ser Glu Ser Gly Glu Val Arg Phe His Ser
610 615 620

Val Glu Pro Tyr Asn Lys Gly Arg Leu Ser Ala Leu Pro Phe Ala Asp
625 630 635 640

Ile Leu Arg Asp Tyr Lys Val Ile Met Ala Glu Asn Ile Pro Glu Asn
645 650 655

Pro Leu Lys Tyr Leu Tyr Pro Asp Ile Pro Lys Asp Lys Ala Phe Gly
660 665 670

Lys His Tyr Ser Ser Gln Pro Cys Glu Val Ser Arg Pro Thr Glu Arg
675 680 685

Gly Asp Lys Gly Tyr Val Pro Ser Val Phe Ile Pro Ile Ser Thr Ile
690 695 700

Arg Ser Asp Ser Thr Glu Pro His Ser Pro Ser Asp Leu Leu Pro Met
705 710 715 720

Ser Pro Ser Val Tyr Ala Val Leu Arg Glu Asn Leu Ser Pro Thr Thr
725 730 735

Ile Glu Thr Ala Met Lys Ser Pro Tyr Ser Ala Glu
740 745

<210> 3013
<211> 92
<212> PRT
<213> Homo sapiens

<400> 3013

Met Lys Leu Cys Val Thr Val Leu Ser Leu Leu Met Leu Val Ala Ala
1 5 10 15

Phe Cys Ser Pro Ala Leu Ser Ala Pro Met Gly Ser Asp Pro Pro Thr
20 25 30

```
Ala Cys Cys Phe Ser Tyr Thr Ala Arg Lys Leu Pro Arg Asn Phe Val
        35                  40                  45

Val Asp Tyr Tyr Glu Thr Ser Ser Leu Cys Ser Gln Pro Ala Val Val
    50                  55                  60

Phe Gln Thr Lys Arg Ser Lys Gln Val Cys Ala Asp Pro Ser Glu Ser
65                  70                  75                  80

Trp Val Gln Glu Tyr Val Tyr Asp Leu Glu Leu Asn
                85                  90
```

<210> 3014
<211> 444
<212> PRT
<213> Homo sapiens

<400> 3014

```
Met Val Ser Gln Ala Leu Arg Leu Leu Cys Leu Leu Leu Gly Leu Gln
1               5                   10                  15

Gly Cys Leu Ala Ala Val Phe Val Thr Gln Glu Glu Ala His Gly Val
            20                  25                  30

Leu His Arg Arg Arg Arg Ala Asn Ala Phe Leu Glu Glu Leu Arg Pro
        35                  40                  45

Gly Ser Leu Glu Arg Glu Cys Lys Glu Glu Gln Cys Ser Phe Glu Glu
    50                  55                  60

Ala Arg Glu Ile Phe Lys Asp Ala Glu Arg Thr Lys Leu Phe Trp Ile
65                  70                  75                  80

Ser Tyr Ser Asp Gly Asp Gln Cys Ala Ser Ser Pro Cys Gln Asn Gly
                85                  90                  95

Gly Ser Cys Lys Asp Gln Leu Gln Ser Tyr Ile Cys Phe Cys Leu Pro
            100                 105                 110

Ala Phe Glu Gly Arg Asn Cys Glu Thr His Lys Asp Asp Gln Leu Ile
        115                 120                 125

Cys Val Asn Glu Asn Gly Gly Cys Glu Gln Tyr Cys Ser Asp His Thr
    130                 135                 140

Gly Thr Lys Arg Ser Cys Arg Cys His Glu Gly Tyr Ser Leu Leu Ala
```

```
145                 150                 155                 160

Asp Gly Val Ser Cys Thr Pro Thr Val Glu Tyr Pro Cys Gly Lys Ile
                165                 170                 175

Pro Ile Leu Glu Lys Arg Asn Ala Ser Lys Pro Gln Gly Arg Ile Val
            180                 185                 190

Gly Gly Lys Val Cys Pro Lys Gly Glu Cys Pro Trp Gln Val Leu Leu
        195                 200                 205

Leu Val Asn Gly Ala Gln Leu Cys Gly Gly Thr Leu Ile Asn Thr Ile
    210                 215                 220

Trp Val Val Ser Ala Ala His Cys Phe Asp Lys Ile Lys Asn Trp Arg
225                 230                 235                 240

Asn Leu Ile Ala Val Leu Gly Glu His Asp Leu Ser Glu His Asp Gly
                245                 250                 255

Asp Glu Gln Ser Arg Arg Val Ala Gln Val Ile Ile Pro Ser Thr Tyr
            260                 265                 270

Val Pro Gly Thr Thr Asn His Asp Ile Ala Leu Leu Arg Leu His Gln
        275                 280                 285

Pro Val Val Leu Thr Asp His Val Val Pro Leu Cys Leu Pro Glu Arg
    290                 295                 300

Thr Phe Ser Glu Arg Thr Leu Ala Phe Val Arg Phe Ser Leu Val Ser
305                 310                 315                 320

Gly Trp Gly Gln Leu Leu Asp Arg Gly Ala Thr Ala Leu Glu Leu Met
                325                 330                 335

Val Leu Asn Val Pro Arg Leu Met Thr Gln Asp Cys Leu Gln Gln Ser
            340                 345                 350

Arg Lys Val Gly Asp Ser Pro Asn Ile Thr Glu Tyr Met Phe Cys Ala
        355                 360                 365

Gly Tyr Ser Asp Gly Ser Lys Asp Ser Cys Lys Gly Asp Ser Gly Gly
    370                 375                 380

Pro His Ala Thr His Tyr Arg Gly Thr Trp Tyr Leu Thr Gly Ile Val
385                 390                 395                 400
```

```
Ser Trp Gly Gln Gly Cys Ala Thr Val Gly His Phe Gly Val Tyr Thr
                405                 410                 415

Arg Val Ser Gln Tyr Ile Glu Trp Leu Gln Lys Leu Met Arg Ser Glu
            420                 425                 430

Pro Arg Pro Gly Val Leu Leu Arg Ala Pro Phe Pro
        435                 440
```

