

(19) AUSTRALIAN PATENT OFFICE

(54) Title
Compositions and methods for the treatment of immune related diseases

(51)⁶ International Patent Classification(s)
C07K 17/00 (2006.01) **OBMEP** **A61P**
A61K 6/00 (2006.01) 37/02
A61K 38/00 (2006.01) 20060101ALI2005111
A61K 38/17 (2006.01) **OBMEP** **C07K**
A61K 39/395 14/47
(2006.01) 20060101ALI2006072
A61P 37/02 (2006.01) **2BMEP** **C07K**
C07K 14/47 (2006.01) 14/52
C07K 14/52 (2006.01) 20060101ALI2008053
C07K 16/18 (2006.01) **1BMEP** **C07K**
C07K 19/00 (2006.01) 16/18
C07K 19/00 (2006.01) 20060101ALI2005111
C12N 15/12 (2006.01) **OBMEP** **C07K**
C12P 21/02 (2006.01) 19/00
C12Q 1/68 (2006.01) 20060101ALI2005111
G01N 33/53 (2006.01) **OBMEP** **C12N**
C07K 17/00 15/12
20060101AFI2006113 20060101ALI2005111
OBHUS **A61K** **OBMEP** **C12P**
6/00 21/02
20060101ALI2005111 20060101ALI2006050
OBMEP **A61K** **6BMEP** **C12Q**
38/00 1/68
20060101ALI2006010 20060101ALI2005111
1BMAU **A61K** **OBMEP** **G01N**
38/17 33/53
20060101ALI2005111 20060101ALI2005111
OBMEP **A61K** **OBMEP**
39/395 PCT/US2003/035971
20060101ALI2005111

(21) Application No: 2003302386

(22) Application Date: 2003 .11.24

(87) WIPO No: W004/047728

(30) Priority Data

(31) Number	(32) Date	(33) Country
60/429,069	2002 .11.26	US

(43) Publication Date : 2004 .06.18

(43) Publication Journal Date : 2004 .07.22

(71) Applicant(s)
Genentech, Inc.

(72) Inventor(s)
Jackman, Janet; Wu, Thomas D.; Wood, William I.; Bodary, Sarah; Clark, Hilary; Schoenfeld, Jill; Hunte, Bridsell; Williams, Mickey P.

(74) Agent/Attorney
Griffith Hack, Level 3 509 St Kilda Road, Melbourne, VIC, 3004

(56) Related Art
WO 2001/093983 A1 (GENENTECH, INC.) 13 December 2001
STRAUSBERG, R. L. et al, Proc. Natl. Acad. Sci, 2002, Vol. 99, No. 26, pages 16899-16903 and
GenBank Accession No. BC020568, 3 January 2002
WO 2000/012708 A2 (GENENTECH, INC.) 9 March 2000
WO 2000/000610 A2 (INCYTE PHARMACEUTICALS, INC.) 6 January 2000
WO 2001/004297 A2 (SAGAMI CHEMICAL RESEARCH CENTRE) 18 January 2001

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
10 June 2004 (10.06.2004)

PCT

(10) International Publication Number
WO 2004/047728 A2

- (51) International Patent Classification⁷: **A61K** [US/US]: 41 Nevada Street, San Francisco, CA 94110 (US). **BODARY, Sarah** [US/US]: 3530 Crestmoor Drive, San Bruno, CA 94066 (US).
- (21) International Application Number:
PCT/US2003/035971
- (22) International Filing Date:
24 November 2003 (24.11.2003)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:
60/429,069 26 November 2002 (26.11.2002) US
- (74) Agents: **CARPENTER, David, A.** et al.; Genentech, Inc., 1 DNA Way, South San Francisco, CA 94080-4990 (US).
- (81) Designated States (*national*): AF, AG, AI, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GH, GI, GM, GR, GU, HD, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SI, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (71) Applicant (*for all designated States except US*): **GENENTECH, INC.** [US/US]: 1 DNA Way, South San Francisco, CA 94080 4990 (US).
- (72) Inventors; and
- (75) Inventors/Applicants (*for US only*): **CLARK, Hilary** [US/US]: 495 Harkness Avenue, San Francisco, CA 94134 (US). **HUNTE, Bridsell** [US/US]: 1133 Dolores Street #16, San Francisco, CA 94110 (US). **JACKMAN, Janet** [US/US]: 94 Patrick Way, Half Moon Bay, CA 94019 (US). **SCHOENFELD, Jill** [US/US]: 680 Spring Creek Drive, Ashland, OR 97520 (US). **WILLIAMS, Mickey, P.** [US/US]: 509 Alto Avenue, Half Moon Bay, CA 94019 (US). **WOOD, William, I.** [US/US]: 35 Southdown Court, Hillsborough, CA 94010 (US). **WU, Thomas, D.**
- (84) Designated States (*regional*): ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NI, SN, TD, TG).

