



(11) **EP 2 806 272 A1**

(12) **EUROPEAN PATENT APPLICATION**

(43) Date of publication:
26.11.2014 Bulletin 2014/48

(51) Int Cl.:
G01N 33/48 (2006.01) **G01N 33/53 (2006.01)**
G01N 33/68 (2006.01)

(21) Application number: **14180229.8**

(22) Date of filing: **06.08.2010**

(84) Designated Contracting States:
**AL AT BE BG CH CY CZ DE DK EE ES FI FR GB
GR HR HU IE IS IT LI LT LU LV MC MK MT NL NO
PL PT RO SE SI SK SM TR**

(30) Priority: **07.08.2009 US 232091 P**
23.04.2010 US 327389 P

(62) Document number(s) of the earlier application(s) in
accordance with Art. 76 EPC:
10807278.6 / 2 462 438

(71) Applicant: **Myriad RBM, Inc.**
Austin TX 78759 (US)

(72) Inventors:
• **Spain, Michael**
Austin, TX 78729 (US)
• **Mapes, James P.**
Lakeway, TX 78734 (US)
• **Labrie, Samuel**
Austin, TX 78717 (US)
• **McDade, Ralph**
Austin, TX 78730 (US)

- **Eisinger, Dominic**
Keene, NY 12942 (US)
- **Ballard, Karri**
Austin, TX 78732 (US)
- **Salomon, Daniel**
San Diego, CA 92130 (US)
- **Abecassis, Michael**
Chicago, IL 60611 (US)

(74) Representative: **Vossius & Partner**
Siebertstrasse 4
81675 München (DE)

Remarks:

- This application was filed on 07-08-2014 as a
divisional application to the application mentioned
under INID code 62.
- A request for correction of part of the description has
been filed pursuant to Rule 139 EPC. A decision on
the request will be taken during the proceedings
before the Examining Division (Guidelines for
Examination in the EPO, A-V, 3.).

(54) **Methods and devices for detecting kidney transplant rejection**

(57) Methods and devices for diagnosing, monitor-
ing, or determining kidney transplant rejection or an as-
sociated disorder in a mammal are described. In partic-
ular, methods and devices for diagnosing, monitoring, or

determining kidney transplant rejection or an associated
disorder using measured concentrations of a combina-
tion of three or more analytes in a test sample taken from
the mammal are described.

EP 2 806 272 A1

Description**CROSS REFERENCE TO RELATED APPLICATIONS**

5 **[0001]** This application claims the priority of US provisional application serial no. 61/327,389, filed April 23, 2010, and US provisional application serial no. 61/232,091, filed August 7, 2009, each of which is hereby incorporated by reference in its entirety and is related to U.S. Patent Application Nos. [Not Yet Assigned], entitled Methods and Devices for Detecting Obstructive Uropathy and Associated Disorders, Methods and Devices for Detecting Kidney Damage, Devices for De-
 10 tecting Renal Disorders, Computer Methods and Devices for Detecting Kidney Damage, Methods and Devices for Detecting Diabetic Nephropathy and Associated Disorders, and Methods and Devices for Detecting Glomerulonephritis and Associated Disorders, Attorney Docket Nos. 060075- , filed on the same date as this application, the entire contents of which are incorporated herein by reference..

FIELD OF THE INVENTION

15 **[0002]** The invention encompasses methods and devices for diagnosing, monitoring, or determining kidney transplant rejection or an associated disorder in a mammal. In particular, the present invention provides methods and devices for diagnosing, monitoring, or determining kidney transplant rejection or an associated disorder using measured concen-
 20 trations of a combination of three or more analytes in a test sample taken from the mammal.

BACKGROUND OF THE INVENTION

25 **[0003]** The urinary system, in particular the kidneys, perform several critical functions such as maintaining electrolyte balance and eliminating toxins from the bloodstream. In the human body, the pair of kidneys together process roughly 20% of the total cardiac output, amounting to about 1 L/min in a 70-kg adult male. Because compounds in circulation are concentrated in the kidney up to 1000-fold relative to the plasma concentration, the kidney is especially vulnerable to injury due to exposure to toxic compounds.

30 **[0004]** Severe kidney damage that results in end-stage renal disease (ESRD) may be treated with a kidney transplant. ESRD is defined as a drop in the glomerular filtration rate (GFR) to 20-25% of normal. Common diseases leading to ESRD may include malignant hypertension, infections, diabetes mellitus, and focal segmental glomerulosclerosis; genetic causes include polycystic kidney disease, a number of inborn errors of metabolism, and autoimmune conditions such as lupus and Goodpasture's syndrome. Diabetes is the most common cause of kidney transplantation, accounting for approximately 25% of those in the US. Despite the success of a kidney transplant in extending the patient's life, rejection is still a significant complication to the procedure, and may result in failure of the transplant. Detecting early signs of a
 35 rejection may enable faster, more aggressive treatment, resulting in less damage to the kidney. Existing diagnostic tests such as BUN and serum creatine tests, however, typically detect only advanced stages of kidney damage. Other diagnostic tests such as kidney tissue biopsies or CAT scans have the advantage of enhanced sensitivity to earlier stages of kidney damage, but these tests are also generally costly, slow, and/or invasive.

40 **[0005]** A need exists in the art for a fast, simple, reliable, and sensitive method of detecting kidney transplant rejection or an associated disorder. In a clinical setting, the early detection of kidney damage would help medical practitioners to diagnose and treat kidney damage more quickly and effectively.

SUMMARY OF THE INVENTION

45 **[0006]** The present invention provides methods and devices for diagnosing, monitoring, or determining a renal disorder in a mammal. In particular, the present invention provides methods and devices for diagnosing, monitoring, or determining a renal disorder using measured concentrations of a combination of three or more analytes in a test sample taken from the mammal.

50 **[0007]** One aspect of the invention encompasses a method for diagnosing, monitoring, or determining kidney transplant rejection or an associated disorder in a mammal. The method typically comprises providing a test sample comprising a sample of bodily fluid taken from the mammal. Then, the method comprises determining a combination of sample concentrations for three or more sample analytes in the test sample, wherein the sample analytes are selected from the group consisting of alpha-1 microglobulin, beta-2 microglobulin, calbindin, clusterin, CTGF, creatinine, cystatin C, GST-
 55 alpha, KIM-1, microalbumin, NGAL, osteopontin, THP, TIMP-1, TFF-3, VEGF, BLC, CD40, IGF BP2, MMP3, peptide YY, stem cell factor, TNF RII, AXL, Eotaxin 3, FABP, FGF basic, myoglobin, resistin, TRAIL R3, endothelin 1, NrCAM, Tenascin C, VCAM1, and cortisol. The combination of sample concentrations may be compared to a data set comprising at least one entry, wherein each entry of the data set comprises a list comprising three or more minimum diagnostic concentrations indicative of kidney transplant rejection or an associated disorder. Each minimum diagnostic concentration

comprises a maximum of a range of analyte concentrations for a healthy mammal. Next, the method comprises determining a matching entry of the dataset in which all minimum diagnostic concentrations are less than the corresponding sample concentrations and identifying an indicated disorder comprising the particular disorder of the matching entry.

[0008] Another aspect of the invention encompasses a method for diagnosing, monitoring, or determining kidney transplant rejection or an associated disorder in a mammal. The method generally comprises providing a test sample comprising a sample of bodily fluid taken from the mammal. Then the method comprises determining the concentrations of three or more sample analytes in a panel of biomarkers in the test sample, wherein the sample analytes are selected from the group consisting of alpha-1 microglobulin, beta-2 microglobulin, calbindin, clusterin, CTGF, creatinine, cystatin C, GST-alpha, KIM-1, microalbumin, NGAL, osteopontin, THP, TIMP-1, TFF-3, VEGF, BLC, CD40, IGF BP2, MMP3, peptide YY, stem cell factor, TNF RII, AXL, Eotaxin 3, FABP, FGF basic, myoglobin, resistin, TRAIL R3, endothelin 1, NrCAM, Tenascin C, VCAM1, and cortisol. Diagnostic analytes are identified in the test sample, wherein the diagnostic analytes are the sample analytes whose concentrations are statistically different from concentrations found in a control group of humans who do not suffer from kidney transplant rejection or an associated disorder. The combination of diagnostic analytes is compared to a dataset comprising at least one entry, wherein each entry of the dataset comprises a combination of three or more diagnostic analytes reflective of kidney transplant rejection or an associated disorder. The particular disorder having the combination of diagnostic analytes that essentially match the combination of sample analytes is then identified.

[0009] An additional aspect of the invention encompasses a method for diagnosing, monitoring, or determining kidney transplant rejection or an associated disorder in a mammal. The method usually comprises providing an analyte concentration measurement device comprising three or more detection antibodies. Each detection antibody comprises an antibody coupled to an indicator, wherein the antigenic determinants of the antibodies are sample analytes associated with kidney transplant rejection or an associated disorder. The sample analytes are generally selected from the group consisting of alpha-1 microglobulin, beta-2 microglobulin, calbindin, clusterin, CTGF, creatinine, cystatin C, GST-alpha, KIM-1, microalbumin, NGAL, osteopontin, THP, TIMP-1, TFF-3, VEGF, BLC, CD40, IGF BP2, MMP3, peptide YY, stem cell factor, TNF RII, AXL, Eotaxin 3, FABP, FGF basic, myoglobin, resistin, TRAIL R3, endothelin 1, NrCAM, Tenascin C, VCAM1, and cortisol. The method next comprises providing a test sample comprising three or more sample analytes and a bodily fluid taken from the mammal. The test sample is contacted with the detection antibodies and the detection antibodies are allowed to bind to the sample analytes. The concentrations of the sample analytes are determined by detecting the indicators of the detection antibodies bound to the sample analytes in the test sample. The concentrations of each sample analyte correspond to a corresponding minimum diagnostic concentration reflective of kidney transplant rejection or an associated disorder.

[0010] Other aspects and iterations of the invention are described in more detail below.

DESCRIPTION OF FIGURES

[0011]

FIG. 1 depicts a sample clustering tree (dendrogram) together with set and status indicators. Below the tree the set that each sample belongs to (black encodes Set 1, red Set 2; see Examples) is shown, and the patient status (black encodes AR (acute rejection), red CAN (chronic allograft nephropathy), green TX (successful, non-rejected transplant)). The sample tree contains two large branches, one of which corresponds to the Set 1 (the large black block in the set indicator color bar), and one that corresponds to Set 2 (the large red block in the set indicator color bar). This two-branch structure points to a batch effect.

FIG. 2 depicts scatterplots of protein significance for the comparisons TX vs. AR, TX vs. CAN, AR vs. CAN (in each case, the samples belonging to the third group are ignored), and for the comparisons TX vs. all others, AR vs. all others, CAN vs. all others, in Set 2 (y-axis) vs. Set 1 (x-axis). Each dot represents a protein; protein significance is defined as biweight midcorrelation [1] of the protein level with status. The correlation and p-value, and a linear model fit line are also included.

FIG. 3 depicts a scatterplot of protein significance for TX vs. AR in Set 2 (y-axis) vs. Set 1 (x-axis). Positive significance identifies proteins whose levels are higher in AR than TX, and negative the opposite. Each dot represents a protein; in this plot the negative logarithm of the association p-value multiplied by the sign of the robust correlation of the protein is plotted with TX vs. AR status. Kidney injury markers identified in previous work are plotted in blue, while all other proteins are black. Proteins with relatively high overall significance are labeled by their names or symbols. The green and red lines denote p-value thresholds of 0.01 and 0.05, respectively.

FIG. 4 depicts a scatterplot of protein significance for TX vs. CAN in Set 2 (y-axis) vs. Set 1 (x-axis). Positive significance identifies proteins whose levels are higher in CAN than TX, and negative the opposite. Each dot represents a protein; in this plot the negative logarithm of the association p-value multiplied by the sign of the robust correlation of the protein is plotted with TX vs. CAN status. Kidney injury markers identified in previous work are

plotted in blue, while all other proteins are black. Proteins with relatively high overall significance are labeled by their names or symbols. The green and red lines denote p-value thresholds of 0.01 and 0.05, respectively.

FIG. 5 depicts a scatterplot of protein significance for AR vs. CAN in Set 2 (y-axis) vs. Set 1 (x-axis). Positive significance identifies proteins whose levels are higher in CAN than AR, and negative the opposite. Each dot represents a protein; in this plot the negative logarithm of the association p-value multiplied by the sign of the robust correlation of the protein is plotted with AR vs. CAN status. Kidney injury markers identified in previous work are plotted in blue, while all other proteins are black. Proteins with relatively high overall significance are labeled by their names or symbols. The green and red lines denote p-value thresholds of 0.01 and 0.05, respectively.

FIG. 6 depicts a scatterplot of protein significance for TX vs. all others in Set 2 (y-axis) vs. Set 1 (x-axis). Positive significance identifies proteins whose levels are higher in others than TX, and negative the opposite. Each dot represents a protein; in this plot the negative logarithm of the association p-value multiplied by the sign of the robust correlation of the protein is plotted with TX vs. all others status. Kidney injury markers identified in previous work are plotted in blue, while all other proteins are black. Proteins with relatively high overall significance are labeled by their names or symbols. The green and red lines denote p-value thresholds of 0.01 and 0.05, respectively.

FIG. 7 depicts a scatterplot of protein significance for AR vs. all others in Set 2 (y-axis) vs. Set 1 (x-axis). Positive significance identifies proteins whose levels are higher in others than AR, and negative the opposite. Each dot represents a protein; in this plot the negative logarithm of the association p-value multiplied by the sign of the robust correlation of the protein is plotted with AR vs. all others status. Kidney injury markers identified in previous work are plotted in blue, while all other proteins are black. Proteins with relatively high overall significance are labeled by their names or symbols. The green and red lines denote p-value thresholds of 0.01 and 0.05, respectively.

FIG. 8 depicts a scatterplot of protein significance for CAN vs. all others in Set 2 (y-axis) vs. Set 1 (x-axis). Positive significance identifies proteins whose levels are higher in others than CAN, and negative the opposite. Each dot represents a protein; in this plot the negative logarithm of the association p-value multiplied by the sign of the robust correlation of the protein is plotted with CAN vs. all others status. Kidney injury markers identified in previous work are plotted in blue, while all other proteins are black. Proteins with relatively high overall significance are labeled by their names or symbols. The green and red lines denote p-value thresholds of 0.01 and 0.05, respectively.

FIG. 9 depicts a chart showing the p-values for finding the observed numbers of genes by chance. Each row corresponds to one significance level and sign of the relationship between protein level and trait, while each column corresponds to a comparison. Thus, for example, the p-value of finding 9 genes with p-values less than 0.01 in the TX vs AR comparison (upper left square) is 0.0018.

DETAILED DESCRIPTION OF THE INVENTION

[0012] It has been discovered that a multiplexed panel of at least three, six, or preferably 16 biomarkers may be used to detect kidney transplant rejection and associated disorders. In particular, a panel or method of the invention may be used to detect acute kidney rejection or chronic allograft nephropathy. Importantly, a panel or method of the invention may be used to distinguish between an acute rejection reaction and a chronic allograft nephropathy. Alternatively, a panel or method of the invention may be used to distinguish between a successful transplant and rejection. As used herein, the term "rejection" refers to a recipient response to a foreign antigen derived from the transplanted kidney. The phrase "acute rejection" refers to an immune related response to the foreign kidney. The response is primarily T-cell driven and originates from an HLC mismatch between the donor and recipient. The phrase "chronic allograft nephropathy" refers to a chronic inflammatory and immune response mediated reaction to a foreign kidney. Chronic allograft nephropathy may result in damage to the kidney manifested by diffuse interstitial fibrosis glomerular changes, typically membranous and sclerotic in nature, as well as intimal fibrosis of the blood vessels with tubular atrophy and loss of tubular structures.

[0013] Additionally, the present invention encompasses biomarkers that may be used to detect a disorder associated with kidney transplant rejection. As used herein, the phrase "a disorder associated with kidney transplant rejection" refers to a disorder that stems from a host response to a foreign antigen derived from the transplanted kidney. For instance, non-limiting examples of associated disorders may include chronic kidney failure and end-stage kidney disease.

[0014] The biomarkers included in a multiplexed panel of the invention are analytes known in the art that may be detected in the urine, serum, plasma and other bodily fluids of mammals. As such, the analytes of the multiplexed panel may be readily extracted from the mammal in a test sample of bodily fluid. The concentrations of the analytes within the test sample may be measured using known analytical techniques such as a multiplexed antibody-based immunological assay. The combination of concentrations of the analytes in the test sample may be compared to empirically determined combinations of minimum diagnostic concentrations and combinations of diagnostic concentration ranges associated with healthy kidney function or kidney transplant rejection or an associated disorder to determine whether kidney transplant rejection, and if so, what type of rejection, is indicated in the mammal.

[0015] One embodiment of the present invention provides a method for diagnosing, monitoring, or determining kidney

transplant rejection or an associated disorder in a mammal that includes determining the presence or concentration of a combination of three or more sample analytes in a test sample containing the bodily fluid of the mammal. The measured concentrations of the combination of sample analytes is compared to the entries of a dataset in which each entry contains the minimum diagnostic concentrations of a combination of three or more analytes reflective of kidney transplant rejection or an associated disorder. Other embodiments provide computer-readable media encoded with applications containing executable modules, systems that include databases and processing devices containing executable modules configured to diagnose, monitor, or determine a renal disorder in a mammal. Still other embodiments provide antibody-based devices for diagnosing, monitoring, or determining kidney transplant rejection or an associated disorder in a mammal.

[0016] The analytes used as biomarkers in the multiplexed assay, methods of diagnosing, monitoring, or determining a renal disorder using measurements of the analytes, systems and applications used to analyze the multiplexed assay measurements, and antibody-based devices used to measure the analytes are described in detail below.

I. Analytes in Multiplexed Assay

[0017] One embodiment of the invention measures the concentrations of three, six, sixteen, or more than 16 biomarker analytes within a test sample taken from a mammal and compares the measured analyte concentrations to minimum diagnostic concentrations to diagnose, monitor, or determine kidney transplant rejection or an associated disorder in a mammal. In this aspect, the biomarker analytes are known in the art to occur in the urine, plasma, serum and other bodily fluids of mammals. The biomarker analytes are proteins that have known and documented associations with early renal damage in humans. As diagnosed herein, the biomarker analytes may include but are not limited to alpha-1 microglobulin, beta-2 microglobulin, calbindin, clusterin, CTGF, creatinine, cystatin C, GST-alpha, KIM-1, microalbumin, NGAL, osteopontin, THP, TIMP-1, TFF-3, VEGF, BLC, CD40, IGF BP2, MMP3, peptide YY, stem cell factor, TNF RII, AXL, Eotaxin 3, FABP, FGF basic, myoglobin, resistin, TRAIL R3, endothelin 1, NrCAM, Tenascin C, VCAM1, and cortisol. A description of each biomarker analyte is given below.

(a) Alpha-1 Microglobulin (A1M)

[0018] Alpha-1 microglobulin (A1M, Swiss-Prot Accession Number P02760) is a 26 kDa glycoprotein synthesized by the liver and reabsorbed in the proximal tubules. Elevated levels of A1 M in human urine are indicative of glomerulotubular dysfunction. A1 M is a member of the lipocalin super family and is found in all tissues. Alpha-1-microglobulin exists in blood in both a free form and complexed with immunoglobulin A (IgA) and heme. Half of plasma A1 M exists in a free form, and the remainder exists in complexes with other molecules including prothrombin, albumin, immunoglobulin A and heme. Nearly all of the free A1M in human urine is reabsorbed by the megalin receptor in proximal tubular cells, where it is then catabolized. Small amounts of A1 M are excreted in the urine of healthy humans. Increased A1 M concentrations in human urine may be an early indicator of renal damage, primarily in the proximal tubule.

(b) Beta-2 Microglobulin (B2M)

[0019] Beta-2 microglobulin (B2M, Swiss-Prot Accession Number P61769) is a protein found on the surfaces of all nucleated cells and is shed into the blood, particularly by tumor cells and lymphocytes. Due to its small size, B2M passes through the glomerular membrane, but normally less than 1% is excreted due to reabsorption of B2M in the proximal tubules of the kidney. Therefore, high plasma levels of B2M occur as a result of renal failure, inflammation, and neoplasms, especially those associated with B-lymphocytes.

(c) Calbindin

[0020] Calbindin (Calbindin D-28K, Swiss-Prot Accession Number P05937) is a Ca-binding protein belonging to the troponin C superfamily. It is expressed in the kidney, pancreatic islets, and brain. Calbindin is found predominantly in subpopulations of central and peripheral nervous system neurons, in certain epithelial cells involved in Ca²⁺ transport such as distal tubular cells and cortical collecting tubules of the kidney, and in enteric neuroendocrine cells.

(d) Clusterin

[0021] Clusterin (Swiss-Prot Accession Number P10909) is a highly conserved protein that has been identified independently by many different laboratories and named SGP2, S35-S45, apolipoprotein J, SP-40, 40, ADHC-9, gp80, GPIII, and testosterone-repressed prostate message (TRPM-2). An increase in clusterin levels has been consistently detected in apoptotic heart, brain, lung, liver, kidney, pancreas, and retinal tissue both *in vivo* and *in vitro*, establishing clusterin as a ubiquitous marker of apoptotic cell loss. However, clusterin protein has also been implicated in physiological

processes that do not involve apoptosis, including the control of complement-mediated cell lysis, transport of beta-amyloid precursor protein, shuttling of aberrant beta-amyloid across the blood-brain barrier, lipid scavenging, membrane remodeling, cell aggregation, and protection from immune detection and tumor necrosis factor induced cell death.

(e) *Connective Tissue Growth Factor (CTGF)*

[0022] Connective tissue growth factor (CTGF, Swiss-Prot Accession Number P29279) is a 349-amino acid cysteine-rich polypeptide belonging to the CCN family. *In vitro* studies have shown that CTGF is mainly involved in extracellular matrix synthesis and fibrosis. Up-regulation of CTGF mRNA and increased CTGF levels have been observed in various diseases, including diabetic nephropathy and cardiomyopathy, fibrotic skin disorders, systemic sclerosis, biliary atresia, liver fibrosis and idiopathic pulmonary fibrosis, and nondiabetic acute and progressive glomerular and tubulointerstitial lesions of the kidney. A recent cross-sectional study found that urinary CTGF may act as a progression promoter in diabetic nephropathy.

(f) *Creatinine*

[0023] Creatinine is a metabolite of creatine phosphate in muscle tissue, and is typically produced at a relatively constant rate by the body. Creatinine is chiefly filtered out of the blood by the kidneys, though a small amount is actively secreted by the kidneys into the urine. Creatinine levels in blood and urine may be used to estimate the creatinine clearance, which is representative of the overall glomerular filtration rate (GFR), a standard measure of renal function. Variations in creatinine concentrations in the blood and urine, as well as variations in the ratio of urea to creatinine concentration in the blood, are common diagnostic measurements used to assess renal function.

(g) *Cystatin C (Cyst C)*

[0024] Cystatin C (Cyst C, Swiss-Prot Accession Number P01034) is a 13 kDa protein that is a potent inhibitor of the C1 family of cysteine proteases. It is the most abundant extracellular inhibitor of cysteine proteases in testis, epididymis, prostate, seminal vesicles and many other tissues. Cystatin C, which is normally expressed in vascular wall smooth muscle cells, is severely reduced in both atherosclerotic and aneurismal aortic lesions.

(h) *Glutathione S-Transferase alpha (GST-alpha)*

[0025] Glutathione S-transferase alpha (GST-alpha, Swiss-Prot Accession Number P08263) belongs to a family of enzymes that utilize glutathione in reactions contributing to the transformation of a wide range of compounds, including carcinogens, therapeutic drugs, and products of oxidative stress. These enzymes play a key role in the detoxification of such substances.

(i) *Kidney Injury Molecule-1 (KIM-1)*

[0026] Kidney injury molecule-1 (KiM-1, Swiss-Prot Accession Number Q96D42) is an immunoglobulin superfamily cell-surface protein highly upregulated on the surface of injured kidney epithelial cells. It is also known as TIM-1 (T-cell immunoglobulin mucin domain-1), as it is expressed at low levels by subpopulations of activated T-cells and hepatitis A virus cellular receptor-1 (HAVCR-1). KIM-1 is increased in expression more than any other protein in the injured kidney and is localized predominantly to the apical membrane of the surviving proximal epithelial cells.

(j) *Microalbumin*

[0027] Albumin is the most abundant plasma protein in humans and other mammals. Albumin is essential for maintaining the osmotic pressure needed for proper distribution of body fluids between intravascular compartments and body tissues. Healthy, normal kidneys typically filter out albumin from the urine. The presence of albumin in the urine may indicate damage to the kidneys. Albumin in the urine may also occur in patients with long-standing diabetes, especially type 1 diabetes. The amount of albumin eliminated in the urine has been used to differentially diagnose various renal disorders. For example, nephrotic syndrome usually results in the excretion of about 3.0 to 3.5 grams of albumin in human urine every 24 hours. Microalbuminuria, in which less than 300mg of albumin is eliminated in the urine every 24 hours, may indicate the early stages of diabetic nephropathy.

(k) Neutrophil Gelatinase-Associated Lipocalin (NGAL)

[0028] Neutrophil gelatinase-associated lipocalin (NGAL, Swiss-Prot Accession Number P80188) forms a disulfide bond-linked heterodimer with MMP-9. It mediates an innate immune response to bacterial infection by sequestering iron. Lipocalins interact with many different molecules such as cell surface receptors and proteases, and play a role in a variety of processes such as the progression of cancer and allergic reactions.

(l) Osteopontin (OPN)

[0029] Osteopontin (OPN, Swiss-Prot Accession Number P10451) is a cytokine involved in enhancing production of interferon-gamma and IL-12, and inhibiting the production of IL-10. OPN is essential in the pathway that leads to type I immunity. OPN appears to form an integral part of the mineralized matrix. OPN is synthesized within the kidney and has been detected in human urine at levels that may effectively inhibit calcium oxalate crystallization. Decreased concentrations of OPN have been documented in urine from patients with renal stone disease compared with normal individuals.

(m) Tamm-Horsfall Protein (THP)

[0030] Tamm-Horsfall protein (THP, Swiss-Prot Accession Number P07911), also known as uromodulin, is the most abundant protein present in the urine of healthy subjects and has been shown to decrease in individuals with kidney stones. THP is secreted by the thick ascending limb of the loop of Henley. THP is a monomeric glycoprotein of ~ 85 kDa with ~30% carbohydrate moiety that is heavily glycosylated. THP may act as a constitutive inhibitor of calcium crystallization in renal fluids.

(n) Tissue Inhibitor of Metalloproteinase-1 (TIMP-1)

[0031] Tissue inhibitor of metalloproteinase-1 (TIMP-1, Swiss-Prot Accession Number P01033) is a major regulator of extracellular matrix synthesis and degradation. A certain balance of MMPs and TIMPs is essential for tumor growth and health. Fibrosis results from an imbalance of fibrogenesis and fibrolysis, highlighting the importance of the role of the inhibition of matrix degradation role in renal disease.

(o) Trefoil Factor 3 (TFF3)

[0032] Trefoil factor 3 (TFF3, Swiss-Prot Accession Number Q07654), also known as intestinal trefoil factor, belongs to a small family of mucin-associated peptides that include TFF1, TFF2, and TFF3. TFF3 exists in a 60-amino acid monomeric form and a 118-amino acid dimeric form. Under normal conditions TFF3 is expressed by goblet cells of the intestine and the colon. TFF3 expression has also been observed in the human respiratory tract, in human goblet cells and in the human salivary gland. In addition, TFF3 has been detected in the human hypothalamus.

(p) Vascular Endothelial Growth Factor (VEGF)

[0033] Vascular endothelial growth factor (VEGF, Swiss-Prot Accession Number P15692) is an important factor in the pathophysiology of neuronal and other tumors, most likely functioning as a potent promoter of angiogenesis. VEGF may also be involved in regulating blood-brain-barrier functions under normal and pathological conditions. VEGF secreted from the stromal cells may be responsible for the endothelial cell proliferation observed in capillary hemangioblastomas, which are typically composed of abundant microvasculature and primitive angiogenic elements represented by stromal cells.

(q) B-lymphocyte Chemoattractant (BLC)

[0034] B-lymphocyte chemoattractant (BLC, Swiss-Prot Accession Number 043927) is also referred to as C-X-C motif chemokine 13, Small-inducible cytokine B13, B lymphocyte chemoattractant, CXC chemokine BLC, and B cell-attracting chemokine 1. BLC functions as a potent chemoattractant for B lymphocytes, but not T lymphocytes, monocytes, or neutrophils. Its specific receptor BLR1 is a G protein-coupled receptor originally isolated from Burkitt's lymphoma cells. Among cells of the hematopoietic lineages, the expression of BRL1, now designated CXCR5, is restricted to B lymphocytes and a subpopulation of T helper memory cells.

(r) Cluster of Differentiation Surface Receptors 40 (CD40)

[0035] Cluster of Differentiation Surface Receptors 40 (CD40, Swiss Prot Accession Number P25942) is also referred to TNFRSF5 (Tumor necrosis factor receptor superfamily member 5. CD40 is a member of the tumor necrosis factor-receptor superfamily of proteins. CD40 has been found to be essential in mediating a broad variety of immune and inflammatory responses including T cell-dependent immunoglobulin class switching, memory B cell development, and germinal center formation.

(s) Insulin-like Growth Factor Binding Protein 2 (IGF BP2)

[0036] Insulin-like Growth Factor Binding Protein 2 (IGF BP2, Swiss Prot Accession Number P18065) functions to prolong the half-life of the insulin growth factors and have been shown to either inhibit or stimulate the growth promoting effects of the insulin growth factors on cell culture. Specifically, during development, insulin-like growth factor binding protein-2 is expressed in a number of tissues with the highest expression level found in the central nervous system. IGFBP-2 exhibits a 2-10 fold higher affinity for IGF II than for IGF I.

(t) Matrix Metalloproteinase-3 (MMP3)

[0037] Matrix Metalloproteinase-3 (MMP3, Swiss Prot Accession Number P08254) is also known as stromelysin-1 and Transin-1. MMP3 is involved in the breakdown of extracellular matrix in normal physiological processes, such as embryonic development, reproduction, and tissue remodeling, as well as in disease processes, such as arthritis and metastasis. Most MMP's are secreted as inactive proproteins which are activated when cleaved by extracellular proteinases. MMP3 encodes an enzyme which degrades fibronectin, laminin, collagens III, IV, IX, and X, and cartilage proteoglycans. The enzyme is thought to be involved in wound repair, progression of atherosclerosis, and tumor initiation. MMP3 is part of a cluster of MMP genes which localize to chromosome 11q22.3.

(u) Peptide YY (PYY)

[0038] Peptide YY (PYY, Swiss-Prot Accession Number P10082) is also known as peptide tyrosine tyrosine and pancreatic peptide YY₃₋₃₆. Peptide YY exerts its action through neuropeptide Y receptors, inhibits gastric motility and increases water and electrolyte absorption in the colon. PYY may also suppress pancreatic secretion. It is secreted by the neuroendocrine cells in the ileum and colon in response to a meal, and has been shown to reduce appetite. PYY works by slowing the gastric emptying; hence, it increases efficiency of digestion and nutrient absorption after meal. Research has also indicated that PYY may be useful in removing aluminum accumulated in the brain.

(v) Stem Cell Factor (SCF)

[0039] Stem Cell Factor (SCF, UniProtKB/TrEMBL Q13528) is also known as kit-ligand, KL, and steel factor. SCF functions SCF plays an important role in the hematopoiesis during embryonic development. Sites where hematopoiesis takes place, such as the fetal liver and bone marrow, all express SCF. SCF may serve as guidance cues that direct hematopoietic stem cells (HSCs) to their stem cell niche (the microenvironment in which a stem cell resides), and it plays an important role in HSC maintenance. Non-lethal point mutants on the c-Kit receptor can cause anemia, decreased fertility, and decreased pigmentation. During development, the presence of the SCF also plays an important role in the localization of melanocytes, cells that produce melanin and control pigmentation. In melanogenesis, melanoblasts migrate from the neural crest to their appropriate locations in the epidermis. Melanoblasts express the Kit receptor, and it is believed that SCF guides these cells to their terminal locations. SCF also regulates survival and proliferation of fully differentiated melanocytes in adults. In spermatogenesis, c-Kit is expressed in primordial germ cells, spermatogonia, and in primordial oocytes. It is also expressed in the primordial germ cells of females. SCF is expressed along the pathways that the germ cells use to reach their terminal destination in the body. It is also expressed in the final destinations for these cells. Like for melanoblasts, this helps guide the cells to their appropriate locations in the body.

(w) Tumor Necrosis Factor Receptor Type II (TNF RII)

[0040] Tumor Necrosis Factor Receptor Type II (TNF RII, Swiss-Prot Accession Number P20333) is also known as p75, p80 TNF alpha receptor, and TNFRSF1 B. TNF RII is a protein that in humans is encoded by the TNFRSF1 B gene. The protein encoded by this gene is a member of the Tumor necrosis factor receptor superfamily, which also contains TNFRSF1 A. The protein encoded by this gene is a member of the TNF-receptor superfamily. This protein and TNF-receptor 1 form a heterocomplex that mediates the recruitment of two anti-apoptotic proteins, c-IAP1 and c-IAP2, which

possess E3 ubiquitin ligase activity. The function of IAPs in TNF-receptor signaling is unknown; however, c-IAP1 is thought to potentiate TNF-induced apoptosis by the ubiquitination and degradation of TNF-receptor-associated factor 2, which mediates anti-apoptotic signals. Knockout studies in mice also suggest a role of this protein in protecting neurons from apoptosis by stimulating antioxidative pathways.

(x) AXL Oncogene

[0041] AXL (Swiss-Prot Accession Number P30530) is also known as UFO, ARK, and tyrosine-protein kinase receptor UFO. The protein encoded by AXL is a member of the receptor tyrosine kinase subfamily. Although it is similar to other receptor tyrosine kinases, the AXL protein represents a unique structure of the extracellular region that juxtaposes IgL and FNIII repeats. AXL transduces signals from the extracellular matrix into the cytoplasm by binding growth factors like vitamin K-dependent protein growth-arrest-specific gene 6. It is involved in the stimulation of cell proliferation. This receptor can also mediate cell aggregation by homophilic binding. AXL is a chronic myelogenous leukemia-associated oncogene and also associated with colon cancer and melanoma.

(y) Eotaxin 3

[0042] Eotaxin 3 (Swiss-Prot Accession Number P51671) is also known as C-C motif chemokine 11 (CCL11), small inducible cytokine A11, and eosinophil chemotactic protein. Eotaxin 3 is a small cytokine belonging to the CC chemokine family that is also called Eotaxin-3, Macrophage inflammatory protein 4-alpha (MIP-4-alpha), Thymic stroma chemokine-1 (TSC-1), and IMAC. It is expressed by several tissues including heart, lung and ovary, and in endothelial cells that have been stimulated with the cytokine interleukin 4.[1][2] CCL26 is chemotactic for eosinophils and basophils and elicits its effects by binding to the cell surface chemokine receptor CCR3.

(z) Fatty Acid Binding Protein (FABP)

[0043] Fatty Acid Binding Protein (FABP, Swiss-Prot Accession Number Q01469) is also known as epidermal-type fatty acid binding protein, and fatty-acid binding protein 5. This gene encodes the fatty acid binding protein found in epidermal cells, and was first identified as being upregulated in psoriasis tissue. Fatty acid binding proteins are a family of small, highly conserved, cytoplasmic proteins that bind longchain fatty acids and other hydrophobic ligands. It is thought that FABPs roles include fatty acid uptake, transport, and metabolism..

(aa) Basic Fibroblast Growth Factor (FGF basic)

[0044] Basic Fibroblast Growth Factor (FGF basic, Swiss-Prot Accession Number P09038) is also known as heparin-binding growth factor. In normal tissue, basic fibroblast growth factor is present in basement membranes and in the subendothelial extracellular matrix of blood vessels. It stays membrane-bound as long as there is no signal peptide. It has been hypothesized that, during both wound healing of normal tissues and tumor development, the action of heparan sulfate-degrading enzymes activates FGF basic, thus mediating the formation of new blood vessels. Additionally, FGF basic is a critical component of human embryonic stem cell culture medium; the growth factor is necessary for the cells to remain in an undifferentiated state, although the mechanisms by which it does this are poorly defined. It has been demonstrated to induce gremlin expression which in turn is known to inhibit the induction of differentiation by bone morphogenetic proteins. It is necessary in mouse-feeder cell dependent culture systems, as well as in feeder and serum-free culture systems.

(bb) Myoglobin

[0045] Myoglobin (Swiss-Prot Accession Number P02144) is released from damaged muscle tissue (rhabdomyolysis), which has very high concentrations of myoglobin. The released myoglobin is filtered by the kidneys but is toxic to the renal tubular epithelium and so may cause acute renal failure. Myoglobin is a sensitive marker for muscle injury, making it a potential marker for heart attack in patients with chest pain.

(cc) Resistin (RETN)

[0046] Resistin (RETN, UniProtKB/TrEMBL Q76B53) is theorized to participate in the inflammatory response. Resistin has also been shown to increase transcriptional events leading to an increased expression of several pro-inflammatory cytokines including (but not limited to) interleukin-1 (IL-1), interleukin-6 (IL-6), interleukin-12 (IL-12), and tumor necrosis factor- α (TNF- α) in an NF- κ B-mediated fashion. It has also been demonstrated that resistin upregulates intracellular

adhesion molecule-1 (ICAM1) vascular cell-adhesion molecule-1 (VCAM1) and CCL2, all of which are occupied in chemotactic pathways involved in leukocyte recruitment to sites of infection. Resistin itself can be upregulated by interleukins and also by microbial antigens such as lipopolysaccharide, which are recognized by leukocytes. Taken together, because resistin is reputed to contribute to insulin resistance, results such as those mentioned suggest that resistin may be a link in the well-known association between inflammation and insulin resistance. In fact, recent data have shown positive correlations between obesity, insulin resistance, and chronic inflammation which is believed to be directed in part by resistin signaling.

(dd) Tumor Necrosis Factor-Related Apoptosis-Inducing Ligand Receptor 3 (TRAIL R3)

[0047] TRAIL R3 (Swiss-Prot Accession Number P83626 (mouse)) is also known as tumor necrosis factor-related apoptosis-inducing ligand receptor 3, and tumor necrosis factor receptor mouse homolog. TRAIL R3 is a decoy receptor for TRAIL, a member of the tumor necrosis factor family. In several cell types decoy receptors inhibit TRAIL-induced apoptosis by binding TRAIL and thus preventing its binding to proapoptotic TRAIL receptors.

(ee) Endothelin 1 (ET1)

[0048] Endothelin 1 (ET1, UniProtKB/TrEMBL Q6FH53) is also known as EDN1 and EDN1 protein. Endothelin 1 is a protein that constricts blood vessels and raises blood pressure. It is normally kept in balance by other mechanisms, but when over-expressed, it contributes to high blood pressure (hypertension) and heart disease. Endothelin 1 peptides and receptors are implicated in the pathogenesis of a number of disease states, including cancer and heart disease.

(ff) Neuronal Cell Adhesion Molecule (NrCAM)

[0049] Neuronal Cell Adhesion Molecule (NrCAM, UniProtKB/TrEMBL Q14CA1) encodes a neuronal cell adhesion molecule with multiple immunoglobulin-like C2-type domains and fibronectin type-III domains. This ankyrin-binding protein is involved in neuron-neuron adhesion and promotes directional signaling during axonal cone growth. This gene is also expressed in non-neural tissues and may play a general role in cell-cell communication via signaling from its intracellular domain to the actin cytoskeleton during directional cell migration. Allelic variants of this gene have been associated with autism and addiction vulnerability.

(gg) Tenascin C (TN-C)

[0050] Tenascin C (TN-C, UniProt/TrEMBL Q99857) has anti-adhesive properties, causing cells in tissue culture to become rounded after it is added to the medium. One mechanism to explain this may come from its ability to bind to the extracellular matrix glycoprotein fibronectin and block fibronectin's interactions with specific syndecans. The expression of tenascin-C in the stroma of certain tumors is associated with a poor prognosis.

(hh) Vascular Cell Adhesion Molecule 1 (VCAM1)

[0051] Vascular Cell Adhesion Molecule 1 (VCAM1, Swiss-Prot Accession Number P19320) is also known as vascular cell adhesion protein 1. VCAM1 mediates the adhesion of lymphocytes, monocytes, eosinophils, and basophils to vascular endothelium. It also functions in leukocyte-endothelial cell signal transduction, and it may play a role in the development of atherosclerosis and rheumatoid arthritis. Upregulation of VCAM-1 in endothelial cells by cytokines occurs as a result of increased gene transcription (e.g., in response to Tumor necrosis factor-alpha (TNF- α) and Interleukin-1 (IL-1)) and through stabilization of Messenger RNA (mRNA) (e.g., Interleukin-4 (IL-4)). The promoter region of the VCAM-1 gene contains functional tandem NF- κ B (nuclear factor-kappa B) sites. The sustained expression of VCAM-1 lasts over 24 hours. Primarily, the VCAM-1 protein is an endothelial ligand for VLA-4 (Very Late Antigen-4 or α 4 β 1) of the β 1 subfamily of integrins, and for integrin α 4 β 7. VCAM-1 expression has also been observed in other cell types (e.g., smooth muscle cells). It has also been shown to interact with EZR and Moesin. Certain melanoma cells can use VCAM-1 to adhere to the endothelium, and VCAM-1 may participate in monocyte recruitment to atherosclerotic sites.

(ii) Cortisol

[0052] Cortisol (Swiss-Prot Accession Number P08185) is also known as corticosteroid-binding globulin, transcortin, and Serpin A6. Cortisol is a steroid hormone or glucocorticoid produced by the adrenal gland. It is released in response to stress, and to a low level of blood glucocorticoids. Its primary functions are to increase blood sugar through gluconeogenesis, suppress the immune system, and aid in fat, protein and carbohydrate metabolism. It also decreases bone

formation. In addition, cortisol can weaken the activity of the immune system. Cortisol prevents proliferation of T-cells by rendering the interleukin-2 producer T-cells unresponsive to interleukin-1 (IL-1), and unable to produce the T-cell growth factor. Cortisol also has a negative feedback effect on interleukin-1. IL-1 must be especially useful in combating some diseases; however, endotoxin bacteria have gained an advantage by forcing the hypothalamus to increase cortisol levels via forcing secretion of CRH hormone, thus antagonizing IL-1 in this case. The suppressor cells are not affected by GRMF, so that the effective set point for the immune cells may be even higher than the set point for physiological processes. It reflects leukocyte redistribution to lymph nodes, bone marrow, and skin.

II. Combinations of Analytes Measured by Multiplexed Assay

[0053] The method for diagnosing, monitoring, or determining a transplant rejection involves determining the presence or concentrations of a combination of sample analytes in a test sample. The combinations of sample analytes, as defined herein, are any group of three or more analytes selected from the biomarker analytes, including but not limited to alpha-1 microglobulin, beta-2 microglobulin, calbindin, clusterin, CTGF, creatinine, cystatin C, GST-alpha, KIM-1, microalbumin, NGAL, osteopontin, THP, TIMP-1, TFF-3, VEGF, BLC, CD40, IGF BP2, MMP3, peptide YY, stem cell factor, TNF RII, AXL, Eotaxin 3, FABP, FGF basic, myoglobin, resistin, TRAIL R3, endothelin 1, NrCAM, Tenascin C, VCAM1, and cortisol. In one embodiment, the combination of analytes may be selected to provide a group of analytes associated with kidney transplant rejection or an associated disorder.

[0054] In one embodiment, the combination of sample analytes may be any three of the biomarker analytes. In other embodiments, the combination of sample analytes may be any four, any five, any six, any seven, any eight, any nine, any ten, any eleven, any twelve, any thirteen, any fourteen, any fifteen, any sixteen, any seventeen, any eighteen, any nineteen, any twenty, or more of biomarker analytes listed in Section I above. In some embodiments, the combination of sample analytes comprises B2M and VEGF. In another embodiment, the combination of sample analytes may be a combination listed in **Table A** below.