<210> 3015
<211> 769
<212> PRT
<213> Homo sapiens

<400> 3015

```
Met Leu Gly Leu Arg Pro Pro Leu Leu Ala Leu Val Gly Leu Leu Ser
1               5                   10                  15

Leu Gly Cys Val Leu Ser Gln Glu Cys Thr Lys Phe Lys Val Ser Ser
            20                  25                  30

Cys Arg Glu Cys Ile Glu Ser Gly Pro Gly Cys Thr Trp Cys Gln Lys
        35                  40                  45

Leu Asn Phe Thr Gly Pro Gly Asp Pro Asp Ser Ile Arg Cys Asp Thr
    50                  55                  60

Arg Pro Gln Leu Leu Met Arg Gly Cys Ala Ala Asp Asp Ile Met Asp
65                  70                  75                  80

Pro Thr Ser Leu Ala Glu Thr Gln Glu Asp His Asn Gly Gly Gln Lys
                85                  90                  95

Gln Leu Ser Pro Gln Lys Val Thr Leu Tyr Leu Arg Pro Gly Gln Ala
            100                 105                 110

Ala Ala Phe Asn Val Thr Phe Arg Arg Ala Lys Gly Tyr Pro Ile Asp
        115                 120                 125

Leu Tyr Tyr Leu Met Asp Leu Ser Tyr Ser Met Leu Asp Asp Leu Arg
    130                 135                 140

Asn Val Lys Lys Leu Gly Gly Asp Leu Leu Arg Ala Leu Asn Glu Ile
145                 150                 155                 160
```