Published:

— without international search report and to be republished upon receipt of that report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 2004/047728 A2

(54) Title: COMPOSITIONS AND METHODS FOR THE TREATMENT OF IMMUNE RELATED DISEASES

(57) Abstract: The present invention relates to compositions containing novel proteins and methods of using those compositions for the diagnosis and treatment of immune related diseases.

COMPOSITIONS AND METHODS FOR THE TREATMENT OF IMMUNE
RELATED DISEASES

Field of the Invention

5 The present invention relates to compositions and methods
useful for the diagnosis and treatment of immune related
diseases.

10 Background of the Invention

It is to be understood that, if any prior art
publication is referred to herein, such reference does not
constitute an admission that the publication forms a part
15 of the common general knowledge in the art, in Australia
or any other country.

Immune related and inflammatory diseases are the
manifestation or consequence of fairly complex, often
20 multiple interconnected biological pathways which in
normal physiology are critical to respond to insult or
injury, initiate repair from insult or injury, and mount
innate and acquired defense against foreign organisms.
Disease or pathology occurs when these normal
25 physiological pathways cause additional insult or injury
either as directly related to the intensity of the
response, as a consequence of abnormal regulation or
excessive stimulation, as a reaction to self, or as a
combination of these.

30 Though the genesis of these diseases often involves
multistep pathways and often multiple different biological
systems/pathways, intervention at critical points in one
or more of these pathways can have an ameliorative or
therapeutic effect. Therapeutic intervention can occur by
35 either antagonism of a detrimental process/pathway or
stimulation of a beneficial process/pathway.

Many immune related diseases are known and have been extensively studied. Such diseases include immune-mediated inflammatory diseases, non-immune-mediated inflammatory diseases, infectious diseases, immunodeficiency diseases, neoplasia, etc.

T lymphocytes (T cells) are an important component of a mammalian immune response. T cells recognize antigens which are associated with a self-molecule encoded by genes within the major histocompatibility complex (MHC). The antigen may be displayed together with MHC molecules on the surface of antigen presenting cells, virus infected cells, cancer cells, grafts, etc. The T cell system eliminates these altered cells which pose a health threat to the host mammal. T cells include helper T cells and cytotoxic T cells. Helper T cells proliferate extensively following recognition of an antigen-MHC complex on an antigen presenting cell. Helper T cells also secrete a variety of cytokines, i.e., lymphokines, which play a central role in the activation of B cells, cytotoxic T cells and a variety of other cells which participate in the immune response.

Immune related diseases could be treated by suppressing the immune response. Using neutralizing antibodies that inhibit molecules having immune stimulatory activity would be beneficial in the treatment of immune-mediated and inflammatory diseases. Molecules which inhibit the immune response can be utilized (proteins directly or via the use of antibody agonists) to inhibit the immune response and thus ameliorate immune related disease.

CD4+ T cells are known to be important regulators of inflammation. Herein, CD4+ T cells were activated and the profile of genes differentially expressed upon activation was analyzed. As such, the activation specific genes may be potential therapeutic targets. *In vivo* co-stimulation is necessary for a productive immune proliferative response. The list of costimulatory molecules is quite

- 2a -

extensive and it is still unclear just which co-stimulatory molecules play critical roles in different types and stages of inflammation. In this application the focus is on genes which are specifically upregulated or
5 downregulated by stimulation with anti-CD3/ICAM, or anti-CD3/anti-CD28 and may be useful in targeting inflammatory processes which are associated with these different molecules.

Despite the above identified advances in T cell
10 research, there is a great need for additional diagnostic and therapeutic agents capable of detecting the presence of a T cell mediated disorders in a mammal and for effectively reducing these disorders. Accordingly, it is an objective of the present invention to identify
15 polypeptides that are overexpressed in activated T cells as compared to resting T cells, and to use those polypeptides, and their encoding nucleic acids, to produce compositions of matter useful in the therapeutic treatment and diagnostic detection of T cell mediated disorders in
20 mammals.