Table A

BLC	CD40	IGF BP2
BLC	CD40	MMP3
BLC	CD40	peptide YY
BLC	CD40	stem cell factor
BLC	CD40	TNF RII
BLC	CD40	AXL
BLC	CD40	Eotaxin 3
BLC	CD40	FABP
BLC	CD40	FGF basic
BLC	CD40	myoglobin
BLC	CD40	resistin
BLC	CD40	TRAIL R3
BLC	CD40	endothelin 1
BLC	CD40	NrCAM
BLC	CD40	Tenascin C
BLC	CD40	VCAM1
BLC	CD40	cortisol
BLC	IGF BP2	MMP3
BLC	IGF BP2	peptide YY
BLC	IGF BP2	stem cell factor
BLC	IGF BP2	TNF RII
BLC	IGF BP2	AXL

EP 2 806 272 A1

(continued)

5

10

15

20

25

30

35

40

45

50

55

BLC	IGF BP2	Eotaxin 3
BLC	IGF BP2	FABP
BLC	IGF BP2	FGF basic
BLC	IGF BP2	myoglobin
BLC	IGF BP2	resistin
BLC	IGF BP2	TRAIL R3
BLC	IGF BP2	endothelin 1
BLC	IGF BP2	NrCAM
BLC	IGF BP2	Tenascin C
BLC	IGF BP2	VCAM1
BLC	IGF BP2	cortisol
BLC	MMP3	peptide YY
BLC	MMP3	stem cell factor
BLC	MMP3	TNF RII
BLC	MMP3	AXL
BLC	MMP3	Eotaxin 3
BLC	MMP3	FABP
BLC	MMP3	FGF basic
BLC	MMP3	myoglobin
BLC	MMP3	resistin
BLC	MMP3	TRAIL R3
BLC	MMP3	endothelin 1
BLC	MMP3	NrCAM
BLC	MMP3	Tenascin C
BLC	MMP3	VCAM1
BLC	MMP3	cortisol
BLC	peptide YY	stem cell factor
BLC	peptide YY	TNF RII
BLC	peptide YY	AXL
BLC	peptide YY	Eotaxin 3
BLC	peptide YY	FABP
BLC	peptide YY	FGF basic
BLC	peptide YY	myoglobin
BLC	peptide YY	resistin
BLC	peptide YY	TRAIL R3
BLC	peptide YY	endothelin 1
BLC	peptide YY	NrCAM
BLC	peptide YY	Tenascin C
BLC	peptide YY	VCAM1

EP 2 806 272 A1

(continued)

5

10

15

20

25

30

35

40

45

50

55

BLC	peptide YY	cortisol
BLC	stem cell factor	TNF RII
BLC	stem cell factor	AXL
BLC	stem cell factor	Eotaxin 3
BLC	stem cell factor	FABP
BLC	stem cell factor	FGF basic
BLC	stem cell factor	myoglobin
BLC	stem cell factor	resistin
BLC	stem cell factor	TRAIL R3
BLC	stem cell factor	endothelin 1
BLC	stem cell factor	NrCAM
BLC	stem cell factor	Tenascin C
BLC	stem cell factor	VCAM1
BLC	stem cell factor	cortisol
BLC	TNF RII	AXL
BLC	TNF RII	Eotaxin 3
BLC	TNF RII	FABP
BLC	TNF RII	FGF basic
BLC	TNF RII	myoglobin
BLC	TNF RII	resistin
BLC	TNF RII	TRAIL R3
BLC	TNF RII	endothelin 1
BLC	TNF RII	NrCAM
BLC	TNF RII	Tenascin C
BLC	TNF RII	VCAM1
BLC	TNF RII	cortisol
BLC	AXL	Eotaxin 3
BLC	AXL	FABP
BLC	AXL	FGF basic
BLC	AXL	myoglobin
BLC	AXL	resistin
BLC	AXL	TRAIL R3
BLC	AXL	endothelin 1
BLC	AXL	NrCAM
BLC	AXL	Tenascin C
BLC	AXL	VCAM1
BLC	AXL	cortisol
BLC	Eotaxin 3	FABP
BLC	Eotaxin 3	FGF basic

EP 2 806 272 A1

(continued)

5

10

15

20

25

30

35

40

45

50

55

BLC	Eotaxin 3	myoglobin
BLC	Eotaxin 3	resistin
BLC	Eotaxin 3	TRAIL R3
BLC	Eotaxin 3	endothelin 1
BLC	Eotaxin 3	NrCAM
BLC	Eotaxin 3	Tenascin C
BLC	Eotaxin 3	VCAM1
BLC	Eotaxin 3	cortisol
BLC	FABP	FGF basic
BLC	FABP	myoglobin
BLC	FABP	resistin
BLC	FABP	TRAIL R3
BLC	FABP	endothelin 1
BLC	FABP	NrCAM
BLC	FABP	Tenascin C
BLC	FABP	VCAM1
BLC	FABP	cortisol
BLC	FGF basic	myoglobin
BLC	FGF basic	resistin
BLC	FGF basic	TRAIL R3
BLC	FGF basic	endothelin 1
BLC	FGF basic	NrCAM
BLC	FGF basic	Tenascin C
BLC	FGF basic	VCAM1
BLC	FGF basic	cortisol
BLC	myoglobin	resistin
BLC	myoglobin	TRAIL R3
BLC	myoglobin	endothelin 1
BLC	myoglobin	NrCAM
BLC	myoglobin	Tenascin C
BLC	myoglobin	VCAM1
BLC	myoglobin	cortisol
BLC	resistin	TRAIL R3
BLC	resistin	endothelin 1
BLC	resistin	NrCAM
BLC	resistin	Tenascin C
BLC	resistin	VCAM1
BLC	resistin	cortisol
BLC	TRAIL R3	endothelin 1

EP 2 806 272 A1

(continued)

5

10

15

20

25

30

35

40

45

50

55

BLC	TRAIL R3	NrCAM
BLC	TRAIL R3	Tenascin C
BLC	TRAIL R3	VCAM1
BLC	TRAIL R3	cortisol
BLC	endothilin 1	NrCAM
BLC	endothilin 1	Tenascin C
BLC	endothilin 1	VCAM1
BLC	endothilin 1	cortisol
BLC	NrCAM	Tenascin C
BLC	NrCAM	VCAM1
BLC	NrCAM	cortisol
BLC	Tenascin C	VCAM1
BLC	Tenascin C	cortisol
BLC	VCAM1	cortisol
CD40	IGF BP2	MMP3
CD40	IGF BP2	peptide YY
CD40	IGF BP2	stem cell factor
CD40	IGF BP2	TNF RII
CD40	IGF BP2	AXL
CD40	IGF BP2	Eotaxin 3
CD40	IGF BP2	FABP
CD40	IGF BP2	FGF basic
CD40	IGF BP2	myoglobin
CD40	IGF BP2	resistin
CD40	IGF BP2	TRAIL R3
CD40	IGF BP2	endothilin 1
CD40	IGF BP2	NrCAM
CD40	IGF BF2	Tenascin C
CD40	IGF BP2	VCAM1
CD40	IGF BP2	cortisol
CD40	MMP3	peptide YY
CD40	MMP3	stem cell factor
CD40	MMP3	TNF RII
CD40	MMP3	AXL
CD40	MMP3	Eotaxin 3
CD40	MMP3	FABP
CD40	MMP3	FGF basic
CD40	MMP3	myoglobin
CD40	MMP3	resistin

EP 2 806 272 A1

(continued)

5

10

15

20

25

30

35

40

45

50

55

CD40	MMP3	TRAIL R3
CD40	MMP3	endothelin 1
CD40	MMP3	NrCAM
CD40	MMP3	Tenascin C
CD40	MMP3	VCAM1
CD40	MMP3	cortisol
CD40	peptide YY	stem cell factor
CD40	peptide YY	TNF RII
CD40	peptide YY	AXL
CD40	peptide YY	Eotaxin 3
CD40	peptide YY	FABP
CD40	peptide YY	FGF basic
CD40	peptide YY	myoglobin
CD40	peptide YY	resistin
CD40	peptide YY	TRAIL R3
CD40	peptide YY	endothelin 1
CD40	peptide YY	NrCAM
CD40	peptide YY	Tenascin C
CD40	peptide YY	VCAM1
CD40	peptide YY	cortisol
CD40	stem cell factor	TNF RII
CD40	stem cell factor	AXL
CD40	stem cell factor	Eotaxin 3
CD40	stem cell factor	FABP
CD40	stem cell factor	FGF basic
CD40	stem cell factor	myoglobin
CD40	stem cell factor	resistin
CD40	stem cell factor	TRAIL R3
CD40	stem cell factor	endothelin 1
CD40	stem cell factor	NrCAM
CD40	stem cell factor	Tenascin C
CD40	stem cell factor	VCAM1
CD40	stem cell factor	cortisol
CD40	TNF RII	AXL
CD40	TNF RII	Eotaxin 3
CD40	TNF RII	FABP
CD40	TNF RII	FGF basic
CD40	TNF RII	myoglobin
CD40	TNF RII	resistin

EP 2 806 272 A1

(continued)

5

10

15

20

25

30

35

40

45

50

55

CD40	TNF RII	TRAIL R3
CD40	TNF RII	endothilin 1
CD40	TNF RII	NrCAM
CD40	TNF RII	Tenascin C
CD40	TNF RII	VCAM1
CD40	TNF RII	cortisol
CD40	AXL	Eotaxin 3
CD40	AXL	FABP
CD40	AXL	FGF basic
CD40	AXL	myoglobin
CD40	AXL	resistin
CD40	AXL	TRAIL R3
CD40	AXL	endothilin 1
CD40	AXL	NrCAM
CD40	AXL	Tenascin C
CD40	AXL	VCAM1
CD40	AXL	cortisol
CD40	Eotaxin 3	FABP
CD40	Eotaxin 3	FGF basic
CD40	Eotaxin 3	myoglobin
CD40	Eotaxin 3	resistin
CD40	Eotaxin 3	TRAIL R3
CD40	Eotaxin 3	endothilin 1
CD40	Eotaxin 3	NrCAM
CD40	Eotaxin 3	Tenascin C
CD40	Eotaxin 3	VCAM1
CD40	Eotaxin 3	cortisol
CD40	FABP	FGF basic
CD40	FABP	myoglobin
CD40	FABP	resistin
CD40	FABP	TRAIL R3
CD40	FABP	endothilin 1
CD40	FABP	NrCAM
CD40	FABP	Tenascin C
CD40	FABP	VCAM1
CD40	FABP	cortisol
CD40	FGF basic	myoglobin
CD40	FGF basic	resistin
CD40	FGF basic	TRAIL R3

EP 2 806 272 A1

(continued)

5

10

15

20

25

30

35

40

45

50

55

CD40	FGF basic	endothilin 1
CD40	FGF basic	NrCAM
CD40	FGF basic	Tenascin C
CD40	FGF basic	VCAM1
CD40	FGF basic	cortisol
CD40	myoglobin	resistin
CD40	myoglobin	TRAIL R3
CD40	myoglobin	endothilin 1
CD40	myoglobin	NrCAM
CD40	myoglobin	Tenascin C
CD40	myoglobin	VCAM1
CD40	myoglobin	cortisol
CD40	resistin	TRAIL R3
CD40	resistin	endothilin 1
CD40	resistin	NrCAM
CD40	resistin	Tenascin C
CD40	resistin	VCAM1
CD40	resistin	cortisol
CD40	TRAIL R3	endothilin 1
CD40	TRAIL R3	NrCAM
CD40	TRAIL R3	Tenascin C
CD40	TRAIL R3	VCAM1
CD40	TRAIL R3	cortisol
CD40	endothilin 1	NrCAM
CD40	endothilin 1	Tenascin C
CD40	endothilin 1	VCAM1
CD40	endothilin 1	cortisol
CD40	NrCAM	Tenascin C
CD40	NrCAM	VCAM1
CD40	NrCAM	cortisol
CD40	Tenascin C	VCAM1
CD40	Tenascin C	cortisol
CD40	VCAM1	cortisol
IGF BP2	MMP3	peptide YY
IGF BP2	MMP3	stem cell factor
IGF BP2	MMP3	TNF RII
IGF BP2	MMP3	AXL
IGF BP2	MMP3	Eotaxin 3
IGF BP2	MMP3	FABP

EP 2 806 272 A1

(continued)

5

10

15

20

25

30

35

40

45

50

55

IGF BP2	MMP3	FGF basic
IGF BP2	MMP3	myoglobin
IGF BP2	MMP3	resistin
IGF BP2	MMP3	TRAIL R3
IGF BP2	MMP3	endothelin 1
IGF BP2	MMP3	NrCAM
IGF BP2	MMP3	Tenascin C
IGF BP2	MMP3	VCAM1
IGF BP2	MMP3	cortisol
IGF BP2	peptide YY	stem cell factor
IGF BP2	peptide YY	TNF RII
IGF BP2	peptide YY	AXL
IGF BP2	peptide YY	Eotaxin 3
IGF BP2	peptide YY	FABP
IGF BP2	peptide YY	FGF basic
IGF BP2	peptide YY	myoglobin
IGF BP2	peptide YY	resistin
IGF BP2	peptide YY	TRAIL R3
IGF BP2	peptide YY	endothelin 1
IGF BP2	peptide YY	NrCAM
IGF BP2	peptide YY	Tenascin C
IGF BP2	peptide YY	VCAM1
IGF BP2	peptide YY	cortisol
IGF BP2	stem cell factor	TNF RII
IGF BP2	stem cell factor	AXL
IGF BP2	stem cell factor	Eotaxin 3
IGF BP2	stem cell factor	FABP
IGF BP2	stem cell factor	FGF basic
IGF BP2	stem cell factor	myoglobin
IGF BP2	stem cell factor	resistin
IGF BP2	stem cell factor	TRAIL R3
IGF BP2	stem cell factor	endothelin 1
IGF BP2	stem cell factor	NrCAM
IGF BP2	stem cell factor	Tenascin C
IGF BP2	stem cell factor	VCAM1
IGF BP2	stem cell factor	cortisol
IGF BP2	TNF RII	AXL
IGF BP2	TNF RII	Eotaxin 3
IGF BP2	TNF RII	FABP

EP 2 806 272 A1

(continued)

5

10

15

20

25

30

35

40

45

50

55

IGF BP2	TNF RII	FGF basic
IGF BP2	TNF RII	myoglobin
IGF BP2	TNF RII	resistin
IGF BP2	TNF RII	TRAIL R3
IGF BP2	TNF RII	endothelin 1
IGF BP2	TNF RII	NrCAM
IGF BP2	TNF RII	Tenascin C
IGF BP2	TNF RII	VCAM1
IGF BP2	TNF RII	cortisol
IGF BP2	AXL	Eotaxin 3
IGF BP2	AXL	FABP
IGF BP2	AXL	FGF basic
IGF BP2	AXL	myoglobin
IGF BP2	AXL	resistin
IGF BP2	AXL	TRAIL R3
IGF BP2	AXL	endothelin 1
IGF BP2	AXL	NrCAM
IGF BP2	AXL	Tenascin C
IGF BP2	AXL	VCAM1
IGF BP2	AXL	cortisol
IGF BP2	Eotaxin 3	FABP
IGF BP2	Eotaxin 3	FGF basic
IGF BP2	Eotaxin 3	myoglobin
IGF BP2	Eotaxin 3	resistin
IGF BP2	Eotaxin 3	TRAIL R3
IGF BP2	Eotaxin 3	endothelin 1
IGF BP2	Eotaxin 3	NrCAM
IGF BP2	Eotaxin 3	Tenascin C
IGF BP2	Eotaxin 3	VCAM1
IGF BP2	Eotaxin 3	cortisol
IGF BP2	FABP	FGF basic
IGF BP2	FABP	myoglobin
IGF BP2	FABP	resistin
IGF BP2	FABP	TRAIL R3
IGF BP2	FABP	endothelin 1
IGF BP2	FABP	NrCAM
IGF BP2	FABP	Tenascin C
IGF BP2	FABP	VCAM1
IGF BP2	FABP	cortisol

EP 2 806 272 A1

(continued)

5

10

15

20

25

30

35

40

45

50

55

IGF BP2	FGF basic	myoglobin
IGF BP2	FGF basic	resistin
IGF BP2	FGF basic	TRAIL R3
IGF BP2	FGF basic	endothilin 1
IGF BP2	FGF basic	NrCAM
IGF BP2	FGF basic	Tenascin C
IGF BP2	FGF basic	VCAM1
IGF BP2	FGF basic	cortisol
IGF BP2	myoglobin	resistin
IGF BP2	myoglobin	TRAIL R3
IGF BP2	myoglobin	endothilin 1
IGF BP2	myoglobin	NrCAM
IGF BP2	myoglobin	Tenascin C
IGF BP2	myoglobin	VCAM1
IGF BP2	myoglobin	cortisol
IGF BP2	resistin	TRAIL R3
IGF BP2	resistin	endothilin 1
IGF BP2	resistin	NrCAM
IGF BP2	resistin	Tenascin C
IGF BP2	resistin	VCAM1
IGF BP2	resistin	cortisol
IGF BP2	TRAIL R3	endothilin 1
IGF BP2	TRAIL R3	NrCAM
IGF BP2	TRAIL R3	Tenascin C
IGF BP2	TRAIL R3	VCAM1
IGF BP2	TRAIL R3	cortisol
IGF BP2	endothilin 1	NrCAM
IGF BP2	endothilin 1	Tenascin C
IGF BP2	endothilin 1	VCAM1
IGF BP2	endothilin 1	cortisol
IGF BP2	NrCAM	Tenascin C
IGF BP2	NrCAM	VCAM1
IGF BP2	NrCAM	cortisol
IGF BP2	Tenascin C	VCAM1
IGF BP2	Tenascin C	cortisol
IGF BP2	VCAM1	cortisol
MMP3	peptide YY	stem cell factor
MMP3	peptide YY	TNF RII
MMP3	peptide YY	AXL

EP 2 806 272 A1

(continued)

5

10

15

20

25

30

35

40

45

50

55

MMP3	peptide YY	Eotaxin 3
MMP3	peptide YY	FABP
MMP3	peptide YY	FGF basic
MMP3	peptide YY	myoglobin
MMP3	peptide YY	resistin
MMP3	peptide YY	TRAIL R3
MMP3	peptide YY	endothelin 1
MMP3	peptide YY	NrCAM
MMP3	peptide YY	Tenascin C
MMP3	peptide YY	VCAM1
MMP3	peptide YY	cortisol
MMP3	stem cell factor	TNF RII
MMP3	stem cell factor	AXL
MMP3	stem cell factor	Eotaxm 3
MMP3	stem cell factor	FABP
MMP3	stem cell factor	FGF basic
MMP3	stem cell factor	myoglobin
MMP3	stem cell factor	resistin
MMP3	stem cell factor	TRAIL R3
MMP3	stem cell factor	endothelin 1
MMP3	stem cell factor	NrCAM
MMP3	stem cell factor	Tenascin C
MMP3	stem cell factor	VCAM1
MMP3	stem cell factor	cortisol
MMP3	TNF RII	AXL
MMP3	TNF RII	Eotaxin 3
MMP3	TNF RII	FABP
MMP3	TNF RII	FGF basic
MMP3	TNF RII	myoglobin
MMP3	TNF RII	resistin
MMP3	TNF RII	TRAIL R3
MMP3	TNF RII	endothelin 1
MMP3	TNF RII	NrCAM
MMP3	TNF RII	Tenascin C
MMP3	TNF RII	VCAM1
MMP3	TNF RII	cortisol
MMP3	AXL	Eotaxin 3
MMP3	AXL	FABP
MMP3	AXL	FGF basic

EP 2 806 272 A1

(continued)

5

10

15

20

25

30

35

40

45

50

55

MMP3	AXL	myoglobin
MMP3	AXL	resistin
MMP3	AXL	TRAIL R3
MMP3	AXL	endothelin 1
MMP3	AXL	NrCAM
MMP3	AXL	Tenascin C
MMP3	AXL	VCAM1
MMP3	AXL	cortisol
MMP3	Eotaxin 3	FABP
MMP3	Eotaxin 3	FGF basic
MMP3	Eotaxin 3	myoglobin
MMP3	Eotaxin 3	resistin
MMP3	Eotaxin 3	TRAIL R3
MMP3	Eotaxin 3	endothelin 1
MMP3	Eotaxin 3	NrCAM
MMP3	Eotaxin 3	Tenascin C
MMP3	Eotaxin 3	VCAM1
MMP3	Eotaxin 3	cortisol
MMP3	FABP	FGF basic
MMP3	FABP	myoglobin
MMP3	FABP	resistin
MMP3	FABP	TRAIL R3
MMP3	FABP	endothelin 1
MMP3	FABP	NrCAM
MMP3	FABP	Tenascin C
MMP3	FABP	VCAM1
MMP3	FABP	cortisol
MMP3	FGF basic	myoglobin
MMP3	FGF basic	resisti n
MMP3	FGF basic	TRAIL R3
MMP3	FGF basic	endothelin 1
MMP3	FGF basic	NrCAM
MMP3	FGF basic	Tenascin C
MMP3	FGF basic	VCAM1
MMP3	FGF basic	cortisol
MMP3	myoglobin	resistin
MMP3	myoglobin	TRAIL R3
MMP3	myoglobin	endothelin 1
MMP3	myoglobin	NrCAM

EP 2 806 272 A1

(continued)

5

10

15

20

25

30

35

40

45

50

55

MMP3	myoglobin	Tenascin C
MMP3	myoglobin	VCAM1
MMP3	myoglobin	cortisol
MMP3	resistin	TRAIL R3
MMP3	resistin	endothelin 1
MMP3	resistin	NrCAM
MMP3	resistin	Tenascin C
MMP3	resistin	VCAM1
MMP3	resistin	cortisol
MMP3	TRAIL R3	endothelin 1
MMP3	TRAIL R3	NrCAM
MMP3	TRAIL R3	Tenascin C
MMP3	TRAIL R3	VCAM1
MMP3	TRAIL R3	cortisol
MMP3	endothelin 1	NrCAM
MMP3	endothelin 1	Tenascin C
MMP3	endothelin 1	VCAM1
MMP3	endothelin 1	cortisol
MMP3	NrCAM	Tenascin C
MMP3	NrCAM	VCAM1
MMP3	NrCAM	cortisol
MMP3	Tenascin C	VCAM1
MMP3	Tenascin C	cortisol
MMP3	VCAM1	cortisol
peptide YY	stem cell factor	TNF RII
peptide YY	stem cell factor	AXL
peptide YY	stem cell factor	Eotaxin 3
peptide YY	stem cell factor	FABP
peptide YY	stem cell factor	FGF basic
peptide YY	stem cell factor	myoglobin
peptide YY	stem cell factor	resistin
peptide YY	stem cell factor	TRAIL R3
peptide YY	stem cell factor	endothelin 1
peptide YY	stem cell factor	NrCAM
peptide YY	stem cell factor	Tenascin C
peptide YY	stem cell factor	VCAM1
peptide YY	stem cell factor	cortisol
peptide YY	TNF RII	AXL
peptide YY	TNF RII	Eotaxin 3

EP 2 806 272 A1

(continued)

5

10

15

20

25

30

35

40

45

50

55

peptide YY	TNF RII	FABP
peptide YY	TNF RII	FGF basic
peptide YY	TNF RII	myoglobin
peptide YY	TNF RII	resistin
peptide YY	TNF RII	TRAIL R3
peptide YY	TNF RII	endothilin 1
peptide YY	TNF RII	NrCAM
peptide YY	TNF RII	Tenascin C
peptide YY	TNF RII	VCAM1
peptide YY	TNF RII	cortisol
peptide YY	AXL	Eotaxin 3
peptide YY	AXL	FABP
peptide YY	AXL	FGF basic
peptide YY	AXL	myoglobin
peptide YY	AXL	resistin
peptide YY	AXL	TRAIL R3
peptide YY	AXL	endothilin 1
peptide YY	AXL	NrCAM
peptide YY	AXL	Tenascin C
peptide YY	AXL	VCAM1
peptide YY	AXL	cortisol
peptide YY	Eotaxin 3	FABP
peptide YY	Eotaxin 3	FGF basic
peptide YY	Eotaxin 3	myoglobin
peptide YY	Eotaxin 3	resistin
peptide YY	Eotaxin 3	TRAIL R3
peptide YY	Eotaxm 3	endothilin 1
peptide YY	Eotaxin 3	NrCAM
peptide YY	Eotaxin 3	Tenascin C
peptide YY	Eotaxin 3	VCAM1
peptide YY	Eotaxin 3	cortisol
peptide YY	FABP	FGF basic
peptide YY	FABP	myoglobin
peptide YY	FABP	resistin
peptide YY	FABP	TRAIL R3
peptide YY	FABP	endothilin 1
peptide YY	FABP	NrCAM
peptide YY	FABP	Tenascin C
peptide YY	FABP	VCAM1

EP 2 806 272 A1

(continued)

	peptide YY	FABP	cortisol
5	peptide YY	FGF basic	myoglobin
	peptide YY	FGF basic	resistin
	peptide YY	FGF basic	TRAIL R3
	peptide YY	FGF basic	endothelin 1
10	peptide YY	FGF basic	NrCAM
	peptide YY	FGF basic	Tenascin C
	peptide YY	FGF basic	VCAM1
15	peptide YY	FGF basic	cortisol
	peptide YY	myoglobin	resistin
	peptide YY	myoglobin	TRAIL R3
	peptide YY	myoglobin	endothelin 1
20	peptide YY	myoglobin	NrCAM
	peptide YY	myoglobin	Tenascin C
	peptide YY	myoglobin	VCAM1
25	peptide YY	myoglobin	cortisol
	peptide YY	resistin	TRAIL R3
	peptide YY	resistin	endothelin 1
	peptide YY	resistin	NrCAM
30	peptide YY	resistin	Tenascin C
	peptide YY	resistin	VCAM1
	peptide YY	resistin	cortisol
35	peptide YY	TRAIL R3	endothelin 1
	peptide YY	TRAIL R3	NrCAM
	peptide YY	TRAIL R3	Tenascin C
	peptide YY	TRAIL R3	VCAM1
40	peptide YY	TRAIL R3	cortisol
	peptide YY	endothelin 1	NrCAM
	peptide YY	endothelin 1	Tenascin C
45	peptide YY	endothelin 1	VCAM1
	peptide YY	endothelin 1	cortisol
	peptide YY	NrCAM	Tenascin C
	peptide YY	NrCAM	VCAM1
50	peptide YY	NrCAM	cortisol
	peptide YY	Tenascin C	VCAM1
	peptide YY	Tenascin C	cortisol
55	peptide YY	VCAM1	cortisol
	stem cell factor	TNF RII	AXL
	stem cell factor	TNF RII	Eotaxin 3

EP 2 806 272 A1

(continued)

5

10

15

20

25

30

35

40

45

50

55

stem cell factor	TNF RII	FABP
stem cell factor	TNF RII	FGF basic
stem cell factor	TNF RII	myoglobin
stem cell factor	TNF RII	resistin
stem cell factor	TNF RII	TRAIL R3
stem cell factor	TNF RII	endothelin 1
stem cell factor	TNF RII	NrCAM
stem cell factor	TNF RII	Tenascin C
stem cell factor	TNF RII	VCAM1
stem cell factor	TNF RII	cortisol
stem cell factor	AXL	Eotaxin 3
stem cell factor	AXL	FABP
stem cell factor	AXL	FGF basic
stem cell factor	AXL	myoglobin
stem cell factor	AXL	resistin
stem cell factor	AXL	TRAIL R3
stem cell factor	AXL	endothelin 1
stem cell factor	AXL	NrCAM
stem cell factor	AXL	Tenascin C
stem cell factor	AXL	VCAM1
stem cell factor	AXL	cortisol
stem cell factor	Eotaxin 3	FABP
stem cell factor	Eotaxin 3	FGF basic
stem cell factor	Eotaxin 3	myoglobin
stem cell factor	Eotaxin 3	resistin
stem cell factor	Eotaxin 3	TRAIL R3
stem cell factor	Eotaxin 3	endothelin 1
stem cell factor	Eotaxin 3	NrCAM
stem cell factor	Eotaxin 3	Tenascin C
stem cell factor	Eotaxin 3	VCAM1
stem cell factor	Eotaxin 3	cortisol
stem cell factor	FABP	FGF basic
stem cell factor	FABP	myoglobin
stem cell factor	FABP	resistin
stem cell factor	FABP	TRAIL R3
stem cell factor	FABP	endothelin 1
stem cell factor	FABP	NrCAM
stem cell factor	FABP	Tenascin C
stem cell factor	FABP	VCAM1

EP 2 806 272 A1

(continued)

	stem cell factor	FABP	cortisol
5	stem cell factor	FGF basic	myoglobin
	stem cell factor	FGF basic	resistin
	stem cell factor	FGF basic	TRAIL R3
	stem cell factor	FGF basic	endothelin 1
10	stem cell factor	FGF basic	NrCAM
	stem cell factor	FGF basic	Tenascin C
	stem cell factor	FGF basic	VCAM1
15	stem cell factor	FGF basic	cortisol
	stem cell factor	myoglobin	resistin
	stem cell factor	myoglobin	TRAIL R3
	stem cell factor	myoglobin	endothelin 1
20	stem cell factor	myoglobin	NrCAM
	stem cell factor	myoglobin	Tenascin C
	stem cell factor	myoglobin	VCAM1
25	stem cell factor	myoglobin	cortisol
	stem cell factor	resistin	TRAIL R3
	stem cell factor	resistin	endothelin 1
	stem cell factor	resistin	NrCAM
30	stem cell factor	resistin	Tenascin C
	stem cell factor	resistin	VCAM1
	stem cell factor	resistin	cortisol
35	stem cell factor	TRAIL R3	endothelin 1
	stem cell factor	TRAIL R3	NrCAM
	stem cell factor	TRAIL R3	Tenascin C
	stem cell factor	TRAIL R3	VCAM1
40	stem cell factor	TRAIL R3	cortisol
	stem cell factor	endothelin 1	NrCAM
	stem cell factor	endothelin 1	Tenascin C
45	stem cell factor	endothelin 1	VCAM1
	stem cell factor	endothelin 1	cortisol
	stem cell factor	NrCAM	Tenascin C
	stem cell factor	NrCAM	VCAM1
50	stem cell factor	NrCAM	cortisol
	stem cell factor	Tenascin C	VCAM1
	stem cell factor	Tenascin C	cortisol
55	stem cell factor	VCAM1	cortisol
	TNF RII	AXL	Eotaxin 3
	TNF RII	AXL	FABP

EP 2 806 272 A1

(continued)

5

10

15

20

25

30

35

40

45

50

55

TNF RII	AXL	FGF basic
TNF RII	AXL	myoglobin
TNF RII	AXL	resistin
TNF RII	AXL	TRAIL R3
TNF RII	AXL	endothelin 1
TNF RII	AXL	NrCAM
TNF RII	AXL	Tenascin C
TNF RII	AXL	VCAM1
TNF RII	AXL	cortisol
TNF RII	Eotaxin 3	FABP
TNF RII	Eotaxin 3	FGF basic
TNF RII	Eotaxin 3	myoglobin
TNF RII	Eotaxin 3	resistin
TNF RII	Eotaxin 3	TRAIL R3
TNF RII	Eotaxin 3	endothelin 1
TNF RII	Eotaxin 3	NrCAM
TNF RII	Eotaxin 3	Tenascin C
TNF RII	Eotaxin 3	VCAM1
TNF RII	Eotaxin 3	cortisol
TNF RII	FABP	FGF basic
TNF RII	FABP	myoglobin
TNF RII	FABP	resistin
TNF RII	FABP	TRAIL R3
TNF RII	FABP	endothelin 1
TNF RII	FABP	NrCAM
TNF RII	FABP	Tenascin C
TNF RII	FABP	VCAM1
TNF RII	FABP	cortisol
TNF RII	FGF basic	myoglobin
TNF RII	FGF basic	resistin
TNF RII	FGF basic	TRAIL R3
TNF RII	FGF basic	endothelin 1
TNF RII	FGF basic	NrCAM
TNF RII	FGF basic	Tenascin C
TNF RII	FGF basic	VCAM1
TNF RII	FGF basic	cortisol
TNF RII	myoglobin	resistin
TNF RII	myoglobin	TRAIL R3
TNF RII	myoglobin	endothelin 1

EP 2 806 272 A1

(continued)

5

10

15

20

25

30

35

40

45

50

55

TNF RII	myoglobin	NrCAM
TNF RII	myoglobin	Tenascin C
TNF RII	myoglobin	VCAM1
TNF RII	myoglobin	cortisol
TNF RII	resistin	TRAIL R3
TNF RII	resistin	endothilin 1
TNF RII	resistin	NrCAM
TNF RII	resistin	Tenascin C
TNF RII	resistin	VCAM1
TNF RII	resistin	cortisol
TNF RII	TRAIL R3	endothilin 1
TNF RII	TRAIL R3	NrCAM
TNF RII	TRAIL R3	Tenascin C
TNF RII	TRAIL R3	VCAM1
TNF RII	TRAIL R3	cortisol
TNF RII	endothilin 1	NrCAM
TNF RII	endothilin 1	Tenascin C
TNF RII	endothilin 1	VCAM1
TNF RII	endothilin 1	cortisol
TNF RII	NrCAM	Tenascin C
TNF RII	NrCAM	VCAM1
TNF RII	NrCAM	cortisol
TNF RII	Tenascin C	VCAM1
TNF RII	Tenascin C	cortisol
TNF RII	VCAM1	cortisol
AXL	Eotaxin 3	FABP
AXL	Eotaxin 3	FGF basic
AXL	Eotaxin 3	myoglobin
AXL	Eotaxin 3	resistin
AXL	Eotaxin 3	TRAIL R3
AXL	Eotaxin 3	endothilin 1
AXL	Eotaxin 3	NrCAM
AXL	Eotaxm 3	Tenascin C
AXL	Eotaxin 3	VCAM1
AXL	Eotaxin 3	cortisol
AXL	FABP	FGF basic
AXL	FABP	myoglobin
AXL	FABP	resistin
AXL	FABP	TRAIL R3

EP 2 806 272 A1

(continued)

5

10

15

20

25

30

35

40

45

50

55

AXL	FABP	endothilin 1
AXL	FABP	NrCAM
AXL	FABP	Tenascin C
AXL	FABP	VCAM1
AXL	FABP	cortisol
AXL	FGF basic	myoglobin
AXL	FGF basic	resistin
AXL	FGF basic	TRAIL R3
AXL	FGF basic	endothilin 1
AXL	FGF basic	NrCAM
AXL	FGF basic	Tenascin C
AXL	FGF basic	VCAM1
AXL	FGF basic	cortisol
AXL	myoglobin	resistin n
AXL	myoglobin	TRAIL R3
AXL	myoglobin	endothilin 1
AXL	myoglobin	NrCAM
AXL	myoglobin	Tenascin C
AXL	myoglobin	VCAM1
AXL	myoglobin	cortisol
AXL	resistin	TRAIL R3
AXL	resistin	endothilin 1
AXL	resistin	NrCAM
AXL	resistin	Tenascin C
AXL	resistin	VCAM1
AXL	resistin	cortisol
AXL	TRAIL R3	endothilin 1
AXL	TRAIL R3	NrCAM
AXL	TRAIL R3	Tenascin C
AXL	TRAIL R3	VCAM1
AXL	TRAIL R3	cortisol
AXL	endothilin 1	NrCAM
AXL	endothilin 1	Tenascin C
AXL	endothilin 1	VCAM1
AXL	endothilin 1	cortisol
AXL	NrCAM	Tenascin C
AXL	NrCAM	VCAM1
AXL	NrCAM	cortisol
AXL	Tenascin C	VCAM1

EP 2 806 272 A1

(continued)

5

10

15

20

25

30

35

40

45

50

55

AXL	Tenascin C	cortisol
AXL	VCAM1	cortisol
Eotaxin 3	FABP	FGF basic
Eotaxin 3	FABP	myoglobin
Eotaxin 3	FABP	resistin
Eotaxin 3	FABP	TRAIL R3
Eotaxin 3	FABP	endothilin 1
Eotaxin 3	FABP	NrCAM
Eotaxin 3	FABP	Tenascin C
Eotaxin 3	FABP	VCAM1
Eotaxin 3	FABP	cortisol
Eotaxin 3	FGF basic	myoglobin
Eotaxin 3	FGF basic	resistin
Eotaxin 3	FGF basic	TRAIL R3
Eotaxin 3	FGF basic	endothilin 1
Eotaxin 3	FGF basic	NrCAM
Eotaxin 3	FGF basic	Tenascin C
Eotaxin 3	FGF basic	VCAM1
Eotaxin 3	FGF basic	cortisol
Eotaxin 3	myoglobin	resistin
Eotaxin 3	myoglobin	TRAIL R3
Eotaxin 3	myoglobin	endothilin 1
Eotaxin 3	myoglobin	NrCAM
Eotaxin 3	myoglobin	Tenascin C
Eotaxin 3	myoglobin	VCAM1
Eotaxin 3	myoglobin	cortisol
Eotaxin 3	resistin	TRAIL R3
Eotaxin 3	resistin	endothilin 1
Eotaxin 3	resistin	NrCAM
Eotaxin 3	resistin	Tenascin C
Eotaxin 3	resistin	VCAM1
Eotaxin 3	resistin	cortisol
Eotaxin 3	TRAIL R3	endothilin 1
Eotaxin 3	TRAIL R3	NrCAM
Eotaxin 3	TRAIL R3	Tenascin C
Eotaxin 3	TRAIL R3	VCAM1
Eotaxin 3	TRAIL R3	cortisol
Eotaxin 3	endothilin 1	NrCAM
Eotaxin 3	endothilin 1	Tenascin C

EP 2 806 272 A1

(continued)

5

10

15

20

25

30

35

40

45

50

55

Eotaxin 3	endothilin 1	VCAM1
Eotaxin 3	endothilin 1	cortisol
Eotaxin 3	NrCAM	Tenascin C
Eotaxin 3	NrCAM	VCAM1
Eotaxin 3	NrCAM	cortisol
Eotaxin 3	Tenascin C	VCAM1
Eotaxin 3	Tenascin C	cortisol
Eotaxin 3	VCAM1	cortisol
FABP	FGF basic	myoglobin
FABP	FGF basic	resistin
FABP	FGF basic	TRAIL R3
FABP	FGF basic	endothilin 1
FABP	FGF basic	NrCAM
FABP	FGF basic	Tenascin C
FABP	FGF basic	VCAM1
FABP	FGF basic	cortisol
FABP	myoglobin	resistin
FABP	myoglobin	TRAIL R3
FABP	myoglobin	endothilin 1
FABP	myoglobin	NrCAM
FABP	myoglobin	Tenascin C
FABP	myoglobin	VCAM1
FABP	myoglobin	cortisol
FABP	resistin	TRAIL R3
FABP	resistin	endothilin 1
FABP	resistin	NrCAM
FABP	resistin	Tenascin C
FABP	resistin	VCAM1
FABP	resistin	cortisol
FABP	TRAIL R3	endothilin 1
FABP	TRAIL R3	NrCAM
FABP	TRAIL R3	Tenascin C
FABP	TRAIL R3	VCAM1
FABP	TRAIL R3	cortisol
FABP	endothilin 1	NrCAM
FABP	endothilin 1	Tenascin C
FABP	endothilin 1	VCAM1
FABP	endothilin 1	cortisol
FABP	NrCAM	Tenascin C

EP 2 806 272 A1

(continued)

5

10

15

20

25

30

35

40

45

50

55

FABP	NrCAM	VCAM1
FABP	NrCAM	cortisol
FABP	Tenascin C	VCAM1
FABP	Tenascin C	cortisol
FABP	VCAM1	cortisol
FGF basic	myoglobin	resistin
FGF basic	myoglobin	TRAIL R3
FGF basic	myoglobin	endothelin 1
FGF basic	Myoglobin	NrCAM
FGF basic	myoglobin	Tenascin C
FGF basic	myoglobin	VCAM1
FGF basic	myoglobin	cortisol
FGF basic	resistin	TRAIL R3
FGF basic	resistin	endothelin 1
FGF basic	resistin	NrCAM
FGF basic	resistin	Tenascin C
FGF basic	resistin	VCAM1
FGF basic	resistin	cortisol
FGF basic	TRAIL R3	endothelin 1
FGF basic	TRAIL R3	NrCAM
FGF basic	TRAIL R3	Tenascin C
FGF basic	TRAIL R3	VCAM1
FGF basic	TRAIL R3	cortisol
FGF basic	endothelin 1	NrCAM
FGF basic	endothelin 1	Tenascin C
FGF basic	endothelin 1	VCAM1
FGF basic	endothelin 1	cortisol
FGF basic	NrCAM	Tenascin C
FGF basic	NrCAM	VCAM1
FGF basic	NrCAM	cortisol
FGF basic	Tenascin C	VCAM1
FGF basic	Tenascin C	cortisol
FGF basic	VCAM1	cortisol
myoglobin	resistin	TRAIL R3
myoglobin	resistin	endothelin 1
myoglobin	resistin	NrCAM
myoglobin	resistin	Tenascin C
myoglobin	resistin	VCAM1
myoglobin	resistin	cortisol

EP 2 806 272 A1

(continued)

5

10

15

20

25

30

35

40

45

50

55

myoglobin	TRAIL R3	endothilin 1
myoglobin	TRAIL R3	NrCAM
myoglobin	TRAIL R3	Tenascin C
myoglobin	TRAIL R3	VCAM1
myoglobin	TRAIL R3	cortisol
myoglobin	endothilin 1	NrCAM
myoglobin	endothilin 1	Tenascin C
myoglobin	endothilin 1	VCAM1
myoglobin	endothilin 1	cortisol
myoglobin	NrCAM	Tenascin C
myoglobin	NrCAM	VCAM1
myoglobin	NrCAM	cortisol
myoglobin	Tenascin C	VCAM1
myoglobin	Tenascin C	cortisol
myoglobin	VCAM1	cortisol
resistin	TRAIL R3	endothelin 1
resistin	TRAIL R3	NrCAM
resistin	TRAIL R3	Tenascin C
resistin	TRAIL R3	VCAM1
resistin	TRAIL R3	cortisol
resistin	endothilin 1	NrCAM
resistin	endothilin 1	Tenascin C
resistin	endothilin 1	VCAM1
resistin	endothilin 1	cortisol
resistin	NrCAM	Tenascin C
resistin	NrCAM	VCAM1
resistin	NrCAM	cortisol
resistin	Tenascin C	VCAM1
resistin	Tenascin C	cortisol
resistin	VCAM1	cortisol
TRAIL R3	endothilin 1	NrCAM
TRAIL R3	endothilin 1	Tenascin C
TRAIL R3	endothilm 1	VCAM1
TRAIL R3	endothilin 1	cortisol
TRAIL R3	NrCAM	Tenascin C
TRAIL R3	NrCAM	VCAM1
TRAIL R3	NrCAM	cortisol
TRAIL R3	Tenascin C	VCAM1
TRAIL R3	Tenascin C	cortisol

(continued)

TRAIL R3	VCAM1	cortisol
endothelin 1	NrCAM	Tenascin C
endothelin 1	NrCAM	VCAM1
endothelin 1	NrCAM	cortisol
endothelin 1	Tenascin C	VCAM1
endothelin 1	Tenascin C	cortisol
endothelin 1	VCAM1	cortisol
NrCAM	Tenascin C	VCAM1
NrCAM	Tenascin C	cortisol
NrCAM	VCAM1	cortisol
Tenascin C	VCAM1	cortisol

[0055] In one exemplary embodiment, the combination of sample analytes may include Beta 2 Microglobulin, BLC, CD40, IGF BP2, MMP3, Peptide YY, Stem Cell Factor, TNF RII, and VEGF. In another exemplary embodiment, the combination of sample analytes may include AXL, Beta 2 Microglobulin, CD40, Eotaxin 3, FABP, FGF basic, IGF BP2, MMP3, Myoglobin, Resistin, Stem Cell Factor, TNF RII, TRAIL R3, and VEGF. In yet another exemplary embodiment, the combination of sample analytes may include AXL, Beta 2 Microglobulin, BLC, CD40, Endothelin 1, Eotaxin 3, FABP, FGF basic, IGF BP2, MMP3, Myoglobin, NrCAM, Peptide YY, Resistin, Stem Cell Factor, Tenascin C, TNF RII, TRAIL R3, VCAM 1, and VEGF. In still yet another exemplary embodiment, the combination of sample analytes may include Beta 2 Microglobulin, CD40, Cortisol, FGF.basic, Stem Cell Factor, TNF RII, and VEGF.

III. Test Sample

[0056] The method for diagnosing, monitoring, or determining a renal disorder involves determining the presence of sample analytes in a test sample. A test sample, as defined herein, is an amount of bodily fluid taken from a mammal. Non-limiting examples of bodily fluids include urine, blood, plasma, serum, saliva, semen, perspiration, tears, mucus, and tissue lysates. In an exemplary embodiment, the bodily fluid contained in the test sample is urine, plasma, or serum.

(a) Mammals

[0057] A mammal, as defined herein, is any organism that is a member of the class Mammalia. Non-limiting examples of mammals appropriate for the various embodiments may include humans, apes, monkeys, rats, mice, dogs, cats, pigs, and livestock including cattle and oxen. In an exemplary embodiment, the mammal is a human.

(b) Devices and Methods of Taking Bodily Fluids from Mammals

[0058] The bodily fluids of the test sample may be taken from the mammal using any known device or method so long as the analytes to be measured by the multiplexed assay are not rendered undetectable by the multiplexed assay. Non-limiting examples of devices or methods suitable for taking bodily fluid from a mammal include urine sample cups, urethral catheters, swabs, hypodermic needles, thin needle biopsies, hollow needle biopsies, punch biopsies, metabolic cages, and aspiration.

[0059] In order to adjust the expected concentrations of the sample analytes in the test sample to fall within the dynamic range of the multiplexed assay, the test sample may be diluted to reduce the concentration of the sample analytes prior to analysis. The degree of dilution may depend on a variety of factors including but not limited to the type of multiplexed assay used to measure the analytes, the reagents utilized in the multiplexed assay, and the type of bodily fluid contained in the test sample. In one embodiment, the test sample is diluted by adding a volume of diluent ranging from about ½ of the original test sample volume to about 50,000 times the original test sample volume.

[0060] In one exemplary embodiment, if the test sample is human urine and the multiplexed assay is an antibody-based capture-sandwich assay, the test sample is diluted by adding a volume of diluent that is about 100 times the original test sample volume prior to analysis. In another exemplary embodiment, if the test sample is human serum and the multiplexed assay is an antibody-based capture-sandwich assay, the test sample is diluted by adding a volume of

diluent that is about 5 times the original test sample volume prior to analysis. In yet another exemplary embodiment, if the test sample is human plasma and the multiplexed assay is an antibody-based capture-sandwich assay, the test sample is diluted by adding a volume of diluent that is about 2,000 times the original test sample volume prior to analysis.

[0061] The diluent may be any fluid that does not interfere with the function of the multiplexed assay used to measure the concentration of the analytes in the test sample. Non-limiting examples of suitable diluents include deionized water, distilled water, saline solution, Ringer's solution, phosphate buffered saline solution, TRIS-buffered saline solution, standard saline citrate, and HEPES-buffered saline.

IV. Multiplexed Assay Device

[0062] In one embodiment, the concentration of a combination of sample analytes is measured using a multiplexed assay device capable of measuring the concentrations of up to sixteen of the biomarker analytes. A multiplexed assay device, as defined herein, is an assay capable of simultaneously determining the concentration of three or more different sample analytes using a single device and/or method. Any known method of measuring the concentration of the biomarker analytes may be used for the multiplexed assay device. Non-limiting examples of measurement methods suitable for the multiplexed assay device may include electrophoresis, mass spectrometry, protein microarrays, surface plasmon resonance and immunoassays including but not limited to western blot, immunohistochemical staining, enzyme-linked immunosorbent assay (ELISA) methods, and particle-based capture-sandwich immunoassays.

(a) Multiplexed Immunoassay Device

[0063] In one embodiment, the concentrations of the analytes in the test sample are measured using a multiplexed immunoassay device that utilizes capture antibodies marked with indicators to determine the concentration of the sample analytes.

(i) capture antibodies

[0064] In the same embodiment, the multiplexed immunoassay device includes three or more capture antibodies. Capture antibodies, as defined herein, are antibodies in which the antigenic determinant is one of the biomarker analytes. Each of the at least three capture antibodies has a unique antigenic determinant that is one of the biomarker analytes. When contacted with the test sample, the capture antibodies form antigen-antibody complexes in which the analytes serve as antigens.

[0065] The term "antibody," as used herein, encompasses a monoclonal ab, an antibody fragment, a chimeric antibody, and a single-chain antibody.

[0066] In some embodiments, the capture antibodies may be attached to a substrate in order to immobilize any analytes captured by the capture antibodies. Non-limiting examples of suitable substrates include paper, cellulose, glass, or plastic strips, beads, or surfaces, such as the inner surface of the well of a microtitration tray. Suitable beads may include polystyrene or latex microspheres.

(ii) indicators

[0067] In one embodiment of the multiplexed immunoassay device, an indicator is attached to each of the three or more capture antibodies. The indicator, as defined herein, is any compound that registers a measurable change to indicate the presence of one of the sample analytes when bound to one of the capture antibodies. Non-limiting examples of indicators include visual indicators and electrochemical indicators.

[0068] Visual indicators, as defined herein, are compounds that register a change by reflecting a limited subset of the wavelengths of light illuminating the indicator, by fluorescing light after being illuminated, or by emitting light via chemiluminescence. The change registered by visual indicators may be in the visible light spectrum, in the infrared spectrum, or in the ultraviolet spectrum. Non-limiting examples of visual indicators suitable for the multiplexed immunoassay device include nanoparticulate gold, organic particles such as polyurethane or latex microspheres loaded with dye compounds, carbon black, fluorophores, phycoerythrin, radioactive isotopes, nanoparticles, quantum dots, and enzymes such as horseradish peroxidase or alkaline phosphatase that react with a chemical substrate to form a colored or chemiluminescent product.

[0069] Electrochemical indicators, as defined herein, are compounds that register a change by altering an electrical property. The changes registered by electrochemical indicators may be an alteration in conductivity, resistance, capacitance, current conducted in response to an applied voltage, or voltage required to achieve a desired current. Non-limiting examples of electrochemical indicators include redox species such as ascorbate (vitamin C), vitamin E, glutathione, polyphenols, catechols, quercetin, phytoestrogens, penicillin, carbazole, murrans, phenols, carbonyls, benzoates, and

trace metal ions such as nickel, copper, cadmium, iron and mercury.

[0070] In this same embodiment, the test sample containing a combination of three or more sample analytes is contacted with the capture antibodies and allowed to form antigen-antibody complexes in which the sample analytes serve as the antigens. After removing any uncomplexed capture antibodies, the concentrations of the three or more analytes are determined by measuring the change registered by the indicators attached to the capture antibodies.

[0071] In one exemplary embodiment, the indicators are polyurethane or latex microspheres loaded with dye compounds and phycoerythrin.