Thr Glu Ser Gly Arg Ile Gly Phe Gly Ser Phe Val Asp Lys Thr Val
165 170 175

Leu Pro Phe Val Asn Thr His Pro Asp Lys Leu Arg Asn Pro Cys Pro
180 185 190

Asn Lys Glu Lys Glu Cys Gln Pro Pro Phe Ala Phe Arg His Val Leu
195 200 205

Lys Leu Thr Asn Asn Ser Asn Gln Phe Gln Thr Glu Val Gly Lys Gln
210 215 220

Leu Ile Ser Gly Asn Leu Asp Ala Pro Glu Gly Gly Leu Asp Ala Met
225 230 235 240

Met Gln Val Ala Ala Cys Pro Glu Glu Ile Gly Trp Arg Asn Val Thr
245 250 255

Arg Leu Leu Val Phe Ala Thr Asp Asp Gly Phe His Phe Ala Gly Asp
260 265 270

Gly Lys Leu Gly Ala Ile Leu Thr Pro Asn Asp Gly Arg Cys His Leu
275 280 285

Glu Asp Asn Leu Tyr Lys Arg Ser Asn Glu Phe Asp Tyr Pro Ser Val
290 295 300

Gly Gln Leu Ala His Lys Leu Ala Glu Asn Asn Ile Gln Pro Ile Phe
305 310 315 320

Ala Val Thr Ser Arg Met Val Lys Thr Tyr Glu Lys Leu Thr Glu Ile
325 330 335

Ile Pro Lys Ser Ala Val Gly Glu Leu Ser Glu Asp Ser Ser Asn Val
340 345 350

Val His Leu Ile Lys Asn Ala Tyr Asn Lys Leu Ser Ser Arg Val Phe
355 360 365

Leu Asp His Asn Ala Leu Pro Asp Thr Leu Lys Val Thr Tyr Asp Ser
370 375 380

Phe Cys Ser Asn Gly Val Thr His Arg Asn Gln Pro Arg Gly Asp Cys
385 390 395 400

Asp Gly Val Gln Ile Asn Val Pro Ile Thr Phe Gln Val Lys Val Thr

405 410 415

Ala Thr Glu Cys Ile Gln Glu Gln Ser Phe Val Ile Arg Ala Leu Gly
420 425 430

Phe Thr Asp Ile Val Thr Val Gln Val Leu Pro Gln Cys Glu Cys Arg
435 440 445

Cys Arg Asp Gln Ser Arg Asp Arg Ser Leu Cys His Gly Lys Gly Phe
450 455 460

Leu Glu Cys Gly Ile Cys Arg Cys Asp Thr Gly Tyr Ile Gly Lys Asn
465 470 475 480

Cys Glu Cys Gln Thr Gln Gly Arg Ser Ser Gln Glu Leu Glu Gly Ser
485 490 495

Cys Arg Lys Asp Asn Asn Ser Ile Ile Cys Ser Gly Leu Gly Asp Cys
500 505 510

Val Cys Gly Gln Cys Leu Cys His Thr Ser Asp Val Pro Gly Lys Leu
515 520 525

Ile Tyr Gly Gln Tyr Cys Glu Cys Asp Thr Ile Asn Cys Glu Arg Tyr
530 535 540

Asn Gly Gln Val Cys Gly Gly Pro Gly Arg Gly Leu Cys Phe Cys Gly
545 550 555 560

Lys Cys Arg Cys His Pro Gly Phe Glu Gly Ser Ala Cys Gln Cys Glu
565 570 575

Arg Thr Thr Glu Gly Cys Leu Asn Pro Arg Arg Val Glu Cys Ser Gly
580 585 590

Arg Gly Arg Cys Arg Cys Asn Val Cys Glu Cys His Ser Gly Tyr Gln
595 600 605

Leu Pro Leu Cys Gln Glu Cys Pro Gly Cys Pro Ser Pro Cys Gly Lys
610 615 620

Tyr Ile Ser Cys Ala Glu Cys Leu Lys Phe Glu Lys Gly Pro Phe Gly
625 630 635 640

Lys Asn Cys Ser Ala Ala Cys Pro Gly Leu Gln Leu Ser Asn Asn Pro
645 650 655

Val Lys Gly Arg Thr Cys Lys Glu Arg Asp Ser Glu Gly Cys Trp Val
660 665 670

Ala Tyr Thr Leu Glu Gln Gln Asp Gly Met Asp Arg Tyr Leu Ile Tyr
675 680 685

Val Asp Glu Ser Arg Glu Cys Val Ala Gly Pro Asn Ile Ala Ala Ile
690 695 700

Val Gly Gly Thr Val Ala Gly Ile Val Leu Ile Gly Ile Leu Leu Leu
705 710 715 720

Val Ile Trp Lys Ala Leu Ile His Leu Ser Asp Leu Arg Glu Tyr Arg
725 730 735

Arg Phe Glu Lys Glu Lys Leu Lys Ser Gln Trp Asn Asn Asp Asn Pro
740 745 750

Leu Phe Lys Ser Ala Thr Thr Thr Val Met Asn Pro Lys Phe Ala Glu
755 760 765

Ser

<210> 3016
<211> 50
<212> DNA
<213> Homo sapiens

<400> 3016
gggaggaaca ctgcactctt aagcttccgc cgtctcaacc cctcacagga 50

<210> 3017
<211> 50
<212> DNA
<213> Homo sapiens

<400> 3017
aggagtcttt tacccggtgt gctttgccgc agtcatccaa aataaattca 50

<210> 3018