Summary of the Invention

In the claims which follow and in the preceding description of the invention, except where the context
25 requires otherwise due to express language or necessary implication, the word "comprise" or variations such as "comprises" or "comprising" is used in an inclusive sense, i.e. to specify the presence of the stated features but not to preclude the presence or addition of further
30 features in various embodiments of the invention.

A. Embodiments

The present invention concerns compositions and methods useful for the diagnosis and treatment of immune
35 related disease in mammals, including humans. The present invention is based on the identification of proteins (including agonist and antagonist antibodies) which are a

451601_1 (GHMatters) 19/08/09

result of stimulation of the immune response in mammals. Immune related diseases can be treated by suppressing or enhancing the immune response. Molecules that enhance the immune response stimulate or potentiate the immune response to an antigen. Molecules which stimulate the immune response can be used therapeutically where enhancement of the immune response would be beneficial. Alternatively, molecules that suppress the immune response attenuate or reduce the immune response to an antigen (e.g., neutralizing antibodies) can be used therapeutically where attenuation of the immune response would be beneficial (e.g., inflammation).

Accordingly, the PRO polypeptides, agonists and antagonists thereof are also useful to prepare medicines and medicaments for the treatment of immune-related and inflammatory diseases. In a specific aspect, such medicines and medicaments comprise a therapeutically effective amount of a PRO polypeptide, agonist or antagonist thereof with a pharmaceutically acceptable carrier. Preferably, the admixture is sterile.

In a first aspect, the present invention provides an isolated nucleic acid having at least 80% nucleic acid sequence identity to a nucleotide sequence identity to: (a) the nucleotide sequence shown in Figure 4569 (SEQ ID NO: 4569); or (b) the nucleotide sequence encoding the polypeptide shown in Figure 4570 (SEQ ID NO: 4570).

In a second aspect, the present invention provides an isolated polypeptide having at least 95% amino acid sequence identity to: (a) a polypeptide shown in Figure 4570 (SEQ ID NO: 4570); or (b) a polypeptide encoded by the full length coding region of the nucleotide sequence shown in Figure 4569 (SEQ ID NO: 4569).

In a third aspect, the present invention provides a method for determining the presence of a polypeptide as described

- 2c -

in Figure 4570 (SEQ ID NO: 4570), in a sample suspected of containing said polypeptide, said method comprising exposing said sample to an antibody that specifically binds to a polypeptide described in Figure 4570 (SEQ ID NO: 4570), where the and determining binding of said antibody to a component of said sample.

In a fourth aspect, the present invention provides a method of diagnosing an immune related disease in a mammal, said method comprising detecting the level of expression of a gene encoding a polypeptide as described in Figure 4570 (SEQ ID NO: 4570), (a) in a test sample of tissue cells obtained from the mammal, and (b) in a control sample of known normal tissue cells of the same cell type, wherein a higher or lower level of expression of said gene in the test sample as compared to the control sample is indicative of the presence of an immune related disease in the mammal from which the test tissue cells were obtained.

In a fifth aspect, the present invention provides a method of diagnosing an immune related disease in a mammal, said method comprising (a) contacting an antibody that specifically binds to a polypeptide as described in Figure 4570 (SEQ ID NO: 4570), with a test sample of tissue cells obtained from said mammal and (b) detecting the formation of a complex between the antibody and the polypeptide in the test sample, wherein formation of said complex is indicative of the presence of an immune related disease in the mammal from which the test tissue cells were obtained.

In a sixth aspect, the present invention provides a method of identifying a compound that inhibits the activity of a polypeptide as described in Figure 4570 (SEQ ID NO: 4570), said method comprising contacting cells which normally respond to said polypeptide with (a) said polypeptide and (b) a candidate compound, and determining the lack

461601_1 (GH/Matters) 19/08/09

- 2d -

responsiveness by said cell to (a).

In a seventh aspect, the present invention provides a method of identifying a compound that inhibits the expression of a gene encoding a polypeptide as described in Figure 4570 (SEQ ID NO: 4570), said method comprising contacting cells which normally express said polypeptide with a candidate compound, and determining the lack of expression of said gene.