(b) Multiplexed Sandwich Immunoassay Device

[0072] In another embodiment, the multiplexed immunoassay device has a sandwich assay format. In this embodiment, the multiplexed sandwich immunoassay device includes three or more capture antibodies as previously described. However, in this embodiment, each of the capture antibodies is attached to a capture agent that includes an antigenic moiety. The antigenic moiety serves as the antigenic determinant of a detection antibody, also included in the multiplexed immunoassay device of this embodiment. In addition, an indicator is attached to the detection antibody.

[0073] In this same embodiment, the test sample is contacted with the capture antibodies and allowed to form antigen-antibody complexes in which the sample analytes serve as antigens. The detection antibodies are then contacted with the test sample and allowed to form antigen-antibody complexes in which the capture agent serves as the antigen for the detection antibody. After removing any uncomplexed detection antibodies the concentration of the analytes are determined by measuring the changes registered by the indicators attached to the detection antibodies.

(c) Multiplexing Approaches

[0074] In the various embodiments of the multiplexed immunoassay devices, the concentrations of each of the sample analytes may be determined using any approach known in the art. In one embodiment, a single indicator compound is attached to each of the three or more antibodies. In addition, each of the capture antibodies having one of the sample analytes as an antigenic determinant is physically separated into a distinct region so that the concentration of each of the sample analytes may be determined by measuring the changes registered by the indicators in each physically separate region corresponding to each of the sample analytes.

[0075] In another embodiment, each antibody having one of the sample analytes as an antigenic determinant is marked with a unique indicator. In this manner, a unique indicator is attached to each antibody having a single sample analyte as its antigenic determinant. In this embodiment, all antibodies may occupy the same physical space. The concentration of each sample analyte is determined by measuring the change registered by the unique indicator attached to the antibody having the sample analyte as an antigenic determinant.

(d) Microsphere-Based Capture-Sandwich immunoassay Device

[0076] In an exemplary embodiment, the multiplexed immunoassay device is a microsphere-based capture-sandwich immunoassay device. In this embodiment, the device includes a mixture of three or more capture-antibody microspheres, in which each capture-antibody microsphere corresponds to one of the biomarker analytes. Each capture-antibody microsphere includes a plurality of capture antibodies attached to the outer surface of the microsphere. In this same embodiment, the antigenic determinant of all of the capture antibodies attached to one microsphere is the same biomarker analyte.

[0077] In this embodiment of the device, the microsphere is a small polystyrene or latex sphere that is loaded with an indicator that is a dye compound. The microsphere may be between about 3 μm and about 5 μm in diameter. Each capture-antibody microsphere corresponding to one of the biomarker analytes is loaded with the same indicator. In this manner, each capture-antibody microsphere corresponding to a biomarker analyte is uniquely color-coded.

[0078] In this same exemplary embodiment, the multiplexed immunoassay device further includes three or more biotinylated detection antibodies in which the antigenic determinant of each biotinylated detection antibody is one of the biomarker analytes. The device further includes a plurality of streptavidin proteins complexed with a reporter compound. A reporter compound, as defined herein, is an indicator selected to register a change that is distinguishable from the indicators used to mark the capture-antibody microspheres.

[0079] The concentrations of the sample analytes may be determined by contacting the test sample with a mixture of capture-antigen microspheres corresponding to each sample analyte to be measured. The sample analytes are allowed to form antigen-antibody complexes in which a sample analyte serves as an antigen and a capture antibody attached to the microsphere serves as an antibody. In this manner, the sample analytes are immobilized onto the capture-antigen microspheres. The biotinylated detection antibodies are then added to the test sample and allowed to form antigen-antibody complexes in which the analyte serves as the antigen and the biotinylated detection antibody serves as the

antibody. The streptavidin-reporter complex is then added to the test sample and allowed to bind to the biotin moieties of the biotinylated detection antibodies. The antigen-capture microspheres may then be rinsed and filtered.

[0080] In this embodiment, the concentration of each analyte is determined by first measuring the change registered by the indicator compound embedded in the capture-antigen microsphere in order to identify the particular analyte. For each microsphere corresponding to one of the biomarker analytes, the quantity of analyte immobilized on the microsphere is determined by measuring the change registered by the reporter compound attached to the microsphere.

[0081] For example, the indicator embedded in the microspheres associated with one sample analyte may register an emission of orange light, and the reporter may register an emission of green light. In this example, a detector device may measure the intensity of orange light and green light separately. The measured intensity of the green light would determine the concentration of the analyte captured on the microsphere, and the intensity of the orange light would determine the specific analyte captured on the microsphere.

[0082] Any sensor device may be used to detect the changes registered by the indicators embedded in the microspheres and the changes registered by the reporter compound, so long as the sensor device is sufficiently sensitive to the changes registered by both indicator and reporter compound. Non-limiting examples of suitable sensor devices include spectrophotometers, photosensors, colorimeters, cyclic coulometry devices, and flow cytometers. In an exemplary embodiment, the sensor device is a flow cytometer.

V. Method for Diagnosing, Monitoring, or Determining a Renal Disorder

[0083] In one embodiment, a method is provided for diagnosing, monitoring, or determining kidney transplant rejection or an associated disorder that includes providing a test sample, determining the concentration of a combination of three or more sample analytes, comparing the measured concentrations of the combination of sample analytes to the entries of a dataset, and identifying kidney transplant rejection or an associated disorder based on the comparison between the concentrations of the sample analytes and the minimum diagnostic concentrations contained within each entry of the dataset.

(a) Diagnostic Dataset

[0084] In an embodiment, the concentrations of the sample analytes are compared to the entries of a dataset. In this embodiment, each entry of the dataset includes a combination of three or more minimum diagnostic concentrations indicative of a particular renal disorder. A minimum diagnostic concentration, as defined herein, is the concentration of an analyte that defines the limit between the concentration range corresponding to normal, healthy renal function and the concentration reflective of a particular renal disorder. In one embodiment, each minimum diagnostic concentration is the maximum concentration of the range of analyte concentrations for a healthy, normal individual. The minimum diagnostic concentration of an analyte depends on a number of factors including but not limited to the particular analyte and the type of bodily fluid contained in the test sample. As an illustrative example, Table 1 lists the expected normal ranges of the biomarker analytes in human plasma, serum, and urine.

TABLE 1: Normal Concentration Ranges In Human Plasma, Serum, and Urine Samples

Analyte	Units	Plasma		Sera		Urine	
		low	high	low	high	low	high
Calbindin	ng/ml	-	< 5.0	-	< 2.6	4.2	233
Clusterin	μg/ml	86	134	37	152	-	< 0.089
CTGF	ng/ml	2.8	7.5	-	< 8.2	-	< 0.90
GST-alpha	ng/ml	6.7	62	1.2	52	-	< 26
KIM-1	ng/ml	0.053	0.57	-	< 0.35	0.023	0.67
VEGF	pg/ml	222	855	219	1630	69	517
B2M	μg/ml	0.68	2.2	1.00	2.6		< 0.17
Cyst C	ng/ml	608	1170	476	1250	3.9	79
NGAL	ng/ml	89	375	102	822	2.9	81
OPN	ng/ml	4.1	25	0.49	12	291	6130
TIMP-1	ng/ml	50	131	100	246	-	< 3.9

(continued)

Analyte	Units	Plasma		Sera		Urine	
		low	high	low	high	low	high
A1M	μg/ml	6.2	16	5.7	17	-	< 4.2
THP	μg/ml	0.0084	0.052	0.007 9	0.053	0.39	2.6
TFF3	μg/ml	0.040	0.49	0.021	0.17	-	< 21
Creatinine	mg/dL	-	-	-	-	13	212
Microalbumin	μg/ml	-	-	-	-	-	> 16

[0085] In one embodiment, the high values shown for each of the biomarker analytes in Table 1 for the analytic concentrations in human plasma, sera and urine are the minimum diagnostics values for the analytes in human plasma, sera, and urine, respectively. In one exemplary embodiment, the minimum diagnostic concentration in human plasma of alpha-1 microglobulin is about 16 μg/ml, beta-2 microglobulin is about 2.2 μg/ml, calbindin is greater than about 5 ng/ml, clusterin is about 134 μg/ml, CTGF is about 16 ng/ml, cystatin C is about 1170 ng/ml, GST-alpha is about 62 ng/ml, KIM-1 is about 0.57 ng/ml, NGAL is about 375 ng/ml, osteopontin is about 25 ng/ml, THP is about 0.052 μg/ml, TIMP-1 is about 131 ng/ml, TFF-3 is about 0.49 μg/ml, and VEGF is about 855 pg/ml.

[0086] In another exemplary embodiment, the minimum diagnostic concentration in human sera of alpha-1 microglobulin is about 17 μg/ml, beta-2 microglobulin is about 2.6 μg/ml, calbindin is greater than about 2.6 ng/ml, clusterin is about 152 μg/ml, CTGF is greater than about 8.2 ng/ml, cystatin C is about 1250 ng/ml, GST-alpha is about 52 ng/ml, KIM-1 is greater than about 0.35 ng/ml, NGAL is about 822 ng/ml, osteopontin is about 12 ng/ml, THP is about 0.053 μg/ml, TIMP-1 is about 246 ng/ml, TFF-3 is about 0.17 μg/ml, and VEGF is about 1630 pg/ml.

[0087] In yet another exemplary embodiment, the minimum diagnostic concentration in human urine of alpha-1 microglobulin is about 233 μg/ml, beta-2 microglobulin is greater than about 0.17 μg/ml, calbindin is about 233 ng/ml, clusterin is greater than about 0.089 μg/ml, CTGF is greater than about 0.90 ng/ml, cystatin C is about 1170 ng/ml, GST-alpha is greater than about 26 ng/ml, KIM-1 is about 0.67 ng/ml, NGAL is about 81 ng/ml, osteopontin is about 6130 ng/ml, THP is about 2.6 μg/ml, TIMP-1 is greater than about 3.9 ng/ml, TFF-3 is greater than about 21 μg/ml, and VEGF is about 517 pg/ml.

[0088] In one embodiment, the minimum diagnostic concentrations represent the maximum level of analyte concentrations falling within an expected normal range. Kidney transplant rejection or an associated disorder may be indicated if the concentration of an analyte is higher than the minimum diagnostic concentration for the analyte.

[0089] If diminished concentrations of a particular analyte are known to be associated with kidney transplant rejection or an associated disorder, the minimum diagnostic concentration may not be an appropriate diagnostic criterion for identifying kidney transplant rejection or an associated disorder indicated by the sample analyte concentrations. In these cases, a maximum diagnostic concentration may define the limit between the expected normal concentration range for the analyte and a sample concentration reflective of kidney transplant rejection or an associated disorder. In those cases in which a maximum diagnostic concentration is the appropriate diagnostic criterion, sample concentrations that fall below a maximum diagnostic concentration may indicate kidney transplant rejection or an associated disorder.

[0090] A critical feature of the method of the multiplexed analyte panel is that a combination of sample analyte concentrations may be used to diagnose kidney transplant rejection or an associated disorder. In addition to comparing subsets of the biomarker analyte concentrations to diagnostic criteria, the analytes may be algebraically combined and compared to corresponding diagnostic criteria. In one embodiment, two or more sample analyte concentrations may be added and/or subtracted to determine a combined analyte concentration. In another embodiment, two or more sample analyte concentrations may be multiplied and/or divided to determine a combined analyte concentration. To identify kidney transplant rejection or an associated disorder, the combined analyte concentration may be compared to a diagnostic criterion in which the corresponding minimum or maximum diagnostic concentrations are combined using the same algebraic operations used to determine the combined analyte concentration.

[0091] In yet another embodiment, the analyte concentration measured from a test sample containing one type of body fluid may be algebraically combined with an analyte concentration measured from a second test sample containing a second type of body fluid to determine a combined analyte concentration. For example, the ratio of urine calbindin to plasma calbindin may be determined and compared to a corresponding minimum diagnostic urine: plasma calbindin ratio to identify a particular renal disorder.

[0092] A variety of methods known in the art may be used to define the diagnostic criteria used to identify kidney transplant rejection or an associated disorder. In one embodiment, any sample concentration falling outside the expected normal range indicates kidney transplant rejection or an associated disorder. In another embodiment, the multiplexed

analyte panel may be used to evaluate the analyte concentrations in test samples taken from a population of patients having kidney transplant rejection or an associated disorder and compared to the normal expected analyte concentration ranges. In this same embodiment, any sample analyte concentrations that are significantly higher or lower than the expected normal concentration range may be used to define a minimum or maximum diagnostic concentration, respectively. A number of studies comparing the biomarker concentration ranges of a population of patients having a renal disorder to the corresponding analyte concentrations from a population of normal healthy subjects are described in the examples section below.

VI. Automated Method for Diagnosing, Monitoring, or Determining a Renal Disorder

[0093] In one embodiment, a system for diagnosing, monitoring, or determining kidney transplant rejection or an associated disorder in a mammal is provided that includes a database to store a plurality of kidney transplant rejection or an associated disorder database entries, and a processing device that includes the modules of a kidney transplant rejection or an associated disorder determining application. In this embodiment, the modules are executable by the processing device, and include an analyte input module, a comparison module, and an analysis module.

[0094] The analyte input module receives three or more sample analyte concentrations that include the biomarker analytes. In one embodiment, the sample analyte concentrations are entered as input by a user of the application. In another embodiment, the sample analyte concentrations are transmitted directly to the analyte input module by the sensor device used to measure the sample analyte concentration via a data cable, infrared signal, wireless connection or other methods of data transmission known in the art.

[0095] The comparison module compares each sample analyte concentration to an entry of a kidney transplant rejection or an associated disorder database. Each entry of the kidney transplant rejection or an associated disorder database includes a list of minimum diagnostic concentrations reflective of a particular type of kidney transplant rejection or an associated disorder. The entries of the kidney transplant rejection or an associated disorder database may further contain additional minimum diagnostic concentrations to further define diagnostic criteria including but not limited to minimum diagnostic concentrations for additional types of bodily fluids, additional types of mammals, and severities of a particular kidney transplant rejection or an associated disorder.

[0096] The analysis module determines a most likely kidney transplant rejection or an associated disorder by combining the particular renal disorders identified by the comparison module for all of the sample analyte concentrations. In one embodiment, the most likely kidney transplant rejection or an associated disorder is the particular type of kidney transplant rejection or an associated disorder from the database entry having the most minimum diagnostic concentrations that are less than the corresponding sample analyte concentrations. In another embodiment, the most likely type of kidney transplant rejection or an associated disorder is the particular renal disorder from the database entry having minimum diagnostic concentrations that are all less than the corresponding sample analyte concentrations. In yet other embodiments, the analysis module combines the sample analyte concentrations algebraically to calculate a combined sample analyte concentration that is compared to a combined minimum diagnostic concentration calculated from the corresponding minimum diagnostic criteria using the same algebraic operations. Other combinations of sample analyte concentrations from within the same test sample, or combinations of sample analyte concentrations from two or more different test samples containing two or more different bodily fluids may be used to determine a particular type of kidney transplant rejection or an associated disorder in still other embodiments.

[0097] The system includes one or more processors and volatile and/or nonvolatile memory and can be embodied by or in one or more distributed or integrated components or systems. The system may include computer readable media (CRM) on which one or more algorithms, software, modules, data, and/or firmware is loaded and/or operates and/or which operates on the one or more processors to implement the systems and methods identified herein. The computer readable media may include volatile media, nonvolatile media, removable media, non-removable media, and/or other media or mediums that can be accessed by a general purpose or special purpose computing device. For example, computer readable media may include computer storage media and communication media, including but not limited to computer readable media. Computer storage media further may include volatile, nonvolatile, removable, and/or non-removable media implemented in a method or technology for storage of information, such as computer readable instructions, data structures, program modules, and/or other data. Communication media may, for example, embody computer readable instructions, data structures, program modules, algorithms, and/or other data, including but not limited to as or in a modulated data signal. The communication media may be embodied in a carrier wave or other transport mechanism and may include an information delivery method. The communication media may include wired and wireless connections and technologies and may be used to transmit and/or receive wired or wireless communications. Combinations and/or subcombinations of the above and systems, components, modules, and methods and processes described herein may be made.

[0098] The following examples are included to demonstrate preferred embodiments of the invention.

EXAMPLES

[0099] The following examples illustrate various iterations of the invention.

Example 1: Least Detectable Dose and Lower Limit of Quantitation of Assay for Analytes Associated with Renal Disorders

[0100] To assess the least detectable doses (LDD) and lower limits of quantitation (LLOQ) of a variety of analytes associated with renal disorders, the following experiment was conducted. The analytes measured were alpha-1 microglobulin (A1 M), beta-2 microglobulin (B2M), calbindin, clusterin, CTGF, cystatin C, GST-alpha, KIM-1, NGAL, osteopontin (OPN), THP, TIMP-1, TFF-3, and VEGF.

[0101] The concentrations of the analytes were measured using a capture-sandwich assay using antigen-specific antibodies. For each analyte, a range of standard sample dilutions ranging over about four orders of magnitude of analyte concentration were measured using the assay in order to obtain data used to construct a standard dose response curve. The dynamic range for each of the analytes, defined herein as the range of analyte concentrations measured to determine its dose response curve, is presented below.

[0102] To perform the assay, 5 μ L of a diluted mixture of capture-antibody microspheres were mixed with 5 μ L of blocker and 10 μ L of pre-diluted standard sample in each of the wells of a hard-bottom microtiter plate. After incubating the hard-bottom plate for 1 hour, 10 μ L of biotinylated detection antibody was added to each well, and then the hard-bottom plate was incubated for an additional hour. 10 μ L of diluted streptavidin-phycoerythrin was added to each well and then the hard-bottom plate was incubated for another 60 minutes.

[0103] A filter-membrane microtiter plate was pre-wetted by adding 100 μ L wash buffer, and then aspirated using a vacuum manifold device. The contents of the wells of the hard-bottom plate were then transferred to the corresponding wells of the filter-membrane plate. All wells of the hard-bottom plate were vacuum-aspirated and the contents were washed twice with 100 μ L of wash buffer. After the second wash, 100 μ L of wash buffer was added to each well, and then the washed microspheres were resuspended with thorough mixing. The plate was then analyzed using a Luminex 100 Analyzer (Luminex Corporation, Austin, Texas, USA). Dose response curves were constructed for each analyte by curve-fitting the median fluorescence intensity (MFI) measured from the assays of diluted standard samples containing a range of analyte concentrations.

[0104] The least detectable dose (LDD) was determined by adding three standard deviations to the average of the MFI signal measured for 20 replicate samples of blank standard solution (i.e. standard solution containing no analyte). The MFI signal was converted to an LDD concentration using the dose response curve and multiplied by a dilution factor of 2.

[0105] The lower limit of quantification (LLOQ), defined herein as the point at which the coefficient of variation (CV) for the analyte measured in the standard samples was 30%, was determined by the analysis of the measurements of increasingly diluted standard samples. For each analyte, the standard solution was diluted by 2 fold for 8 dilutions. At each stage of dilution, samples were assayed in triplicate, and the CV of the analyte concentration at each dilution was calculated and plotted as a function of analyte concentration. The LLOQ was interpolated from this plot and multiplied by a dilution factor of 2.

[0106] The LDD and LLOQ results for each analyte are summarized in **Table 2**:

TABLE 2: LDD, LLOQ, and Dynamic Range of Analyte Assay

Analyte	Units	LDD	LLOQ	Dynamic Range	
				minimum	maximum
Calbindin	ng/mL	1.1	3.1	0.516	2580
Clusterin	ng/mL	2.4	2.3	0.676	3378
CTGF	ng/mL	1.3	3.8	0.0794	400
GST-alpha	ng/mL	1.4	3.6	0.24	1,200
KIM-1	ng/mL	0.016	0.028	0.00478	24
VEGF	pg/mL	4.4	20	8.76	44,000
β -2M	μ g/mL	0.012	0.018	0.0030	15
Cystatin C	ng/mL	2.8	3.7	0.60	3,000
NGAL	ng/mL	4.1	7.8	1.2	6,000

(continued)

Analyte	Units	LDD	LLOQ	Dynamic Range	
				minimum	maximum
Osteopontin	ng/mL	29	52	3.9	19,500
TIMP-1	ng/mL	0.71	1.1	0.073	365
A-1 M	μg/mL	0.059	0.29	0.042	210
THP	μg/mL	0.46	0.30	0.16	800
TFF-3	μg/mL	0.06	0.097	0.060	300

[0107] The results of this experiment characterized the least detectible dose and the lower limit of quantification for fourteen analytes associated with various renal disorders using a capture-sandwich assay.

Example 2: Precision of Assay for Analytes Associated with Renal Disorders

[0108] To assess the precision of an assay used to measure the concentration of analytes associated with renal disorders, the following experiment was conducted. The analytes measured were alpha-1 microglobulin (A1M), beta-2 microglobulin (B2M), calbindin, clusterin, CTGF, cystatin C, GST-alpha, KIM-1, NGAL, osteopontin (OPN), THP, TIMP-1, TFF-3, and VEGF. For each analyte, three concentration levels of standard solution were measured in triplicate during three runs using the methods described in Example 1. The percent errors for each run at each concentration are presented in Table 3 for all of the analytes tested:

TABLE 3: Precision of Analyte Assay

Analyte	Average concentration (ng/mL)	Run 1 Error (%)	Run 2 Error (%)	Run 2 Error (%)	Interrun Error (%)
Calbindin	4.0	6	2	6	13
	36	5	3	2	7
	281	1	6	0	3
Clusterin	4.4	4	9	2	6
	39	5	1	6	8
	229	1	3	0	2
CTGF	1.2	10	17	4	14
	2.5	19	19	14	14
	18	7	5	13	9
GST-alpha	3.9	14	7	5	10
	16	13	7	10	11
	42	1	16	6	8
KIM-1	0.035	2	0	5	13
	0.32	4	5	2	8
	2.9	0	5	7	4
VEGF	65	10	1	6	14
	534	9	2	12	7
	5,397	1	13	14	9

(continued)

Analyte	Average concentration (ng/mL)	Run 1 Error (%)	Run 2 Error (%)	Run 2 Error (%)	Interrun Error (%)
β -2M	0.040	6	1	8	5
	0.43	2	2	0	10
	6.7	6	5	11	6
Cystatin C	10.5	4	1	7	13
	49	0	0	3	9
	424	2	6	2	5
NGAL	18.1	11	3	6	13
	147	0	0	6	5
	1,070	5	1	2	5
Osteopontin	44	1	10	2	11
	523	9	9	9	7
	8,930	4	10	1	10
TIMP-1	2.2	13	6	3	13
	26	1	1	4	14
	130	1	3	1	4
A-1 M	1.7	11	7	7	14
	19	4	1	8	9
	45	3	5	2	4
THP	9.4	3	10	11	11
	15	3	7	8	6
	37	4	5	0	5
TFF-3	0.3	13	3	11	12
	4.2	5	8	5	7
	1.2	3	7	0	13

[0109] The results of this experiment characterized the precision of a capture-sandwich assay for fourteen analytes associated with various renal disorders over a wide range of analyte concentrations. The precision of the assay varied between about 1 % and about 15% error within a given run, and between about 5% and about 15% error between different runs. The percent errors summarized in Table 2 provide information concerning random error to be expected in an assay measurement caused by variations in technicians, measuring instruments, and times of measurement.

Example 3: Linearity of Assay for Analytes Associated with Renal Disorders

[0110] To assess the linearity of an assay used to measure the concentration of analytes associated with renal disorders, the following experiment was conducted. The analytes measured were alpha-1 microglobulin (A1M), beta-2 microglobulin (B2M), calbindin, clusterin, CTGF, cystatin C, GST-alpha, KIM-1, NGAL, osteopontin (OPN), THP, TIMP-1, TFF-3, and VEGF. For each analyte, three concentration levels of standard solution were measured in triplicate during three runs using the methods described in Example 1. Linearity of the assay used to measure each analyte was determined by measuring the concentrations of standard samples that were serially-diluted throughout the assay range. The % recovery was calculated as observed vs. expected concentration based on the dose-response curve. The results of the linearity analysis are summarized in **Table 4**.

TABLE 4: Linearity of Analyte Assay

Analyte	Dilution	Expected concentration	Observed concentration	Recovery (%)
Calbindin (ng/mL)	1:2	61	61	100
	1:4	30	32	106
	1:8	15	17	110
Clusterin (ng/mL)	1:2	41	41	100
	1:4	21	24	116
	1:8	10	11	111
CTGF (ng/mL)	1:2	1.7	1.7	100
	1:4	0.84	1.0	124
	1:8	0.42	0.51	122
GST-alpha (ng/mL)	1:2	25	25	100
	1:4	12	14	115
	1:8	6.2	8.0	129
KIM-1 (ng/mL)	1:2	0.87	0.87	100
	1:4	0.41	0.41	101
	1:8	0.21	0.19	93
VEGF (pg/mL)	1:2	2,525	2,525	100
	1:4	1,263	1,340	106
	1:8	631	686	109
β -2M (μ g/mL)	1:100	0.63	0.63	100
	1:200	0.31	0.34	106
	1:400	0.16	0.17	107
Cystatin C (ng/mL)	1:100	249	249	100
	1:200	125	122	102
	1:400	62	56	110
NGAL (ng/mL)	1:100	1,435	1,435	100
	1:200	718	775	108
	1:400	359	369	103
Osteopontin (ng/mL)	1:100	6,415	6,415	100
	1:200	3,208	3,275	102
	1:400	1,604	1,525	95
TIMP-1 (ng/mL)	1:100	35	35	100
	1:200	18	18	100
	1:400	8.8	8.8	100
A-1 M (μ g/mL)	1:2000	37	37	100
	1:4000	18	18	99
	1:8000	9.1	9.2	99

(continued)

Analyte	Dilution	Expected concentration	Observed concentration	Recovery (%)
THP (µg/mL)	1:2000	28	28	100
	1:4000	14	14	96
	1:8000	6.7	7.1	94
TFF-3 (µg/mL)	1:2000	8.8	8.8	100
	1:4000	3.8	4.4	86
	1:8000	1.9	2.2	86

[0111] The results of this experiment demonstrated reasonably linear responses of the sandwich-capture assay to variations in the concentrations of the analytes in the tested samples.

Example 4: Spike Recovery of Analytes Associated with Renal Disorders

[0112] To assess the recovery of analytes spiked into urine, serum, and plasma samples by an assay used to measure the concentration of analytes associated with renal disorders, the following experiment was conducted. The analytes measured were alpha-1 microglobulin (A1 M), beta-2 microglobulin (B2M), calbindin, clusterin, CTGF, cystatin C, GST-alpha, KIM-1, NGAL, osteopontin (OPN), THP, TIMP-1, TFF-3, and VEGF. For each analyte, three concentration levels of standard solution were spiked into known urine, serum, and plasma samples. Prior to analysis, all urine samples were diluted 1:2000 (sample: diluent), all plasma samples were diluted 1:5 (sample: diluent), and all serum samples were diluted 1:2000 (sample: diluent).

[0113] The concentrations of the analytes in the samples were measured using the methods described in Example 1. The average % recovery was calculated as the proportion of the measurement of analyte spiked into the urine, serum, or plasma sample (observed) to the measurement of analyte spiked into the standard solution (expected). The results of the spike recovery analysis are summarized in Table 5.

TABLE 5: Spike Recovery of Analyte Assay in Urine, Serum, and Plasma Samples

Analyte	Spike Concentration	Recovery in Urine Sample (%)	Recovery in Serum Sample (%)	Recovery in Plasma Sample (%)
Calbindin (ng/mL)	66	76	82	83
	35	91	77	71
	18	80	82	73
	average	82	80	76
Clusterin (ng/mL)	80	72	73	75
	37	70	66	72
	20	90	73	70
	average	77	70	72
CTGF (ng/mL)	8.4	91	80	79
	4.6	114	69	78
	2.4	76	80	69
	average	94	77	75
GST-alpha (ng/mL)	27	75	84	80
	15	90	75	81
	7.1	82	84	72
	average	83	81	78

EP 2 806 272 A1

(continued)

Analyte	Spike Concentration	Recovery in Urine Sample (%)	Recovery in Serum Sample (%)	Recovery in Plasma Sample (%)
KIM-1 (ng/mL)	0.63	87	80	83
	.029	119	74	80
	0.14	117	80	78
	average	107	78	80
VEGF (pg/mL)	584	88	84	82
	287	101	77	86
	123	107	84	77
	average	99	82	82
β -2 M (μ g/mL)	0.97	117	98	98
	0.50	124	119	119
	0.24	104	107	107
	average	115	108	105
Cystatin C (ng/mL)	183	138	80	103
	90	136	97	103
	40	120	97	118
	average	131	91	108
NGAL (ng/mL)	426	120	105	111
	213	124	114	112
	103	90	99	113
	average	111	106	112
Osteopontin (ng/mL)	1,245	204	124	68
	636	153	112	69
	302	66	103	67
	average	108	113	68
TIMP-1 (ng/mL)	25	98	97	113
	12	114	89	103
	5.7	94	99	113
	average	102	95	110
A-1 M (μ g/mL)	0.0028	100	101	79
	0.0012	125	80	81
	0.00060	118	101	82
	Average	114	94	81
THP (μ g/mL)	0.0096	126	108	90
	0.0047	131	93	91
	0.0026	112	114	83
	average	123	105	88

(continued)

Analyte	Spike Concentration	Recovery in Urine Sample (%)	Recovery in Serum Sample (%)	Recovery in Plasma Sample (%)
TFF-3 ($\mu\text{g/mL}$)	0.0038	105	114	97
	0.0019	109	104	95
	0.0010	102	118	93
	average	105	112	95

[0114] The results of this experiment demonstrated that the sandwich-type assay is reasonably sensitive to the presence of all analytes measured, whether the analytes were measured in standard samples, urine samples, plasma samples, or serum samples.

Example 5: Matrix Interferences of Analytes Associated with Renal Disorders

[0115] To assess the matrix interference of hemoglobin, bilirubin, and triglycerides spiked into standard samples, the following experiment was conducted. The analytes measured were alpha-1 microglobulin (A1M), beta-2 microglobulin (B2M), calbindin, clusterin, CTGF, cystatin C, GST-alpha, KIM-1, NGAL, osteopontin (OPN), THP, TIMP-1, TFF-3, and VEGF. For each analyte, three concentration levels of standard solution were spiked into known urine, serum, and plasma samples. Matrix interference was assessed by spiking hemoglobin, bilirubin, and triglyceride into standard analyte samples and measuring analyte concentrations using the methods described in Example 1. A % recovery was determined by calculating the ratio of the analyte concentration measured from the spiked sample (observed) divided by the analyte concentration measured from the standard sample (expected). The results of the matrix interference analysis are summarized in **Table 6**.

TABLE 6: Matrix Interference of Hemoglobin, Bilirubin, and Triglyceride on the Measurement of Analytes

Analyte	Matrix Compound Spiked into Sample	Maximum Spike Concentration	Overall Recovery (%)
Calbindin (mg/mL)	Hemoglobin	500	110
	Bilirubin	20	98
	Triglyceride	500	117
Clusterin (mg/mL)	Hemoglobin	500	125
	Bilirubin	20	110
	Triglyceride	500	85
CTGF (mg/mL)	Hemoglobin	500	91
	Bilirubin	20	88
	Triglyceride	500	84
GST-alpha (mg/mL)	Hemoglobin	500	100
	Bilirubin	20	96
	Triglyceride	500	96
KIM-1 (mg/mL)	Hemoglobin	500	108
	Bilirubin	20	117
	Triglyceride	500	84
VEGF (mg/mL)	Hemoglobin	500	112
	Bilirubin	20	85
	Triglyceride	500	114

(continued)

Analyte	Matrix Compound Spiked into Sample	Maximum Spike Concentration	Overall Recovery (%)
β-2 M (μg/mL)	Hemoglobin	500	84
	Bilirubin	20	75
	Triglyceride	500	104
Cystatin C (ng/mL)	Hemoglobin	500	91
	Bilirubin	20	102
	Triglyceride	500	124
NGAL (ng/mL)	Hemoglobin	500	99
	Bilirubin	20	92
	Triglyceride	500	106
Osteopontin (ng/mL)	Hemoglobin	500	83
	Bilirubin	20	86
	Triglyceride	500	106
TIMP-1 (ng/mL)	Hemoglobin	500	87
	Bilirubin	20	86
	Triglyceride	500	93
A-1 M (μg/mL)	Hemoglobin	500	103
	Bilirubin	20	110
	Triglyceride	500	112
THP (μg/mL)	Hemoglobin	500	108
	Bilirubin	20	101
	Triglyceride	500	121
TFF-3 (μg/mL)	Hemoglobin	500	101
	Bilirubin	20	101
	Triglyceride	500	110

[0116] The results of this experiment demonstrated that hemoglobin, bilirubin, and triglycerides, three common compounds found in urine, plasma, and serum samples, did not significantly degrade the ability of the sandwich-capture assay to detect any of the analytes tested.

Example 6: Sample Stability of Analytes Associated with Renal Disorders

[0117] To assess the ability of analytes spiked into urine, serum, and plasma samples to tolerate freeze-thaw cycles, the following experiment was conducted. The analyses measured were alpha-1 microglobulin (A1M), beta-2 microglobulin (B2M), calbindin, clusterin, CTGF, cystatin C, GST-alpha, KIM-1, NGAL, osteopontin (OPN), THP, TIMP-1, TFF-3, and VEGF. Each analyte was spiked into known urine, serum, and plasma samples at a known analyte concentration. The concentrations of the analytes in the samples were measured using the methods described in Example 1 after the initial addition of the analyte, and after one, two and three cycles of freezing and thawing. In addition, analyte concentrations in urine, serum and plasma samples were measured immediately after the addition of the analyte to the samples as well as after storage at room temperature for two hours and four hours, and after storage at 40 C for 2 hours, four hours, and 24 hours.

[0118] The results of the freeze-thaw stability analysis are summarized in **Table 7**. The % recovery of each analyte was calculated as a percentage of the analyte measured in the sample prior to any freeze-thaw cycles.

TABLE 7: Freeze-Thaw Stability of the Analytes in Urine, Serum, and Plasma

Analyte	Period and Temp	Urine Sample		Serum Sample		Plasma Sample	
		Concentration	Recovery (%)	Concentration	Recovery (%)	Concentration	Recovery (%)
Calbindin (ng/mL)	Control	212	100	31	100	43	100
	1X	221	104	30	96	41	94
	2X	203	96	30	99	39	92
	3X	234	110	30	97	40	93
Clusterin (ng/mL)	0	315	100	232	100	187	100
	1X	329	104	227	98	177	95
	2X	341	108	240	103	175	94
	3X	379	120	248	107	183	98
CTGF (ng/mL)	0	6.7	100	1.5	100	1.2	100
	1X	7.5	112	1.3	82	1.2	94
	2X	6.8	101	1.4	90	1.2	100
	3X	7.7	115	1.2	73	1.3	107
GST-alpha (ng/mL)	0	12	100	23	100	11	100
	1X	13	104	24	105	11	101
	2X	14	116	21	92	11	97
	3X	14	111	23	100	12	108
KIM-1 (ng/mL)	0	1.7	100	0.24	100	0.24	100
	1X	1.7	99	0.24	102	0.22	91
	2X	1.7	99	0.22	94	0.19	78
	3X	1.8	107	0.23	97	0.22	93
VEGF (pg/mL)	0	1,530	100	1,245	100	674	100
	1X	1,575	103	1,205	97	652	97
	2X	1,570	103	1,140	92	612	91
	3X	1,700	111	1,185	95	670	99

(continued)

Analyte	Period and Temp	Urine Sample		Serum Sample		Plasma Sample	
		Concentration	Recovery (%)	Concentration	Recovery (%)	Concentration	Recovery (%)
β 3-2 M (μ g/mL)	0	0.0070	100	1.2	100	15	100
	1X	0.0073	104	1.1	93	14	109
	2X	0.0076	108	1.2	103	15	104
	3X	0.0076	108	1.1	97	13	116
Cystatin C (ng/mL)	0	1,240	100	1,330	100	519	100
	1X	1,280	103	1,470	111	584	113
	2X	1,410	114	1,370	103	730	141
	3X	1,420	115	1,380	104	589	113
NGAL (ng/mL)	0	45	100	245	100	84	100
	1X	46	102	179	114	94	112
	2X	47	104	276	113	91	108
	3X	47	104	278	113	91	109
Osteopo ntin (ng/mL)	0	38	100	1.7	100	5.0	100
	1X	42	110	1.8	102	5.5	110
	2X	42	108	1.5	87	5.5	109
	3X	42	110	1.3	77	5.4	107
TIMP-1 (ng/mL)	0	266	100	220	100	70	100
	1X	265	100	220	10	75	108
	2X	255	96	215	98	77	110
	3X	295	111	228	104	76	109
A-1 M (μ g/mL)	0	14	100	26	100	4.5	100
	1X	13	92	25	96	4.2	94
	2X	15	107	25	96	4.3	97
	3X	16	116	23	88	4.0	90

(continued)

Analyte	Period and Temp	Urine Sample		Serum Sample		Plasma Sample	
		Concentration	Recovery (%)	Concentration	Recovery (%)	Concentration	Recovery (%)
THP (µg/mL)	0	4.6	100	31	100	9.2	100
	1X	4.4	96	31	98	8.8	95
	2X	5.0	110	31	100	9.2	100
	3X	5.2	114	27	85	9.1	99
TFF-3 (µg/mL)	0	4.6	100	24	100	22	100
	1X	4.4	96	23	98	22	103
	2X	5.0	110	24	103	22	101
	3X	5.2	114	19	82	22	102

[0119] The results of the short-term stability assessment are summarized in **Table 8**. The % recovery of each analyte was calculated as a percentage of the analyte measured in the sample prior to any short-term storage.

TABLE 8: Short-Term Stability of Analytes in Urine, Serum, and Plasma

Analyte	Storage Time/Temp	Urine Sample		Serum Sample		Plasma Sample	
		Sample Conc.	Recovery (%)	Sample Conc.	Recovery (%)	Sample Conc.	Recovery (%)
Calbindin (ng/mL)	Control	226	100	33	100	7	100
	2 hr/ room temp	242	107	30	90	6.3	90
	2 hr. @ 4° C	228	101	29	89	6.5	93
	4 hr @ room temp	240	106	28	84	5.6	79
	4 hr. @ 4° C	202	89	29	86	5.5	79
	24 hr. @ 4° C	199	88	26	78	7.1	101
Clusterin (ng/mL)	Control	185	100	224	100	171	100
	2 hr @ room temp	173	94	237	106	180	105
	2 hr. @ 4° C	146	79	225	100	171	100
	4 hr @ room temp	166	89	214	96	160	94
	4 hr. @ 4° C	157	85	198	88	143	84
	24 hr. @ 4° C	185	100	207	92	162	94
CTGF	Control	1.9	100	8.8	100	1.2	100
(ng/mL)	2 hr. @ room temp	1.9	99	6.7	76	1	83
	2 hr. @ 4° C	1.8	96	8.1	92	1.1	89
	4 hr. @ room temp	2.1	113	5.6	64	1	84
	4 hr. @ 4° C	1.7	91	6.4	74	0.9	78
	24 hr. @ 4° C	2.2	116	5.9	68	1.1	89
GST-alpha (ng/mL)	Control	14	100	21	100	11	100
	2 hr. @ room temp	11	75	23	107	11	103
	2 hr. @ 4° C	13	93	22	104	9.4	90
	4 hr. @ room temp	11	79	21	100	11	109
	4 hr. @ 4° C	12	89	21	98	11	100
	24 hr. @ 4° C	13	90	22	103	14	129

EP 2 806 272 A1

(continued)

Analyte	Storage Time/ Temp	Urine Sample		Serum Sample		Plasma Sample	
		Sample Conc.	Recovery (%)	Sample Conc.	Recovery (%)	Sample Conc.	Recovery (%)
KIM-1 (ng/mL)	Control	1.5	100	0.23	100	0.24	100
	2 hr. @ room temp	1.2	78	0.2	86	0.22	90
	2 hr. @ 4° C	1.6	106	0.23	98	0.21	85
	4 hr. @ room temp	1.3	84	0.19	82	0.2	81
	4 hr. @ 4° C	1.4	90	0.22	93	0.19	80
	24 hr. @ 4° C	1.1	76	0.18	76	0.23	94
VEGF	Control	851	100	1215	100	670	100
(pg/mL)	2 hr @ room temp	793	93	1055	87	622	93
	2 hr. @ 4° C	700	82	1065	88	629	94
	4 hr @ room temp	704	83	1007	83	566	84
	4 hr. @ 4° C	618	73	1135	93	544	81
	24 hr. @ 4° C	653	77	1130	93	589	88
β-2 M (μg/mL)	Control	0.064	100	2.6	100	1.2	100
	2 hr @ room temp	0.062	97	2.4	92	1.1	93
	2 hr. @ 4° C	0.058	91	2.2	85	1.2	94
	4 hr @ room temp	0.064	101	2.2	83	1.2	94
	4 hr. @ 4° C	0.057	90	2.2	85	1.2	98
	24 hr. @ 4° C	0.06	94	2.5	97	1.3	103
Cystatin C (ng/mL)	Control	52	100	819	100	476	100
	2 hr @ room temp	50	96	837	102	466	98
	2 hr. @ 4° C	44	84	884	108	547	115
	4 hr @ room temp	49	93	829	101	498	105
	4 hr. @ 4° C	46	88	883	108	513	108
	24 hr. @ 4° C	51	97	767	94	471	99
NGAL	Control	857	100	302	100	93	100

EP 2 806 272 A1

(continued)

Analyte	Storage Time/ Temp	Urine Sample		Serum Sample		Plasma Sample	
		Sample Conc.	Recovery (%)	Sample Conc.	Recovery (%)	Sample Conc.	Recovery (%)
(ng/mL)	2 hr @ room temp	888	104	287	95	96	104
	2 hr. @ 4° C	923	108	275	91	92	100
	4 hr @ room temp	861	101	269	89	88	95
	4 hr. @ 4° C	842	98	283	94	94	101
	24 hr. @ 4° C	960	112	245	81	88	95
Osteopontin (ng/mL)	Control	2243	100	6.4	100	5.2	100
	2 hr @ room temp	2240	100	6.8	107	5.9	114
	2 hr. @ 4° C	2140	95	6.4	101	6.2	120
	4 hr @ room temp	2227	99	6.9	108	5.8	111
	4 hr. @ 4° C	2120	95	7.7	120	5.2	101
	24 hr. @ 4° C	2253	100	6.5	101	6	116
TIMP-1 (ng/mL)	Control	17	100	349	100	72	100
	2 hr @ room temp	17	98	311	89	70	98
	2 hr. @ 4° C	16	94	311	89	68	95
	4 hr @ room temp	17	97	306	88	68	95
	4 hr. @ 4° C	16	93	329	94	74	103
	24 hr. @ 4° C	18	105	349	100	72	100
A-1 M	Control	3.6	100	2.2	100	1	100
(μg/mL)	2 hr @ room temp	3.5	95	2	92	1	105
	2 hr. @ 4° C	3.4	92	2.1	97	0.99	99
	4 hr @ room temp	3.2	88	2.2	101	0.99	96
	4 hr. @ 4° C	3	82	2.2	99	0.97	98
	24 hr. @ 4° C	3	83	2.2	100	1	101

(continued)

Analyte	Storage Time/ Temp	Urine Sample		Serum Sample		Plasma Sample	
		Sample Conc.	Recovery (%)	Sample Conc.	Recovery (%)	Sample Conc.	Recovery (%)
THP (µg/mL)	Control	1.2	100	34	100	2.1	100
	2 hr @ room temp	1.2	99	34	99	2	99
	2 hr. @ 4° C	1.1	90	34	100	2	98
	4 hr @ room temp	1.1	88	27	80	2	99
	4 hr. @ 4° C	0.95	79	33	97	2	95
	24 hr. @ 4° C	0.91	76	33	98	2.4	116
TFF-3 (µg/mL)	Control	1230	100	188	100	2240	100
	2 hr @ room temp	1215	99	179	95	2200	98
	2 hr. @ 4° C	1200	98	195	104	2263	101
	4 hr @ room temp	1160	94	224	119	2097	94
	4 hr. @ 4° C	1020	83	199	106	2317	103
	24 hr. @ 4° C	1030	84	229	122	1940	87

[0120] The results of this experiment demonstrated that the analytes associated with renal disorders tested were suitably stable over several freeze/thaw cycles, and up to 24 hrs of storage at a temperature of 4° C.

Example 8: Diagnosis of Renal Damage Using Detection of Analytes in Human Plasma Samples

[0121] To assess the effectiveness of a human kidney toxicity panel to detect renal damage due to disease states, the following experiment was conducted. Plasma samples were obtained from healthy control patients as well as patients experiencing acute kidney rejection (AR) or chronic allograft nephropathy (CAN). All plasma samples were diluted as described in Example 4 and subjected to a sandwich-capture assay as described in Example 1. Plasma concentrations of analytes included in a human kidney toxicity panel were measured by the assay, including alpha-1 microglobulin (A1M), beta-2 microglobulin (B2M), calbindin, clusterin, CTGF, cystatin C, GST-alpha, KIM-1, NGAL, osteopontin (OPN), THP, TIMP-1, TFF-3, and VEGF.

[0122] FIG. 1 summarizes the plasma concentrations of those analytes that differed significantly from control plasma concentrations. The plasma analyte concentrations of the AR and CAN groups are expressed as a percentage difference relative to the corresponding control plasma analyte concentrations. The A1M plasma concentrations of the CAN and AR groups were both significantly lower than control concentrations. Plasma levels of B2M, KIM-1, NGAL, and OPN had changes between about 100% and 200% of control levels for both the CAN and AR groups. VEGF and Cyst C plasma levels were between about 30% and about 100% higher than control levels for both the CAN and AR groups.

[0123] The results of this experiment demonstrated that panels of analytes detected in plasma samples were capable of identifying patients having renal damage caused by CAN and AR conditions.

Example 9: Analysis of the statistical importance of proteins associated with kidney transplant.

[0124] To assess the statistical importance of the proteins associated with kidney transplant success, the following experiments were conducted. Six two-way comparisons were performed: TX vs. AR, TX vs. CAN, AR vs. CAN, TX vs. all other, AR vs. all other, and CAN vs. all other where TX= successful, non-rejected transplant, AR=acute rejection, and CAN=chronic allograft nephropathy. Two different sets of patient data were evaluated. Set characteristics are in Table 9 below.

Table 9

	Set 1	Set 2	total
AR	25	20	45
CAN/IFTA	25	48	73
TX	18	3	21
acute dysfunction no rejection (ADNR)	0	47	47
	68	118	186

[0125] In **FIG. 2**, samples were clustered to check for batch effects. A moderate batch effect was identified. Because robust statistics are used to identify proteins associated with status, there is no attempt to remove outliers. All protein levels are scaled to mean zero and variance one to equalize their units. The resulting sample dendrogram is shown in **FIG. 2**. The sample dendrogram shows evidence of a moderate batch effect since samples tend to cluster together with other samples from the same data set.