<211> 50
<212> DNA
<213> Homo sapiens

<400> 3018
cacctgattc cccctcttgc ccacaggact ctgctgttgt tttcattctg 50

<210> 3019
<211> 50
<212> DNA
<213> Homo sapiens

<400> 3019
attatatttg tccctatcag aatcctcgaa tccctagcag ccagtccctg 50

<210> 3020
<211> 50
<212> DNA
<213> Homo sapiens

<400> 3020
gtcccttagg ggagggagag ttgtcctctt tgcccacagt ctaccctcag 50

<210> 3021
<211> 50
<212> DNA
<213> Homo sapiens

<400> 3021
cttgggccag actgtcaggg ttcaaggagg gcatcaggag cagacggaga 50

<210> 3022
<211> 50
<212> DNA
<213> Homo sapiens

<400> 3022
ctcttcaagg ggtctacatg gcaactgtga ggaggggaga ttcagtgtgg 50

<210> 3023
<211> 50
<212> DNA
<213> Homo sapiens

<400> 3023
taagcataaa acctgacacg ttaaaatccc tgccctttgg tgagcccact 50

<210> 3024
<211> 50
<212> DNA
<213> Homo sapiens

<400> 3024
tgctggtatt ctcactgcca catttttgga aacctgtatt acaccttaaa 50

<210> 3025
<211> 50
<212> DNA
<213> Homo sapiens

<400> 3025
cagtcactgg gtctatatta aacagcaacc agagcaacaa atggcaaaca 50

<210> 3026
<211> 50
<212> DNA
<213> Homo sapiens

<400> 3026
tctagcccag cattgatcta gaagcagagg aatcccagcg ccttttaaaa 50

<210> 3027
<211> 50
<212> DNA
<213> Homo sapiens

<400> 3027
tgggcaagac atgattaatg aatcagaatc ctgtttcatt ggtgacttgg 50

<210> 3028
<211> 50
<212> DNA
<213> Homo sapiens

<400> 3028
tgcagattcc tagtagcatg ccttacctac agcactatgt gcatttgctg 50

<210> 3029
<211> 50
<212> DNA
<213> Homo sapiens

<400> 3029
ggtctgagag tctgtgaaga tggcccagtc ttctatcccc cacctaaaaa 50

<210> 3030
<211> 50
<212> DNA
<213> Homo sapiens

<400> 3030
cttgaccaaa cccacagcct gtctcttctc ttgtttagtt acttacggca 50

<210> 3031
<211> 50
<212> DNA
<213> Homo sapiens

<400> 3031
ccactgtcac tgtttctctg ctgttgcaaa tacatggata acacatttga 50

<210> 3032
<211> 50
<212> DNA
<213> Homo sapiens

<400> 3032
tgcagccact attgttagtc tcttgattca taatgactta agcacacttg 50

<210> 3033
<211> 50
<212> DNA
<213> Homo sapiens

<400> 3033
cctgatggag agaagaaggc atatgttcga ctggctcctg attacgatgc 50

<210> 3034
<211> 50
<212> DNA
<213> Homo sapiens

<400> 3034
gccgaattgt ctttggtgct tttcacttgt gttttaaaat aaggattttt 50

<210> 3035
<211> 50
<212> DNA
<213> Homo sapiens

<400> 3035
ctggaggacc tgttgatgct agttcagagt atcaccaaga gctggagagg 50

<210> 3036
<211> 50
<212> DNA
<213> Homo sapiens

<400> 3036
accatccaat cggacaagct ttcagaacct tattgaagga tttgaagcac 50

<210> 3037
<211> 50
<212> DNA
<213> Homo sapiens

<400> 3037
agaaatgttc agtaatgaaa aaatatatcc aatcagagcc atcccgaaaa 50

<210> 3038
<211> 50
<212> DNA
<213> Homo sapiens

<400> 3038
agcggactca ggctccagct gtggctacaa catagggttt ttatacaaga 50

<210> 3039
<211> 50
<212> DNA

<213> Homo sapiens

<400> 3039
accagactga caaatgtgta tcggatgctt ttgttcaggg ctgtgatcgg 50

<210> 3040
<211> 50
<212> DNA
<213> Homo sapiens

<400> 3040
ccactgtcac tgtttctctg ctgttgcaaa tacatggata acacatttga 50

<210> 3041
<211> 50
<212> DNA
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gactcctggg cctagtatct tttgcccctg gcagaatgta acagcaaaat gtctccttct 240

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gaaccttgga taccccttcga attttaaaat accttaaagt cttccattaa tcttatttttt 480

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caagcacaga cttatattga ttctaaaaga ataagagaca ttttcagcat gttgctttgt 300

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