In an eighth aspect, the present invention provides a method of identifying a compound that mimics the activity of a polypeptide as described in Figure 4570 (SEQ ID NO: 4570), said method comprising contacting cells which normally respond to said polypeptide with a candidate compound, and determining the responsiveness by said cell to said candidate compound.

In a ninth aspect, method of stimulating the immune response in a mammal, said method comprising administering to said mammal an effective amount of a polypeptide as described in Figure 4570 (SEQ ID NO: 4570), wherein said immune response is stimulated.

In a tenth aspect, the present invention provides method of diagnosing an inflammatory immune response in a mammal, said method comprising detecting the level of expression of a gene encoding a polypeptide as described in Figure 4570 (SEQ ID NO: 4570), (a) in a test sample of tissue cells obtained from the mammal, and (b) in a control sample of known normal tissue cells of the same cell type, wherein a higher or lower level of expression of said gene in the test sample as compared to the control sample is indicative of the presence of an inflammatory immune response in the mammal from which the test tissue cells were obtained.

451601_1 (GHMatters) 19/08/09

In a further embodiment, the invention concerns a method of identifying agonists or antagonists to a PRO polypeptide which comprises contacting the PRO polypeptide with a candidate molecule and monitoring a biological activity mediated by said PRO polypeptide. Preferably, the PRO polypeptide is a native sequence PRO polypeptide. In a specific aspect, the PRO agonist or antagonist is an anti-PRO antibody.

In another embodiment, the invention concerns a composition of matter comprising a PRO polypeptide or an agonist or antagonist antibody which binds the polypeptide in admixture with a carrier or excipient. In one aspect, the composition comprises a therapeutically effective amount of the polypeptide or antibody. In another aspect, when the composition comprises an immune stimulating molecule, the composition is useful for: (a) increasing infiltration of inflammatory cells into a tissue of a mammal in need thereof, (b) stimulating or enhancing an immune response in a mammal in need thereof, (c) increasing the proliferation of T-lymphocytes in a mammal in need thereof in response to an antigen, (d) stimulating the activity of T-lymphocytes or (e) increasing the vascular permeability. In a further aspect, when the composition comprises an immune inhibiting molecule, the composition is useful for: (a) decreasing infiltration of inflammatory cells into a tissue of a mammal in need thereof, (b) inhibiting or reducing an

immune response in a mammal in need thereof, (c) decreasing the activity of T-lymphocytes or (d) decreasing the proliferation of T-lymphocytes in a mammal in need thereof in response to an antigen. In another aspect, the composition comprises a further active ingredient, which may, for example, be a further antibody or a cytotoxic or chemotherapeutic agent. Preferably, the composition is sterile.

5 In another embodiment, the invention concerns a method of treating an immune related disorder in a mammal in need thereof, comprising administering to the mammal an effective amount of a PRO polypeptide, an agonist thereof, or an antagonist thereto. In a preferred aspect, the immune related disorder is selected from the group consisting of: systemic lupus erythematosus, rheumatoid arthritis, osteoarthritis, juvenile chronic arthritis, spondyloarthropathies, systemic sclerosis, idiopathic inflammatory myopathies, 10 Sjögren's syndrome, systemic vasculitis, sarcoidosis, autoimmune hemolytic anemia, autoimmune thrombocytopenia, thyroiditis, diabetes mellitus, immune-mediated renal disease, demyelinating diseases of the central and peripheral nervous systems such as multiple sclerosis, idiopathic demyelinating polyneuropathy or Guillain-Barré syndrome, and chronic inflammatory demyelinating polyneuropathy, hepatobiliary diseases such as infectious, autoimmune chronic active hepatitis, primary biliary cirrhosis, 15 granulomatous hepatitis, and sclerosing cholangitis, inflammatory bowel disease, gluten-sensitive enteropathy, and Whipple's disease, autoimmune or immune-mediated skin diseases including bullous skin diseases, erythema multiforme and contact dermatitis, psoriasis, allergic diseases such as asthma, allergic rhinitis, atopic dermatitis, food hypersensitivity and urticaria, immunologic diseases of the lung such as eosinophilic pneumonias, idiopathic pulmonary fibrosis and hypersensitivity pneumonitis, transplantation associated diseases including graft rejection and graft -versus-host-disease. 20