[0126] In **FIGS. 4-9**, the statistical association of protein levels with status is studied. The following proteins were found to be related to clinical status at the level of 0.01:

Table 10

Comparison	Significant Proteins
TX vs. AR	Beta.2.Microglobulin, BLC, CD40, IGF.BP.2, MMP.3, Peptide.YY, Stem.Cell.Factor, TNF.RII, VEGF
TX vs. CAN	AXL, Beta.2.Microglobulin, CD40, Eotaxin.3, FABP, FGF.basica, IGF.BP.2, MMP.3, Myoglobin, Resistin, Stem.Cell.Factor, TNF.RII, TRAIL.R3, VEGF
AR vs. CAN	None
TX vs. all Other	AXL, Beta.2.Microglobulin, BLC, CD40, Endothelin.1, Eotaxin.3, FABP, FGF.basica, IGF.BP.2, MMP.3, Myoglobin, NrCAM, Peptide.YY, Resistin, Stem.Cell.Factor, Tenascin.C, TNF.RII, TRAIL.R3, VCAM.1, VEGF
AR vs. all Other	None
CAN vs. all Other	Beta.2.Microglobulin, CD40, Cortisol, FGF.basica, Stem.Cell.Factor, TNF.RII, VEGF

[0127] The necessary variables for calculation of protein significances were prepared and then the clinical traits for two-way comparisons were defined. One clinical trait is defined for each of the three comparisons TX vs. AR, TX vs. CAN, AR vs. CAN (in each case, the samples belonging to the third group are ignored), and for the comparisons TX vs. all others, AR vs. all others, and CAN vs. all others. The protein significances for each of the 6 "clinical traits" are checked to see how well they agree in the two data sets. The significance scatterplots are shown in **FIG. 3**. In the analysis of gene expression data it was found that subtracting several principal components from the full matrices of the expression data in Test and Validation sets improved the concordance of gene significance for status in the two data sets. Another reason to perform subtraction of principal components was that the histograms of association p-values exhibited anomalies suggesting that the data contained systematic bias(es) that may be removed by subtracting the first few principal components. No significant evidence of such anomalies in the protein data was found, however, and the concordance of protein significance in the Test and Validation data does not improve significantly upon subtracting principal components of the data. Hence, such a subtraction is not performed here.

[0128] For each protein and clinical trait, the following information is contained in **Table 11**: correlation with the trait in set 1, correlation with the trait in set 2, the corresponding Z scores in sets 1 and 2, a combined ("meta-analysis") Z

score determined using the formula

$$Z = \frac{Z_1 + Z_2}{\sqrt{2}}, \quad (1)$$

p-values in set 1 and 2, and meta-analysis determined from the Z scores, and q-values in set 1, set 2, and meta-analysis determined from the corresponding p-values. The q-values are estimates of false discovery rate (FDR). All correlations reported in Table 10 are robust (that is, outlier resistant) biweight midcorrelations. The results are presented in graphical form in FIGS. 4-9.

[0129] Lastly, the statistical significance of the observed significant proteins was studied. For example, in the TX vs. AR comparison 9 proteins were found to be significant at the level of 0.01 or better in both data sets. Provided herein, in FIG. 10 are the p-values for the null hypothesis that the protein significances in the two data sets are not related and the 9 proteins were significant in both sets by chance. The p-values were calculated in the plotting code above and are contained in the variable pTable. FIG. 10 illustrates that most of the findings are highly significant.

[0130] The results of this experiment demonstrate that the three kidney transplant success options (AR, CAN, and TX) can be distinguished via a limited set of significant proteins differentially expressed between the three transplant options.

probelD	cor.TX-vs- AR.Set_1	cor.TX-vs- AR.Set_2	Z.TX-vs- AR.Set_1	Z.TX-vs-AR.Set_2	Z.TX-vs-AR.Meta
Alpha.1.Antitrypsin	0.19651782	0.544745877	1.365014973	3.863540936	3.697147339
ACE..Angiotensin.Converting.Enzyme.	-0.056591672	-0.039749567	0.388387932	0.251530867	0.452490922
ACTH..Adrenocorticotrophic.Hormone.	0.029720353	0.223744359	0.203812495	1.439433005	1.161950036
Adiponectin	0.010447683	0.145646186	0.071628312	0.92774491	0.706663583
AgRP..Agouti.related.Protein.	0.213314725	0.234643509	1.485219539	1.51218797	2.119487175
Alpha.2.Macroglobulin	-0.244305568	0.07626922	1.709442987	0.483307489	1.55050873
Alpha.Fetoprotein	0.044502555	0.062135881	0.3052958	0.39348874	0.494115287
Amphiregulin	-0.032895242	-0.095582587	0.225599813	0.60636848	0.588290422
ANG.2..Angiopoietin.2.	0.192265313	0.360428016	1.334716268	2.386746362	2.631471461
Angiotensinogen	0.189583743	0.190254475	1.315636851	1.218116867	1.791634436
Apolipoprotein.A1	-0.056282705	-0.160553086	0.386262988	1.02428934	0.997411116
Apolipoprotein.CIII	0.140143385	0.425209453	0.967139742	2.871564279	2.714373645
Apolipoprotein.H	-0.086880527	-0.045498485	0.597128338	0.287956498	0.62584949
AXL	0.554118882	0.387462077	4.280025149	2.585543542	4.854690178
Beta.2.Microglobulin	0.603466542	0.596675835	4.789232561	4.351099666	6.4631909
Betacellulin	-0.015920759	-0.169877855	0.109156446	1.084919821	0.844339426
BLC..B.Lymphocyte.Chemoattractant.	0.370923325	0.415254861	2.670231546	2.795101853	3.864574308
BMP.6	0.097069574	-0.162008604	0.667577519	1.033740689	1.203013642
BDNF..Brain.Derived.Neurotrophic.Factor.	-0.286713691	-0.203614904	2.022294107	1.306026587	2.353478133
Complement.3	0.045145682	0.269820563	0.309713726	1.749816529	1.45630781
C.Reactive.Protein	0.127880901	0.325559186	0.881533821	2.13676921	2.134262541
Calcitonin	0.250584789	0.418596757	1.755299073	2.820684937	3.235709324
Cancer.Antigen.125	-0.203022866	-0.006483253	1.411465258	0.041004264	1.027051049
Cancer.Antigen.19.9	-0.114647199	0.205070411	0.789452655	1.315633155	1.488520451
Carcinoembryonic.Antigen	0.039388379	0.085216233	0.270172896	0.540265091	0.573066196
CD40	0.381789854	0.687101268	2.757023753	5.328082139	5.717033203
CD40.Ligand	-0.219592046	0.108533326	1.530370269	0.689139481	1.569430395
CgA..Chromogranin.A.	0.436070921	0.341187247	3.204119198	2.247971959	3.855210629
CNTF..Ciliary.Neurotrophic.Factor.	0.116635413	-0.26836516	0.803267918	1.739893195	1.798286468
Cortisol	-0.167877174	0.157496866	1.161906421	1.00445859	1.53185139
Creatine.Kinase.MB	0.13826237	0.116509942	0.953989327	0.740235241	1.197997681
CTGF..Connective.Tissue.Growth.Factor.	0.247052383	0.1578506	1.729483843	1.006752835	1.93481151
EGF	-0.137649862	0.028490054	0.94970672	0.180235695	0.798991358
EGF.R	-0.342512876	-0.236710848	2.447034166	1.52603192	2.809381972

EP 2 806 272 A1

5	ENA.78	-0.163250369	-0.108029871	1.129292592	0.685917574	1.283547418		
	Endothelin.1	0.147454702	0.406768883	1.018322217	2.730521359	2.650832715		
	EN.RAGE	0.292001087	0.044015515	2.061955147	0.278558546	1.654922392		
	Eotaxin	0.029235107	0.068717319	0.200482927	0.435292511	0.449561124		
	Eotaxin.3	0.2720196	0.565748629	1.913025953	4.05560777	4.22046138		
	Epiregulin	0.192670037	-0.192386614	1.337597654	1.232114051	1.817060572		
	Erythropoietin	-0.189360236	-0.00534035	1.314047505	0.033775662	0.953054901		
	Factor.VII	-0.017829181	0.02127869	0.122243658	0.13459857	0.181614881		
	Fas	0.395920739	0.12113867	2.871162164	0.769929203	2.574640396		
	Fas.Ligand	0.169381265	-0.073827426	1.172519757	0.467776749	1.159864782		
	FABP	0.31695717	0.569528815	2.250442714	4.090881595	4.48399342		
	Ferritin	0.235522216	0.427630472	1.645549201	2.890279169	3.207314998		
10	probelD	p.TX-vs-AR.Set_1	p.TX-vs-AR.Set_2	p.TX-vs-AR.Meta	q.TX-vs-AR.Set_1	q.TX-vs-AR.Set_2	q.TX-vs-AR.Meta	
	Alpha.1.Antitrypsin	0.171367015	0.000158886	0.000218036	0.177198839	0.001563766	0.000106	
	ACE..Angiotensin.Converting.Enzyme.	0.696273788	0.800210605	0.65091536	0.332945168	0.500045635	0.042832	
	ACTH..Adrenocorticotrophic.Hormone.	0.837662442	0.149213752	0.245255761	0.366221249	0.204283128	0.022133	
	Adiponectin	0.942594229	0.351385527	0.479775566	0.382906795	0.321707586	0.035171	
	AgRP..Agouti.related.Protein.	0.136911446	0.129885276	0.034049316	0.152674292	0.182619764	0.005401	
	Alpha.2.Macroglobulin	0.087298478	0.628894564	0.12101946	0.112836688	0.440709451	0.013535	
	Alpha.Fetoprotein	0.758939672	0.692231429	0.621224762	0.34808227	0.465740328	0.042338	
	Amphiregulin	0.820592822	0.542056445	0.556337373	0.364597827	0.395181531	0.039139	
	ANG.2..Angiopoietin.2.	0.181009349	0.017584436	0.008501601	0.18060197	0.041955643	0.001766	
	Angiotensinogen	0.187286716	0.221700639	0.073191543	0.181041825	0.252984397	0.009121	
	Apolipoprotein.A1	0.697852653	0.303721912	0.318564998	0.332945168	0.297054343	0.027245	
20	Apolipoprotein.CIII	0.331697419	0.004477577	0.006640123	0.227793158	0.018555187	0.001448	
	Apolipoprotein.H	0.548548959	0.772036613	0.531413667	0.308880402	0.500045635	0.037998	
	AXL	2.98E-05	0.010257245	1.21E-06	0.000378445	0.027848938	1.75E-06	
	Beta.2.Microglobulin	3.50E-06	2.41E-05	1.03E-10	0.000199245	0.000632919	8.94E-10	
	Betacellulin	0.912618541	0.276119505	0.398479781	0.374357111	0.292391201	0.030762	
	BLC..B.Lymphocyte.Chemoattractant.	0.00800596	0.005622454	0.000111283	0.023963826	0.020122369	6.90E-05	
	BMP.6	0.502468214	0.299301108	0.228971041	0.294600304	0.297054343	0.02162	
	BDNF..Brain.Derived.Neurotrophic.Factor.	0.043518996	0.19032556	0.018598702	0.075	0.23124681	0.003245	
	Complement.3	0.755562875	0.080150828	0.145307548	0.34808227	0.129706391	0.015327	
	C.Reactive.Protein	0.376143256	0.03314323	0.032821296	0.245541216	0.069889867	0.005302	
	30	Calcitonin	0.079223506	0.005212604	0.001213409	0.107275636	0.019870757	0.000407
		Cancer.Antigen.125	0.157346199	0.967087687	0.304396427	0.166042746	0.551302217	0.026291
Cancer.Antigen.19.9		0.427898478	0.187108314	0.136613693	0.267421106	0.23124681	0.014713	
Carcinoembryonic.Antigen		0.78594594	0.586906775	0.566599874	0.351953498	0.416314969	0.039324	
CD40		0.006221717	3.61E-07	1.08E-08	0.020543178	2.84E-05	3.15E-08	
CD40.Ligand		0.12546158	0.488447891	0.116547686	0.14561664	0.367796104	0.013204	
CgA..Chromogranin.A.		0.001547727	0.02515291	0.00011563	0.007335157	0.056584317	6.90E-05	
CNTF..Ciliary.Neurotrophic.Factor.		0.419876518	0.081857321	0.072131623	0.265323312	0.129706391	0.009119	
Cortisol		0.243881693	0.313139689	0.125559111	0.203970152	0.297054343	0.013865	
Creatine.Kinase.MB		0.338292712	0.456856369	0.23091792	0.227793158	0.360957043	0.02162	
CTGF..Connective.Tissue.Growth.Factor.		0.083690413	0.312040284	0.05301343	0.110688776	0.297054343	0.007226	
EGF		0.340457785	0.856090208	0.424295423	0.227793158	0.526605563	0.032468	
40	EGF.R	0.014899123	0.126440621	0.004963672	0.040349463	0.181008852	0.001203	
	ENA.78	0.257307978	0.490479139	0.199300358	0.204286052	0.367796104	0.019318	
	Endothelin.1	0.306833111	0.006791176	0.00802936	0.227793158	0.020565891	0.001708	
	EN.RAGE	0.039626912	0.779278196	0.097940241	0.072698402	0.500045635	0.011537	
	Eotaxin	0.840278075	0.661495266	0.653026925	0.366221249	0.456875397	0.042832	
	Eotaxin.3	0.056001109	7.70E-05	2.44E-05	0.086356261	0.001212281	1.93E-05	
	Epiregulin	0.180075217	0.216468259	0.069207839	0.18060197	0.25064624	0.009011	
	Erythropoietin	0.18781687	0.972887263	0.340562255	0.181041825	0.551302217	0.028844	
	Factor.VII	0.902192356	0.892266152	0.855884969	0.374357111	0.533558766	0.054104	
	Fas	0.004426033	0.439044296	0.010034435	0.015765461	0.360091599	0.001989	
	Fas.Ligand	0.239621608	0.638000542	0.246103863	0.203970152	0.444547822	0.022133	
	FABP	0.024915474	6.72E-05	7.33E-06	0.052262132	0.001212281	7.92E-06	
50	Ferritin	0.099655777	0.004232034	0.001339802	0.120587128	0.018511967	0.000433	
	probelD	cor.TX-vs-CAN.Set_1	cor.TX-vs-CAN.Set_2	Z.TX-vs-CAN.Set_1	Z.TX-vs-CAN.Set_2	Z.TX-vs-CAN.Meta		
	Alpha.1.Antitrypsin	0.403528206	0.286268152	2.933234801	1.862559632	3.391138765		
	ACE..Angiotensin.Converting.Enzyme.	0.249434132	-0.139050564	1.746884618	0.885167625	1.861141199		
	ACTH..Adrenocorticotrophic.Hormone.	-0.075783974	0.314686872	0.520546819	2.060154139	1.824831148		
	Adiponectin	0.312608285	0.293823322	2.217348989	1.91473215	2.921822594		
	AgRP..Agouti.related.Protein.	0.312389911	0.275500502	2.215689871	1.788624921	2.831478143		
	Alpha.2.Macroglobulin	0.183884999	0.052359602	1.27515657	0.331454316	1.136045452		
	Alpha.Fetoprotein	-0.006831019	0.037721445	0.046831837	0.238684616	0.201890621		
	55							

EP 2 806 272 A1

	Amphiregulin	-0.007138139	-0.081358506	0.048937449	0.515696219	0.399256295
	ANG.2..Angiopoietin.2.	0.232399349	0.309748595	1.62290013	2.025548253	2.579842592
	Angiotensinogen	-0.057492856	0.170215517	0.394586302	1.087118979	1.047723852
5	Apolipoprotein.A1	0.057734809	0.249520832	0.396250578	1.612140311	1.420146817
	Apolipoprotein.CIII	0.074687063	0.420587018	0.512983964	2.835962121	2.368062487
	Apolipoprotein.H	-0.012802317	-0.015198422	0.087773059	0.096130665	0.130039571
	AXL	0.48432	0.4861663	3.623986832	3.35851425	4.937373865
	Beta.2.Microglobulin	0.708882508	0.704831924	6.066801827	5.545613163	8.211217385
	Betacellulin	0.25521347	0.238464408	1.789200026	1.537785902	2.352534311
	BLC..B.Lymphocyte.Chemoattractant.	0.231502704	0.494793252	1.616403509	3.430361128	3.568601498
10	BMP.6	0.365975701	0.113504072	2.630984183	0.72096962	2.370189265
	BDNF..Brain.Derived.Neurotrophic.Factor.	-0.469665334	-0.018371957	3.493921767	0.116207535	2.55274691
	Complement.3	-0.604283485	0.08099202	4.798047873	0.513362986	3.755734637
	C.Reactive.Protein	0.000771532	0.159532746	0.005289357	1.017666508	0.723339029
	Calcitonin	0.183886745	0.187188875	1.275168955	1.19801225	1.748803201
	Cancer.Antigen.125	-0.130092925	0.115908416	0.896955278	0.736378779	1.154941588
	Cancer.Antigen.19.9	-0.178600465	0.167765145	1.237697025	1.07116587	1.63261261
15	Carcinoembryonic.Antigen	0.423344093	0.366571377	3.09710585	2.431516135	3.909326096
	CD40	0.647728239	0.720128266	5.288280108	5.742135675	7.7996818
	CD40.Ligand	-0.254880457	0.183465098	1.786758159	1.173623322	2.09330582
	CgA..Chromogranin.A.	0.577392073	0.333524738	4.514734138	2.193285808	4.743286392
	CNTF..Ciliary.Neurotrophic.Factor.	0.086442548	-0.013245829	0.594102988	0.083778879	0.479334865
	Cortisol	-0.478326963	-0.23121892	3.570511538	1.489286369	3.577817412
20	Creatine.Kinase.MB	0.269727283	0.051127151	1.896066231	0.323638689	1.569568401
	CTGF..Connective.Tissue.Growth.Factor.	0.270754049	-0.092497474	1.903659952	0.586682401	1.760937966
	EGF	-0.0140503	0.159857205	0.096330346	1.019772265	0.789203724
	EGF.R	-0.190238772	-0.189118241	1.320295523	1.210662477	1.789657565
	ENA.78	-0.170335194	0.012874577	1.179253854	0.081430475	0.891438438
	Endothelin.1	0.461212433	0.318755037	3.419944788	2.088752274	3.895237048
	EN.RAGE	0.183565096	0.128343284	1.272886808	0.816215627	1.477218499
25	Eotaxin	0.08500313	0.083306843	0.584161781	0.528102688	0.786489749
	Eotaxin.3	0.472591422	0.549187985	3.519704939	3.903628615	5.249689495
	Epiregulin	0.364310979	-0.169763681	2.61781567	1.084176283	2.617703614
	Erythropoietin	-0.021159826	0.106709643	0.145086112	0.677470332	0.581635239
	Factor.VII	0.280903304	0.101899999	1.978970326	0.646716832	1.856641194
	Fas	0.556635954	0.247374844	4.304977883	1.597674992	4.173805875

30

35

Fas.Ligand	0.416300541	0.107624193	3.038485324	0.683321657	2.831714955	
FABP	0.516340296	0.536936453	3.916687217	3.79372791	5.452228244	
Ferritin	0.106030964	0.199676933	0.729654311	1.280085005	1.421086156	

probelD	p.TX-vs-CAN.Set_1	p.TX-vs-CAN.Set_2	p.TX-vs-CAN.Meta	q.TX-vs-CAN.Set_1	q.TX-vs-CAN.Set_2	q.TX-vs-CAN.Meta
Alpha.1.Antitrypsin	0.003662189	0.062739931	0.000696029	0.007837826	0.082680224	0.000167
ACE..Angiotensin.Converting.Enzyme.	0.080657463	0.373853681	0.062724128	0.092951011	0.246336788	0.00693
ACTH..Adrenocorticotrophic.Hormone.	0.600923403	0.039852544	0.068026514	0.39833304	0.059364258	0.007256
Adiponectin	0.027085358	0.055824398	0.003479897	0.038440557	0.076910709	0.000683
AgRP..Agouti.related.Protein.	0.027198354	0.073755746	0.00463334	0.038440557	0.095129113	0.00089
Alpha.2.Macroglobulin	0.201140587	0.73878983	0.255937542	0.171894045	0.370044586	0.019229
Alpha.Fetoprotein	0.962448347	0.810211987	0.840002235	0.522421762	0.377853788	0.052593
Amphiregulin	0.960761329	0.604009183	0.689704367	0.522421762	0.321288138	0.044142
ANG.2..Angiopoietin.2.	0.104360888	0.043246653	0.009884536	0.11156188	0.062419265	0.001675
Angiotensinogen	0.691675916	0.275151949	0.294765855	0.431761907	0.206125327	0.021583
Apolipoprotein.A1	0.690443323	0.106605017	0.155564943	0.431761907	0.129247776	0.013577
Apolipoprotein.CIII	0.606217218	0.004981073	0.017881516	0.39833304	0.015097616	0.002628
Apolipoprotein.H	0.929685968	0.922939664	0.89653512	0.519702006	0.407633958	0.055728
AXL	0.00036546	0.000948795	7.92E-07	0.001244342	0.004424299	4.89E-07
Beta.2.Microglobulin	8.38E-09	1.32E-07	2.19E-16	2.09E-07	2.67E-06	9.46E-16
Betacellulin	0.073656939	0.123572863	0.018645969	0.086666091	0.144057278	0.002641
BLC..B.Lymphocyte.Chemoattractant.	0.10574291	0.000743778	0.000358892	0.11156188	0.003757316	9.12E-05
BMP.6	0.008955433	0.468629468	0.017778982	0.016361596	0.289880472	0.002628
BDNF..Brain.Derived.Neurotrophic.Factor.	0.000579461	0.906913337	0.010687713	0.001669452	0.404242826	0.001742
Complement.3	3.37E-06	0.605645066	0.000172834	1.80E-05	0.321288138	5.15E-05
C.Reactive.Protein	0.995757217	0.306845734	0.46947162	0.53505063	0.216290319	0.032193
Calcitonin	0.201136236	0.229375635	0.080325043	0.171894045	0.193127626	0.008165
Cancer.Antigen.125	0.367873357	0.459199478	0.248114347	0.272834871	0.286975678	0.018971
Cancer.Antigen.19.9	0.21462049	0.282224043	0.102550497	0.18063591	0.206125327	0.009845
Carcinoembryonic.Antigen	0.002189573	0.015616193	9.26E-05	0.005290792	0.032643191	3.03E-05
CD40	3.69E-07	5.23E-08	6.21E-15	3.95E-06	1.58E-06	1.34E-14
CD40.Ligand	0.074046795	0.238940751	0.036321863	0.086666091	0.193127626	0.004551
CgA..Chromogranin.A.	1.13E-05	0.028842798	2.10E-06	5.31E-05	0.049955667	1.14E-06
CNTF..Ciliary.Neurotrophic.Factor.	0.550574078	0.932815641	0.631700423	0.375560341	0.407633958	0.040732
Cortisol	0.000442371	0.135745025	0.000346475	0.001380698	0.146793727	9.07E-05

EP 2 806 272 A1

	Creatine.Kinase.MB	0.058185878	0.744729306	0.116515555	0.073873469	0.370044586	0.01071
	CTGF..Connective.Tissue.Growth.Factor.	0.057198956	0.555230637	0.078248903	0.073872538	0.314561151	0.008049
	EGF	0.922851486	0.305850175	0.429992945	0.519702006	0.216290319	0.029832
	EGF.R	0.185739167	0.224524361	0.073508978	0.165633097	0.193127626	0.007746
5	ENA.78	0.236946251	0.93469456	0.372694004	0.190799565	0.407633958	0.02618
	Endothelin.1	0.000749031	0.037222795	9.81E-05	0.002078064	0.057945364	3.03E-05
	EN.RAGE	0.20193918	0.412099983	0.139617077	0.171894045	0.268617986	0.012436
	Eotaxin	0.557254626	0.595344675	0.431580622	0.37605695	0.321288138	0.029832
	Eotaxin.3	0.000529376	0.000136858	1.53E-07	0.00158616	0.001185187	1.32E-07
	Epiregulin	0.009296074	0.276447168	0.008852366	0.016579567	0.206125327	0.00153
	Erythropoietin	0.884036307	0.495826451	0.560812401	0.501671103	0.291815199	0.037273
10	Factor.VII	0.048150986	0.515557342	0.063362219	0.063278073	0.295470966	0.00693
	Fas	2.70E-05	0.109750897	3.00E-05	0.000118763	0.130452782	1.13E-05
	Fas.Ligand	0.00263811	0.49211907	0.008495511	0.006026802	0.291815199	0.001498
	FABP	0.000123838	0.000205523	4.97E-08	0.000488227	0.001557347	5.37E-08
	Ferritin	0.463644768	0.199226142	0.155291714	0.330649678	0.182985986	0.013577

15	probelD	cor.AR-vs-CAN.Set_1	cor.AR-vs-CAN.Set_2	Z.AR-vs-CAN.Set_1	Z.AR-vs-CAN.Set_2	Z.AR-vs-CAN.Meta
	Alpha.1.Antitrypsin	0.136992841	-0.14875832	0.945117837	1.027459807	1.394823029
	ACE..Angiotensin.Converting.Enzyme.	0.232155898	-0.097879991	1.621135924	0.673186751	1.622331122
	ACTH..Adrenocorticotrophic.Hormone.	-0.169924977	0.124075593	1.176357722	0.855025205	1.436404643
	Adiponectin	0.330238709	0.178540172	2.352148761	1.237270059	2.538102388
	AgRP..Agouti.related.Protein.	0.253734302	0.093056001	1.778357211	0.639810884	1.709903059
20	Alpha.2.Macroglobulin	0.431188103	-0.033871249	3.162891986	0.23229845	2.40076218
	Alpha.Fetoprotein	-0.06999834	-0.010748584	0.480677417	0.073691417	0.391997961
	Amphiregulin	0.050159657	-0.027988775	0.344166116	0.1919315	0.37907826
	ANG.2..Angiopoietin.2.	0.055405474	0.013407126	0.380230183	0.091920133	0.33386069
	Angiotensinogen	-0.251895593	0.03412023	1.764890946	0.234007352	1.413434541
	Apolipoprotein.A1	0.120303498	0.367502109	0.828773036	2.643074881	2.454967206
	Apolipoprotein.CIII	-0.07300405	-0.010749203	0.501382539	0.073695664	0.406641697
	Apolipoprotein.H	0.043364499	0.039796017	0.297478586	0.272971913	0.403369416
25	AXL	0.033240726	0.125177011	0.227970923	0.862695276	0.771217486
	Beta.2.Microglobulin	0.1402783	0.254781493	0.968083226	1.786032577	1.94745396
	Betacellulin	0.225867951	0.253082628	1.575641742	1.773582976	2.38825951

30	BLC..B.Lymphocyte.Chemoattractant.	-0.074356718	0.090476337	0.510706586	0.621975394	0.800927109
	BMP.6	0.353408403	0.245916539	2.532021413	1.721193193	3.007476889
	BDNF..Brain.Derived.Neurotrophic.Factor.	-0.120532581	0.169252235	0.830366659	1.171609057	1.415610604
	Complement.3	-0.556801163	-0.285827368	4.306619204	2.014162349	4.469481641
	C.Reactive.Protein	-0.144505591	-0.217864375	0.997663879	1.517930818	1.778794069
	Calcitonin	-0.019739972	-0.204916753	0.135348013	1.425012717	1.103341653
	Cancer.Antigen.125	0.083343568	0.151902623	0.572703209	1.049514502	1.147081144
	Cancer.Antigen.19.9	-0.061310956	-0.045948962	0.420854605	0.315232191	0.520491965
35	Carcinoembryonic.Antigen	0.316075125	0.248096186	2.243722466	1.737107046	2.814871543
	CD40	0.113278859	0.104709925	0.77994835	0.720496039	1.060974402
	CD40.Ligand	0.001134959	0.083705309	0.007780892	0.575200599	0.412230166
	CgA..Chromogranin.A.	0.193956508	0.069870528	1.346759641	0.479789984	1.291555627
	CNTF..Ciliary.Neurotrophic.Factor.	-0.052357978	0.233851704	0.359276756	1.633429205	1.409055898
	Cortisol	-0.223299671	-0.442328039	1.55709203	3.257268465	3.404266953
	Creatine.Kinase.MB	0.100819535	-0.118353967	0.69354016	0.815214661	1.066850765
40	CTGF..Connective.Tissue.Growth.Factor.	0.012853541	-0.030586603	0.088124288	0.209756617	0.210633608
	EGF	0.131457611	0.284173355	0.906473883	2.003333557	2.057544572
	EGF.R	0.135750136	0.037557578	0.936436835	0.257602948	0.844313628
	ENA.78	0.021290661	0.21978659	0.145983481	1.531771632	1.186352018
	Endothelin.1	0.278121163	0.010337303	1.958280469	0.070871504	1.43482712
	EN.RAGE	-0.270341451	0.134778632	1.900607929	0.929652409	2.001296278
	Eotaxin	0.055013877	0.006065001	0.37753732	0.04158006	0.296360741
	Eotaxin.3	0.229327065	0.043924253	1.600651801	0.301323395	1.344899559
45	Epiregulin	0.138407422	0.036299336	0.955003154	0.2489651	0.851334117
	Erythropoietin	0.192826	0.079081482	1.338708136	0.543289776	1.330773486
	Factor.VII	0.329855758	0.099473564	2.349202438	0.684219165	2.144952985
	Fas	0.173030867	0.081557022	1.198295729	0.560371431	1.243565475
	Fas.Ligand	0.246060385	0.147903054	1.722242865	1.021464491	1.940094077
	FABP	0.350453011	0.034267974	2.508896037	0.235021418	1.94024264
	Ferritin	-0.170380908	-0.124416508	1.179576616	0.857399044	1.440359303

50	probelD	p.AR-vs-CAN.Set_1	p.AR-vs-CAN.Set_2	p.AR-vs-CAN.Meta	q.AR-vs-CAN.Set_1	q.AR-vs-CAN.Set_2	q.AR-vs-CAN.Meta
	Alpha.1.Antitrypsin	0.342789738	0.302528826	0.163069213	0.417256265	0.718387019	0.012314
	ACE..Angiotensin.Converting.Enzyme.	0.104734745	0.498890163	0.104732468	0.253213935	0.797303461	0.010453

55

EP 2 806 272 A1

5	ACTH..Adrenocorticotrophic.Hormone.	0.238094216	0.390627196	0.150887233	0.393405488	0.718387019	0.012314
	Adiponectin	0.019169947	0.214777839	0.011145537	0.119167562	0.707339939	0.003576
	AgRP..Agouti.related.Protein.	0.075401087	0.5203802	0.087283801	0.218272788	0.821380598	0.009256
	Alpha.2.Macroglobulin	0.001770857	0.815361479	0.018360966	0.027309377	0.865859107	0.003955
	Alpha.Fetoprotein	0.629064408	0.940943787	0.69505972	0.54399002	0.886846611	0.027007
	Amphiregulin	0.729395862	0.847003984	0.70462975	0.592022265	0.866331559	0.027171
	ANG.2..Angiopoietin.2.	0.702342308	0.926373122	0.738484684	0.581902126	0.886846611	0.027883
	Angiotensinogen	0.077614516	0.814028221	0.157527995	0.218272788	0.865859107	0.012314
	Apolipoprotein.A1	0.405303538	0.008652634	0.014089744	0.446458098	0.348403945	0.003955
	Apolipoprotein.CIII	0.614378627	0.94094039	0.684271167	0.54399002	0.886846611	0.027007
10	Apolipoprotein.H	0.764926039	0.7837837	0.686676482	0.599814602	0.865859107	0.027007
	AXL	0.818740153	0.386401575	0.440578043	0.626095116	0.718387019	0.020733
	Beta.2.Microglobulin	0.331227487	0.074162966	0.051480334	0.417256265	0.554575803	0.006835
	Betacellulin	0.114751891	0.076179789	0.017871995	0.253213935	0.554575803	0.003955
	BLC..B.Lymphocyte.Chemoattractant.	0.607815447	0.532058689	0.423173845	0.54399002	0.829572568	0.020321
	BMP.6	0.011816011	0.085167951	0.002634262	0.097098932	0.554575803	0.001341
	BDNF..Brain.Derived.Neurotrophic.Factor.	0.404403234	0.23998506	0.156889545	0.446458098	0.707339939	0.012314
	Complement.3	2.68E-05	0.044356141	7.84E-06	0.001238694	0.554575803	3.99E-05
	C.Reactive.Protein	0.316714685	0.128538176	0.07527353	0.417256265	0.56686451	0.008329
	Calcitonin	0.891769567	0.153427033	0.269878824	0.63965019	0.818687053	0.015435
15	Cancer.Antigen.125	0.565004005	0.292307793	0.251348086	0.520281791	0.718387019	0.014706
	Cancer.Antigen.19.9	0.67231939	0.751351518	0.602720727	0.576011929	0.865859107	0.025147
	Carcinoembryonic.Antigen	0.025343376	0.082350396	0.004879673	0.123421399	0.554575803	0.001911
	CD40	0.433469212	0.469264154	0.288701534	0.459053854	0.789427922	0.015801
	CD40.Ligand	0.993758703	0.563310577	0.680170729	0.661673607	0.841835746	0.027007
	CgA..Chromogranin.A.	0.177128993	0.629697231	0.196507614	0.339367833	0.85129144	0.013142
	CNTF..Ciliary.Neurotrophic.Factor.	0.718016792	0.102151863	0.15881864	0.587943717	0.554575803	0.012314
	Cortisol	0.119048819	0.001298593	0.000663419	0.256174698	0.166028116	0.000844
	Creatine.Kinase.MR	0.486022727	0.413012072	0.286039231	0.48356318	0.733396688	0.015801
	CTGF..Connective.Tissue.Growth.Factor.	0.929405344	0.832997399	0.833173185	0.645312732	0.865859107	0.03051
20	EGF	0.362826467	0.045497182	0.039633872	0.427173306	0.554575803	0.006304
	EGF.R	0.347227406	0.795676579	0.398494173	0.417256265	0.865859107	0.019503
	ENA.78	0.883324234	0.125118652	0.235483312	0.638542447	0.56686451	0.014617
	Endothelin.1	0.050506748	0.943199723	0.151336368	0.186934299	0.886846611	0.012314
	EN.RAGE	0.05759391	0.350721153	0.045360471	0.197375114	0.718387019	0.006601
	Eotaxin	0.704349759	0.9666568	0.766954603	0.581902126	0.892409011	0.028289
25							
30							
35							

30	Eotaxin.3	0.109154691	0.761979913	0.178657673	0.253213935	0.865859107	0.012673
	Epiregulin	0.337781243	0.802382069	0.394583778	0.417256265	0.865859107	0.0195
	Erythropoietin	0.179716172	0.585132507	0.183263555	0.339367833	0.841835746	0.012673
	Factor.VII	0.019318336	0.49189285	0.031956606	0.119167562	0.796071569	0.005887
	Fas	0.229496635	0.573401392	0.213659529	0.393244392	0.841835746	0.013656
	Fas.Ligand	0.08497971	0.305348334	0.052368258	0.21841997	0.718387019	0.006835
	FABP	0.01259262	0.13232732	0.052350209	0.097098932	0.865859107	0.006835
	Ferritin	0.236818561	0.389316371	0.149765771	0.393405488	0.718387019	0.012314
35							

	probeID	cor.TX-vs-allOther.Set_1	cor.TX-vs-allOther.Set_2	Z.TX-vs-allOther.Set_1	Z.TX-vs-allOther.Set_2	Z.TX-vs-allOther.Meta
40	Alpha.1.Antitrypsin	0.279845384	0.37852713	2.439639828	3.211514328	3.995969425
	ACE..Angiotensin.Converting.Enzyme.	0.096793335	-0.07453388	0.823898167	0.60202782	1.008281935
	ACTH..Adrenocorticotrophic.Hormone.	-0.008857328	0.243255635	0.075158883	2.001307259	1.46828329
	Adiponectin	0.150760242	0.193249538	1.289069248	1.577869157	2.027231587
	AgRP..Agouti.related.Protein.	0.244110103	0.218743366	2.114023215	1.792529679	2.762350042
	Alpha.2.Macroglobulin	-0.029520198	0.053719288	0.250559987	0.433516077	0.483714823
	Alpha.Fetoprotein	0.013300076	0.0420251	0.112861545	0.339016885	0.319526288
	Amphiregulin	-0.021654836	-0.106406644	0.183776104	0.8611377	0.738865637
	ANG.2..Angiopoietin.2.	0.200518646	0.311350656	1.724827486	2.596372357	3.055549712
	Angiotensinogen	0.06674839	0.164801807	0.567222262	1.340903321	1.349248539
45	Apolipoprotein.A1	-0.005345643	0.046367386	0.045359717	0.374094066	0.296598614
	Apolipoprotein.CIII	0.101490396	0.362351782	0.864149763	3.060356401	2.775044921
	Apolipoprotein.H	-0.053080003	-0.025333444	0.450822475	0.204288469	0.463233391
	AXL	0.461681682	0.376089168	4.23794338	3.188596164	5.251356472
	Beta.2.Microglobulin	0.605006599	0.578746564	5.948242023	5.325733403	7.971904475
	Betacellulin	0.105269722	0.092410471	0.896564881	0.747168765	1.162295208
	BLC..B.Lymphocyte.Chemoattractant.	0.297784477	0.411667496	2.605717357	3.528183612	4.337322971
	BMP.6	0.180999006	-0.010129333	1.552836642	0.081668085	1.155840087
	BDNF..Brain.Derived.Neurotrophic.Factor.	-0.348230415	-0.092979006	3.093453605	0.751792171	2.718999363
	Complement.3	-0.2706015	0.17998084	2.354773631	1.467031696	2.702424464
55	C.Reactive.Protein	0.05320534	0.208196643	0.451889004	1.703438464	1.524046668
	Calcitonin	0.234709966	0.250195483	2.029409834	2.060885113	2.892275294
	Cancer.Antigen.125	-0.155863586	0.058945623	1.333414996	0.475786373	1.279298556
	Cancer.Antigen.19.9	-0.133090685	0.163958853	1.136051568	1.333918472	1.748532565

5	Carcinoembryonic.Antigen	0.2251489	0.220092828	1.943752193	1.803959686	2.650032484	
	CD40	0.474698782	0.598050125	4.379411479	5.563812856	7.030921354	
	CD40.Ligand	-0.222090096	0.129578406	1.916431141	1.050601135	2.098008642	
	CgA..Chromogranin.A.	0.471759454	0.298897829	4.347273166	2.485665551	4.831617302	
	CNTF..Ciliary.Neurotrophic.Factor.	0.089789189	-0.13317264	0.763943961	1.08008773	1.303927314	
	Cortisol	-0.307729535	-0.04205582	2.698620745	0.339264977	2.148109594	
	Creatine.Kinase.MB	0.20812614	0.072874268	1.792191902	0.588574521	1.683456082	
	CTGF..Connective.Tissue.Growth.Factor.	0.232700389	0.019731599	2.011372848	0.159101889	1.534757405	
	EGF	-0.08973474	0.025948738	0.763478194	0.209252389	0.687824392	
	EGF.R	-0.25408677	-0.19796983	2.204279389	1.617439541	2.702363371	
10	ENA.78	-0.154268945	-0.062454233	1.319550638	0.504178328	1.289571119	
	Endothelin.1	0.298151046	0.328411061	2.609130868	2.749602207	3.789196496	
	EN.RAGE	0.200737016	0.084824994	1.726758132	0.685528324	1.705744112	
	Eotaxin	0.049731896	0.067289204	0.422337541	0.543323925	0.682825771	
	Eotaxin.3	0.350311634	0.499539074	3.103906907	4.423694432	5.322817953	
	Epiregulin	0.255240675	-0.183283852	2.214749624	1.494569957	2.622885029	
	Erythropoietin	-0.103689303	0.039769296	0.883006573	0.32079951	0.851219444	
	Factor.VII	0.130171342	0.046297232	1.110843322	0.37352725	1.049608497	
	Fas	0.432201918	0.192532372	3.925301664	1.571863743	3.887082936	
	Fas.Ligand	0.285196169	0.007882392	2.488981239	0.063551189	1.804912989	
15	FABP	0.400382262	0.476220161	3.598642512	4.176929622	5.498159783	
	Ferritin	0.147124719	0.309648215	1.257520911	2.581182369	2.71437312	
	probelD	p.TX-vs- allOther.Set_1	p.TX-vs- allOther.Set_2	p.TX-vs- allOther.Meta	q.TX-vs- allOther.Set_1	q.TX-vs- allOther.Set_2	q.TX-vs- allOther.Meta
	Alpha.1.Antitrypsin	0.015031282	0.001458204	6.44E-05	0.029332251	0.004336026	1.16E-06
	ACE..Angiotensin.Converting.Enzyme.	0.408737237	0.545798246	0.313319133	0.307990131	0.321376701	0.001164
	ACTH..Adrenocorticotrophic.Hormone.	0.939880702	0.045621081	0.142027288	0.525954037	0.057739158	0.000658
	Adiponectin	0.19667374	0.114346203	0.042638734	0.196945813	0.109239885	0.000266
	AgRP..Agouti.related.Protein.	0.034807476	0.073111562	0.005738692	0.055188078	0.080518547	5.62E-05
	Alpha.2.Macroglobulin	0.801494611	0.663502761	0.628588272	0.487982854	0.34919492	0.002099
	Alpha.Fetoprotein	0.90983043	0.733650722	0.74932746	0.517096004	0.357651942	0.002339
25	Amphiregulin	0.8536933	0.387786017	0.45998859	0.503646861	0.250673222	0.001638
	ANG.2..Angiopoietin.2.	0.084537923	0.009753545	0.002246484	0.102123336	0.017895869	2.48E-05
	Angiotensinogen	0.569366912	0.179272495	0.177257149	0.388933497	0.149947391	0.000777
	Apolipoprotein.A1	0.963694925	0.707312058	0.766772969	0.531464737	0.356691103	0.002376
	Apolipoprotein.CIII	0.38626523	0.00239305	0.005519408	0.29396768	0.006468933	5.53E-05
	Apolipoprotein.H	0.651064027	0.837521539	0.643197084	0.416380812	0.382039757	0.002115
	AXL	3.06E-05	0.00157379	1.51E-07	0.000193849	0.004456883	5.42E-09
	Beta.2.Microglobulin	8.97E-09	2.35E-07	1.56E-15	6.04E-07	3.49E-06	6.73E-16
	Betacellulin	0.368731918	0.453547364	0.245115573	0.286350948	0.280966823	0.000987
	BLC..B.Lymphocyte.Chemoattractant.	0.009466628	0.000487057	1.44E-05	0.020584543	0.002602755	3.27E-07
35	BMP.6	0.120175908	0.934660958	0.247746573	0.13650752	0.408713347	0.000987
	BDNF..Brain.Derived.Neurotrophic.Factor.	0.002133873	0.4507619	0.006547973	0.006246105	0.280966823	6.05E-05
	Complement.3	0.018869074	0.141923213	0.006883582	0.035900836	0.122322957	6.05E-05
	C.Reactive.Protein	0.650293852	0.088431877	0.127497054	0.416380812	0.092265134	0.000604
	Calcitonin	0.042670902	0.039612565	0.003824627	0.064949496	0.052682717	3.92E-05
	Cancer.Antigen.125	0.181770358	0.633019083	0.200791941	0.194262302	0.339154396	0.000832
	Cancer.Antigen.19.9	0.254989931	0.181538098	0.080718454	0.223057971	0.149947391	0.000433
	Carcinoembryonic.Antigen	0.052123571	0.071314727	0.008048403	0.073460583	0.080021554	6.80E-05
	CD40	1.69E-05	7.23E-08	2.05E-12	0.000128322	3.49E-06	2.21E-13
	CD40.Ligand	0.055487099	0.29226379	0.035904382	0.07677915	0.213937108	0.000227
45	CgA..Chromogranin.A.	1.93E-05	0.013287893	1.35E-06	0.00013371	0.022577984	3.89E-08
	CNTF..Ciliary.Neurotrophic.Factor.	0.443625148	0.278967894	0.192258367	0.327992983	0.213937108	0.000812
	Cortisol	0.007236427	0.733463263	0.03170505	0.01776546	0.357651942	0.000204
	Creatine.Kinase.MB	0.073160397	0.554800902	0.092286834	0.092798033	0.323474919	0.000479
	CTGF..Connective.Tissue.Growth.Factor.	0.044529964	0.873109673	0.124843429	0.066325284	0.385246844	0.000603
	EGF	0.443902722	0.833631007	0.491563374	0.327992983	0.382039757	0.001733
	EGF.R	0.027825734	0.105598873	0.006884847	0.047059585	0.105875255	6.05E-05
	ENA.78	0.18633628	0.612886861	0.197199609	0.194262302	0.33828268	0.000825
	Endothelin.1	0.009374834	0.006252799	0.000151135	0.020584543	0.013772549	2.25E-06
	EN.RAGE	0.084192861	0.491605456	0.088055733	0.102123336	0.298328157	0.000463
50	Eotaxin	0.671770502	0.585607816	0.494716943	0.426043214	0.334870587	0.001733
	Eotaxin.3	0.002062402	1.45E-05	1.02E-07	0.006246105	0.000143365	4.31E-09
	Epiregulin	0.027100436	0.134632362	0.008718869	0.046874599	0.118264344	6.96E-05
	Erythropoietin	0.376004089	0.747457718	0.394647463	0.289048914	0.361397502	0.001417
	Factor.VII	0.265654088	0.707734974	0.293898149	0.224640451	0.356691103	0.001111
	Fas	0.000107887	0.115722593	0.000101456	0.00051317	0.109239885	1.56E-06
	Fas.Ligand	0.01313349	0.949132864	0.071088299	0.027764612	0.409026599	0.000393
	FABP	0.000371847	4.05E-05	3.84E-08	0.001572192	0.000343725	2.36E-09
	Ferritin	0.207812107	0.010182338	0.006640133	0.19769461	0.017895869	6.05E-05
	55						

	probeID	cor.AR-vs- allOther.Set_1	cor.AR-vs- allOther.Set_2	Z.AR-vs- allOther.Set_1	Z.AR-vs- allOther.Set_2	Z.AR-vs-allOther.Meta
5	Alpha.1.Antitrypsin	-0.015020208	-0.307755635	0.127460281	2.564316643	1.903373716
	ACE..Angiotensin.Converting.Enzyme.	0.131089293	-0.041373071	1.118767622	0.333750881	1.027085684
	ACTH..Adrenocorticotrophic.Hormone.	-0.098596298	-0.01976877	0.83934424	0.159401686	0.706220017
	Adiponectin	0.154783528	-0.021205629	1.324023829	0.170990882	1.05713504
	AgRP..Agouti.related.Protein.	0.032147075	-0.035899665	0.272871003	0.289556788	0.397696505
10	Alpha.2.Macroglobulin	0.321309921	-0.053016296	2.8265079	0.427832184	2.301165942
	Alpha.Fetoprotein	-0.051408652	-0.029073126	0.436601772	0.234461112	0.474513117
	Amphiregulin	0.031598383	0.028128856	0.268210458	0.22684193	0.3500549
	ANG.2..Angiopoietin.2.	-0.061621128	-0.132504236	0.523535935	1.074602085	1.130054232
	Angiotensinogen	-0.213724215	-0.057191036	1.841905004	0.461592571	1.628818756
15	Apolipoprotein.A1	0.070827041	0.273180253	0.601995356	2.259829403	2.023615694
	Apolipoprotein.CIII	-0.103374911	-0.165591258	0.880309966	1.347446642	1.575261805
	Apolipoprotein.H	0.064692791	0.040509472	0.54970426	0.326776632	0.619765582
	AXL	-0.215531099	-0.077721104	1.857977295	0.627873852	1.757762203
	Beta.2.Microglobulin	-0.193725087	-0.085647421	1.664851473	0.692207466	1.666692359
20	Betacellulin	0.126547444	0.176609189	1.079578372	1.438956049	1.780872767
	BLC..B.Lymphocyte.Chemoattractant.	-0.220523901	-0.172981467	1.902457135	1.408786602	2.3414029
	BMP.6	0.184340403	0.195886242	1.582268107	1.589933372	2.250177459
	BDNF..Brain.Derived.Neurotrophic.Factor.	0.071041332	0.170791175	0.603822865	1.390590282	1.410263061
	Complement.3	-0.266162383	-0.277991552	2.314182666	2.301807578	3.263998004
25	C.Reactive.Protein	-0.130290384	-0.316680813	1.11187086	2.644046582	2.655834693
	Calcitonin	-0.165940828	-0.258618175	1.42119667	2.133490824	2.513543632
	Cancer.Antigen.125	0.132940363	0.084656334	1.134753067	0.684158704	1.286164847
	Cancer.Antigen.19.9	0.02159707	-0.109321988	0.183285715	0.884918657	0.755334555
	Carcinoembryonic.Antigen	0.134925791	0.06625662	1.151907711	0.534961681	1.192796787
30	CD40	-0.119795444	-0.196292102	1.02140292	1.603366376	1.855992169
	CD40.Ligand	0.11006274	0.005028794	0.93771205	0.040543776	0.691731328
	CgA..Chromogranin.A.	-0.107762746	-0.100729093	0.917961667	0.814867384	1.225295172
	CNTF..Ciliary.Neurotrophic.Factor.	-0.086620159	0.251013443	0.736842977	2.067921627	1.983268071
	Cortisol	-0.03013108	-0.328388361	0.255748105	2.749397073	2.124958533
35	Creatine.Kinase.MB	-0.05296598	-0.092535283	0.449852228	0.748183708	0.847139335
	CTGF..Connective.Tissue.Growth.Factor.	-0.104714625	-0.179620584	0.891802224	1.464030188	1.665825074
	EGF	0.141901042	0.191277863	1.212251015	1.561362838	1.961241164

30

35

40

EGF.R	0.227598963	0.118434867	1.965664577	0.95935489	2.0683011
FNA.78	0.085011061	0.176339171	0.723087518	1.436709119	1.527206848
Endothelin.1	0.031548778	-0.142378563	0.267789125	1.155744866	1.006590609
EN.RAGE	-0.246965422	0.058022258	2.139805826	0.468316413	1.844220921
Eotaxin	0.015384566	-0.024153432	0.130552669	0.194769079	0.230037214
Eotaxin.3	-0.020265865	-0.201668158	0.17198511	1.64849649	1.287274885
Epiregulin	-0.023343932	0.103359423	0.198115821	0.836296943	0.73144028
Erythropoietin	0.175989425	0.04664348	1.509029962	0.37632483	1.333147158
Factor.VII	0.164819084	0.047190003	1.411410704	0.380740761	1.267242454
Fas	-0.086941287	-0.021388199	0.739588515	0.172463478	0.644918149
Fas.Ligand	0.037921142	0.104568491	0.321925926	0.84615127	0.825955306
FABP	-0.011280521	-0.194764318	0.095722456	1.590559354	1.192381303
Ferritin	-0.181175703	-0.240084592	1.554486802	1.974155804	2.495126974

45

50

55

probeID	p.AR-vs- allOther.Set_1	p.AR-vs- allOther.Set_2	p.AR-vs- allOther.Meta	q.AR-vs- allOther.Set_1	q.AR-vs- allOther.Set_2	q.AR-vs- allOther.Meta
Alpha.1.Antitrypsin	0.898227154	0.010678177	0.056991798	0.652419976	0.202616126	0.041592
ACE..Angiotensin.Converting.Enzyme.	0.262268954	0.737633147	0.304380119	0.497506659	0.761984693	0.077566
ACTH..Adrenocorticotrophic.Hormone.	0.400022698	0.872872619	0.480051324	0.531527436	0.77994156	0.098993
Adiponectin	0.1848539	0.863717909	0.290449961	0.453458513	0.77994156	0.076046
AgRP..Agouti.related.Protein.	0.784240954	0.771325554	0.690853914	0.63490951	0.770308729	0.122888
Alpha.2.Macroglobulin	0.004941305	0.667646372	0.021382253	0.236366098	0.756466542	0.027681
Alpha.Fetoprotein	0.661368837	0.813938592	0.635134047	0.596913512	0.77994156	0.116182
Amphiregulin	0.787836566	0.819878632	0.726297497	0.63490951	0.77994156	0.128214
ANG.2..Angiopoietin.2.	0.599450473	0.281409536	0.258453374	0.572272522	0.528322812	0.068437
Angiotensinogen	0.665598927	0.643188567	0.103351393	0.298848437	0.754909175	0.047221
Apolipoprotein.A1	0.545952043	0.024196331	0.043009709	0.553515905	0.30608012	0.041592
Apolipoprotein.CIII	0.377461007	0.177169383	0.115196026	0.531527436	0.438489264	0.049593
Apolipoprotein.H	0.581342959	0.742918381	0.535412131	0.572272522	0.761984693	0.102264
AXL	0.063297639	0.52871003	0.078787979	0.298848437	0.684670431	0.044623
Beta.2.Microglobulin	0.095843577	0.48739986	0.095575593	0.356984243	0.667465551	0.044623
Betacellulin	0.279304848	0.149667163	0.074933238	0.513864574	0.419530935	0.044623
BLC..B.Lymphocyte.Chemoattractant.	0.057276687	0.158346378	0.019211423	0.298848437	0.419530935	0.026333
BMP.6	0.113370866	0.10939383	0.024437683	0.384790107	0.409993732	0.029971
BDNF..Brain.Derived.Neurotrophic.Factor.	0.544734889	0.163763747	0.158462022	0.553515905	0.419530935	0.053514

EP 2 806 272 A1

5	Complement.3	0.020992334	0.021714687	0.001098519	0.256481419	0.30608012	0.012799
	C.Reactive.Protein	0.265213438	0.008511066	0.007911238	0.497506659	0.202616126	0.02106
	Calcitonin	0.154783076	0.033216727	0.011952499	0.425139878	0.336242863	0.02106
	Cancer.Antigen.125	0.255531823	0.492470272	0.198385536	0.497506659	0.667465551	0.061579
	Cancer.Antigen.19.9	0.854079287	0.374840671	0.45004827	0.643380681	0.652574559	0.09809
10	Carcinoembryonic.Antigen	0.248437681	0.591387107	0.232948969	0.497506659	0.723964092	0.063162
	CD40	0.305964634	0.108646469	0.063454674	0.528950714	0.409993732	0.044623
	CD40.Ligand	0.347206367	0.967535124	0.489106069	0.528950714	0.80403378	0.099106
	CgA..Chromogranin.A.	0.357436112	0.413748276	0.220464027	0.528950714	0.652574559	0.063162
	CNTF..Ciliary.Neurotrophic.Factor.	0.459941265	0.038949744	0.047337494	0.553515905	0.336242863	0.041592
15	Cortisol	0.797473465	0.006256602	0.033590073	0.63578246	0.202616126	0.037272
	Creatine.Kinase.MB	0.651765	0.452935054	0.396917463	0.594262315	0.663885683	0.091697
	CTGF..Connective.Tissue.Growth.Factor.	0.37127633	0.142735998	0.095748261	0.531527436	0.419530935	0.044623
	EGF	0.224589331	0.118160814	0.049850897	0.497506659	0.409993732	0.041592
	EGF.R	0.049551513	0.336088159	0.038611718	0.298848437	0.607352446	0.040897
20	ENA.78	0.468350416	0.150300693	0.126709584	0.553515905	0.419530935	0.050907
	Endothelin.1	0.78816185	0.246770855	0.314131549	0.63490951	0.528322812	0.078709
	EN.RAGE	0.032673898	0.63836256	0.065150951	0.298848437	0.754909175	0.044623
	Eotaxin	0.895772005	0.844993606	0.818062852	0.852419976	0.77994156	0.142019
	Eotaxin.3	0.862983608	0.099115132	0.197998494	0.64500952	0.409993732	0.061579
25	Epregrulin	0.842422405	0.401597571	0.464510269	0.843380681	0.652574559	0.0984
	Erythropoietin	0.130959409	0.705648514	0.182483516	0.404155562	0.756466542	0.059059
	Factor.VII	0.157630552	0.702359613	0.20506861	0.425139878	0.756466542	0.062059
	Fas	0.458273075	0.862555846	0.51898023	0.553515905	0.77994156	0.102045
	Fas.Ligand	0.746689919	0.396083288	0.408829445	0.63490951	0.652574559	0.09256
30	FABP	0.923477385	0.11148043	0.233111768	0.652723645	0.409993732	0.063162
	Ferritin	0.11980838	0.048606235	0.012591207	0.384790107	0.336242863	0.02106

	probeID	cor.CAN-vs-allOther.Set_1	cor.CAN-vs-allOther.Set_2	Z.CAN-vs-allOther.Set_1	Z.CAN-vs-allOther.Set_2	Z.CAN-vs-allOther.Meta
25	Alpha.1.Antitrypsin	-0.264825175	-0.038593443	2.301975644	0.311304902	1.847868395
	ACE..Angiotensin.Converting.Enzyme.	-0.227882629	0.109570932	1.968203233	0.886950041	2.018898241
	ACTH..Adrenocorticotrophic.Hormone.	0.107453626	-0.20280805	0.915307965	1.658078499	1.819659019
	Adiponectin	-0.30554377	-0.15561604	2.678149022	1.26489378	2.788152303
	AgRP..Agouti.related.Protein.	-0.276257178	-0.164248638	2.406641679	1.336319453	2.646673198

EP 2 806 272 A1

	Alpha.2.Macroglobulin	-0.291789723	0.003863608	2.550008918	0.03114956	1.825154663
	Alpha.Fetoprotein	0.038108576	-0.00937948	0.323518659	0.075622002	0.282235068
	Amphiregulin	-0.009943547	0.06923231	0.084376575	0.55906309	0.454980551
5	ANG.2..Angiopoietin.2.	-0.138897518	-0.152378943	1.186252769	1.238161483	1.714319758
	Angiotensinogen	0.146975825	-0.093601204	1.256229583	0.756852528	1.423464012
	Apolipoprotein.A1	-0.065481399	-0.315606014	0.556424284	2.634419033	2.256266947
	Apolipoprotein.CIII	0.001884515	-0.165957515	0.015990657	1.350482943	0.966242749
	Apolipoprotein.H	-0.011612788	-0.017329588	0.098542204	0.139729592	0.168483603
	AXL	-0.246150583	-0.266397259	2.132444166	2.200849981	3.064101676
10	Beta.2.Microglobulin	-0.411281512	-0.44390072	3.709363342	3.846328724	5.342681096
	Betacellulin	-0.231817166	-0.261163977	2.003451129	2.155502494	2.94082431
	BLC..B.Lymphocyte.Chemoattractant.	-0.077260576	-0.203690761	0.656886839	1.665501802	1.642176756
	BMP.6	-0.365339409	-0.186617989	3.250151157	1.522402727	3.374705214
	BDNF..Brain.Derived.Neurotrophic.Factor.	0.278189084	-0.085716181	2.424399154	0.692765928	2.204168568
	Complement.3	0.536763883	0.113310627	5.087762893	0.917479613	4.246347699
15	C.Reactive.Protein	0.077085045	0.12618267	0.655388485	1.02276865	1.18663629
	Calcitonin	-0.068769139	0.029691454	0.584447978	0.239450541	0.58258423
	Cancer.Antigen.125	0.022923224	-0.138591073	0.194544084	1.124594421	0.932771782
	Cancer.Antigen.19.9	0.111493615	-0.040698956	0.950004276	0.328306827	0.903902449
	Carcinoembryonic.Antigen	-0.360074691	-0.26763967	3.198711085	2.211635624	3.825692846
	CD40	-0.354903338	-0.350918632	3.148400966	2.954745005	4.315575903
	CD40.Ligand	0.112027355	-0.123591924	0.954590497	1.00155044	1.383200522
20	CgA..Chromogranin.A.	-0.363996708	-0.172759857	3.23701047	1.406944884	3.283772322
	CNTF..Ciliary.Neurotrophic.Factor.	-0.00316903	-0.12916162	0.026890203	1.047183696	0.759484937
	Cortisol	0.337860615	0.366869076	2.98406547	3.102360109	4.3037528
	Creatine.Kinase.MB	-0.15516016	0.025855952	1.3272983	0.208503822	1.085976096
	CTGF..Connective.Tissue.Growth.Factor.	-0.127985764	0.16156634	1.091983849	1.314104502	1.701361388
	EGF	-0.052166302	-0.215020735	0.443047934	1.761035409	1.558522278
25	EGF.R	0.026487808	0.062705829	0.224809088	0.506214736	0.516911904
	ENA.78	0.069257945	-0.119194084	0.588615484	0.965563542	1.098970528
	Endothelin.1	-0.329699824	-0.15811474	2.906136164	1.285547171	2.963967711
	EN.RAGE	0.046228406	-0.1356364	0.39254082	1.100316638	1.055609632
	Eotaxin	-0.065116461	-0.037415612	0.553314428	0.301795189	0.604653809
	Eotaxin.3	-0.33004577	-0.255405809	2.909430038	2.105760115	3.546274966
	Epregrulin	-0.231896743	0.064343729	2.004164719	0.519473417	1.784481639
30	Erythropoietin	-0.072300123	-0.083032045	0.61455921	0.670970553	0.909006813

35

40

45

50

55

EP 2 806 272 A1

5	Factor.VII	-0.294990425	-0.089551574	2.579725775	0.723927199	2.336035421
	Fas	-0.345260631	-0.15477727	3.055150186	1.257964499	3.049832642
	Fas.Ligand	-0.323117311	-0.111778081	2.843620811	0.904987514	2.650666437
	FABP	-0.389101741	-0.240973044	3.485253628	1.981758475	3.865761331
	Ferritin	0.034050984	-0.043240878	0.28904393	0.348836628	0.451049669

	probelD	p.CAN-vs- allOther.Set_1	p.CAN-vs- allOther.Set_2	p.CAN-vs- allOther.Meta	q.CAN-vs- allOther.Set_1	q.CAN-vs- allOther.Set_2	q.CAN-vs- allOther.Meta
10	Alpha.1.Antitrypsin	0.02167059	0.754686534	0.064621384	0.031409745	0.409435518	0.000178
	ACE...Angiotensin.Converting.Enzyme.	0.049260576	0.373747487	0.043497797	0.05367358	0.309219617	0.000127
	ACTH..Adrenocorticotropic.Hormone.	0.35882502	0.097180608	0.068810948	0.244729503	0.178671735	0.000181
	Adiponectin	0.00768246	0.205088234	0.005300962	0.015391274	0.250612008	2.75E-05
	AgRP..Agouti.related.Protein.	0.016432536	0.180756914	0.008128787	0.027331201	0.249248427	3.69E-05
	Alpha.2.Macroglobulin	0.011083135	0.975054572	0.067977693	0.020858575	0.467858228	0.000181
	Alpha.Fetoprotein	0.745480251	0.939488433	0.77776327	0.367452772	0.457226373	0.001017
	Amphiregulin	0.93252426	0.574801897	0.649123231	0.426132272	0.355892534	0.000891
	ANG.2..Angiopoietin.2.	0.234654182	0.21478613	0.086470016	0.186839884	0.250612008	0.000214
	Angiotensinogen	0.208277639	0.447724403	0.154601687	0.170202128	0.336477099	0.000319
15	Apolipoprotein.A1	0.576734855	0.00874984	0.024053918	0.326829083	0.052648521	8.74E-05
	Apolipoprotein.CIII	0.987197478	0.176199789	0.33922726	0.438634338	0.249248427	0.000547
	Apolipoprotein.H	0.921230499	0.888450989	0.866202842	0.426132272	0.443264974	0.001124
	AXL	0.033271279	0.028099977	0.002183247	0.042170558	0.094656849	1.42E-05
	Beta.2.Microglobulin	0.000246756	0.000149614	9.16E-08	0.00139319	0.003300871	5.55E-09
	Betaocellulin	0.045367942	0.0314627	0.003273401	0.05122976	0.094656849	1.80E-05
	BLC...B.Lymphocyte.Chemoattractant.	0.509995976	0.095702913	0.100553378	0.317338943	0.178671735	0.000237
	BMP.6	0.001268653	0.127563356	0.000738948	0.004335056	0.211078835	5.84E-06
	BDNF..Brain.Derived.Neurotrophic.Factor.	0.015664739	0.487049107	0.027512491	0.027024434	0.338260484	9.80E-05
	Complement.3	6.90E-07	0.357558257	2.17E-05	1.43E-05	0.30898559	3.59E-07
20	C.Reactive.Protein	0.510960633	0.305201338	0.235371115	0.317338943	0.296895462	0.000447
	Calcitonin	0.557707556	0.810054562	0.560173224	0.326070399	0.425522443	0.000789
	Cancer.Antigen.125	0.845226816	0.258694965	0.350937813	0.400717124	0.296356379	0.000567
	Cancer.Antigen.19.9	0.340935248	0.741757711	0.36604713	0.243382071	0.405747117	0.00057
	Carcinoembryonic.Antigen	0.001508097	0.027347712	0.000130405	0.004683118	0.094656849	1.39E-06
	CD40	0.001782239	0.003346014	1.59E-05	0.005031289	0.024607303	3.05E-07
	CD40.Ligand	0.338614323	0.315317778	0.16660339	0.243382071	0.296895462	0.00034
	CdA...Chromogranin.A.	0.0132621	0.158888392	0.001024276	0.004335056	0.239011192	7.75E-06

35	CNTF..Ciliary.Neurotrophic.Factor.	0.978472728	0.293832046	0.447562521	0.438634338	0.296895462	0.000656
	Cortisol	0.00303159	0.002089145	1.68E-05	0.007845039	0.019753734	3.05E-07
	Creatine.Kinase.MB	0.183774349	0.834217445	0.277489568	0.15423719	0.433193936	0.000485
	CTGF..Connective.Tissue.Growth.Factor.	0.273832013	0.18808138	0.088875147	0.207398828	0.250612008	0.000215
	EGF	0.656689569	0.078256414	0.119109491	0.339871542	0.167084819	0.000263
	EGF.R	0.821529763	0.611453887	0.605217658	0.392478508	0.35814922	0.000839
	ENA.78	0.554904422	0.33297754	0.271780921	0.326070399	0.297476426	0.000482
	Endothelin.1	0.003870077	0.197818186	0.003037002	0.008902085	0.250612008	1.72E-05
	EN.RAGE	0.693702006	0.270089791	0.291146598	0.345474026	0.296895462	0.000501
	Eotaxin	0.578865212	0.76194862	0.545409045	0.326829083	0.410014597	0.000774
40	Eotaxin.3	0.003830725	0.035545968	0.000390718	0.008902085	0.101743848	3.74E-06
	Epregrulin	0.045291913	0.602160863	0.074345436	0.05122976	0.35814922	0.000019
	Erythropoietin	0.537611812	0.500839528	0.36334653	0.326070399	0.338260484	0.00057
	Factor.VII	0.010192464	0.467697012	0.019489396	0.01978177	0.336477099	7.38E-05
	Fas	0.002415748	0.207570681	0.002289689	0.006523185	0.250612008	1.43E-05
	Fas.Ligand	0.004690577	0.364128008	0.008033314	0.01004533	0.30898559	3.69E-05
	FABP	0.00056027	0.047754136	0.000110743	0.002298337	0.117064704	1.26E-06
	Ferritin	0.771799924	0.72624381	0.651953752	0.374488178	0.401863318	0.000891

	probeID	cor.TX-vs-AR.Set_1	cor.TX-vs-AR.Set_2	Z.TX-vs-AR.Set_1	Z.TX-vs-AR.Set_2	Z.TX-vs-AR.Meta
50	FGF.basic	0.219765	0.280834	1.531617	1.825185	2.373617
	FGF_4	-0.09574	-0.09341	0.658352	0.592513	0.884495
	Fibrinogen	0.147901	0.355842	1.021453	2.353476	2.386435
	FSH..Follicle.Stimulating.Hormone.	-0.04907	0.042841	0.336711	0.271115	0.429797
	G.CSF	-0.067	0.297749	0.460046	1.941938	1.898459
	GLP.1.Total	0.271827	0.209249	1.911599	1.343247	2.301523
	Glucagon	0.179278	0.128055	1.242499	0.814361	1.454419
	GST	0.084586	-0.1146	0.581283	0.727987	0.925794
	GM.CSF	-0.05902	-0.12861	0.405107	0.817916	0.864808
	GRO.alpha	-0.04953	0.047844	0.339806	0.30282	0.454405
55	Growth.Hormone	0.175739	0.158776	1.217445	1.012758	1.576991
	Haptoglobin	-0.1762	0.437479	1.220683	2.966907	2.961073
	HB.EGF	0.571612	0.126082	4.45559	0.801549	3.717358
	HCC_4	0.294018	0.443851	2.07698	3.016915	3.601927

EP 2 806 272 A1

5	HGF..Hepatocyte.growth.factor.	0.108491	0.516245	0.746715	3.612628	3.082520
	I.309	0.275878	-0.14381	1.941623	0.915873	2.020555
	ICAM.1	0.019896	0.1718	0.136418	1.097441	0.872469
	IFN.gamma	0.263659	-0.17397	1.851278	1.111559	2.095042
	IgA	-0.07277	-0.00945	0.499804	0.059789	0.395691
10	IgE	0.329333	-0.1608	2.34518	1.025895	2.383710
	IGF.BP.2	0.419807	0.550135	3.067613	3.912215	4.935483
	IGF.1	0.072756	0.067393	0.499675	0.426875	0.655169
	IgM	0.137752	-0.1032	0.950423	0.655044	1.13523
	IL.10	0.551368	0.256702	4.252866	1.660665	4.18149
15	IL.12p40	0.305293	0.135979	2.161907	0.86537	2.140607
	IL.13	0.154889	-0.32294	1.070484	2.118248	2.254773
	IL.15	0.111104	0.005267	0.764845	0.033312	0.56438
	IL.16	0.057034	-0.03483	0.39143	0.220367	0.432606
	IL.18	0.379917	0.243251	2.742004	1.569923	3.048992
20	IL.1.alpha	-0.12688	-0.25815	0.874532	1.670507	1.789614
	IL.1.beta	0.209684	-0.20336	1.45916	1.304315	1.954071
	IL.1.ra	0.14329	0.439819	0.989152	2.985227	2.810310
	IL.2	-0.25366	0.14853	1.777779	0.946386	1.92627
	IL.3	-0.01549	-0.40686	0.106214	2.731189	2.00634
25	IL.4	0.063458	0.123913	0.435629	0.787744	0.86505
	IL.5	0.140371	-0.11078	0.968729	0.703536	1.182470
	IL.6	0.173364	0.194216	1.200654	1.244133	1.728725
	IL.7	0.163832	-0.02217	1.133391	0.140247	0.90059
	IL.8	0.214186	0.506815	1.491476	3.531852	3.552029
30	Insulin	-0.1697	-0.01107	1.174786	0.070041	0.890225
	Leptin	-0.01574	0.011589	0.107883	0.073299	0.128115
	LH..Luteinizing.Hormone.	-0.07687	0.020608	0.528024	0.130355	0.465544
	Lymphotactin	-0.07625	-0.18185	0.52376	1.163044	1.192751
	MCP.1	-0.23898	0.169045	1.67065	1.079496	1.944646
35	MCP.3	-0.10347	-0.06091	0.711899	0.385735	0.776144
	M.CSF	0.202673	0.308927	1.410397	2.019803	2.425517

	probelD	p.TX-vs-AR.Set_1	p.TX-vs-AR.Set_2	p.TX-vs-AR.Meta	q.TX-vs-AR.Set_1	q.TX-vs-AR.Set_2
30	FGF.basic	0.125158	0.068123	0.017615	0.145617	0.116603
	FGF.4	0.508383	0.551312	0.376429	0.295027	0.398241
	Fibrinogen	0.305354	0.019187	0.017013	0.227793	0.044431
	FSH..Follicle.Stimulating.Hormone.	0.735032	0.785028	0.867343	0.342644	0.500045
	G.CSF	0.643847	0.052481	0.089421	0.324042	0.098384
35	GLP.1.Total	0.056182	0.178087	0.021362	0.086356	0.226160
	Glucagon	0.212857	0.41316	0.14583	0.198451	0.353595
	GST	0.559196	0.464321	0.354553	0.309054	0.360957
	GM.CSF	0.683898	0.411129	0.387144	0.332945	0.353595
	GRO.alpha	0.73269	0.760625	0.649537	0.342644	0.49907
40	Growth.Hormone	0.222177	0.309175	0.114797	0.200565	0.297054
	Haptoglobin	0.220956	0.00335	0.003066	0.200565	0.015516
	HB.EGF	1.45E-05	0.420528	0.000201	0.000356	0.356031
	HCC.4	0.03822	0.00287	0.000316	0.072454	0.015516
	HGF..Hepatocyte.growth.factor.	0.453278	0.000395	0.002053	0.274242	0.003452
45	I.309	0.052474	0.357561	0.043326	0.086356	0.323599
	ICAM.1	0.890919	0.270642	0.382952	0.374357	0.291909
	IFN.gamma	0.064302	0.264557	0.036167	0.096236	0.289309
	IgA	0.615493	0.952025	0.692332	0.312583	0.551169
	IgE	0.019523	0.302968	0.017139	0.046262	0.297054
50	IGF.BP.2	0.002406	0.000133	8.00E-07	0.010524	0.001490
	IGF.1	0.615584	0.66764	0.512359	0.312583	0.45710
	IgM	0.340096	0.510174	0.256276	0.227793	0.375414
	IL.10	3.33E-05	0.096577	2.90E-05	0.000378	0.143474
	IL.12p40	0.031091	0.384601	0.032306	0.060972	0.34411
55	IL.13	0.28281	0.034689	0.024148	0.21735	0.06999
	IL.15	0.442409	0.97326	0.572494	0.272928	0.551302
	IL.16	0.694016	0.824527	0.665301	0.332945	0.511183
	IL.18	0.006502	0.115994	0.002296	0.020543	0.169128
	IL.1.alpha	0.379936	0.094639	0.071922	0.245541	0.143299
60	IL.1.beta	0.143881	0.190903	0.050693	0.157361	0.23124

EP 2 806 272 A1

5	IL.1ra	0.320847	0.003166	0.004949	0.227793	0.015516
	IL.2	0.075495	0.341827	0.05407	0.10472	0.316638
	IL.3	0.914965	0.006773	0.044819	0.374357	0.020565
	IL.4	0.661527	0.428555	0.387009	0.330019	0.358782
	IL.5	0.330906	0.479428	0.237019	0.227793	0.366489
	IL.6	0.228586	0.212047	0.083858	0.203126	0.250432
	IL.7	0.255593	0.887775	0.367802	0.204286	0.533558
	IL.8	0.135278	0.000524	0.000382	0.152674	0.003751
10	Insulin	0.238719	0.943812	0.378737	0.20397	0.550462
	Leptin	0.913634	0.941203	0.898058	0.374357	0.550462
	LH...Luteinizing.Hormone.	0.59571	0.895643	0.641542	0.312583	0.533558
	Lymphotoctin	0.59868	0.243177	0.232967	0.312583	0.269674
	MCP.1	0.094643	0.278516	0.051818	0.117011	0.292391
	MCP.3	0.474574	0.697991	0.437664	0.281144	0.465740
	M.CSF	0.157658	0.043833	0.015287	0.166043	0.084177
15	probeID	cor.TX-vs-CAN.Set_1	cor.TX-vs-CAN.Set_2	Z.TX-vs-CAN.Set_1	Z.TX-vs-CAN.Set_2	Z.TX-vs-CAN.Meta
	FGF.basic	0.523011	0.450677	3.979537	3.070885	4.98540
	FGF.4	0.19822	0.140206	1.377157	0.892622	1.604976
	Fibrinogen	0.133795	0.213512	0.922786	1.371466	1.622280
	FSH...Follicle.Stimulating.Hormone.	0.055921	0.080129	0.383775	0.507869	0.630487
	G.CSF	0.033182	0.555745	0.22757	3.963316	2.963403
	GLP.1.Total	0.237364	0.107079	1.658923	0.679835	3.7516
	Glucagon	0.230253	0.1744	1.607354	1.114393	4.566
	GST	-0.2575	-0.27313	1.805987	1.772432	0.323
	GM.CSF	0.244815	-0.19464	1.713154	1.246921	3.089
	GRO.alpha	-0.26424	0.185897	1.855569	1.189547	3.222
	Growth.Hormone	0.227667	0.039176	1.588642	0.247895	8.628
20	Haptoglobin	-0.15782	0.168342	1.091104	1.07492	1.610
	HB.EGF	0.726564	0.156639	6.316865	0.998894	7.302
	HCC.4	0.061449	0.227028	4.21805	1.461314	1.566
	HGF...Hepatocyte.growth.factor.	0.118935	0.378144	0.819253	2.516489	5.726
30	I.309	0.641185	0.07338	5.21155	0.46493	4.013877
	ICAM.1	-0.09089	-0.02329	0.624859	0.147308	0.54600
	IFN.gamma	0.256517	-0.17739	1.798762	1.133885	2.07369
	IgA	0.086241	0.054202	0.592714	0.343138	0.66174
	IgE	0.231625	-0.18461	1.617289	1.181108	1.97876
	IGF.BP.2	0.439736	0.457948	3.23521	3.128831	4.50005
	IGF.1	0.079227	0.226027	0.544291	1.45464	1.413457
	IgM	0.389396	0.356356	2.818277	2.3572	3.659614
	IL.10	0.69784	0.229915	5.916964	1.480573	5.230848
	IL.12p40	0.414912	-0.00237	3.026981	0.014993	2.151000
	IL.13	0.636678	-0.20022	5.159341	1.283613	4.555856
	IL.15	0.415472	0.118059	3.031616	0.750169	2.674126
35	IL.16	0.221892	0.206032	1.546943	1.321984	2.028637
	IL.18	0.436546	0.349692	3.208145	2.30905	3.901246
	IL.1.alpha	0.033517	-0.23162	0.22987	1.491993	1.217541
	IL.1.beta	0.092569	-0.15227	0.636445	0.970606	1.136356
40	IL.1ra	0.213197	0.517812	1.48437	3.626157	3.613688
	IL.2	-0.04594	-0.03644	0.315167	0.230572	0.385895
	IL.3	0.191177	-0.43052	1.32697	2.91265	2.997864
	IL.4	0.070873	0.193002	0.486699	1.236155	1.218241
	IL.5	0.175286	-0.17177	1.21424	1.097247	1.634467
	IL.6	0.193244	0.081119	1.341682	0.514173	1.312287
	IL.7	0.367248	-0.08808	2.641063	0.558525	2.26245
	IL.8	0.172353	0.367558	1.193504	2.438725	2.568374
	Insulin	0.162448	-0.05786	1.123641	0.36632	1.053561
	Leptin	-0.01036	-0.10244	0.071	0.650197	0.50996
	LH...Luteinizing.Hormone.	-0.02933	0.046301	0.201117	0.29304	0.34942
	Lymphotoctin	-0.19403	-0.03644	1.347266	0.230572	1.11570
45	MCP.1	0.02529	0.121622	0.173415	0.773029	0.669
	MCP.3	0.208628	0.124022	1.451591	0.788443	1.58394
	M.CSF	0.348659	0.523007	2.494882	3.671215	4.36008
50	I.309	0.641185	0.07338	5.21155	0.46493	4.013877
	ICAM.1	-0.09089	-0.02329	0.624859	0.147308	0.54600
	IFN.gamma	0.256517	-0.17739	1.798762	1.133885	2.07369
	IgA	0.086241	0.054202	0.592714	0.343138	0.66174
	IgE	0.231625	-0.18461	1.617289	1.181108	1.97876
	IGF.BP.2	0.439736	0.457948	3.23521	3.128831	4.50005
	IGF.1	0.079227	0.226027	0.544291	1.45464	1.413457
	IgM	0.389396	0.356356	2.818277	2.3572	3.659614
	IL.10	0.69784	0.229915	5.916964	1.480573	5.230848
	IL.12p40	0.414912	-0.00237	3.026981	0.014993	2.151000
	IL.13	0.636678	-0.20022	5.159341	1.283613	4.555856
	IL.15	0.415472	0.118059	3.031616	0.750169	2.674126
55	IL.16	0.221892	0.206032	1.546943	1.321984	2.028637
	IL.18	0.436546	0.349692	3.208145	2.30905	3.901246
	IL.1.alpha	0.033517	-0.23162	0.22987	1.491993	1.217541
	IL.1.beta	0.092569	-0.15227	0.636445	0.970606	1.136356
55	IL.1ra	0.213197	0.517812	1.48437	3.626157	3.613688
	IL.2	-0.04594	-0.03644	0.315167	0.230572	0.385895
	IL.3	0.191177	-0.43052	1.32697	2.91265	2.997864
	IL.4	0.070873	0.193002	0.486699	1.236155	1.218241
	IL.5	0.175286	-0.17177	1.21424	1.097247	1.634467
	IL.6	0.193244	0.081119	1.341682	0.514173	1.312287
	IL.7	0.367248	-0.08808	2.641063	0.558525	2.26245
	IL.8	0.172353	0.367558	1.193504	2.438725	2.568374
	Insulin	0.162448	-0.05786	1.123641	0.36632	1.053561
	Leptin	-0.01036	-0.10244	0.071	0.650197	0.50996
	LH...Luteinizing.Hormone.	-0.02933	0.046301	0.201117	0.29304	0.34942
	Lymphotoctin	-0.19403	-0.03644	1.347266	0.230572	1.11570
55	MCP.1	0.02529	0.121622	0.173415	0.773029	0.669
	MCP.3	0.208628	0.124022	1.451591	0.788443	1.58394
	M.CSF	0.348659	0.523007	2.494882	3.671215	4.36008

EP 2 806 272 A1

	probeID	p.TX-vs-CAN.Set_1	p.TX-vs-CAN.Set_2	p.TX-vs-CAN.Meta	q.TX-vs-CAN.Set_1	q.TX-vs-CAN.Set_2
5	FGF.basic	9.75E-05	0.002423	6.18E-07	0.000406	0.0090125
	FGF.4	0.167614	0.369856	0.108499	0.15893	0.2463367
	Fibrinogen	0.35428	0.169211	0.104743	0.265381	0.1654440
	FSH..Follicle.Stimulating.Hormone.	0.699703	0.609505	0.528376	0.433163	0.321288*
	G.CSF	0.819054	0.000109	0.003043	0.483094	0.001105
10	GLP.1.Total	0.096959	0.494326	0.098178	0.106807	0.291815*
	Glucagon	0.107692	0.263347	0.054284	0.112041	0.2061255
	GST	0.071023	0.076371	0.011396	0.086666	0.0964500
	GM.CSF	0.086621	0.211032	0.036341	0.098311	0.1909362
	GRO.alpha	0.063693	0.232664	0.031301	0.079518	0.1931276
15	Growth.Hormone	0.111815	0.803038	0.194072	0.114736	0.3778537
	Haptoglobin	0.273677	0.280549	0.125619	0.213546	0.2061255
	HB.EGF	2.33E-09	0.315817	2.30E-07	8.72E-08	0.2200550
	HCC.4	0.671623	0.14318	0.183003	0.428923	0.14898*
	HGF..Hepatocyte.growth.factor.	0.410707	0.012412	0.018338	0.298688	0.0278683
20	I.309	5.26E-07	0.640046	5.97E-05	4.38E-06	0.3288094
	ICAM.1	0.530162	0.882165	0.585063	0.367712	0.4020812
	IFN.gamma	0.072147	0.25513	0.038108	0.086666	0.2034994
	IgA	0.551505	0.729941	0.508133	0.37556	0.3687412
	IgE	0.105554	0.235976	0.047842	0.111562	0.1931276
25	IGF.BP.2	0.001397	0.002016	6.79E-06	0.003738	0.0081458
	IGF.1	0.584442	0.145	0.157521	0.090883	0.14898*
	IgM	0.005189	0.019001	0.000253	0.010797	71562
	IL.10	1.78E-08	0.138028	1.69E-07	3.33E-07	57937
	IL.12p40	0.002736	0.987963	0.031476	0.006027	77877
30	IL.13	6.69E-07	0.197992	5.22E-06	5.01E-06	29855
	IL.15	0.002696	0.450852	0.007492	0.006027	4694*
	IL.16	0.121453	0.185004	0.042495	0.121303	80145
	IL.18	0.001527	0.021527	9.57E-05	0.003945	07795
	IL.1.alpha	0.817257	0.135042	0.223398	0.483094	67937
35	IL.1.beta	0.522574	0.329661	0.255807	0.365836	49182
	IL.1.ra	0.137134	0.000376	0.000302	0.135162	02280
40	IL.2	0.751401	0.816544	0.699574	0.453914	0.3778537
	IL.3	0.183539	0.003955	0.002719	0.165833	0.0126177
	IL.4	0.624778	0.214975	0.223132	0.406959	0.1916430
	IL.5	0.223339	0.270726	0.102161	0.185928	0.2061255
	IL.6	0.178757	0.605077	0.189423	0.163295	0.321288*
45	IL.7	0.008702	0.574345	0.02367	0.016297	0.321288*
	IL.8	0.231355	0.015318	0.010218	0.190441	0.032643*
	Insulin	0.259686	0.71249	0.292084	0.204762	0.362950*
	Leptin	0.943097	0.513304	0.610077	0.521567	0.2954705
	L.H..Luteinizing.Hormone.	0.839779	0.768128	0.726773	0.487639	0.3725110
50	Lymphotoctin	0.176967	0.816544	0.26455	0.163295	0.3778537
	MCP.1	0.861606	0.437208	0.503344	0.492675	0.2789844
	MCP.3	0.145957	0.428146	0.113207	0.140169	0.2761082
	M.CSF	0.013085	0.00032	1.30E-05	0.021782	0.0021572
55	probeID	cor.AR-vs-CAN.Set_1	cor.AR-vs-CAN.Set_2	Z.AR-vs-CAN.Set_1	Z.AR-vs-CAN.Set_2	Z.AR-vs-CAN.Meta
	FGF.basic	0.366515	0.234035	2.635256	1.634758	3.0193557
	FGF.4	0.275622	0.204225	1.939727	1.420062	2.3757289
	Fibrinogen	-0.0223	-0.12613	0.152872	0.869299	0.7227842
	FSH..Follicle.Stimulating.Hormone.	0.13974	0.012692	0.964316	0.087017	0.7434047
60	G.CSF	0.09501	0.284384	0.653326	2.004906	1.879655
	GLP.1.Total	0.161859	-0.07719	1.119494	0.530258	1.1665506
	Glucagon	0.14622	0.030897	1.009673	0.211889	37746
	GST	-0.31924	-0.15219	2.267855	1.051507	71430
	GM.CSF	0.284358	-0.05099	2.004708	0.349847	49220
65	GRO.alpha	-0.12571	0.158639	0.866405	1.096836	82206
	Growth.Hormone	0.045327	-0.10947	0.31096	0.753501	26876
	Haptoglobin	0.028959	-0.26489	0.19859	1.860386	59160
	HB.EGF	0.208938	0.007886	1.453811	0.054066	6230*
	HCC.4	-0.24625	-0.15785	1.723613	1.09132	0456*
70	HGF..Hepatocyte.growth.factor.	0.009374	-0.07342	0.06427	0.504256	20080
	I.309	0.178034	0.18999	1.233687	1.318526	46860

EP 2 806 272 A1

5	ICAM.1	-0.1297	-0.1094	0.894223	0.752996	1.164760
	IFN.gamma	-0.14298	0.040963	0.986954	0.280989	0.896570
	IgA	0.154911	0.074028	1.070634	0.508437	1.116572
	IgE	-0.19691	0.050105	1.367807	0.343791	1.210282
	IGF.BP.2	-0.04179	0.033413	0.286672	0.229151	0.364741
10	IGF.1	0.070726	0.224356	0.485684	1.564724	1.449857
	IgM	0.168308	0.416427	1.164944	3.039532	2.973013
	IL.10	0.253973	-0.00542	1.780104	0.037135	1.284982
	IL.12p40	0.070853	-0.14277	0.486561	0.985502	1.040905
	IL.13	0.509434	0.169467	3.852638	1.173125	3.553751
15	IL.15	0.261816	0.103229	1.837707	0.710231	1.801663
	IL.16	0.098611	0.346756	0.678245	2.480047	2.233250
	IL.18	-0.00769	0.131812	0.052689	0.908949	0.679980
	IL.1.alpha	0.160743	0.048178	1.111642	0.330545	1.019780
	IL.1.beta	-0.11252	0.232568	0.774667	1.62412	1.696198
20	IL.1.ra	-0.01402	0.05154	0.096101	0.353653	0.318024
	IL.2	0.246858	-0.18707	1.728061	1.297802	2.139608
	IL.3	0.209462	0.046199	1.457568	0.316949	1.254772
	IL.4	0.018434	0.06579	0.126393	0.451689	0.408765
	IL.5	-0.01354	-0.06831	0.092799	0.469043	0.397282
25	IL.6	-0.03488	-0.1224	0.23921	0.843345	0.765482
	IL.7	0.217022	-0.05833	1.511867	0.400359	1.352148
	IL.8	-0.08272	-0.05253	0.568424	0.36049	0.65682
	Insulin	0.310197	-0.06794	2.19904	0.466501	1.884822
	Leptin	-0.00109	-0.13677	0.007501	0.943564	0.672502
30	LH..Luteinizing.Hormone.	0.028652	0.088215	0.196485	0.606351	0.567691
	Lymphotactin	-0.14318	0.142857	0.988402	0.986124	1.396200
	MCP.1	0.251706	0.017496	1.763503	0.11996	1.331809
	MCP.3	0.366232	0.162495	2.633011	1.123976	2.656591
	M.CSF	0.185109	0.243428	1.283843	1.703048	2.112050
25	probeID	p.AR-vs-CAN.Set_1	p.AR-vs-CAN.Set_2	p.AR-vs-CAN.Meta	q.AR-vs-CAN.Set_1	q.AR-vs-CAN.Set_2
35	FGF.basic	0.008847	0.101876	0.002533	0.082388	0.554575
	FGF.4	0.052702	0.15485	0.017514	0.187555	0.618687
	Fibrinogen	0.877861	0.382786	0.469812	0.638542	0.718387
	FSH..Follicle.Stimulating.Hormone.	0.333107	0.93029	0.457237	0.417256	0.886846
	G.CSF	0.511621	0.04533	0.060155	0.493124	0.554575
40	GLP.1.Total	0.261441	0.594157	0.243392	0.39584	0.841835
	Glucagon	0.310945	0.831325	0.387712	0.417256	0.865859
	GST	0.023836	0.291396	0.018918	0.123421	0.718387
	GM.CSF	0.045351	0.72511	0.095928	0.182449	0.865859
	GRO.alpha	0.384368	0.271176	0.16507	0.43615	0.713841
45	Growth.Hormone	0.754611	0.449192	0.451638	0.596784	0.776608
	Haptoglobin	0.841766	0.063016	0.145416	0.628537	0.554575
	HB.EGF	0.145346	0.956653	0.28632	0.292364	0.892409
	HCC.4	0.084735	0.273583	0.04654	0.21842	0.713841
	HGF..Hepatocyte.growth.factor.	0.948483	0.612353	0.687678	0.645313	0.841835
50	I.309	0.216102	0.186326	0.071124	0.377278	0.680634
	ICAM.1	0.36933	0.449495	0.244116	0.427173	0.776608
	IFN.gamma	0.32192	0.7776	0.369948	0.417256	0.865859
	IgA	0.282742	0.60941	0.264177	0.415269	0.841835
	IgE	0.170498	0.729679	0.22617	0.335662	0.865859
55	IGF.BP.2	0.773225	0.817819	0.715304	0.601227	0.865859
	IGF.1	0.6255	0.117266	0.147098	0.54399	0.566686
	IgM	0.242657	0.002629	0.002949	0.39391	0.168087
	IL.10	0.075118	0.97022	0.198798	0.218273	0.892409
	IL.12p40	0.624876	0.32263	0.29792	0.54399	0.718387
60	IL.13	0.000158	0.23938	0.00038	0.004868	0.707339
	IL.15	0.066258	0.475608	0.071598	0.218273	0.789708
	IL.16	0.495675	0.013625	0.025532	0.48792	0.348403
	IL.18	0.957756	0.361521	0.496517	0.646866	0.718387
	IL.1.alpha	0.264787	0.739705	0.307833	0.39584	0.865859
65	IL.1.beta	0.436583	0.104103	0.089848	0.459054	0.554575
	IL.1.ra	0.923034	0.722244	0.750466	0.645313	0.865859
	IL.2	0.083942	0.1933	0.032386	0.21842	0.686496

EP 2 806 272 A1

5	IL3	0.144316	0.750043	0.209561	0.292364	0.865859
	IL4	0.89889	0.649876	0.682712	0.639798	0.856578
	IL5	0.925671	0.637383	0.691159	0.645313	0.85129
	IL6	0.809972	0.397116	0.443984	0.624552	0.718387
	IL7	0.130059	0.687404	0.176328	0.273507	0.865859
	IL8	0.567911	0.717106	0.511283	0.520282	0.865859
	Insulin	0.028355	0.639206	0.059454	0.126639	0.85129
	Leptin	0.993983	0.343582	0.501263	0.661674	0.718387
10	LH..Luteinizing.Hormone.	0.843421	0.542398	0.570245	0.628537	0.835504
	Lymphotactin	0.321213	0.322325	0.162654	0.417256	0.718387
	MCP.1	0.077846	0.904011	0.182923	0.218273	0.886846
	MCP.3	0.008904	0.259545	0.007894	0.082388	0.707339
	M.CSF	0.198106	0.088476	0.034682	0.352512	0.554575

	probelD	cor.TX-vs-allOther.Set_1	cor.TX-vs-allOther.Set_2	Z.TX-vs-allOther.Set_1	Z.TX-vs-allOther.Set_2	Z.TX-vs-allOther.Meta
15	FGF.basic	0.356752	0.316687	3.166363	2.644104	4.108620
	FGF.4	0.06623	0.008563	0.562808	0.069042	0.446785
	Fibrinogen	0.132147	0.249889	1.127801	2.058246	2.252945
	FSH..Follicle.Stimulating.Hormone.	0.012906	0.061867	0.109517	0.499429	0.430590
	G.CSF	-0.01698	0.405008	0.144122	3.46375	2.551150
	GLP.1.Total	0.241127	0.162682	2.087127	1.323338	2.411563
	Glucagon	0.185841	0.131348	1.595454	1.065118	1.881308
	GST	-0.0809	-0.16161	0.687938	1.314491	1.415930
20	GM.CSF	0.088836	-0.14659	0.755793	1.190439	1.376193
	GRO.alpha	-0.14033	0.107268	1.198624	0.868159	1.461436
	Growth.Hormone	0.188339	0.111215	1.617414	0.900372	1.780343
	Haptoglobin	-0.1792	0.264684	1.537199	2.185987	2.632690
	HB.EGF	0.596784	0.123921	5.83904	1.004246	4.838934
	HCC.4	0.165811	0.293487	1.420061	2.437845	2.727950
	HGF..Hepatocyte.growth.factor.	0.108858	0.405882	0.927364	3.472177	3.110945
	I.309	0.457165	-0.0519	4.189365	0.418845	3.25848
25	ICAM.1	-0.03442	0.061185	0.292143	0.493903	0.555819

30	IFN.gamma	0.22996	-0.19664	1.986801	1.636287	2.54069
	IgA	0.001203	0.024518	0.010208	0.197706	0.147017
	IgE	0.204969	-0.18301	1.764207	1.492286	2.302688
	IGF.BP.2	0.408558	0.441961	3.681589	3.826873	5.309284
	IGF.1	0.064733	0.121021	0.55005	0.980509	1.082268
	IgM	0.256502	0.128106	2.226198	1.03553	2.30851
	IL.10	0.581771	0.2282	5.643864	1.872776	5.315067
	IL.12p40	0.321709	0.064355	2.830287	0.519561	2.368700
35	IL.13	0.382378	-0.23417	3.418226	1.923601	3.777242
	IL.15	0.247069	0.080215	2.140746	0.486057	1.857430
	IL.16	0.12106	0.08091	1.032293	0.853747	1.192210
	IL.18	0.382994	0.253633	3.424348	2.080475	3.899568
	IL.1.alpha	-0.04039	-0.22307	0.342891	1.829202	1.535901
	IL.1.beta	0.140032	-0.19632	1.196074	1.603589	1.979660
	IL.1.ra	0.14626	0.419959	1.250024	3.609005	3.435852
	IL.2	-0.13059	0.062868	1.114424	0.507524	1.146890
40	IL.3	0.07995	-0.40658	0.679847	3.47906	2.940791
	IL.4	0.074635	0.14047	0.634481	1.140043	1.254777
	IL.5	0.147486	-0.12791	1.260655	1.036912	1.62462
	IL.6	0.154938	0.12264	1.32537	0.993758	1.639871
	IL.7	0.252337	-0.04699	2.188413	0.379134	1.815530
	IL.8	0.181431	0.400897	1.556724	3.424176	3.522028
	Insulin	-0.04682	-0.03783	0.397611	0.305102	0.496892
	Leptin	-0.02293	-0.04898	0.194563	0.403321	0.422767
45	LH..Luteinizing.Hormone.	-0.08446	0.002961	0.547687	0.023871	0.404152
	Lymphotactin	-0.1349	-0.09284	1.15168	0.750673	1.345166
	MCP.1	-0.1098	0.114035	0.935437	0.923398	1.314394
	MCP.3	0.053832	0.022672	0.457225	0.182822	0.452581
	M.CSF	0.26953	0.378849	2.344968	3.214547	3.931171

	probelD	p.TX-vs-allOther.Set_1	p.TX-vs-allOther.Set_2	p.TX-vs-allOther.Meta	q.TX-vs-allOther.Set_1	q.TX-vs-allOther.Set_2
55	FGF.basic	0.001679	0.00851	3.98E-05	0.005437	0.01686

EP 2 806 272 A1

	FGF.4	0.572373	0.944745	0.65503	0.388933	0.409026
	Fibrinogen	0.258405	0.039864	0.024263	0.223477	0.052682
	FSH.,Follicle.Stimulating.Hormone.	0.912491	0.616235	0.666766	0.517096	0.33828
	G.CSF	0.885011	0.000613	0.010737	0.511167	0.002602
5	GLP.1.Total	0.03716	0.185011	0.015884	0.057715	0.150722
	Glucagon	0.110413	0.285665	0.05993	0.129277	0.219937
	GST	0.490223	0.187952	0.156796	0.349051	0.151049
	GM.CSF	0.448497	0.232919	0.168762	0.328201	0.184691
	GRO.alpha	0.229825	0.383935	0.143896	0.209121	0.250673
	Growth.Hormone	0.105623	0.366574	0.07502	0.125601	0.242227
	Haptoglobin	0.123958	0.029166	0.008471	0.138732	0.045645
10	HB.EGF	1.60E-08	0.314021	1.31E-06	6.04E-07	0.220019
	HCC.4	0.155112	0.015139	0.006373	0.171084	0.025009
	HGF.,Hepatocyte.growth.factor.	0.352543	0.000595	0.001865	0.279482	0.002602
	I.309	3.74E-05	0.674219	0.00112	0.000219	0.351722
	ICAM.1	0.769422	0.62014	0.578335	0.472234	0.33828
	IFN.gamma	0.047173	0.108008	0.011063	0.067738	0.105875
15	IgA	0.991827	0.842686	0.883118	0.543044	0.382039
	IgE	0.077724	0.135226	0.021296	0.09697	0.118264
	IGF.BP.2	0.000274	0.000161	1.10E-07	0.001225	0.001198
	IGF.1	0.581105	0.325567	0.279133	0.389024	0.220019
	IgM	0.026326	0.297829	0.020971	0.046594	0.219937
	IL.10	4.40E-08	0.061252	1.07E-07	6.70E-07	0.071425
	IL.12p40	0.004885	0.602099	0.017851	0.01282	0.33828
20	IL.13	0.00071	0.054605	0.000159	0.002704	0.06494
	IL.15	0.032598	0.625704	0.06325	0.052785	0.33828
	IL.16	0.300849	0.511883	0.233179	0.248871	0.30442
	IL.18	0.000695	0.036889	9.64E-05	0.002704	0.052583
	IL.1.alpha	0.730818	0.067476	0.124563	0.452187	0.077169
	IL.1.beta	0.230815	0.108598	0.047742	0.209121	0.105875
	IL.1.ra	0.210525	0.000364	0.000591	0.197803	0.002162
25	IL.2	0.264121	0.610534	0.251427	0.22464	0.33828
	IL.3	0.495335	0.00058	0.003274	0.349051	0.002602
30	IL.4	0.524521	0.253228	0.208559	0.366227	0.19815
	IL.5	0.206685	0.29858	0.104242	0.197695	0.213937
	IL.6	0.184409	0.319088	0.101032	0.194262	0.220019
	IL.7	0.028957	0.703555	0.069442	0.047908	0.356691
	IL.8	0.119279	0.000704	0.000428	0.136508	0.00279
	Insulin	0.689952	0.759421	0.619265	0.433957	0.364220
	Leptin	0.845212	0.685631	0.672465	0.502539	0.354585
35	LH.,Luteinizing.Hormone.	0.58273	0.980882	0.686101	0.389024	0.416807
	Lymphotactin	0.248531	0.451435	0.178571	0.222398	0.280966
	MCP.1	0.348375	0.354472	0.188713	0.279482	0.236862
	MCP.3	0.646446	0.854391	0.65085	0.416381	0.382039
	M.CSF	0.019364	0.001444	8.45E-05	0.035944	0.004336
40	probelD	cor.AR-vs-allOther.Set_1	cor.AR-vs-allOther.Set_2	Z.AR-vs-allOther.Set_1	Z.AR-vs-allOther.Set_2	Z.AR-vs-allOther.Met
	FGF.basic	0.077346	0.043972	0.657616	0.354742	0.715844
	FGF.4	0.180766	0.150036	1.550891	1.218826	1.958485
	Fibrinogen	-0.08417	-0.2218	0.715929	1.818409	1.792047
	FSH.,Follicle.Stimulating.Hormone.	0.09398	0.00072	0.799805	0.005806	0.569653
	G.CSF	0.078596	0.011635	0.668291	0.093809	0.538866
	GLP.1.Total	-0.02292	-0.14895	0.19453	1.20989	0.993074
45	Glucagon	-0.00253	-0.03584	0.021437	0.289062	0.219555
	GST	-0.19299	-0.05798	1.658401	0.467994	1.50358
	GM.CSF	0.162092	0.030194	1.387639	0.243502	1.153390
	GRO.alpha	-0.0411	0.06681	0.348935	0.53944	0.628175
	Growth.Hormone	-0.05927	-0.12021	0.503544	0.97387	1.04468
	Haptoglobin	0.108033	-0.32387	0.920281	2.708659	2.566048
	HB.EGF	-0.16269	0.03826	1.392849	0.308631	1.203127
50	HCC.4	-0.26526	-0.24324	2.305957	2.001176	3.045602
	HGF.,Hepatocyte.growth.factor.	-0.04898	-0.24028	0.415941	1.975811	1.691223
	I.309	-0.07944	0.169972	0.675508	1.383789	1.456142
	ICAM.1	-0.07212	-0.13676	0.613012	1.109506	1.218004
	IFN.gamma	-0.16881	0.086655	1.446227	0.70039	1.517887

55

EP 2 806 272 A1

5	IgA	0.109341	0.045344	0.931511	0.365824	0.917354
	IgE	-0.27505	0.116888	2.395516	0.946706	2.363307
	IGF.BP.2	-0.22848	-0.19373	1.973557	1.581898	2.514086
	IGF.1	-0.00761	0.107491	0.064549	0.869985	0.660815
	IgM	0.008175	0.282064	0.069372	2.337435	1.701869
10	IL.10	-0.13785	-0.10496	1.177176	0.849368	1.432982
	IL.12p40	-0.12047	-0.14403	1.027189	1.169301	1.553152
	IL.13	0.194134	0.230269	1.668458	1.89039	2.516485
	IL.15	0.072723	0.049583	0.618166	0.400082	0.720010
	IL.16	0.036664	0.216975	0.311242	1.777558	1.477004
15	IL.18	-0.19097	-0.02059	1.640597	0.168406	1.279158
	IL.1.alpha	0.131015	0.136905	1.118128	1.110737	1.576045
	IL.1.beta	-0.15057	0.136774	1.287437	1.109661	1.695004
	IL.1ra	-0.0782	-0.1333	0.664886	1.081138	1.234625
	IL.2	0.238462	-0.1795	2.063134	1.463062	2.493397
20	IL.3	0.111105	0.214391	0.946666	1.755711	1.910869
	IL.4	-0.0262	-0.01034	0.22234	0.08333	0.216141
	IL.5	-0.06083	0.007354	0.516792	0.059292	0.407353
	IL.6	-0.09943	-0.1447	0.846526	1.174848	1.429327
	IL.7	0.021694	-0.02205	0.18411	0.17778	0.255894
25	IL.8	-0.14541	-0.23241	1.242657	1.908651	2.228310
	Insulin	0.224752	-0.03302	1.940204	0.266341	1.560262
	Leptin	0.031308	-0.07819	0.265743	0.631708	0.634593
	LH...Luteinizing.Hormone.	0.079306	0.051326	0.67435	0.414169	0.769696
	Lymphotactin	-0.01584	0.132733	0.134411	1.076479	0.856228
30	MCP.1	0.234783	-0.0559	2.030067	0.451177	1.754504
	MCP.3	0.219624	0.09841	1.894437	0.795985	1.902411
	M-CSF	-0.00806	0.006047	0.068372	0.048756	0.082821
	probed					
	FGF.basic	0.509527	0.721802	0.474087	0.553516	0.756466
35	FGF.4	0.120662	0.222005	0.050173	0.38479	0.523705
	Fibrinogen	0.472761	0.069096	0.073125	0.553516	0.364263
	FSH...Follicle.Stimulating.Hormone.	0.422555	0.99535	0.568913	0.54787	0.811088
	G-CSF	0.502685	0.924974	0.589965	0.553516	0.797781
	GLP.1.Total	0.645238	0.2254	0.320674	0.643381	0.523705
40	Glucagon	0.982838	0.771706	0.826217	0.671626	0.770308
	GST	0.097129	0.638593	0.132687	0.356984	0.754909
	GM-CSF	0.164714	0.806904	0.24875	0.42514	0.779941
	GRO.alpha	0.726264	0.588289	0.529889	0.631649	0.723964
	Growth.Hormone	0.613455	0.328845	0.296167	0.575382	0.603848
45	Haptoglobin	0.356225	0.007055	0.010286	0.528951	0.202616
	HB.EGF	0.163141	0.756727	0.228927	0.42514	0.769217
	HCC.4	0.021447	0.045635	0.002322	0.256481	0.336242
	HGF...Hepatocyte.growth.factor.	0.676456	0.04842	0.090794	0.604824	0.336242
	I.309	0.498088	0.165824	0.145353	0.553516	0.419530
50	ICAM.1	0.536635	0.266122	0.223222	0.553516	0.528322
	IFN.gamma	0.147679	0.482274	0.129043	0.42514	0.667465
	IgA	0.350398	0.713491	0.358957	0.528951	0.756466
	IgE	0.01693	0.342484	0.018113	0.256481	0.609239
	IGF.BP.2	0.048652	0.11343	0.011934	0.298848	0.409993
55	IGF.1	0.948354	0.382938	0.508731	0.652724	0.652574
	IgM	0.944501	0.019787	0.08878	0.652724	0.306080
	IL.10	0.238243	0.394293	0.151863	0.497507	0.652574
	IL.12p40	0.30324	0.241291	0.120387	0.528951	0.528322
	IL.13	0.095131	0.058876	0.011853	0.356984	0.336242
60	IL.15	0.535229	0.688021	0.471519	0.553516	0.756488
	IL.16	0.754821	0.075521	0.139674	0.63491	0.364263
	IL.18	0.100749	0.865759	0.200841	0.356984	0.779941
	IL.1.alpha	0.262541	0.265594	0.115015	0.497507	0.528322
	IL.1.beta	0.197239	0.266055	0.090075	0.471744	0.528322
65	IL.1ra	0.504862	0.278502	0.21697	0.553516	0.528322
	IL.2	0.039372	0.142999	0.012653	0.298848	0.419530
	IL.3	0.342631	0.079155	0.056021	0.528951	0.364263
	IL.4	0.823457	0.933334	0.828878	0.643381	0.798939

EP 2 806 272 A1

5	IL.5	0.604158	0.952538	0.683749	0.572273	0.804035
	IL.6	0.396009	0.239073	0.15291	0.531527	0.528322
	IL.7	0.85343	0.858364	0.798032	0.643381	0.77994
	IL.8	0.213217	0.056494	0.02586	0.497507	0.336242
	Insulin	0.05255	0.789205	0.118698	0.298848	0.774569
	Leptin	0.789742	0.526199	0.525693	0.63491	0.684670
	LH..Luteinizing.Hormone.	0.198824	0.677648	0.441478	0.553516	0.756466
	Lymphotoctin	0.89271	0.280572	0.391871	0.65242	0.528322
	MCP.1	0.042604	0.650694	0.079344	0.298848	0.75592
	MCP.3	0.058325	0.424634	0.057117	0.298848	0.652574
10	M.CSF	0.945301	0.960964	0.833993	0.652724	0.804035
	probeID	cor.CAN-vs-allOther.Set_1	cor.CAN-vs-allOther.Set_2	Z.CAN-vs-allOther.Set_1	Z.CAN-vs-allOther.Set_2	Z.CAN-vs-allOther.Me
	FGF.basie	-0.4341	-0.33374	3.945108	2.797836	4.767981
	FGF.4	-0.247	-0.15787	2.140085	1.283531	2.420862
	Fibrinogen	-0.04797	-0.00685	0.407382	0.055214	0.327105
	FSH..Follicle.Stimulating.Hormone.	-0.10689	-0.05733	0.910434	0.462703	0.970954
	G.CSF	-0.06161	-0.38221	0.523468	3.246267	2.665605
	GLP.1.Total	-0.21821	9.97E-05	1.88179	0.000804	1.331194
	Glucagon	-0.18331	-0.08434	1.573261	0.681625	1.594445
	GST	0.27389	0.205857	2.384914	1.683731	2.876966
15	GM.CSF	-0.25093	0.103937	2.175856	0.841003	2.133100
	GRO.alpha	0.181426	-0.16496	1.556685	1.342202	2.049822
	Growth.Hormone	-0.12906	0.018448	1.101294	0.146753	0.883916
	Haptoglobin	0.071172	0.08169	0.604934	0.660073	0.894495
	HB.EGF	-0.43409	-0.07512	3.945064	0.608817	3.218665
	HCC.4	0.099451	-0.0253	0.846667	0.203999	0.742933
	HGF..Hepatocyte.growth.factor.	-0.05988	-0.1311	0.50869	1.063082	1.111410
	I.309	-0.37772	-0.12248	3.372064	0.992446	3.086174
	ICAM.1	0.106535	0.080772	0.907419	0.652623	1.103116
	IFN.gamma	-0.06115	0.093269	0.519536	0.754154	0.900634
20	IgA	-0.11054	-0.06778	0.941844	0.547276	1.052966
	probeID	p.CAN-vs-allOther.Set_1	p.CAN-vs-allOther.Set_2	p.CAN-vs-allOther.Meta	q.CAN-vs-allOther.Set_1	q.CAN-vs-allOther.Se
	FGF.basie	9.98E-05	0.005415	1.86E-06	0.000689	0.035838
	FGF.4	0.032651	0.198519	0.015484	0.042171	0.250612
	Fibrinogen	0.682744	0.955798	0.743588	0.344738	0.46176
25	IgE	0.070077	0.050565	0.595598	0.408016	0.709662
	IGF.BP.2	-0.18008	-0.21066	1.544854	1.724209	2.311576
	IGF.1	-0.05713	-0.21822	0.485261	1.788138	1.607536
	IgM	-0.26468	-0.39928	2.300624	3.408658	4.037071
	IL.10	-0.44392	-0.10384	4.048377	0.840194	3.456741
	IL.12p40	-0.20124	0.085142	1.731222	0.688099	1.710718
	IL.13	-0.57651	-0.01601	5.576717	0.129079	4.034607
	IL.15	-0.31979	-0.10468	2.812157	0.847057	2.587454
	IL.16	-0.15772	-0.29101	1.349599	2.415981	2.662667
	IL.18	-0.19202	-0.21119	1.649835	1.728653	2.388952
30	IL.1alpha	-0.09063	0.067202	0.771112	0.54262	0.928948
	IL.1beta	0.01054	0.042856	0.089437	0.345728	0.307707
	IL.1ra	-0.06806	-0.25096	0.578425	2.067446	1.870913
	IL.2	-0.10788	0.121981	0.918932	0.988365	1.348662
	IL.3	-0.19105	0.15764	1.641322	1.281618	2.066831
	IL.4	-0.04844	-0.11819	0.411334	0.95738	0.967826
	IL.5	-0.08666	0.109681	0.737155	0.887849	1.149051
	IL.6	-0.0555	0.032485	0.471452	0.261992	0.518622
	IL.7	-0.27403	0.065044	2.386205	0.525142	2.058632
	IL.8	-0.03602	-0.1344	0.305775	1.090194	0.987098
35	Insulin	-0.17793	0.067633	1.526005	0.54611	1.465206
	Leptin	-0.00838	0.123929	0.071129	1.004309	0.760449
	LH..Luteinizing.Hormone.	-0.01485	-0.05404	0.126016	0.436072	0.397456
	Lymphotoctin	0.150739	-0.04778	1.288881	0.385539	1.183994
	MCP.1	-0.12499	-0.04844	1.06611	0.380825	1.030208
	MCP.3	-0.27346	-0.11916	2.380938	0.965246	2.366109
	M.CSF	-0.26147	-0.35269	2.271413	2.971055	3.706994
40	probeID	p.CAN-vs-allOther.Set_1	p.CAN-vs-allOther.Set_2	p.CAN-vs-allOther.Meta	q.CAN-vs-allOther.Set_1	q.CAN-vs-allOther.Se
	FGF.basie	9.98E-05	0.005415	1.86E-06	0.000689	0.035838
	FGF.4	0.032651	0.198519	0.015484	0.042171	0.250612
	Fibrinogen	0.682744	0.955798	0.743588	0.344738	0.46176
45	IL.1	0.070077	0.050565	0.595598	0.408016	0.709662
	IL.2	-0.10788	0.121981	0.918932	0.988365	1.348662
	IL.3	-0.19105	0.15764	1.641322	1.281618	2.066831
	IL.4	-0.04844	-0.11819	0.411334	0.95738	0.967826
	IL.5	-0.08666	0.109681	0.737155	0.887849	1.149051
	IL.6	-0.0555	0.032485	0.471452	0.261992	0.518622
	IL.7	-0.27403	0.065044	2.386205	0.525142	2.058632
	IL.8	-0.03602	-0.1344	0.305775	1.090194	0.987098
	IL.9	-0.03602	-0.1344	0.305775	1.090194	0.987098
	IL.10	-0.44392	-0.10384	4.048377	0.840194	3.456741
50	IL.11	-0.03602	-0.1344	0.305775	1.090194	0.987098
	IL.12	-0.10788	0.121981	0.918932	0.988365	1.348662
	IL.13	-0.57651	-0.01601	5.576717	0.129079	4.034607
	IL.14	-0.31979	-0.10468	2.812157	0.847057	2.587454
	IL.15	-0.31979	-0.10468	2.812157	0.847057	2.587454
	IL.16	-0.15772	-0.29101	1.349599	2.415981	2.662667
	IL.17	-0.15772	-0.29101	1.349599	2.415981	2.662667
	IL.18	-0.19202	-0.21119	1.649835	1.728653	2.388952
	IL.19	-0.19202	-0.21119	1.649835	1.728653	2.388952
	IL.20	-0.19202	-0.21119	1.649835	1.728653	2.388952
55	IL.21	-0.19202	-0.21119	1.649835	1.728653	2.388952
	IL.22	-0.19202	-0.21119	1.649835	1.728653	2.388952
	IL.23	-0.19202	-0.21119	1.649835	1.728653	2.388952
	IL.24	-0.19202	-0.21119	1.649835	1.728653	2.388952
	IL.25	-0.19202	-0.21119	1.649835	1.728653	2.388952
	IL.26	-0.19202	-0.21119	1.649835	1.728653	2.388952
	IL.27	-0.19202	-0.21119	1.649835	1.728653	2.388952
	IL.28	-0.19202	-0.21119	1.649835	1.728653	2.388952
	IL.29	-0.19202	-0.21119	1.649835	1.728653	2.388952
	IL.30	-0.19202	-0.21119	1.649835	1.728653	2.388952

EP 2 806 272 A1

	FSH..Follicle.Stimulating.Hormone.	0.361385	0.64239	0.331571	0.24473	0.372969
	G.CSF	0.599498	0.001298	0.007685	0.333955	0.014317
	GLP.1.Total	0.060012	0.999356	0.183125	0.064261	0.472466
	Glucagon	0.115427	0.494072	0.110836	0.110289	0.338260
5	GST	0.017417	0.092151	0.004015	0.027331	0.178671
	GM.CSF	0.029895	0.398958	0.032917	0.039504	0.314716
	GRO.alpha	0.119289	0.178854	0.040382	0.112251	0.249248
	Growth.Hormone	0.269773	0.8813	0.376741	0.206847	0.443264
	Haptoglobin	0.543995	0.507812	0.371057	0.32607	0.339284
	HB.EGF	9.98E-05	0.542611	0.001288	0.000689	0.345330
	HCC.4	0.395931	0.837748	0.457522	0.261594	0.433193
10	HGF..Hepatocyte.growth.factor.	0.609837	0.286585	0.266392	0.335174	0.296895
	I.309	0.000835	0.319726	0.002027	0.003051	0.296895
	ICAM.1	0.362974	0.512608	0.269977	0.24473	0.339284
	IFN.gamma	0.602241	0.449343	0.367783	0.333955	0.336477
	IgA	0.34509	0.582885	0.292356	0.243549	0.355892
	IgE	0.550223	0.682172	0.477913	0.32607	0.389237
	IGF.BP.2	0.122107	0.084645	0.020801	0.113188	0.169772
15	IGF.1	0.626388	0.073812	0.107937	0.337728	0.162848
	IgM	0.021747	0.000744	5.41E-05	0.03141	0.011747
	IL.10	6.63E-05	0.399411	0.000547	0.000588	0.314716
	IL.12p40	0.083399	0.489984	0.087133	0.08779	0.338260
	IL.13	6.20E-08	0.896904	5.47E-05	1.93E-06	0.443264
	IL.15	0.005161	0.395579	0.009669	0.010684	4716
20	IL.16	0.176547	0.016059	0.007752	0.152287	7675
	IL.18	0.098857	0.083852	0.016896	0.100407	6977
	IL.1.alpha	0.439366	0.586093	0.352916	0.284244	5892
	IL.1.beta	0.928488	0.728586	0.758305	0.426132	1863
	IL.1.ra	0.561771	0.038994	0.061357	0.32607	3238
	IL.2	0.356929	0.321715	0.177445	0.24473	6895
	IL.3	0.100599	0.199186	0.03875	0.100407	0612
25	IL.4	0.679838	0.337082	0.333131	0.344738	7476
	IL.5	0.459751	0.373264	0.250535	0.294366	9219
30	IL.6	0.636234	0.792567	0.604024	0.337728	0.419667
	IL.7	0.017357	0.598208	0.039529	0.027331	0.358145
	IL.8	0.758992	0.274508	0.323594	0.371167	0.296895
	Insulin	0.126704	0.583688	0.142865	0.115722	0.355892
	Leptin	0.943099	0.31399	0.446986	0.427536	0.296895
	LH..Luteinizing.Hormone.	0.899374	0.661643	0.691031	0.423158	0.380806
	Lymphotactin	0.196739	0.698792	0.236415	0.162916	0.391962
35	MCP.1	0.285331	0.69487	0.302912	0.213504	0.391962
	MCP.3	0.017603	0.333136	0.017976	0.027331	0.297476
	M.CSF	0.023454	0.003179	0.00021	0.033105	0.024607
	probelD	cor.TX-vs- AR.Set_1	cor.TX-vs- AR.Set_2	Z.TX-vs- AR.Set_1	Z.TX-vs-AR.Meta AR.Set_2	
	MDC	0.020738	-0.00217	0.14219	0.01375	0.110266
	MIF	0.141713	0.364004	0.978121	2.412778	2.397727
40	MIP.1.alpha	0.271918	0.311548	1.912272	2.038147	2.793368
	MIP.1.beta	0.022338	0.272983	0.153165	1.771405	1.360876
	MMP.2	0.166311	0.184576	1.150864	1.180899	1.648805
	MMP.3	0.441913	0.448621	3.253728	3.054585	4.460651
	MMP.9	0.02408	0.115966	0.165113	0.73675	0.637713
	Myeloperoxidase	0.040536	0.113764	0.278052	0.722634	0.707592
45	Myoglobin	0.315895	0.324539	2.242354	2.129553	3.091405
	NGF.beta	-0.14286	0.117298	0.986124	0.745286	1.224292
	NrCAM	0.334256	0.394634	2.383111	2.63909	3.551232
	PAI.1	-0.07952	-0.04094	0.5463	0.259099	0.569503
	Pancreatic Polypeptide	0.110162	0.119287	0.758313	0.758045	1.072227
50	PAPP.A	0.260508	0.148734	1.828085	0.947706	1.96278
	PDGF	-0.24143	-0.10628	1.688463	0.674692	1.671003
	Progesterone	0.162804	0.408228	1.126152	2.741585	2.734903
	Prolactin	0.365822	0.193777	2.629764	1.241247	2.737218
	Prostate.Specific.Antigen..Free	0.07475	0.122761	0.513415	0.780348	0.914828
55						

5	Prostatic. Acid.Phos phatase	0.090012	-0.21533	0.618763	1.383534	1.415838
	PARC	0.160196	0.160555	1.107793	1.024304	1.50762
	Peptide.Y Y	0.454903	0.412226	3.365202	2.771987	4.339648
10	RANTES	-0.074	-0.08958	0.508249	0.568059	0.761065
	Resistin	0.445155	0.265246	3.281401	1.718656	3.535574
	Secretin	0.084473	0.219683	0.580499	1.412419	1.409206
	Serum.Am yloid.P	0.055371	0.388127	0.379994	2.59049	2.100449
15	SGOT	0.138216	-0.16549	0.953667	1.056337	1.421288
	SHBG	-0.16855	-0.22307	1.166651	1.434921	1.839589
	SOD	-0.02863	0.04003	0.196302	0.253307	0.317921
	Sortilin	0.105133	0.061774	0.723429	0.391191	0.788156
	sRAGE	-0.25618	0.01949	1.796305	0.12328	1.357352
20	Stem.Cell. Factor	0.414095	0.511028	3.020215	3.567812	4.658439
	Tenascin. C	0.315288	0.380769	2.237727	2.535887	3.375455
	Testostero ne	0.07893	0.021649	0.542242	0.136939	0.480253
25	TGF.alpha	-0.13341	0.285182	0.920091	1.855082	1.962343
	TGF.b3	-0.08839	0.132805	0.607575	0.844925	1.027072
	Thrombop oietin	-0.39584	-0.2175	2.870466	1.397888	3.018182
	TECK	0.187007	0.440059	1.297326	2.987114	3.029556
30	Thyroid.St imulating. Hormone	-0.04246	-0.26793	0.291238	1.73696	1.434152
	Thyroxine. Binding.Gl obulin	-0.31751	-0.29424	2.254635	1.917629	2.950236
35	TIMP.1	0.287496	0.473723	2.02814	3.256258	3.736634
	Tissue.Fa ctor	0.073635	-0.05403	0.505732	0.342037	0.599463
	TNF.RII	0.565472	0.609502	4.393389	4.478595	6.273439
40	TNF.alpha	0.33396	0.380832	2.380825	2.536354	3.476971
	TNF.beta	0.055466	-0.13252	0.380644	0.843087	0.865309

45

50

55

TRAIL.R3 0.437182 0.291242 3.213527 1.89688 3.613604
VCAM.1 0.444814 0.329508 3.278484 2.164746 3.848945
VEGF 0.515781 0.550142 3.911663 3.912274 5.532359
von.Willeb 0.122292 0.417867 0.842611 2.815093 2.586388
rand.Fact
or

probelD	p.TX-vs- AR.Set_1	p.TX-vs- AR.Set_2	p.TX-vs- AR.Meta	q.TX-vs- AR.Set_1	q.TX-vs- AR.Set_2	q.TX-vs- AR.Meta
MDC	0.886335	0.988961	0.912198	0.374357	0.556195	0.05684
MIF	0.326255	0.016415	0.016497	0.227793	0.040389	0.003115
MIP.1alph a	0.056097	0.041983	0.005216	0.086356	0.082641	0.00123
MIP.1beta	0.877629	0.076539	0.173553	0.374357	0.128222	0.017121
MMP.2	0.248371	0.236058	0.099188	0.204286	0.26552	0.011537
MMP.3	0.001314	0.002551	8.17E-06	0.007335	0.015448	7.92E-06
MMP.9	0.868168	0.458974	0.52366	0.374047	0.360957	0.037754
Myelopero xidase	0.779864	0.467606	0.479199	0.351953	0.360957	0.035171
Myoglobin	0.025431	0.03373	0.001992	0.052262	0.06989	0.000617
NGF.beta	0.322325	0.453798	0.220842	0.227793	0.360957	0.021171
NrCAM	0.01767	0.008825	0.000383	0.043958	0.025734	0.000152
PAI.1	0.583057	0.794334	0.569015	0.312583	0.500046	0.039324
Pancreatic .Polypepti de	0.446307	0.446124	0.283618	0.272928	0.360957	0.024991
PAPP.A	0.067674	0.341157	0.049672	0.098686	0.316638	0.007111
PDGF	0.091211	0.497592	0.094721	0.115273	0.36961	0.011319
Progeste rone	0.258628	0.006576	0.00624	0.204286	0.020566	0.001396
Prolactin	0.008987	0.213103	0.006196	0.025554	0.250433	0.001396
Prostate.S pecific.Ant igen..Free	0.605915	0.432892	0.360282	0.312583	0.358783	0.029933
Prostatic. Acid.Phos phatase	0.534176	0.165519	0.156823	0.306864	0.213645	0.015908
PARC	0.266437	0.303715	0.131652	0.207572	0.297054	0.014356

	Peptide.Y Y	0.000903	0.006018	1.43E-05	0.007335	0.020566	1.24E-05
5	RANTES	0.609542	0.567838	0.446618	0.312583	0.40645	0.0333
	Resistin	0.001198	0.08561	0.000407	0.007335	0.132169	0.000154
	Secretin	0.559726	0.156931	0.158774	0.309054	0.209428	0.01592
	Serum.Am yloid.P	0.702518	0.010117	0.035689	0.332945	0.027849	0.005535
10	SGOT	0.338455	0.288909	0.155233	0.227793	0.297054	0.015908
	SHBG	0.241971	0.150482	0.065829	0.20397	0.204283	0.008701
	SOD	0.843565	0.798831	0.750545	0.366221	0.500046	0.047791
	Sortilin	0.46746	0.693936	0.430606	0.279845	0.46574	0.032664
	sRAGE	0.072532	0.901276	0.17467	0.103126	0.533559	0.017121
15	Stem.Cell. Factor	0.002794	0.000462	3.19E-06	0.011351	0.003639	3.97E-06
	Tenascin. C	0.025731	0.011769	0.000737	0.052262	0.029893	0.000257
	Testostero ne	0.585856	0.890405	0.631047	0.312583	0.533559	0.042674
20	TGF.alpha	0.355683	0.063788	0.049723	0.235213	0.111609	0.007111
	TGF.b3	0.541585	0.395898	0.304386	0.308009	0.347248	0.026291
	Thrombop oietin	0.004435	0.161208	0.002543	0.015765	0.211549	0.000693
	TECK	0.193463	0.003148	0.002449	0.183376	0.015517	0.000689
25	Thyroid.St imulating. Hormone	0.769716	0.082367	0.151529	0.3502	0.129706	0.015737
	Thyroxine. Binding.Gl obulin	0.024652	0.05546	0.003175	0.052262	0.101552	0.000815
30	TIMP.1	0.042924	0.001333	0.000186	0.075	0.008748	0.000102
	Tissue.Fa ctor	0.611313	0.730772	0.548864	0.312583	0.483516	0.038927
	TNF.RII	1.88E-05	1.44E-05	3.53E-10	0.000356	0.000566	1.54E-09
35	TNF.alpha	0.017777	0.011754	0.000507	0.043958	0.029893	0.000184
	TNF.beta	0.702034	0.396923	0.386869	0.332945	0.347248	0.030154
	TRAIL.R3	0.001501	0.058115	0.000302	0.007335	0.103994	0.000138
	VCAM.1	0.00121	0.03095	0.000119	0.007335	0.067691	6.90E-05
	VEGF	0.000126	0.000133	3.16E-08	0.001197	0.001491	6.89E-08
40	von.Willeb	0.397526	0.0053	0.009699	0.254022	0.019871	0.001968

45

50

55

rand.Fact
or

5

10

15

20

25

30

35

40

45

50

55

probeID	cor.TX-vs- CAN.Set_ 1	cor.TX-vs- CAN.Set_ 2	Z.TX-vs- CAN.Set_ 1	Z.TX-vs- CAN.Set_ 2	Z.TX-vs-CAN.Meta
MDC	0.184673	-0.20418	1.280746	1.30977	1.831771
MIF	-0.03028	0.173263	0.207656	1.106978	0.929587
MIP.1alpha	0.313204	0.271348	2.221875	1.760243	2.815783
MIP.1beta	-0.04866	0.217295	0.333889	1.396561	1.223613
MMP.2	0.289563	0.218129	2.043599	1.402093	2.436472
MMP.3	0.590033	0.498382	4.646195	3.460484	5.732288
MMP.9	0.147526	-0.0469	1.018823	0.29681	0.930293
Myeloperoxidase	-0.32289	0.164726	2.295728	1.051399	2.366777
Myoglobin	0.485366	0.439982	3.633357	2.986508	4.680952
NGF.beta	-0.14286	0.289265	0.986124	1.883221	2.028934
NrCAM	0.4261	0.387812	3.120157	2.588144	4.036379
PAI.1	-0.24008	0.078037	1.678639	0.494557	1.536681
Pancreatic Polypeptide	0.334016	0.318936	2.381255	2.090024	3.161671
PAPP.A	0.371781	0.036952	2.677054	0.233814	2.058295
PDGF	-0.35852	0.1521	2.572147	0.969488	2.504314
Progesterone	0.112085	0.140025	0.771657	0.891451	1.175995
Prolactin	0.606472	0.30348	4.821735	1.981791	4.810819
Prostate.Specific.Antigen..Free	0.171232	0.083955	1.185586	0.532233	1.214682
Prostatic.Acid.Phosphatase	0.125276	-0.34453	0.863383	2.271932	2.217002
PARC	0.155144	-0.10163	1.072272	0.645016	1.214306
Peptide.Y.Y	0.305702	0.359425	2.165	2.379455	3.213415
RANTES	-0.37216	0.036513	2.680046	0.231032	2.058443

EP 2 806 272 A1

	Resistin	0.741489	0.465578	6.538783	3.190168	6.879407
	Secretin	0.223501	0.236074	1.558552	1.521769	2.178115
5	Serum.Am yloid.P	-0.10503	0.184815	0.722717	1.182458	1.347162
	SGOT	0.478992	-0.11072	3.576428	0.703143	3.026114
	SHBG	0.361378	0.086673	2.594657	0.549548	2.223289
	SOD	-0.64202	0.10839	5.221275	0.688222	4.178645
10	Sortilin	-0.20894	0.031076	1.453793	0.196605	1.167008
	sRAGE	0.194518	0.018859	1.350757	0.119287	1.039478
	Stem.Cell. Factor	0.621128	0.653251	4.982956	4.939153	7.01599
	Tenascin. C	0.315348	0.448986	2.238184	3.057479	3.744599
15	Testostero ne	-0.06065	-0.233	0.41628	1.50117	1.355842
	TGF.alpha	-0.06146	0.318665	0.421897	2.08812	1.774849
	TGF.b3	0.026359	0.185642	0.180747	1.187878	0.967764
20	Thrombop oietin	-0.31356	-0.38236	2.224602	2.547646	3.374489
	TECK	0.32947	0.334517	2.346236	2.200346	3.214919
	Thyroid.St imulating. Hormone	0.050745	-0.31956	0.348192	2.094415	1.727184
25	Thyroxine. Binding.Gl obulin	0.043194	-0.07695	0.29631	0.487635	0.554333
	TIMP.1	0.169449	0.399849	1.172995	2.678252	2.723243
30	Tissue.Fa ctor	0.297355	0.047158	2.10205	0.298473	1.697426
	TNF.RII	0.68866	0.680426	5.795793	5.248792	7.8097
	TNF.alpha	0.386616	0.31424	2.795844	2.057015	3.431489
	TNF.beta	2.08E-17	-0.02166	0	0.136981	0.09686
35	TRAIL.R3	0.607785	0.409098	4.835988	2.748192	5.362825
	VCAM.1	0.510293	0.382044	3.860593	2.545326	4.529669
	VEGF	0.691197	0.727241	5.828977	5.83659	8.248802
	von.Willeb rand.Fact or	0.009654	0.412935	0.066189	2.777391	2.010714

	probeID	p.TX-vs- CAN.Set_ 1	p.TX-vs- CAN.Set_ 2	p.TX-vs- CAN.Meta	q.TX-vs- CAN.Set_ 1	q.TX-vs- CAN.Set_ 2	q.TX-vs- CAN.Meta
5	MDC	0.199184	0.189067	0.066986	0.171894	0.179082	0.007235
	MIF	0.834645	0.266521	0.352585	0.487639	0.206125	0.024971
	MIP.1alpha	0.026779	0.078389	0.004866	0.038441	0.096979	0.000914
	MIP.1beta	0.73717	0.161603	0.221098	0.448937	0.160596	0.017644
10	MMP.2	0.041384	0.159961	0.014831	0.055357	0.160596	0.002288
	MMP.3	6.50E-06	0.000671	9.91E-09	3.25E-05	0.003697	1.22E-08
	MMP.9	0.306596	0.765233	0.352219	0.234349	0.372511	0.024971
	Myeloperoxidase	0.022193	0.291158	0.017944	0.034634	0.210119	0.002628
15	Myoglobin	0.000353	0.003154	2.86E-06	0.001244	0.010621	1.45E-06
	NGF.beta	0.322325	0.05992	0.042465	0.243883	0.080719	0.004962
	NrCAM	0.002033	0.010183	5.43E-05	0.005077	0.025721	1.95E-05
	PAI.1	0.093091	0.618903	0.124371	0.104077	0.323211	0.011306
20	Pancreatic .Polypeptide	0.017757	0.037109	0.001569	0.028916	0.057945	0.000339
	PAPP.A	0.007851	0.814012	0.039562	0.015078	0.377854	0.004748
	PDGF	0.01057	0.330217	0.012269	0.017994	0.224918	0.001927
	Progesterone	0.438363	0.370482	0.239597	0.315736	0.246337	0.01865
25	Prolactin	3.04E-06	0.04789	1.50E-06	1.75E-05	0.067513	8.66E-07
	Prostate.Specific.Antigen..Free	0.23445	0.592473	0.224487	0.1908	0.321288	0.017644
30	Prostatic.Acid.Phosphatase	0.386024	0.023671	0.026623	0.28349	0.043483	0.003594
	PARC	0.282009	0.516661	0.224631	0.217778	0.295471	0.017644
	Peptide.Y.Y	0.030854	0.017925	0.001312	0.0428	0.03622	0.000291
35	RANTES	0.007783	0.816185	0.039548	0.015078	0.377854	0.004748
	Resistin	7.31E-10	0.001654	6.01E-12	5.47E-08	0.007164	8.65E-12
	Secretin	0.118706	0.127494	0.029397	0.120161	0.145824	0.003908
	Serum.Am	0.467898	0.235443	0.177928	0.33065	0.193128	0.015072

	ylويد.P						
	SGOT	0.000433	0.479673	0.002477	0.001381	0.291815	0.000522
5	SHBG	0.009924	0.580505	0.026196	0.017287	0.321288	0.003593
	SOD	5.03E-07	0.489026	2.93E-05	4.38E-06	0.291815	1.13E-05
	Sortilin	0.145351	0.843184	0.243207	0.140169	0.387226	0.018762
	sRAGE	0.175855	0.904459	0.298582	0.163295	0.404243	0.021679
	Stem.Cell. Factor	1.49E-06	2.05E-06	2.28E-12	1.01E-05	2.48E-05	3.95E-12
10	Tenascin. C	0.025701	0.002527	0.000181	0.038441	0.009013	5.20E-05
	Testostero ne	0.675675	0.132679	0.17515	0.428923	0.146794	0.014983
15	TGF.alpha	0.671556	0.037279	0.075923	0.428923	0.057945	0.007903
	TGF.b3	0.855818	0.233316	0.333162	0.492675	0.193128	0.023988
	Thrombop oietin	0.026596	0.011394	0.00074	0.038441	0.026737	0.000173
	TECK	0.019469	0.028341	0.001305	0.031029	0.049956	0.000291
20	Thyroid.St imulating. Hormone	0.726358	0.03672	0.084135	0.445978	0.057945	0.008453
	Thyroxine. Binding.Gl obulin	0.765822	0.623815	0.579351	0.458924	0.323211	0.038212
25	TIMP.1	0.239432	0.007894	0.006464	0.1908	0.020807	0.001188
	Tissue.Fa ctor	0.035982	0.763957	0.089616	0.049006	0.372511	0.0089
	TNF.RII	3.24E-08	5.17E-07	5.73E-15	4.04E-07	7.84E-06	1.34E-14
30	TNF.alpha	0.005548	0.040151	0.0006	0.011231	0.059364	0.000148
	TNF.beta	1	0.890371	0.922837	0.535051	0.402793	0.056954
	TRAIL.R3	2.85E-06	0.006451	8.19E-08	1.75E-05	0.017776	7.87E-08
	VCAM.1	0.000153	0.011467	5.91E-06	0.000574	0.026737	2.69E-06
	VEGF	2.75E-08	3.33E-08	1.60E-16	4.04E-07	1.58E-06	9.46E-16
35	von.Willeb rand.Fact or	0.946947	0.005923	0.044356	0.521567	0.017098	0.00511

probelD	cor.AR-vs-	cor.AR-vs-	Z.AR-vs-	Z.AR-vs-	Z.AR-vs-
	CAN.Set_	CAN.Set_	CAN.Set_	CAN.Set_	CAN.Meta

	1	2	1	2	
5	MDC	0.103413	-0.167	0.711505	1.155692 1.320308
	MIF	-0.10158	-0.1924	0.698807	1.335643 1.438573
	MIP.1alph	0.045648	-0.02223	0.313167	0.152442 0.329236
	a				
	MIP.1beta	-0.04728	-0.04417	0.324356	0.303 0.443608
10	MMP.2	0.161158	0.121929	1.114561	0.840083 1.382142
	MMP.3	0.125146	0.076195	0.862482	0.523379 0.979952
	MMP.9	0.110438	-0.14408	0.760225	0.994719 1.240933
	Myelopero	-0.4953	0.040019	3.723039	0.274501 2.826688
	xidase				
	Myoglobin	0.280657	0.197606	1.977136	1.37278 2.368748
15	NGF.beta	NA	0.017836	NA	0.12229 0.12229
	NrCAM	0.087839	0.028086	0.603747	0.192599 0.563102
	PAI.1	-0.16141	0.128355	1.116356	0.88484 1.415059
	Pancreatic	0.187375	0.17151	1.299934	1.187552 1.758919
	.Polypepti				
20	de				
	PAPP.A	0.092539	-0.14486	0.636233	1.000163 1.157106
	PDGF	-0.02785	0.241131	0.190953	1.686315 1.327429
	Progester	-0.07019	-0.25156	0.481967	1.76246 1.58705
	one				
25	Prolactin	0.442612	0.162334	3.259687	1.122836 3.098911
	Prostate.S	0.145264	-0.35282	1.002975	2.527376 2.496336
	pecific.Ant				
	igen..Free				
	Prostatic.	-0.02486	-0.13245	0.170494	0.913422 0.766444
30	Acid.Phos				
	phatase				
	PARC	-0.0276	-0.16478	0.189263	1.140064 0.939976
	Peptide.Y	0.011431	-0.05506	0.078371	0.377834 0.322586
	Y				
35	RANTES	-0.22576	0.137612	1.574834	0.949447 1.784936
	Resistin	0.300631	0.209598	2.126714	1.458547 2.535163
	Secretin	0.086681	-0.01147	0.595753	0.078617 0.476852
	Serum.Am	-0.15056	-0.27262	1.040095	1.917472 2.091316
	yloid.P				
40	SGOT	0.258178	0.048635	1.810955	0.333687 1.516491

	SHBG	0.424867	0.224435	3.109835	1.565293	3.305814
	SOD	-0.58662	0.125594	4.610396	0.865603	3.872116
5	Sortilin	-0.31869	-0.03931	2.263645	0.269604	1.791278
	sRAGE	0.316927	0.001461	2.25021	0.010013	1.598219
	Stem.Cell. Factor	0.236723	0.24356	1.654269	1.704009	2.374661
	Tenascin. C	0.058677	0.182305	0.402735	1.263948	1.178523
10	Testostero ne	-0.16059	-0.29424	1.110594	2.078635	2.255126
	TGF.alpha	0.18877	0.032865	1.309849	0.22539	1.085578
	TGF.b3	0.115033	0.085377	0.792132	0.586742	0.975012
15	Thrombop oietin	0.138222	-0.17447	0.953708	1.208463	1.528886
	TECK	0.117975	-0.01031	0.812578	0.070668	0.624549
	Thyroid.St imulating. Hormone	0.105729	-0.10608	0.72756	0.730024	1.030667
20	Thyroxine. Binding.Gl obulin	0.399715	0.22207	2.902068	1.548231	3.146837
	TIMP.1	-0.14848	-0.03518	1.025495	0.241276	0.895742
25	Tissue.Fa ctor	0.309481	0.100877	2.193614	0.69394	2.041809
	TNF.RII	0.150577	0.272693	1.040216	1.918015	2.091785
	TNF.alpha	0.095617	-0.07475	0.657525	0.513393	0.827964
	TNF.beta	-0.05864	0.077571	0.402446	0.532868	0.661367
30	TRAIL.R3	0.228393	0.175987	1.593894	1.219199	1.989157
	VCAM.1	-0.01033	0.122415	0.070845	0.843465	0.646515
	VEGF	0.344022	0.269567	2.458765	1.894885	3.078495
	von.Willeb rand.Fact or	-0.13041	-0.01308	0.899169	0.089651	0.699201

probeID	p.AR-vs- CAN.Set_ 1	p.AR-vs- CAN.Set_ 2	p.AR-vs- CAN.Meta	q.AR-vs- CAN.Set_ 1	q.AR-vs- CAN.Set_ 2	q.AR-vs- CAN.Meta
MDC	0.474818	0.246401	0.186732	0.482798	0.70734	0.012673

	MIF	0.482723	0.180709	0.150272	0.483563	0.67953	0.012314
	MIP.1alpha	0.752927	0.878202	0.741978	0.596784	0.886847	0.027883
5	MIP.1beta	0.744405	0.760696	0.657326	0.596784	0.865859	0.026983
	MMP.2	0.26354	0.398941	0.166928	0.39584	0.718387	0.012314
	MMP.3	0.386519	0.598946	0.32711	0.43615	0.841836	0.017117
	MMP.9	0.445164	0.31814	0.214631	0.462817	0.718387	0.013656
10	Myeloperoxidase	0.000255	0.782603	0.004703	0.005903	0.865859	0.001911
	Myoglobin	0.048356	0.16896	0.017848	0.186431	0.654602	0.003955
	NGF.beta	NA	0.902155	0.902669	NA	0.886847	0.032819
	NrCAM	0.544132	0.846478	0.573366	0.513556	0.866332	0.02412
15	PAI.1	0.262774	0.374361	0.157051	0.39584	0.718387	0.012314
	Pancreatic .Polypeptide	0.192574	0.233679	0.078591	0.349387	0.70734	0.008511
	PAPP.A	0.522712	0.315508	0.247229	0.498621	0.718387	0.014633
20	PDGF	0.847774	0.091619	0.184367	0.628537	0.554576	0.012673
	Progesterone	0.628145	0.07802	0.112501	0.54399	0.554576	0.010805
	Prolactin	0.001288	0.260026	0.001942	0.023839	0.70734	0.001324
	Prostate.Specific.Antigen..Free	0.314154	0.011968	0.012548	0.417256	0.348404	0.003757
25	Prostatic.Acid.Phosphatase	0.863914	0.35917	0.443412	0.634424	0.718387	0.020733
	PARC	0.849105	0.252817	0.34723	0.628537	0.70734	0.017853
30	Peptide.Y.Y	0.937201	0.704128	0.747009	0.645313	0.865859	0.027883
	RANTES	0.114936	0.340591	0.074272	0.253214	0.718387	0.008329
	Resistin	0.033892	0.144049	0.01124	0.142544	0.613899	0.003576
	Secretin	0.549469	0.937005	0.633468	0.513556	0.886847	0.026215
35	Serum.Amyloid.P	0.296644	0.05544	0.0365	0.417256	0.554576	0.005993
	SGOT	0.070258	0.737323	0.129395	0.218273	0.865859	0.011975
	SHBG	0.002102	0.117134	0.000947	0.027785	0.566686	0.000964
40	SOD	7.57E-06	0.384807	0.000108	0.000701	0.718387	0.000275

5	Sortilin	0.024093	0.786385	0.073249	0.123421	0.865859	0.008329
	sRAGE	0.02493	0.991968	0.109994	0.123421	0.905896	0.010767
	Stem.Cell. Factor	0.097891	0.088298	0.017565	0.244804	0.554576	0.003955
	Tenascin. C	0.685649	0.205107	0.238588	0.576931	0.70734	0.014618
10	Testostero ne	0.265235	0.038068	0.024125	0.39584	0.554576	0.004912
	TGF.alpha	0.189223	0.820757	0.277666	0.349387	0.865859	0.015704
	TGF.b3	0.426336	0.555517	0.329555	0.458704	0.841836	0.017117
	Thrombop oietin	0.338435	0.225589	0.126293	0.417256	0.70734	0.011904
15	TECK	0.414521	0.943363	0.532267	0.45124	0.886847	0.022767
	Thyroid.St imulating. Hormone	0.464926	0.463419	0.302697	0.477993	0.789428	0.016218
20	Thyroxine. Binding.Gl obulin	0.004029	0.121146	0.00165	0.046602	0.566686	0.001324
	TIMP.1	0.303451	0.808363	0.37039	0.417256	0.865859	0.018666
	Tissue.Fa ctor	0.028741	0.485772	0.04117	0.126639	0.796072	0.00635
25	TNF.RII	0.296588	0.055372	0.036458	0.417256	0.554576	0.005993
	TNF.alpha	0.508915	0.605931	0.407691	0.493124	0.841836	0.019764
	TNF.beta	0.685862	0.592344	0.508377	0.576931	0.841836	0.022243
	TRAIL.R3	0.110645	0.221515	0.046684	0.253214	0.70734	0.006601
	VCAM.1	0.943221	0.397049	0.517946	0.645313	0.718387	0.022342
30	VEGF	0.014435	0.058341	0.00208	0.102742	0.554576	0.001324
	von.Willeb rand.Fact or	0.366696	0.928185	0.484426	0.427173	0.886847	0.021821
35	probeID	cor.TX-vs- allOther.S et_1	cor.TX-vs- allOther.S et_2	Z.TX-vs- allOther.S et_1	Z.TX-vs- allOther.S et_2	Z.TX-vs- allOther.Meta	
	MDC	0.085351	-0.08747	0.725997	0.706989	1.013274	
	MIF	0.016748	0.262886	0.142128	2.170413	1.635214	
40	MIP.1alph	0.28169	0.253312	2.456629	2.087715	3.213336	

a

MIP.1beta	-0.0122	0.213583	0.103531	1.748883	1.309854
MMP.2	0.216655	0.190024	1.867983	1.550873	2.417496
MMP.3	0.477651	0.433179	4.411809	3.7393	5.763705
MMP.9	0.080224	0.024681	0.682187	0.199023	0.62311
Myeloperoxidase	-0.14194	0.121186	1.212547	0.981862	1.551681
Myoglobin	0.370785	0.34722	3.303594	2.920786	4.401301
NGF.beta	-0.1644	0.130386	1.407747	1.057225	1.742999
NrCAM	0.356109	0.343946	3.160111	2.890808	4.278646
PAI.1	-0.15094	0.024729	1.290667	0.199409	1.053643
Pancreatic .Polypeptide	0.23187	0.210082	2.003922	1.719335	2.63274
PAPP.A	0.306516	0.191152	2.687255	1.560309	3.003482
PDGF	-0.28215	0.025756	2.460882	0.207698	1.886971
Progesterone	0.150933	0.242195	1.290568	1.99222	2.321282
Prolactin	0.454698	0.199473	4.162936	1.630054	4.096262
Prostate.Specific.Antigen..Free	0.109009	-0.04202	0.928658	0.338956	0.896338
Prostatic.Acid.Phosphatase	0.072363	-0.25033	0.615094	2.062057	1.893032
PARC	0.148516	0.043472	1.269588	0.350704	1.14572
Peptide.Y.Y	0.363236	0.34968	3.229568	2.943362	4.364921
RANTES	-0.20822	-0.02349	1.793052	0.189391	1.401799
Resistin	0.518695	0.323071	4.875244	2.701438	5.357523
Secretin	0.125258	0.189078	1.068462	1.542963	1.846556
Serum.Amyloid.P	-0.01967	0.242773	0.166901	1.997174	1.530232
SGOT	0.264746	-0.12352	2.301251	1.000984	2.335033
SHBG	0.112484	-0.06857	0.958512	0.553691	1.069289
SOD	-0.30918	0.08366	2.712198	0.676069	2.395867
Sortilin	-0.04429	0.034962	0.376087	0.28199	0.465331
sRAGE	-0.05465	0.019511	0.464221	0.15732	0.439496

	Stem.Cell. Factor	0.485245	0.5154	4.49569	4.595932	6.428748	
5	Tenascin. C	0.304279	0.39645	2.66632	3.381555	4.276493	
	Testostero ne	0.007738	-0.09854	0.065663	0.797077	0.61005	
	TGF.alpha	-0.10708	0.274568	0.912099	2.271924	2.251444	
10	TGF.b3	-0.02423	0.129616	0.205642	1.050909	0.888516	
	Thrombop oietin	-0.33237	-0.23915	2.931586	1.966158	3.463228	
	TECK	0.214433	0.339491	1.848212	2.850142	3.322237	
	Thyroid.St imulating. Hormone	1.53E-05	-0.25996	0.000129	2.145112	1.516914	
15	Thyroxine. Binding.Gl obulin	-0.13412	-0.17346	1.144912	1.412786	1.808566	
	TIMP.1	0.21861	0.391884	1.88539	3.33797	3.693474	
20	Tissue.Fa ctor	0.149151	0.002911	1.275101	0.023467	0.918226	
	TNF.RII	0.58186	0.578802	5.645007	5.326405	7.757959	
	TNF.alpha	0.342067	0.309458	3.024426	2.579487	3.962565	
25	TNF.beta	0.027471	-0.05735	0.233157	0.462882	0.492174	
	TRAIL.R3	0.480544	0.32049	4.443666	2.67823	5.035941	
	VCAM.1	0.441897	0.315102	4.026989	2.62991	4.707138	
	VEGF	0.590959	0.581946	5.76268	5.364633	7.868198	
30	von.Willeb rand.Fact or	0.060914	0.38273	0.51751	3.251136	2.664835	
	probeID	p.TX-vs- allOther.S et_1	p.TX-vs- allOther.S et_2	p.TX-vs- allOther.M eta	q.TX-vs- allOther.S et_1	q.TX-vs- allOther.S et_2	q.TX-vs- allOther.M eta
35	MDC	0.466565	0.478162	0.310929	0.338171	0.293162	0.001164
	MIF	0.886591	0.030321	0.102004	0.511167	0.046236	0.000517
	MIP.1alph a	0.014352	0.037136	0.001312	0.028744	0.052583	1.53E-05
40	MIP.1beta	0.917257	0.080319	0.190245	0.517096	0.086848	0.000811

	MMP.2	0.061899	0.120637	0.015628	0.082646	0.110375	0.000118
	MMP.3	1.47E-05	0.000224	8.23E-09	0.000124	0.001483	5.91E-10
5	MMP.9	0.493853	0.841653	0.533212	0.349051	0.38204	0.001852
	Myeloperoxidase	0.224477	0.324901	0.120739	0.208339	0.220019	0.000598
	Myoglobin	0.001058	0.00372	1.08E-05	0.003833	0.009217	2.73E-07
	NGF.beta	0.158707	0.28924	0.081334	0.172549	0.213937	0.000433
10	NrCAM	0.001715	0.004081	1.88E-05	0.005437	0.009708	3.89E-07
	PAI.1	0.196122	0.841349	0.292046	0.196946	0.38204	0.001111
	Pancreatic .Polypeptide	0.045318	0.085522	0.00847	0.066325	0.090822	6.89E-05
15	PAPP.A	0.007481	0.118408	0.002669	0.017792	0.110028	2.87E-05
	PDGF	0.014186	0.834849	0.059164	0.028744	0.38204	0.000354
	Progesterone	0.196156	0.046602	0.020272	0.196946	0.057739	0.000141
	Prolactin	4.16E-05	0.102926	4.20E-05	0.000226	0.105536	7.86E-07
20	Prostate.Specific.Antigen..Free	0.351872	0.733697	0.370072	0.279482	0.357652	0.001351
	Prostatic. Acid.Phosphatase	0.537258	0.039502	0.058354	0.37171	0.052683	0.000354
25	PARC	0.203498	0.724838	0.251911	0.197695	0.357652	0.000987
	Peptide.Y Y	0.00136	0.003467	1.27E-05	0.004704	0.008965	3.04E-07
	RANTES	0.073024	0.849221	0.160975	0.092798	0.38204	0.000722
30	Resistin	1.87E-06	0.007206	8.44E-08	2.37E-05	0.015304	4.31E-09
	Secretin	0.284272	0.122531	0.064811	0.237743	0.110409	0.000372
	Serum.Amyloid.P	0.866995	0.046065	0.125959	0.50756	0.057739	0.000603
	SGOT	0.021711	0.315591	0.019542	0.039342	0.220019	0.000138
35	SHBG	0.336638	0.57848	0.284939	0.275482	0.334006	0.001096
	SOD	0.006954	0.497595	0.016581	0.01764	0.298913	0.000121
	Sortilin	0.705926	0.77714	0.641695	0.440365	0.369737	0.002115
	sRAGE	0.641416	0.874519	0.660302	0.416381	0.385247	0.002123
40	Stem.Cell. Factor	1.02E-05	6.87E-06	1.29E-10	0.000111	8.18E-05	1.11E-11

	Tenascin. C	0.007951	0.000817	1.90E-05	0.018338	0.003038	3.89E-07
5	Testostero ne	0.947465	0.424	0.541829	0.526328	0.271136	0.001867
	TGF.alpha	0.360509	0.023457	0.024357	0.282852	0.037703	0.000159
	TGF.b3	0.83652	0.292123	0.374263	0.501287	0.213937	0.001355
10	Thrombop oietin	0.003575	0.049516	0.000534	0.009718	0.060098	6.97E-06
	TECK	0.064688	0.004622	0.000893	0.084881	0.010573	1.10E-05
	Thyroid.St imulating. Hormone	0.999896	0.03228	0.129288	0.543552	0.047994	0.000605
15	Thyroxine. Binding.Gl obulin	0.251314	0.157174	0.070519	0.222398	0.133532	0.000393
	TIMP.1	0.059528	0.00095	0.000221	0.080899	0.003324	3.07E-06
	Tissue.Fa ctor	0.20155	0.981206	0.3585	0.197695	0.416808	0.00132
20	TNF.RII	4.38E-08	2.34E-07	8.63E-15	6.70E-07	3.49E-06	1.24E-15
	TNF.alpha	0.002666	0.010231	7.41E-05	0.007515	0.017896	1.28E-06
	TNF.beta	0.815021	0.642262	0.622596	0.49228	0.341034	0.002095
	TRAIL.R3	1.28E-05	0.00771	4.76E-07	0.000122	0.015811	1.58E-08
25	VCAM.1	7.22E-05	0.008864	2.51E-06	0.000366	0.017004	6.76E-08
	VEGF	2.38E-08	1.94E-07	3.60E-15	6.04E-07	3.49E-06	7.75E-16
	von.Willeb rand.Fact or	0.603656	0.001277	0.007703	0.39949	0.004218	6.64E-05
30	probelD	cor.AR-vs- allOther.S et_1	cor.AR-vs- allOther.S et_2	Z.AR-vs- allOther.S et_1	Z.AR-vs- allOther.S et_2	Z.AR-vs- allOther.Meta	
	MDC	0.044152	-0.10158	0.374886	0.821797	0.846182	
35	MIF	-0.07082	-0.26011	0.601937	2.146353	1.943335	
	MIP.1alph a	-0.11093	-0.13617	0.945173	1.104693	1.449474	
	MIP.1beta	-0.03377	-0.13205	0.286655	1.07088	0.959922	
	MMP.2	0.01271	-0.00345	0.107854	0.027818	0.095934	
40	MMP.3	-0.14378	-0.14949	1.228546	1.214319	1.727366	
45							
50							
55							

5	MMP.9	0.035644	-0.09215	0.302578	0.745027	0.740768
	Myeloperoxidase	-0.25356	-0.02434	2.199488	0.196244	1.694038
	Myoglobin	-0.01328	-0.01769	0.112693	0.142663	0.180564
	NGF.beta	0.082199	-0.04409	0.699063	0.355716	0.745841
	NrCAM	-0.09995	-0.1394	0.85092	1.131277	1.401625
10	PAI.1	-0.03942	0.09006	0.334695	0.72806	0.751481
	Pancreatic .Polypeptide	0.024146	0.071138	0.204922	0.574506	0.551139
	PAPP.A	-0.0615	-0.19526	0.522541	1.594702	1.497117
15	PDGF	0.11224	0.175323	0.956416	1.428259	1.68622
	Progesterone	-0.10165	-0.31134	0.865538	2.596236	2.447844
	Prolactin	0.052892	0.016995	0.449223	0.137034	0.414547
	Prostate.Specific.Antigen..Free	0.047086	-0.2301	0.399836	1.888941	1.61841
20	Prostatic .Acid .Phosphatase	-0.01399	0.000403	0.118733	0.003249	0.086255
	PARC	-0.09259	-0.17231	0.787868	1.403169	1.549298
25	Peptide.Y.Y	-0.21813	-0.21381	1.881145	1.750815	2.568184
	RANTES	-0.07018	0.105098	0.596467	0.850469	1.023138
	Resistin	-0.07343	-0.00506	0.624197	0.0408	0.470224
	Secretin	0.00886	-0.0961	0.075181	0.777203	0.602727
30	Serum.Amyloid.P	-0.10016	-0.32046	0.852751	2.677962	2.496591
	SGOT	0.060979	0.097092	0.518064	0.785253	0.921585
	SHBG	0.287531	0.214779	2.510558	1.758993	3.019029
	SOD	-0.26796	0.04512	2.330599	0.364018	1.905381
35	Sortilin	-0.19383	-0.04644	1.665734	0.37466	1.442776
	sRAGE	0.2925	-0.0175	2.556594	0.141099	1.907557
	Stem.Cell .Factor	-0.08241	-0.07763	0.700877	0.627097	0.939019
	Tenascin.C	-0.13667	-0.08143	1.166982	0.657936	1.290412
40	Testosterone	-0.1135	-0.17285	0.967285	1.407653	1.679335

45

50

55

ne

TGF.alpha	0.108733	-0.09836	0.926292	0.795538	1.217517
TGF.b3	0.089999	0.015428	0.765735	0.124393	0.629415
Thrombopoietin	0.240406	-0.03481	2.080632	0.280745	1.669746
TECK	-0.02747	-0.18083	0.233126	1.474139	1.207218
Thyroid.Stimulating.Hormone	0.072018	0.043569	0.612154	0.351487	0.681397
Thyroxine.Binding.Globulin	0.334454	0.248786	2.951476	2.048769	3.535707
TIMP.1	-0.20876	-0.2303	1.797789	1.890625	2.608103
Tissue.Factor	0.131736	0.075439	1.12435	0.609366	1.225922
TNF.RII	-0.16053	-0.08516	1.374063	0.688222	1.458256
TNF.alpha	-0.10733	-0.19093	0.914248	1.558468	1.748474
TNF.beta	-0.05494	0.086686	0.466667	0.700646	0.825415
TRAIL.R3	-0.09299	-0.02429	0.791365	0.195899	0.698101
VCAM.1	-0.17067	-0.06317	1.462463	0.510008	1.394748
VEGF	-0.06845	-0.06687	0.581686	0.53991	0.793088
von.Willebrand.Factor	-0.11453	-0.17101	0.976073	1.392382	1.674751

probeID	p.AR-vs-allOther.S et_1	p.AR-vs-allOther.S et_2	p.AR-vs-allOther.M eta	q.AR-vs-allOther.S et_1	q.AR-vs-allOther.S et_2	q.AR-vs-allOther.M eta
MDC	0.706821	0.409795	0.397451	0.620378	0.652575	0.091697
MIF	0.545991	0.032182	0.051976	0.553516	0.336243	0.041592
MIP.1alpha	0.343391	0.268195	0.147205	0.528951	0.528323	0.052399
MIP.1beta	0.773634	0.283075	0.337095	0.63491	0.528323	0.082684
MMP.2	0.913815	0.977722	0.923573	0.65242	0.806612	0.155457
MMP.3	0.218442	0.223713	0.084102	0.497507	0.523705	0.044623
MMP.9	0.761434	0.454841	0.458834	0.63491	0.663886	0.09809
Myeloperoxidase	0.028163	0.843835	0.090258	0.298848	0.779942	0.044623

	Myoglobin	0.909965	0.886125	0.85671	0.65242	0.779942	0.145716
	NGF.beta	0.483241	0.72107	0.455763	0.553516	0.756467	0.09809
5	NrCAM	0.393566	0.256883	0.161027	0.531527	0.528323	0.053526
	PAI.1	0.73701	0.465163	0.452363	0.63491	0.667466	0.09809
	Pancreatic .Polypepti de	0.837084	0.564293	0.581538	0.643381	0.713822	0.108408
10	PAPP.A	0.600144	0.110557	0.134363	0.572273	0.409994	0.051327
	PDGF	0.337693	0.152702	0.091753	0.528951	0.419531	0.044623
	Progester one	0.385504	0.009757	0.014371	0.531527	0.202616	0.022325
	Prolactin	0.65222	0.890589	0.678474	0.594262	0.779942	0.122557
15	Prostate.S pecific.Ant igen..Free	0.688308	0.059068	0.105574	0.609723	0.336243	0.04731
	Prostatic. Acid.Phos phatase	0.905161	0.997397	0.931264	0.65242	0.811089	0.155457
20	PARC	0.429502	0.160004	0.12131	0.54787	0.419531	0.049593
	Peptide.Y Y	0.060099	0.079989	0.010223	0.298848	0.364264	0.02106
	RANTES	0.549642	0.393682	0.306242	0.553516	0.652575	0.077566
25	Resistin	0.531258	0.96733	0.638195	0.553516	0.804034	0.116182
	Secretin	0.939863	0.435628	0.54669	0.652724	0.652575	0.103569
	Serum.Am yloid.P	0.392551	0.007716	0.012539	0.531527	0.202616	0.02106
	SGOT	0.603269	0.430896	0.356745	0.572273	0.652575	0.085351
30	SHBG	0.012373	0.0786	0.002536	0.256481	0.364264	0.014773
	SOD	0.02011	0.714844	0.056731	0.256481	0.756467	0.041592
	Sortilin	0.095669	0.70689	0.149084	0.356984	0.756467	0.052399
	sRAGE	0.01088	0.887365	0.056449	0.256481	0.779942	0.041592
	Stern.Cell. Factor	0.482107	0.52922	0.347721	0.553516	0.68467	0.084402
35	Tenascin. C	0.242319	0.509185	0.196908	0.497507	0.682001	0.061579
	Testostero ne	0.332243	0.15868	0.093087	0.528951	0.419531	0.044623
40	TGF.alpha	0.353098	0.424894	0.223407	0.528951	0.652575	0.063162
	TGF.b3	0.442559	0.900627	0.529077	0.553516	0.782712	0.102045

45

50

55

	Thrombopoietin	0.037748	0.778098	0.09497	0.298848	0.770309	0.044623
5	TECK	0.815046	0.140013	0.227348	0.643381	0.419531	0.063162
	Thyroid.Stimulating.Hormone	0.539204	0.724249	0.49562	0.553516	0.756467	0.09956
	Thyroxine.Binding.Globulin	0.00336	0.040776	0.000407	0.236366	0.336243	0.009477
10	TIMP.1	0.072275	0.058845	0.009105	0.314295	0.336243	0.02106
	Tissue.Factor	0.259902	0.540919	0.220228	0.497507	0.691943	0.063162
	TNF.RII	0.168866	0.489907	0.14477	0.42514	0.667466	0.052399
15	TNF.alpha	0.359381	0.11884	0.080382	0.528951	0.409994	0.044623
	TNF.beta	0.639661	0.482114	0.409136	0.594137	0.667466	0.09256
	TRAIL.R3	0.42746	0.844106	0.485114	0.54787	0.779942	0.099106
	VCAM.1	0.143207	0.608788	0.163092	0.42514	0.737338	0.053526
20	VEGF	0.559569	0.587964	0.427726	0.557643	0.723964	0.095835
	von.Willebrand.Factor	0.327879	0.163224	0.093983	0.528951	0.419531	0.044623
25	probeID	cor.CAN-vs-allOther.S et_1	cor.CAN-vs-allOther.S et_2	Z.CAN-vs-allOther.S et_1	Z.CAN-vs-allOther.S et_2	Z.CAN-vs-allOther.Meta	
	MDC	-0.1295	0.181611	1.105078	1.480622	1.828367	
30	MIF	0.054072	0.019567	0.459262	0.157778	0.436313	
	MIP.1.alpha	-0.17076	-0.09561	1.463268	0.77319	1.581414	
	MIP.1.beta	0.04597	-0.06338	0.390347	0.511637	0.637798	
	MMP.2	-0.22937	-0.17042	1.981477	1.387508	2.382232	
35	MMP.3	-0.33387	-0.24687	2.945889	2.032273	3.520092	
	MMP.9	-0.11587	0.069564	0.987606	0.561753	1.095563	
	Myeloperoxidase	0.395494	-0.08655	3.549356	0.699525	3.004413	
	Myoglobin	-0.3575	-0.30001	3.173678	2.495514	4.008724	
40	NGF.beta	0.082199	-0.07521	0.699063	0.607507	0.923885	

5	NrCAM	-0.25616	-0.1753	2.223113	1.428091	2.581792
	PAI.1	0.190368	-0.11269	1.635274	0.912383	1.801466
	Pancreatic .Polypepti de	-0.25602	-0.26336	2.221782	2.17453	3.108662
10	PAPP.A	-0.24501	0.020356	2.122164	0.16414	1.616661
	PDGF	0.169911	-0.19889	1.455865	1.625162	2.178615
	Progester one	-0.04928	0.089729	0.418499	0.725371	0.808838
	Prolactin	-0.50759	-0.19951	4.747326	1.630377	4.509717
15	Prostate.S pecific.Ant igen..Free	-0.15609	0.268545	1.335426	2.2195	2.513712
	Prostatic. Acid.Phos phatase	-0.05837	0.228648	0.495857	1.876594	1.677576
20	PARC	-0.05593	0.132529	0.475082	1.074804	1.095935
	Peptide.Y Y	-0.1451	-0.10614	1.239988	0.858987	1.484199
	RANTES	0.278402	-0.08361	2.426357	0.675646	2.193447
	Resistin	-0.44527	-0.29055	4.062575	2.41193	4.578167
25	Secretin	-0.13412	-0.0769	1.144928	0.621232	1.248864
	Serum.Am yloid.P	0.119828	0.098325	1.02168	0.795292	1.284793
	SGOT	-0.32572	0.01593	2.868346	0.128445	2.119051
	SHBG	-0.40001	-0.15204	3.594924	1.235355	3.415524
30	SOD	0.577136	-0.12167	5.584658	0.985806	4.646019
	Sortilin	0.238118	0.014447	2.060044	0.116485	1.539038
	sRAGE	-0.23785	-0.00035	2.057585	0.002844	1.456944
	Stem.Cell. Factor	-0.40283	-0.39396	3.62344	3.357771	4.936462
35	Tenascin. C	-0.16761	-0.28132	1.435763	2.330941	2.663461
	Testostero ne	0.105766	0.263012	0.900824	2.171504	2.172464
	TGF.alpha	-0.00165	-0.15287	0.014028	1.242231	0.888309
40	TGF.b3	-0.06577	-0.13403	0.558868	1.087087	1.163866
	Thrombop oietin	0.091965	0.253628	0.782556	2.090432	2.031509

45

50

55

EP 2 806 272 A1

	TECK	-0.18697	-0.1298	1.605344	1.052396	1.879306	
	Thyroid.Stimulating.Hormone	-0.07203	0.194295	0.612284	1.586624	1.554863	
5	Thyroxine.Binding.Globulin	-0.20034	-0.09007	1.723227	0.728136	1.733376	
	TIMP.1	-0.00985	-0.12827	0.083603	1.039904	0.794439	
10	Tissue.Factor	-0.28089	-0.0781	2.449232	0.630965	2.178028	
	TNF.RII	-0.42133	-0.44444	3.812464	3.851766	5.419429	
	TNF.alpha	-0.23474	-0.09222	2.029656	0.745616	1.962414	
	TNF.beta	0.027471	-0.03421	0.233157	0.275927	0.359977	
15	TRAIL.R3	-0.38755	-0.26895	3.469748	2.223041	4.02541	
	VCAM.1	-0.27123	-0.22514	2.360531	1.846785	2.975022	
	VEGF	-0.52251	-0.46561	4.919693	4.066991	6.354545	
	von.Willebrand.Factor	0.053613	-0.17919	0.455358	1.460421	1.35466	
20							
	probelD	p.CAN-vs-allOther.S et_1	p.CAN-vs-allOther.S et_2	p.CAN-vs-allOther.M eta	q.CAN-vs-allOther.S et_1	q.CAN-vs-allOther.S et_2	q.CAN-vs-allOther.M eta
25	MDC	0.268136	0.138288	0.067495	0.206847	0.223243	0.000181
	MIF	0.64498	0.874157	0.662609	0.338084	0.443265	0.000898
	MIP.1alpha	0.142988	0.437998	0.113783	0.128659	0.336477	0.000255
	MIP.1beta	0.695328	0.607646	0.523605	0.345474	0.358149	0.000749
30	MMP.2	0.047763	0.164695	0.017208	0.052971	0.242241	6.80E-05
	MMP.3	0.003419	0.042408	0.000431	0.008494	0.107958	3.92E-06
	MMP.9	0.322208	0.572964	0.27327	0.235426	0.355893	0.000482
	Myeloperoxidase	0.000445	0.482815	0.002661	0.001974	0.33826	1.61E-05
35	Myoglobin	0.001639	0.012932	6.10E-05	0.004848	0.071331	7.39E-07
	NGF.beta	0.483241	0.542153	0.355546	0.306248	0.34533	0.000567
	NrCAM	0.026533	0.15275	0.009829	0.035944	0.23512	4.25E-05
	PAI.1	0.101852	0.360229	0.07163	0.100407	0.308986	0.000186
40							
45							
50							
55							

5	Pancreatic .Polypepti de	0.026623	0.030012	0.001879	0.035944	0.094657	1.31E-05
	PAPP.A	0.034121	0.869127	0.105951	0.042383	0.443265	0.000247
	PDGF	0.145011	0.103956	0.02936	0.128659	0.181069	9.85E-05
	Progester one	0.674581	0.466811	0.418609	0.344738	0.336477	0.000629
10	Prolactin	3.35E-06	0.102858	6.49E-06	4.16E-05	0.181069	1.47E-07
	Prostate.S pecific.Ant igen..Free	0.181115	0.02681	0.011947	0.154088	0.094657	5.05E-05
	Prostatic. Acid.Phos phatase	0.618878	0.06073	0.09343	0.33716	0.143558	0.000223
15	PARC	0.63364	0.281319	0.273107	0.337728	0.296895	0.000482
	Peptide.Y Y	0.214198	0.38897	0.137756	0.172767	0.314717	0.000294
20	RANTES	0.015582	0.497864	0.028275	0.027024	0.33826	9.85E-05
	Resistin	6.26E-05	0.016235	4.69E-06	0.000588	0.076754	1.22E-07
	Secretin	0.251307	0.533075	0.211715	0.197567	0.34533	0.000409
	Serum.Am yloid.P	0.305834	0.425037	0.198865	0.226122	0.330969	0.000389
25	SGOT	0.004349	0.897407	0.034086	0.009646	0.443265	0.000109
	SHBG	0.000377	0.215823	0.000637	0.001801	0.250612	5.26E-06
	SOD	5.96E-08	0.322966	3.38E-06	1.93E-06	0.296895	1.02E-07
	Sortilin	0.039665	0.906914	0.123795	0.047654	0.444643	0.000268
	sRAGE	0.039899	0.997722	0.145132	0.047654	0.472467	0.000303
30	Stem.Cell. Factor	0.00034	0.000887	7.96E-07	0.001757	0.011747	3.61E-08
	Tenascin. C	0.150618	0.020126	0.007734	0.131751	0.088808	3.69E-05
	Testostero ne	0.366466	0.030238	0.029821	0.24473	0.094657	9.85E-05
35	TGF.alpha	0.988769	0.213289	0.374374	0.438634	0.250612	0.00057
	TGF.b3	0.575063	0.275874	0.244478	0.326829	0.296895	0.000458
	Thrombop oietin	0.432615	0.036893	0.042203	0.282823	0.101744	0.000126
40	TECK	0.108235	0.291443	0.060203	0.105032	0.296895	0.000171
	Thyroid.St	0.539117	0.112363	0.119979	0.32607	0.190694	0.000263

45

50

55

	imulating.						
	Hormone						
5	Thyroxine.	0.084825	0.465116	0.083029	0.087803	0.336477	0.00021
	Binding.Gl						
	obulin						
	TIMP.1	0.933141	0.297192	0.42694	0.426132	0.296895	0.000636
	Tissue.Fa	0.014644	0.526685	0.029404	0.02675	0.34515	9.85E-05
10	ctor						
	TNF.RII	0.000167	0.000147	5.98E-08	0.001037	0.003301	5.43E-09
	TNF.alpha	0.042646	0.454485	0.049714	0.049973	0.336477	0.000143
	TNF.beta	0.815021	0.781808	0.718864	0.392387	0.417308	0.00096
	TRAIL.R3	0.000592	0.026571	5.69E-05	0.002298	0.094657	7.38E-07
15	VCAM.1	0.018584	0.064904	0.00293	0.02815	0.148133	1.72E-05
	VEGF	1.52E-06	6.31E-05	2.09E-10	2.36E-05	0.003301	3.80E-11
	von.Willeb	0.647791	0.143718	0.175526	0.338084	0.226486	0.000354
	rand.Fact						
20	or						

[0131] It should be appreciated by those of skill in the art that the techniques disclosed in the examples above represent techniques discovered by the inventors to function well in the practice of the invention. Those of skill in the art should, however, in light of the present disclosure, appreciate that many changes can be made in the specific embodiments that are disclosed and still obtain a like or similar result without departing from the spirit and scope of the invention, therefore all matter set forth or shown in the accompanying drawings is to be interpreted as illustrative and not in a limiting sense.

[0132] Furthermore, the present invention relates to the following items:

1. A method for diagnosing, monitoring, or determining kidney transplant rejection or an associated disorder in a mammal, the method comprising:

- a. providing a test sample comprising a sample of bodily fluid taken from the mammal;
- b. determining sample concentrations for sample analytes in the test sample, wherein the sample analytes are microalbumin, VEGF, BLC, CD40, IGF BP2, MMP3, peptide YY, stem cell factor, TNF RII, AXL, Eotaxin 3, FABP, FGF basic, myoglobin, resistin, TRAIL R3, endothelin 1, NrCAM, Tenascin C, VCAM1, and cortisol;
- c. comparing the combination of sample concentrations to a data set comprising at least one entry, wherein each entry of the data set comprises a list comprising three or more minimum diagnostic concentrations indicative of kidney transplant rejection or an associated disorder, wherein each minimum diagnostic concentration comprises a maximum of a range of analyte concentrations for a healthy mammal;
- d. determining a matching entry of the dataset in which all minimum diagnostic concentrations are less than the corresponding sample concentrations; and,
- e. identifying an indicated disorder comprising the particular disorder of the matching entry.

2. A method for diagnosing, monitoring, or determining kidney transplant rejection or an associated disorder in a mammal, the method comprising:

- a. providing a test sample comprising a sample of bodily fluid taken from the mammal;
- b. determining a combination of sample concentrations for three or more sample analytes in the test sample, wherein the sample analytes are selected from the group consisting of alpha-1 microglobulin, beta-2 microglobulin, calbindin, clusterin, CTGF, creatinine, cystatin C, GST-alpha, KIM-1, microalbumin, NGAL, osteopontin, THP, TIMP-1, TFF-3, VEGF, BLC, CD40, IGF BP2, MMP3, peptide YY, stem cell factor, TNF RII, AXL, Eotaxin 3, FABP, FGF basic, myoglobin, resistin, TRAIL R3, endothelin 1, NrCAM, Tenascin C, VCAM1, and cortisol;
- c. comparing the combination of sample concentrations to a data set comprising at least one entry, wherein each entry of the data set comprises a list comprising three or more minimum diagnostic concentrations indicative of kidney transplant rejection or an associated disorder, wherein each minimum diagnostic concentration comprises a maximum of a range of analyte concentrations for a healthy mammal;
- d. determining a matching entry of the dataset in which all minimum diagnostic concentrations are less than the

corresponding sample concentrations; and,

e. identifying an indicated disorder comprising the particular disorder of the matching entry.

3. The method of item 2, wherein the mammal is selected from the group consisting of humans, apes, monkeys, rats, mice, dogs, cats, pigs, and livestock including cattle and oxen.

4. The method of item 2, wherein the bodily fluid is selected from the group consisting of urine, blood, plasma, serum, saliva, semen, and tissue lysates.

5. The method of item 2, wherein the minimum diagnostic concentration in human plasma of alpha-1 microglobulin is about 16 $\mu\text{g/ml}$, beta-2 microglobulin is about 2.2 $\mu\text{g/ml}$, calbindin is greater than about 5 ng/ml, clusterin is about 134 $\mu\text{g/ml}$, CTGF is about 16 ng/ml, cystatin C is about 1170 ng/ml, GST-alpha is about 62 ng/ml, KIM-1 is about 0.57 ng/ml, NGAL is about 375 ng/ml, osteopontin is about 25 ng/ml, THP is about 0.052 $\mu\text{g/ml}$, TIMP-1 is about 131 ng/ml, TFF-3 is about 0.49 $\mu\text{g/ml}$, and VEGF is about 855 $\mu\text{g/ml}$.

6. The method of item 2, wherein the minimum diagnostic concentration in human sera of alpha-1 microglobulin is about 17 $\mu\text{g/ml}$, beta-2 microglobulin is about 2.6 $\mu\text{g/ml}$, calbindin is greater than about 2.6 ng/ml, clusterin is about 152 $\mu\text{g/ml}$, CTGF is greater than about 8.2 ng/ml, cystatin C is about 1250 ng/ml, GST-alpha is about 52 ng/ml, KIM-1 is greater than about 0.35 ng/ml, NGAL is about 822 ng/ml, osteopontin is about 12 ng/ml, THP is about 0.053 $\mu\text{g/ml}$, TIMP-1 is about 246 ng/ml, TFF-3 is about 0.17 $\mu\text{g/ml}$, and VEGF is about 1630 $\mu\text{g/ml}$.

7. The method of item 2, wherein the minimum diagnostic concentration in human urine of alpha-1 microglobulin is about 233 $\mu\text{g/ml}$, beta-2 microglobulin is greater than about 0.17 $\mu\text{g/ml}$, calbindin is about 233 ng/ml, clusterin is greater than about 0.089 $\mu\text{g/ml}$, CTGF is greater than about 0.90 ng/ml, cystatin C is about 1170 ng/ml, GST-alpha is greater than about 26 ng/ml, KIM-1 is about 0.67 ng/ml, NGAL is about 81 ng/ml, osteopontin is about 6130 ng/ml, THP is about 2.6 $\mu\text{g/ml}$, TIMP-1 is greater than about 3.9 ng/ml, TFF-3 is greater than about 21 $\mu\text{g/ml}$, and VEGF is about 517 $\mu\text{g/ml}$.

8. The method of item 2, wherein a combination of sample concentrations for six or more sample analytes in the test sample are determined.

9. The method of item 8, wherein sample concentrations are determined for the analytes selected from the group consisting of BLC, CD40, IGF BP2, MMP3, peptide YY, stem cell factor, TNF RII, AXL, Eotaxin 3, FABP, FGF basic, myoglobin, resistin, TRAIL R3, endothelin 1, NrCAM, Tenascin C, VCAM1, and cortisol.

10. The method of item 2, wherein the kidney transplant rejection is acute rejection.

11. The method of item 2, wherein the kidney transplant rejection is chronic allograft nephropathy.

12. A method for diagnosing, monitoring, or determining kidney transplant rejection or an associated disorder in a mammal, the method comprising:

a. providing a test sample comprising a sample of bodily fluid taken from the mammal;

b. determining the concentrations of three or more sample analytes in a panel of biomarkers in the test sample, wherein the sample analytes are selected from the group consisting of alpha-1 microglobulin, beta-2 microglobulin, calbindin, clusterin, CTGF, creatinine, cystatin C, GST-alpha, KIM-1, microalbumin, NGAL, osteopontin, THP, TIMP-1, TFF-3, VEGF, BLC, CD40, IGF BP2, MMP3, peptide YY, stem cell factor, TNF RII, AXL, Eotaxin 3, FABP, FGF basic, myoglobin, resistin, TRAIL R3, endothelin 1, NrCAM, Tenascin C, VCAM1, and cortisol;

c. identifying diagnostic analytes in the test sample, wherein the diagnostic analytes are the sample analytes whose concentrations are statistically different from concentrations found in a control group of humans who do not suffer from kidney transplant rejection or an associated disorder;

d. comparing the combination of diagnostic analytes to a dataset comprising at least one entry, wherein each entry of the dataset comprises a combination of three or more diagnostic analytes reflective of kidney transplant rejection or an associated disorder; and,

e. identifying the particular disorder having the combination of diagnostic analytes that essentially match the combination of sample analytes.

13. The method of item 12, wherein the mammal is selected from the group consisting of humans, apes, monkeys, rats, mice, dogs, cats, pigs, and livestock including cattle and oxen.

14. The method of item 12, wherein the bodily fluid is selected from the group consisting of urine, blood, plasma, serum, saliva, semen, and tissue lysates.

15. The method of item 12, wherein the kidney transplant rejection is acute rejection.

16. The method of item 12, wherein the kidney transplant rejection is chronic allograft nephropathy.

17. A method for diagnosing, monitoring, or determining kidney transplant rejection or an associated disorder in a mammal, the method comprising:

a. providing an analyte concentration measurement device comprising three or more detection antibodies ,

wherein each detection antibody comprises an antibody coupled to an indicator, wherein the antigenic determinants of the antibodies are sample analytes associated with kidney transplant rejection or an associated disorder, and wherein the sample analytes are selected from the group consisting of alpha-1 microglobulin, beta-2 microglobulin, calbindin, clusterin, CTGF, creatinine, cystatin C, GST-alpha, KIM-1, microalbumin, NGAL, osteopontin, THP, TIMP-1, TFF-3, VEGF, BLC, CD40, IGF BP2, MMP3, peptide YY, stem cell factor, TNF RII, AXL, Eotaxin 3, FABP, FGF basic, myoglobin, resistin, TRAIL R3, endothelin 1, NrCAM, Tenascin C, VCAM1, and cortisol;

b. providing a test sample comprising three or more sample analytes and a bodily fluid taken from the mammal;
 c. contacting the test sample with the detection antibodies and allowing the detection antibodies to bind to the sample analytes;
 d. determining the concentrations of the sample analytes by detecting the indicators of the detection antibodies bound to the sample analytes in the test sample; and,
 e. comparing the concentrations of each sample analyte to a corresponding minimum diagnostic concentration reflective of kidney transplant rejection or an associated disorder.

18. The method of item 17, wherein the bodily fluid is selected from the group consisting of urine, blood, plasma, serum, saliva, semen, and tissue lysates.

19. The method of item 17, wherein the analyte concentration measurement device comprises six or more detection antibodies.

20. The method of item 17, wherein the analyte concentration measurement device comprises sixteen detection antibodies.

21. The method of item 17, wherein the sample analytes are selected from the group consisting of alpha-1 microglobulin, beta-2 microglobulin, cystatin C, KIM-1, THP, and TIMP-1.

22. The method of item 17, wherein the kidney transplant rejection is acute rejection.

23. The method of item 17, wherein the kidney transplant rejection is chronic allograft nephropathy.

24. A method for diagnosing, monitoring, or determining kidney transplant rejection or an associated disorder in a mammal, the method comprising:

a. providing a test sample comprising a sample of bodily fluid taken from the mammal;
 b. determining sample concentrations for sample analytes in the test sample, wherein the sample analytes are microalbumin, VEGF, BLC, CD40, IGF BP2, MMP3, peptide YY, stem cell factor, TNF RII, AXL, Eotaxin 3, FABP, FGF basic, myoglobin, resistin, TRAIL R3, endothelin 1, NrCAM, Tenascin C, VCAM1, and cortisol;
 c. comparing the combination of sample concentrations to a data set comprising at least one entry, wherein each entry of the data set comprises a list comprising three or more minimum diagnostic concentrations indicative of kidney transplant rejection or an associated disorder, wherein each minimum diagnostic concentration comprises a maximum of a range of analyte concentrations for a healthy mammal;
 d. determining a matching entry of the dataset in which all minimum diagnostic concentrations are less than the corresponding sample concentrations; and,
 e. identifying an indicated disorder comprising the particular disorder of the matching entry.

25. A method for diagnosing, monitoring, or determining kidney transplant rejection or an associated disorder in a mammal, the method comprising:

a. providing a test sample comprising a sample of bodily fluid taken from the mammal;
 b. determining sample concentrations for sample analytes in the test sample, wherein the sample analytes are alpha-1 microglobulin, beta-2 microglobulin, calbindin, clusterin, CTGF, creatinine, cystatin C, GST-alpha, KIM-1, microalbumin, NGAL, osteopontin, THP, TIMP-1, TFF-3, VEGF, BLC, CD40, IGF BP2, MMP3, peptide YY, stem cell factor, TNF RII, AXL, Eotaxin 3, FABP, FGF basic, myoglobin, resistin, TRAIL R3, endothelin 1, NrCAM, Tenascin C, VCAM1, and cortisol;
 c. comparing the combination of sample concentrations to a data set comprising at least one entry, wherein each entry of the data set comprises a list comprising three or more minimum diagnostic concentrations indicative of kidney transplant rejection or an associated disorder, wherein each minimum diagnostic concentration comprises a maximum of a range of analyte concentrations for a healthy mammal;
 d. determining a matching entry of the dataset in which all minimum diagnostic concentrations are less than the corresponding sample concentrations; and,
 e. identifying an indicated disorder comprising the particular disorder of the matching entry.

Claims

1. A method for diagnosing, monitoring, or determining kidney transplant rejection or an associated disorder in a mammal, the method comprising:
 - a. providing an analyte concentration measurement device comprising three or more detection antibodies, wherein each detection antibody comprises an antibody coupled to an indicator, wherein the antigenic determinants of the antibodies are sample analytes associated with kidney transplant rejection or an associated disorder, and wherein the sample analytes are selected from the group consisting of TFF-3, beta-2 microglobulin, alpha-1 microglobulin, calbindin, clusterin, CTGF, creatinine, cystatin C, GST-alpha, KIM-1, microalbumin, NGAL, osteopontin, THP, TIMP-1, VEGF, BLC, CD40, IGF BP2, MMP3, peptide YY, stem cell factor, TNF RII, AXL, Eotaxin 3, FABP, FGF basic, myoglobin, resistin, TRAIL R3, endothelin 1, NrCAM, Tenascin C, VCAM1, and cortisol;
 - b. contacting a test sample comprising three or more sample analytes and a bodily fluid taken from the mammal with the detection antibodies and allowing the detection antibodies to bind to the sample analytes;
 - c. determining the concentrations of the sample analytes by detecting the indicators of the detection antibodies bound to the sample analytes in the test sample; and,
 - d. comparing the concentrations of each sample analyte to a corresponding minimum diagnostic concentration reflective of kidney transplant rejection or an associated disorder.
2. The method of claim 1, wherein the analyte concentration measurement device comprises six or more detection antibodies.
3. The method of claim 1, wherein the analyte concentration measurement device comprises sixteen detection antibodies.
4. The method of claim 1, wherein the sample analytes are selected from the group consisting of alpha-1 microglobulin, beta-2 microglobulin, cystatin C, KIM-1, THP, and TIMP-1.
5. The method of any one of claims 1 to 4, wherein the mammal is selected from the group consisting of humans, apes, monkeys, rats, mice, dogs, cats, pigs, and livestock including cattle and oxen.
6. The method of any one of claims 1 to 5, wherein the bodily fluid is selected from the group consisting of urine, blood, plasma, serum, saliva, semen, and tissue lysates.
7. The method of any one of claims 1 to 6, wherein the kidney transplant rejection is acute rejection or chronic allograft nephropathy.

FIG. 1

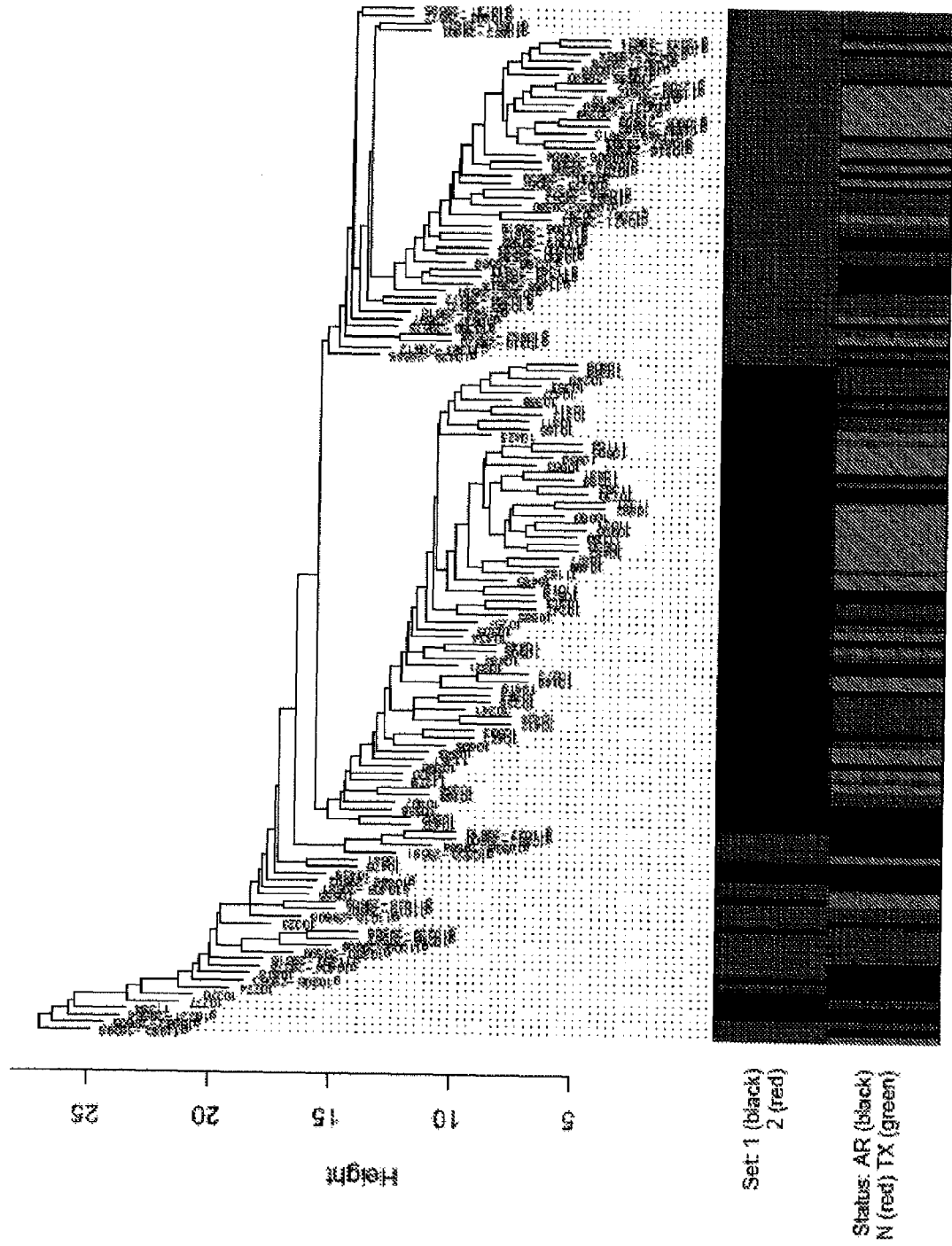


FIG. 2A

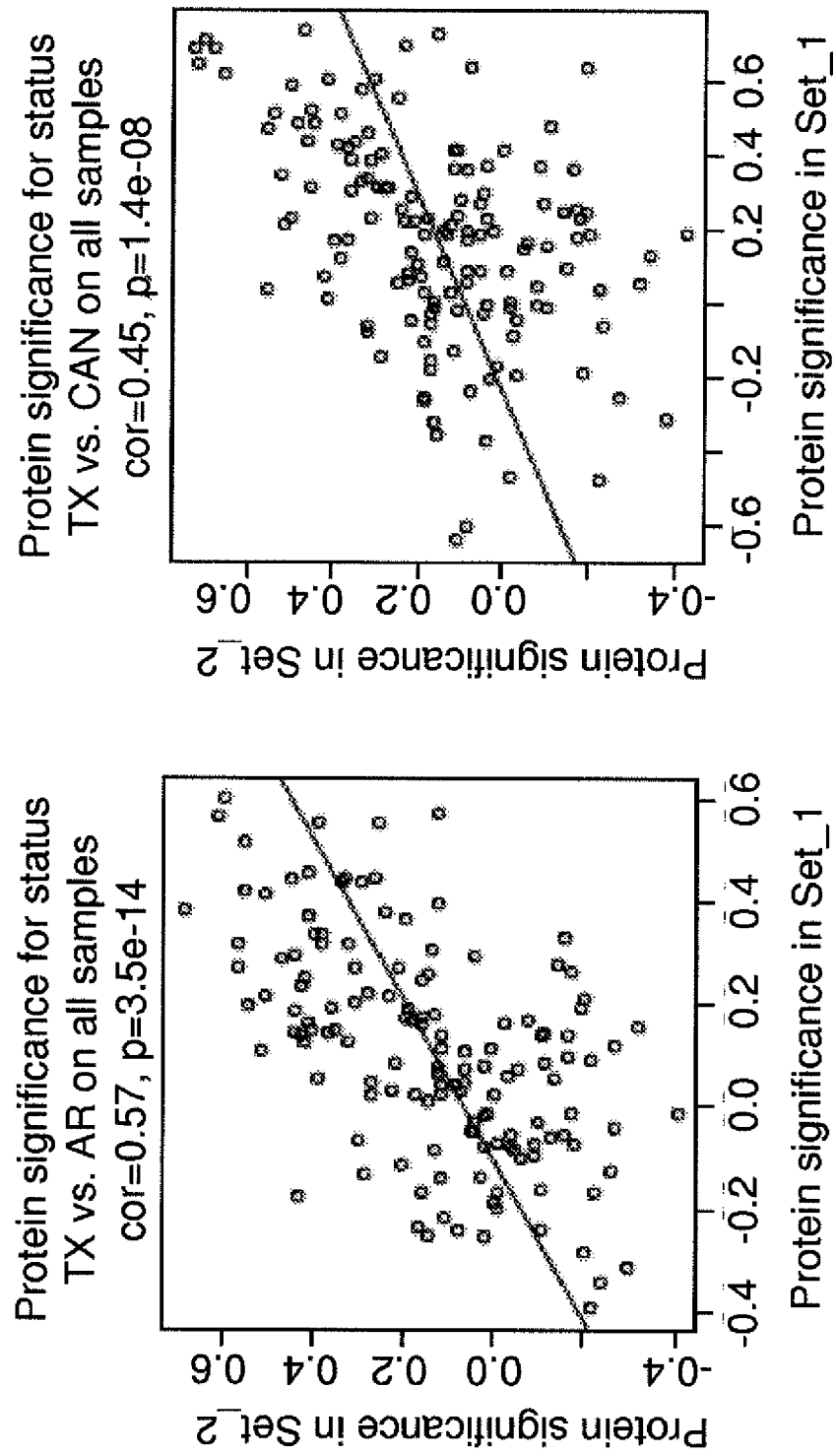


FIG. 2B

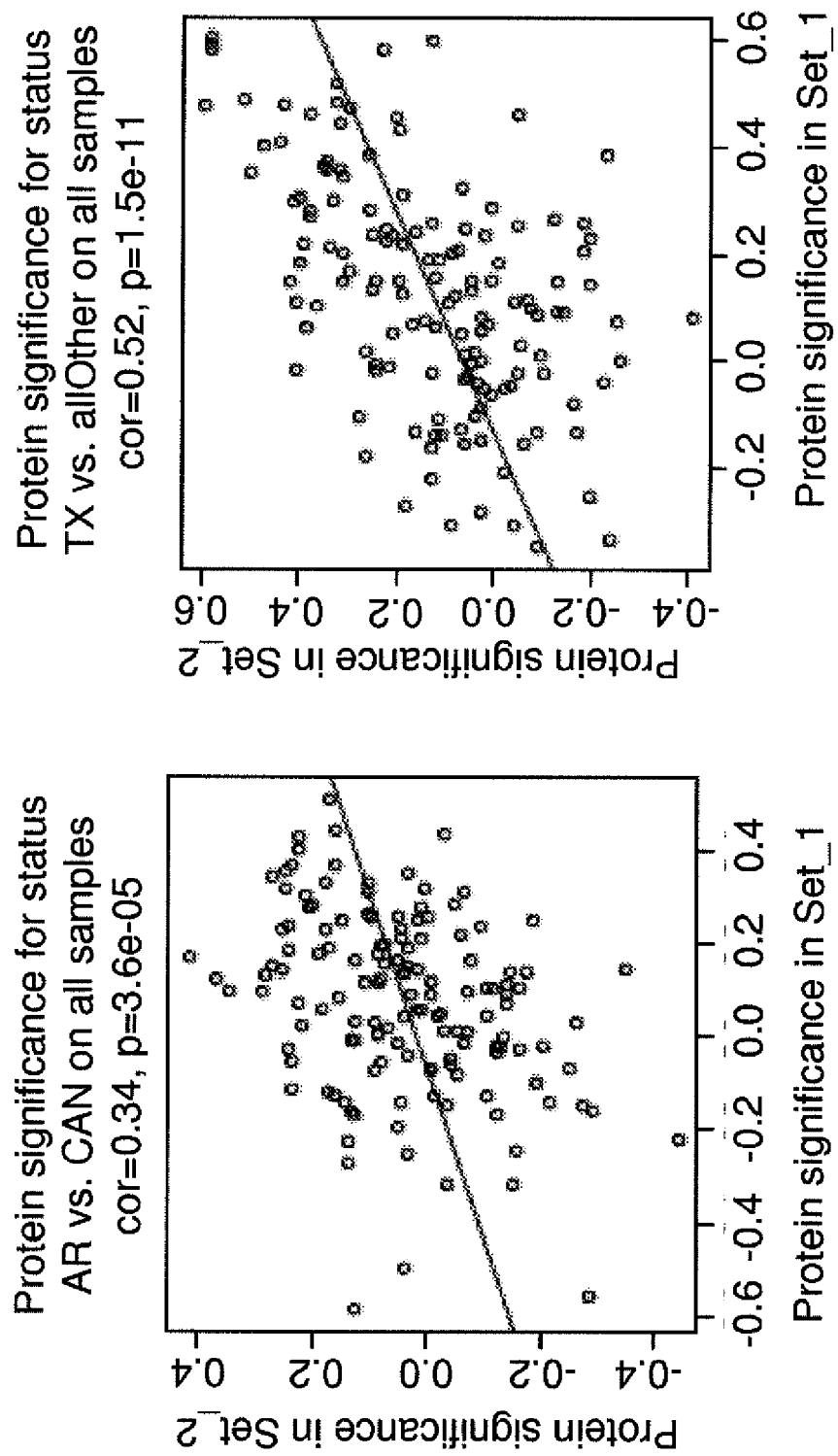


FIG. 2C

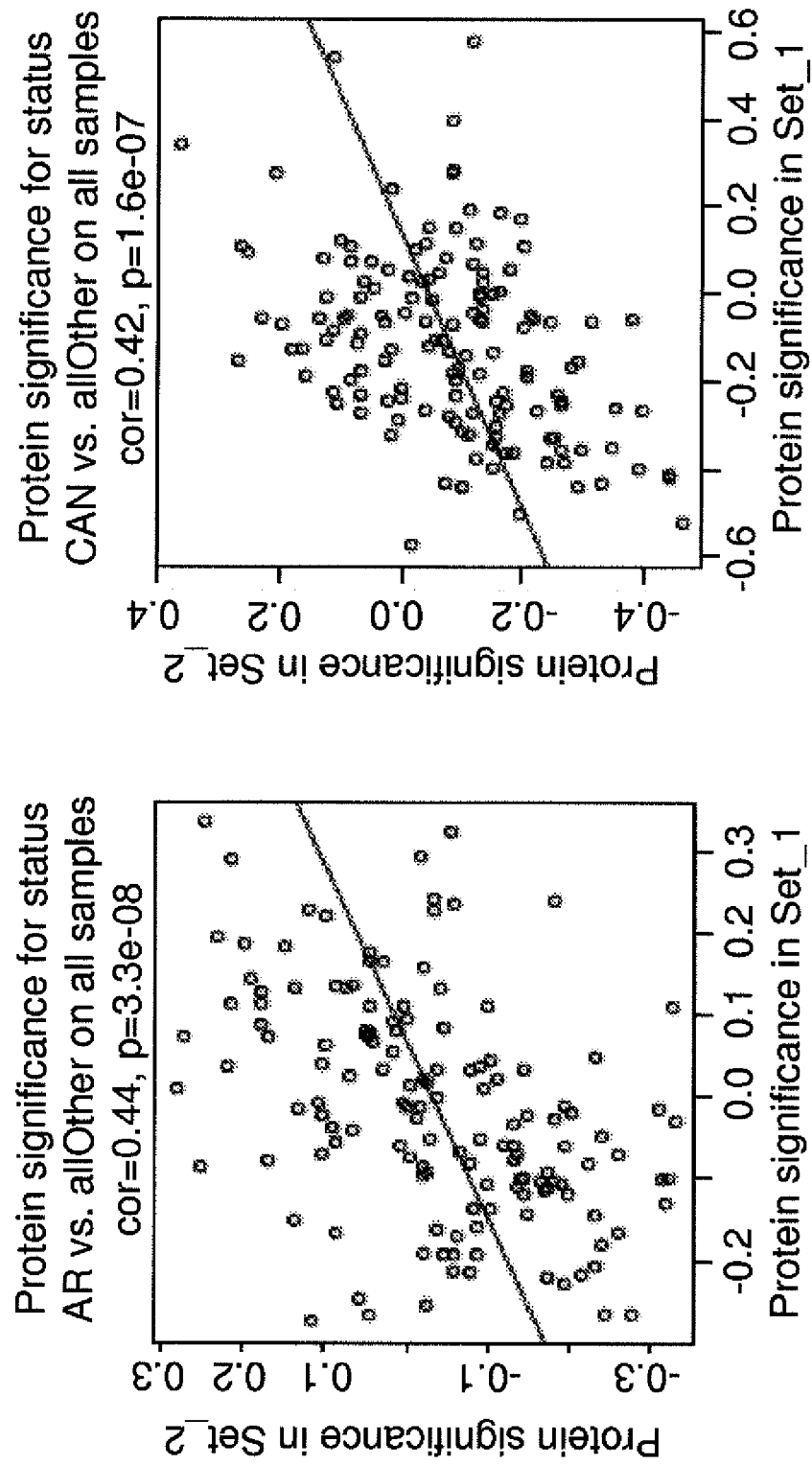


FIG. 3

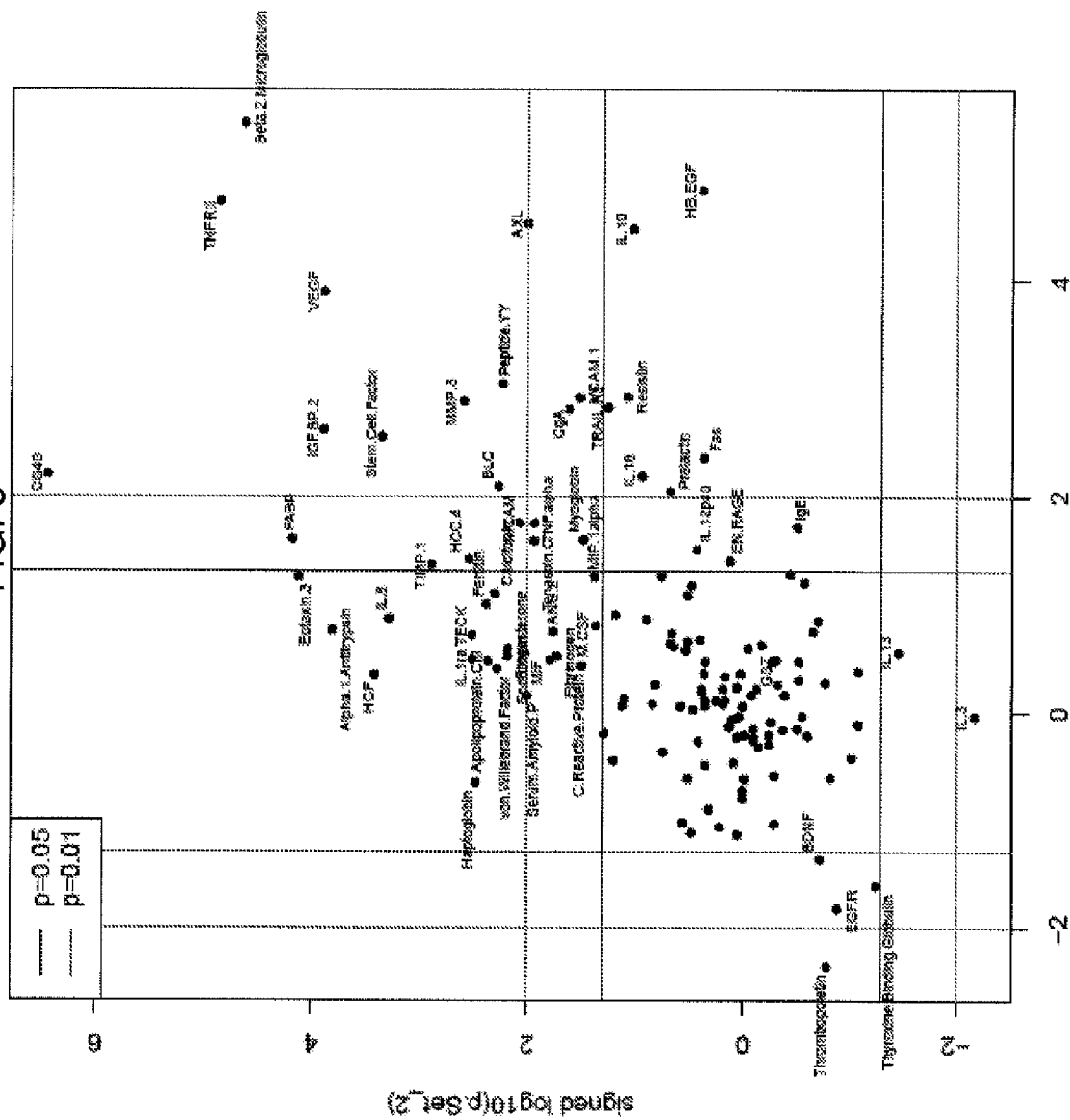


FIG. 4

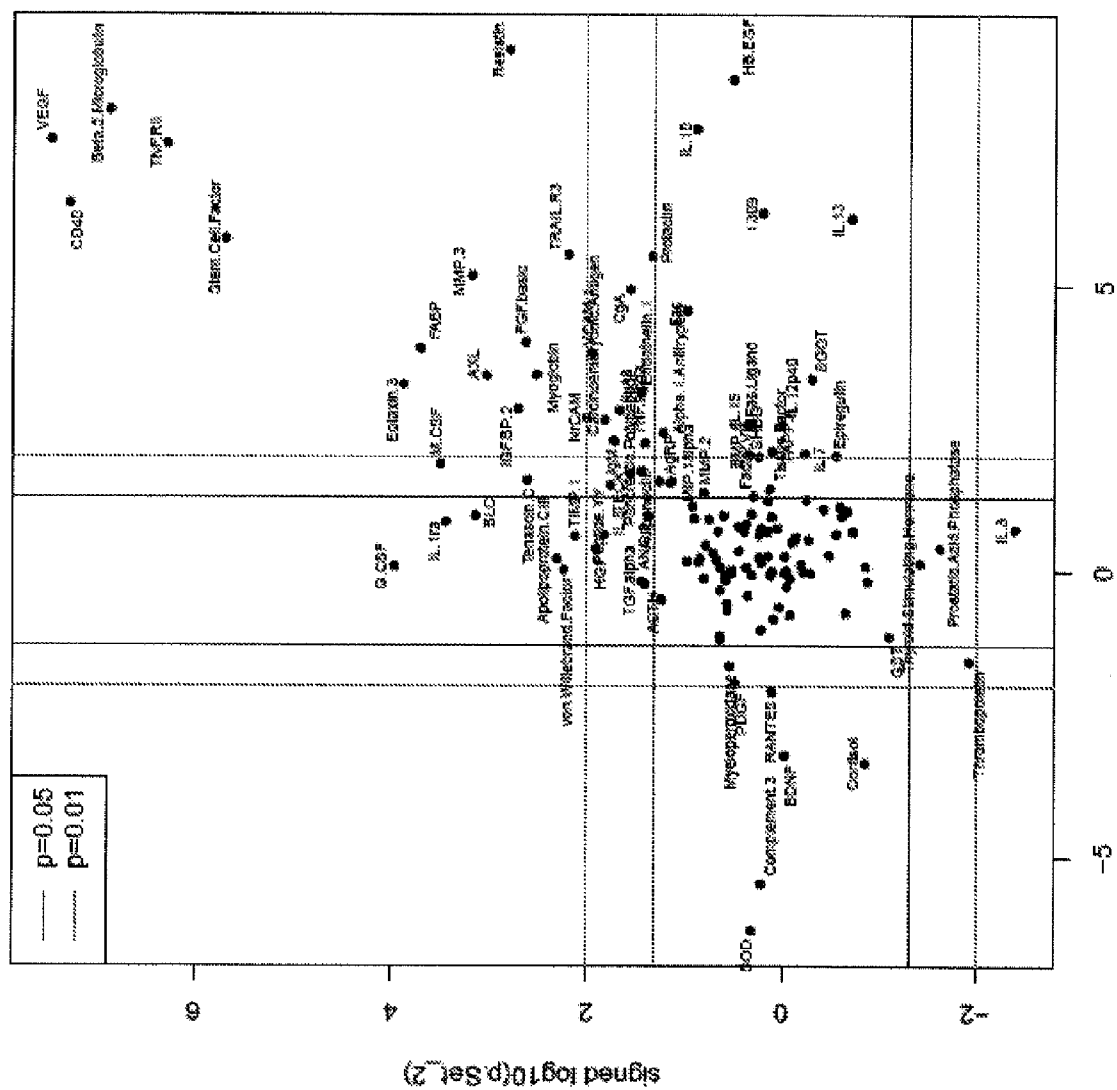


FIG. 5

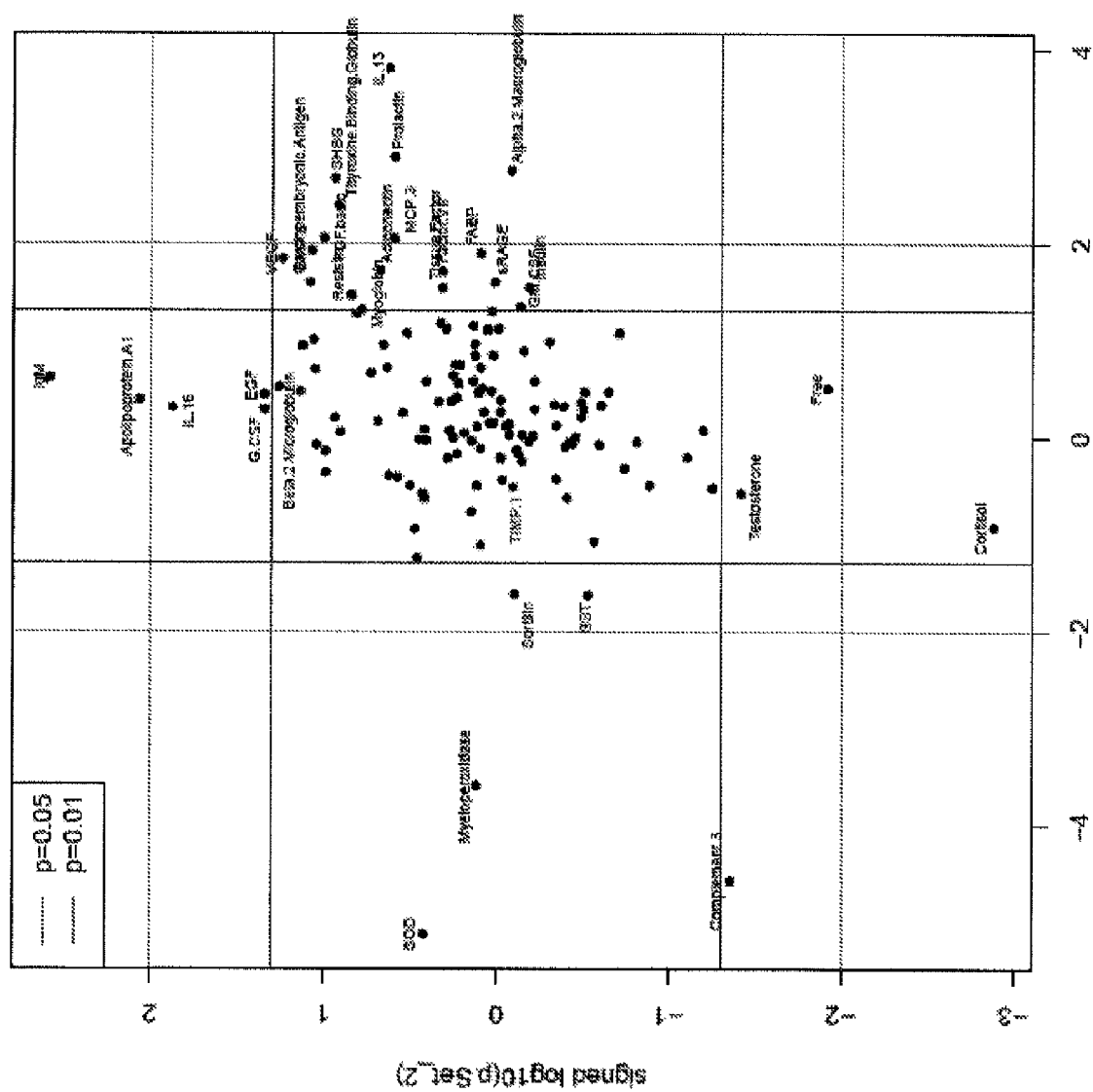


FIG. 6

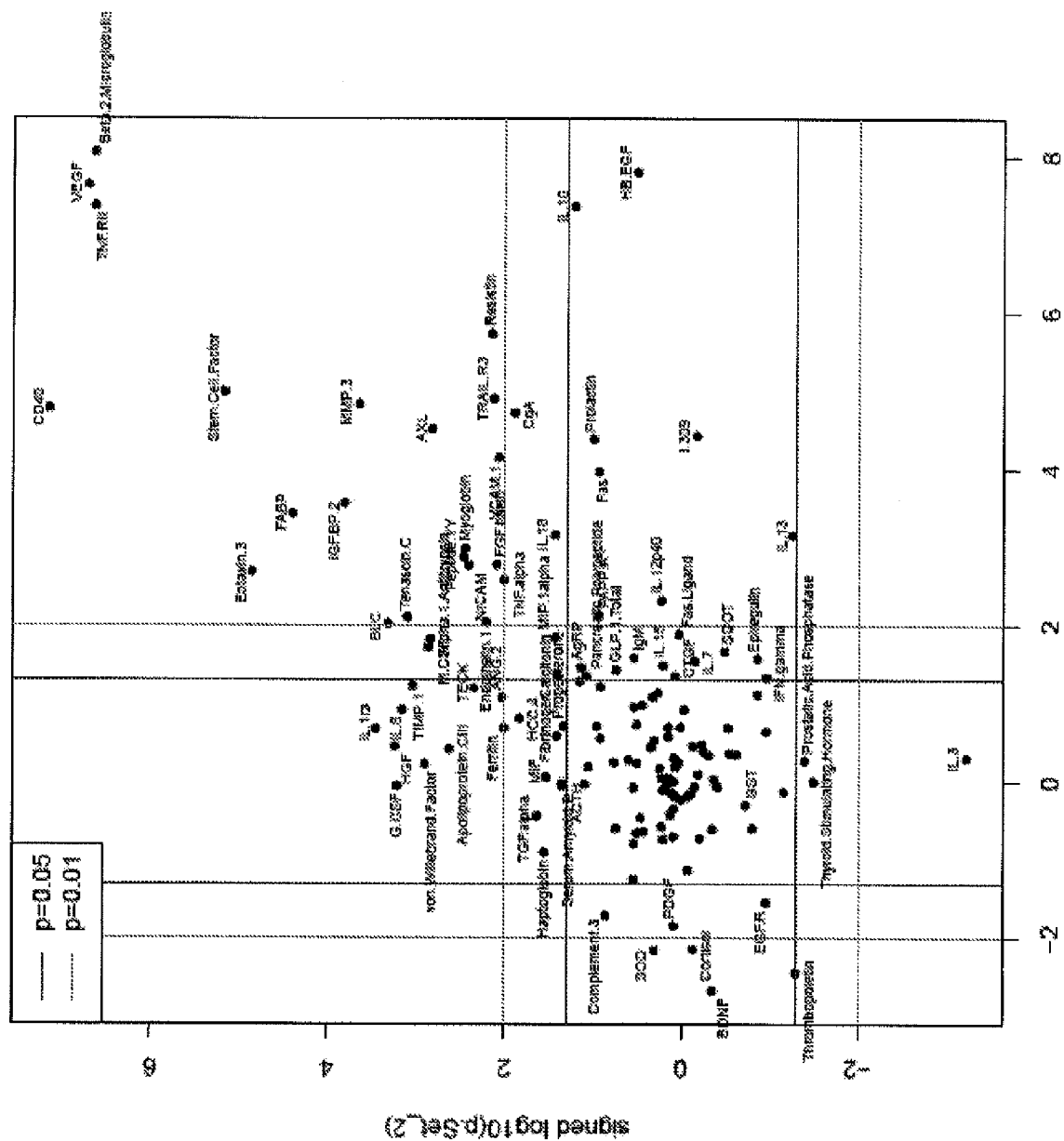


FIG. 7

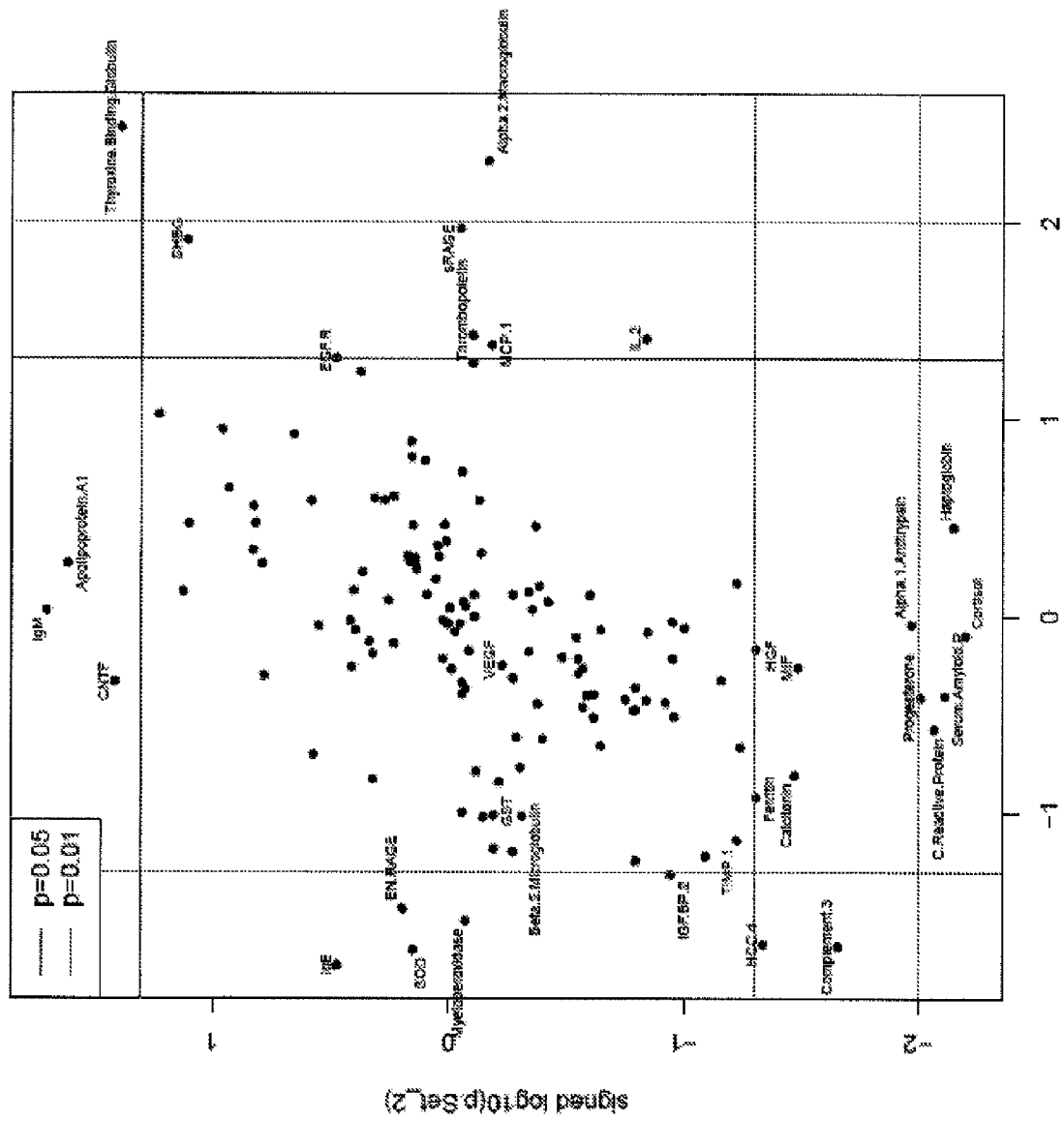


FIG. 8

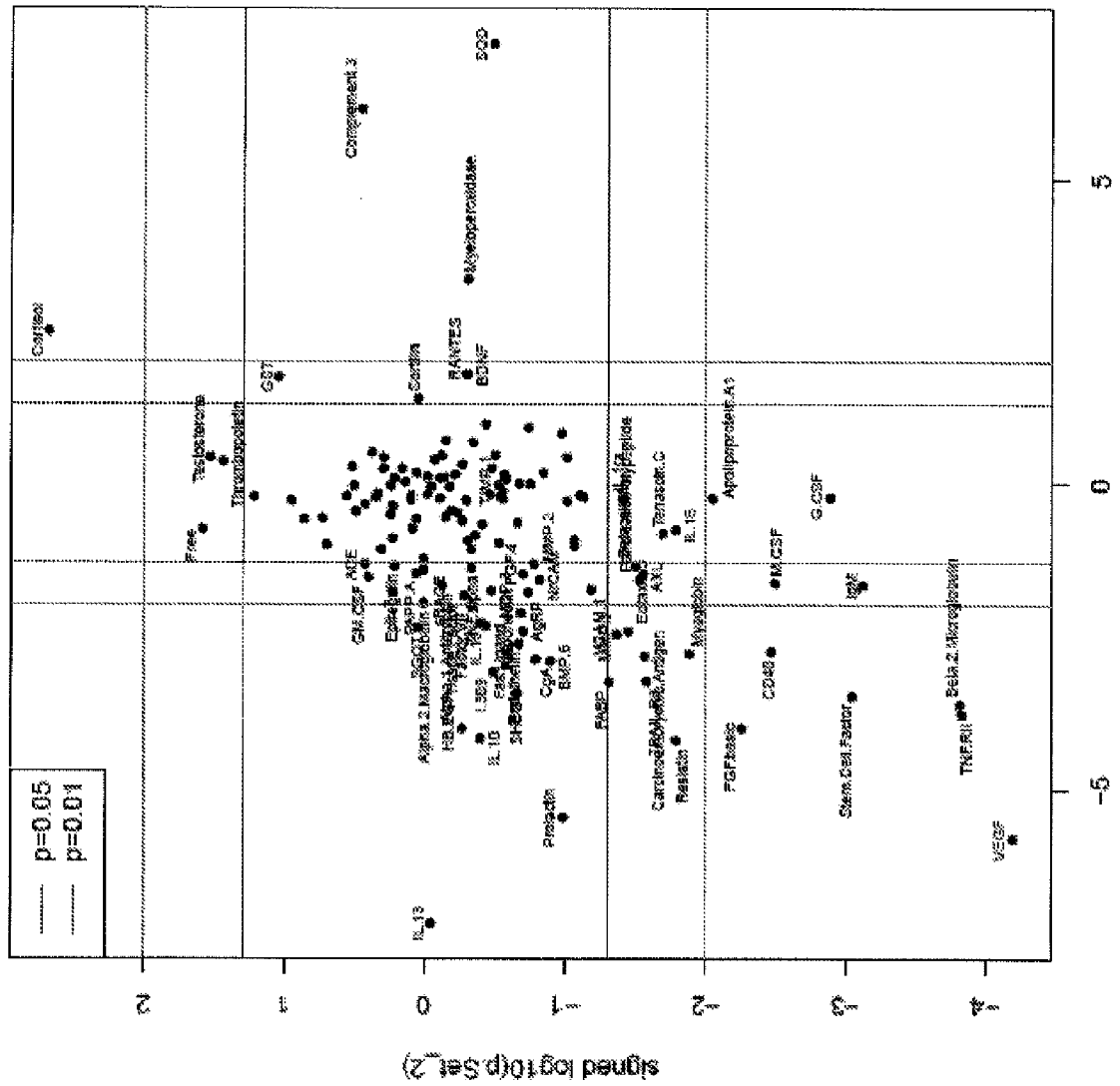
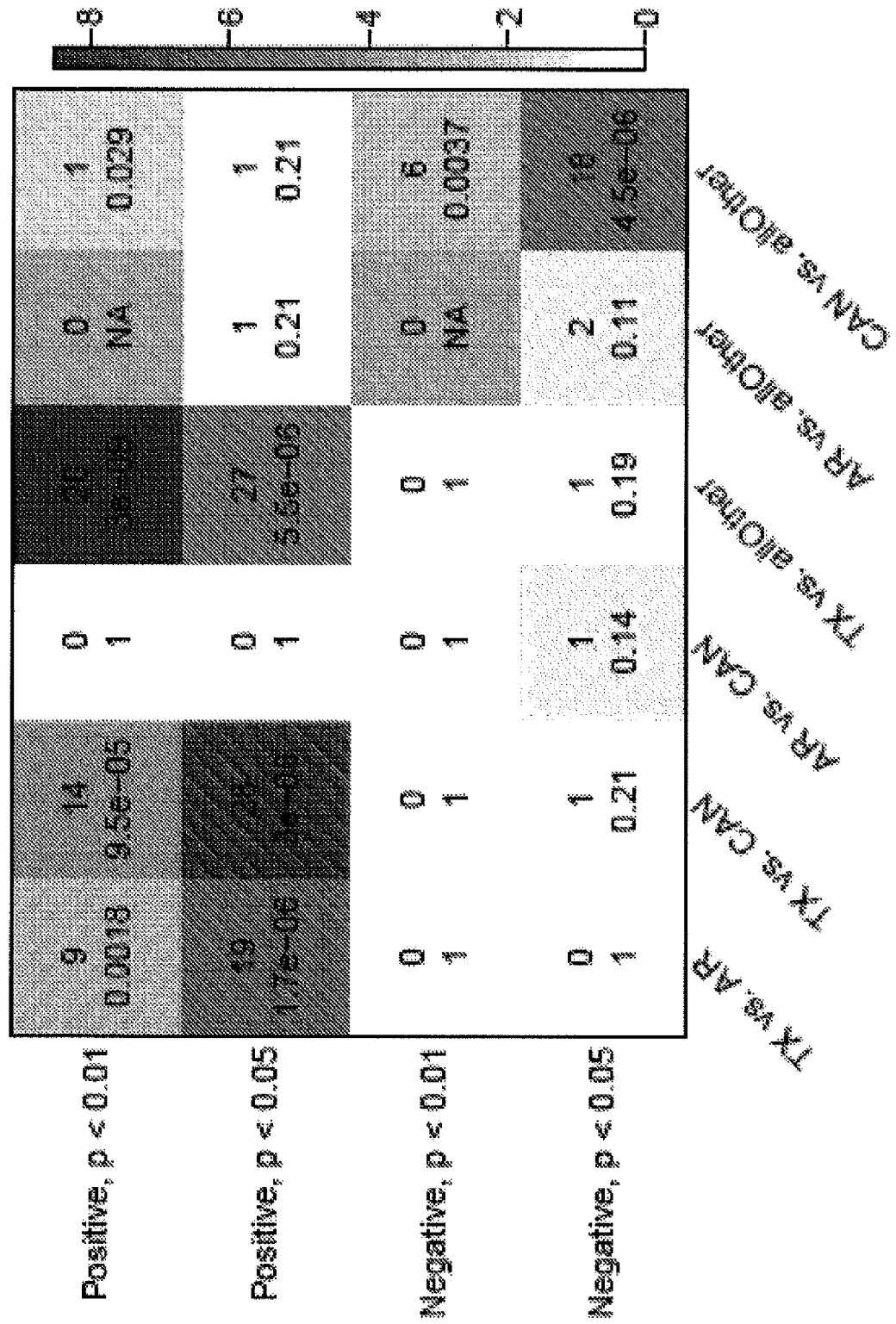


FIG. 9





EUROPEAN SEARCH REPORT

Application Number
EP 14 18 0229

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
A	WO 2004/042346 A2 (EXPRESSION DIAGNOSTICS INC [US]; WOHLGEMUTH JAY [US]; FRY KIRK [US]; W) 21 May 2004 (2004-05-21) * the whole document * * abstract * * table 8 * * claims 17, 21, 42 * -----	1-7	INV. G01N33/48 G01N33/53 G01N33/68
A	GILLESPIE A ET AL: "Biomarkers in renal transplantation", BIOMARKERS IN MEDICINE, FUTURE MEDICINE, LONDON, vol. 2, no. 6, 1 December 2008 (2008-12-01), pages 603-612, XP008158885, ISSN: 1752-0363, DOI: 10.2217/17520363.2.6.603 * the whole document * * abstract * * page 604, right-hand column, last paragraph - page 606, left-hand column, paragraph 1 * * page 605; table 1 * * page 606, left-hand column, last paragraph - right-hand column, paragraph 3 * * page 607, left-hand column, paragraph 2 - paragraph 3 * * Executive summary; page 610 * ----- -/--	1-7	TECHNICAL FIELDS SEARCHED (IPC) G01N
The present search report has been drawn up for all claims			
Place of search The Hague		Date of completion of the search 8 October 2014	Examiner Gall-Truchot, A
CATEGORY OF CITED DOCUMENTS X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document		T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons ----- & : member of the same patent family, corresponding document	

1
EPO FORM 1503 03.02 (P04C01)



EUROPEAN SEARCH REPORT

 Application Number
EP 14 18 0229

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
A	UWE POGE ET AL: "Time course of low molecular weight proteins in the early kidney transplantation period--influence of corticosteroids", NEPHROLOGY DIALYSIS TRANSPLANTATION, vol. 19, no. 11, 22 September 2004 (2004-09-22), pages 2858-2863, XP55048192, DOI: 10.1093/ndt/gfh341 * the whole document * * abstract * * page 2858, right-hand column, paragraph 1 - paragraph 3 * * page 2863, left-hand column, last paragraph *	1-7	
A,P	----- NICKERSON ET AL: "Post-transplant monitoring of renal allografts: are we there yet?", CURRENT OPINION IN IMMUNOLOGY, ELSEVIER, OXFORD, GB, vol. 21, no. 5, 26 August 2009 (2009-08-26), - 1 October 2009 (2009-10-01), pages 563-568, XP026682570, ISSN: 0952-7915, DOI: 10.1016/J.COI.2009.07.014 [retrieved on 2009-08-26] * the whole document * * abstract * * page 563, right-hand column, paragraph 2 * ----- -----	1-7	TECHNICAL FIELDS SEARCHED (IPC)
The present search report has been drawn up for all claims			
Place of search The Hague		Date of completion of the search 8 October 2014	Examiner Gall-Truchot, A
CATEGORY OF CITED DOCUMENTS X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document		T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document	

EPO FORM 1503 03.82 (P04C01)



EUROPEAN SEARCH REPORT

Application Number
EP 14 18 0229

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
A,P	TRUONG D Q ET AL: "The immunological monitoring of kidney and liver transplants in adult and pediatric recipients", TRANSPLANT IMMUNOLOGY, ELSEVIER, NL, vol. 22, no. 1-2, 1 December 2009 (2009-12-01), pages 18-27, XP026755846, ISSN: 0966-3274, DOI: 10.1016/J.TRIM.2009.09.008 [retrieved on 2009-09-30] * the whole document * * abstract * * page 19, left-hand column, paragraph 1 * -----	1-7	
			TECHNICAL FIELDS SEARCHED (IPC)
The present search report has been drawn up for all claims			
Place of search		Date of completion of the search	Examiner
The Hague		8 October 2014	Gall-Truchot, A
CATEGORY OF CITED DOCUMENTS X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document			

EPO FORM 1503 03.82 (P04C01)

**ANNEX TO THE EUROPEAN SEARCH REPORT
ON EUROPEAN PATENT APPLICATION NO.**

EP 14 18 0229

5

This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report.
The members are as contained in the European Patent Office EDP file on
The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

08-10-2014

10

15

20

25

30

35

40

45

50

55

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2004042346 A2	21-05-2004	AU 2003299465 A1	07-06-2004
		CA 2483481 A1	21-05-2004
		EP 1585972 A2	19-10-2005
		EP 2194145 A1	09-06-2010
		EP 2253719 A2	24-11-2010
		EP 2292786 A2	09-03-2011
		JP 2005536230 A	02-12-2005
		JP 2010022375 A	04-02-2010
		US 2006088836 A1	27-04-2006
		US 2007031890 A1	08-02-2007
		US 2010099098 A1	22-04-2010
		WO 2004042346 A2	21-05-2004

EPO FORM P0459

For more details about this annex : see Official Journal of the European Patent Office, No. 12/82

REFERENCES CITED IN THE DESCRIPTION

This list of references cited by the applicant is for the reader's convenience only. It does not form part of the European patent document. Even though great care has been taken in compiling the references, errors or omissions cannot be excluded and the EPO disclaims all liability in this regard.

Patent documents cited in the description

- US 61327389 A [0001]
- US 61232091 A [0001]

专利名称(译)	用于检测肾移植排斥的方法和装置		
公开(公告)号	EP2806272A1	公开(公告)日	2014-11-26
申请号	EP2014180229	申请日	2010-08-06
[标]发明人	SPAIN MICHAEL MAPES JAMES P LABRIE SAMUEL MCDADE RALPH EISINGER DOMINIC BALLARD KARRI SALOMON DANIEL ABECASSIS MICHAEL		
发明人	SPAIN, MICHAEL MAPES, JAMES P. LABRIE, SAMUEL MCDADE, RALPH EISINGER, DOMINIC BALLARD, KARRI SALOMON, DANIEL ABECASSIS, MICHAEL		
IPC分类号	G01N33/48 G01N33/53 G01N33/68		
CPC分类号	G01N33/6893 G01N33/5302 G01N33/566 G01N2333/47 G01N2333/4703 G01N2333/4706 G01N2333/4725 G01N2333/4727 G01N2333/475 G01N2333/52 G01N2333/70503 G01N2333/70539 G01N2333/765 G01N2333/775 G01N2333/8139 G01N2333/8146 G01N2333/82 G01N2333/91177 G01N2800/34 G01N2800/347 G01N2800/52 G01N2800/56 G01N2800/60 Y10T436/147777		
代理机构(译)	法思博事务所		
优先权	61/232091 2009-08-07 US 61/327389 2010-04-23 US		
外部链接	Espacenet		

摘要(译)

描述了用于诊断，监测或确定哺乳动物中肾移植排斥或相关病症的方法和装置。具体地，描述了使用从哺乳动物取得的测试样品中测量浓度的三种或更多种分析物的组合来诊断，监测或确定肾移植排斥或相关病症的方法和装置。

Table 9

	Set 1	Set 2	total
AR	25	20	45
CAN/IFTA	25	48	73
TX	18	3	21
acute dysfunction no rejection (ADNR)	0	47	47
	68	118	186