In another embodiment, the invention provides an antibody which specifically binds to any of the above or below described polypeptides. Optionally, the antibody is a monoclonal antibody, humanized antibody, antibody fragment or single-chain antibody. In one aspect, the present invention concerns an isolated antibody which binds a PRO polypeptide. In another aspect, the antibody mimics the activity of a 25 PRO polypeptide (an agonist antibody) or conversely the antibody inhibits or neutralizes the activity of a PRO polypeptide (an antagonist antibody). In another aspect, the antibody is a monoclonal antibody, which preferably has nonhuman complementarity determining region (CDR) residues and human framework region (FR) residues. The antibody may be labeled and may be immobilized on a solid support. In a further aspect, the antibody is an antibody fragment, a monoclonal antibody, a single-chain antibody, or an anti-idiotypic 30 antibody.

In yet another embodiment, the present invention provides a composition comprising an anti-PRO antibody in admixture with a pharmaceutically acceptable carrier. In one aspect, the composition comprises a therapeutically effective amount of the antibody. Preferably, the composition is sterile. The composition may be administered in the form of a liquid pharmaceutical formulation, which may be preserved to achieve 35 extended storage stability. Alternatively, the antibody is a monoclonal antibody, an antibody fragment, a humanized antibody, or a single-chain antibody.

In a further embodiment, the invention concerns an article of manufacture, comprising:

- (a) a composition of matter comprising a PRO polypeptide or agonist or antagonist thereof;
- (b) a container containing said composition; and

(c) a label affixed to said container, or a package insert included in said container referring to the use of said PRO polypeptide or agonist or antagonist thereof in the treatment of an immune related disease. The composition may comprise a therapeutically effective amount of the PRO polypeptide or the agonist or antagonist thereof.

5 In yet another embodiment, the present invention concerns a method of diagnosing an immune related disease in a mammal, comprising detecting the level of expression of a gene encoding a PRO polypeptide (a) in a test sample of tissue cells obtained from the mammal, and (b) in a control sample of known normal tissue cells of the same cell type, wherein a higher or lower expression level in the test sample as compared to the control sample indicates the presence of immune related disease in the mammal
10 from which the test tissue cells were obtained.

In another embodiment, the present invention concerns a method of diagnosing an immune disease in a mammal, comprising (a) contacting an anti-PRO antibody with a test sample of tissue cells obtained from the mammal, and (b) detecting the formation of a complex between the antibody and a PRO polypeptide, in the test sample; wherein the formation of said complex is indicative of the presence or
15 absence of said disease. The detection may be qualitative or quantitative, and may be performed in comparison with monitoring the complex formation in a control sample of known normal tissue cells of the same cell type. A larger quantity of complexes formed in the test sample indicates the presence or absence of an immune disease in the mammal from which the test tissue cells were obtained. The antibody preferably carries a detectable label. Complex formation can be monitored, for example, by light
20 microscopy, flow cytometry, fluorimetry, or other techniques known in the art. The test sample is usually obtained from an individual suspected of having a deficiency or abnormality of the immune system.

In another embodiment, the invention provides a method for determining the presence of a PRO polypeptide in a sample comprising exposing a test sample of cells suspected of containing the PRO polypeptide to an anti-PRO antibody and determining the binding of said antibody to said cell sample. In a
25 specific aspect, the sample comprises a cell suspected of containing the PRO polypeptide and the antibody binds to the cell. The antibody is preferably detectably labeled and/or bound to a solid support.

In another embodiment, the present invention concerns an immune-related disease diagnostic kit, comprising an anti-PRO antibody and a carrier in suitable packaging. The kit preferably contains instructions for using the antibody to detect the presence of the PRO polypeptide. Preferably the carrier is
30 pharmaceutically acceptable.

In another embodiment, the present invention concerns a diagnostic kit, containing an anti-PRO antibody in suitable packaging. The kit preferably contains instructions for using the antibody to detect the PRO polypeptide.

35 In another embodiment, the invention provides a method of diagnosing an immune-related disease in a mammal which comprises detecting the presence or absence of a PRO polypeptide in a test sample of tissue cells obtained from said mammal, wherein the presence or absence of the PRO polypeptide in said test sample is indicative of the presence of an immune-related disease in said mammal.

In another embodiment, the present invention concerns a method for identifying an agonist of a PRO polypeptide comprising:

(a) contacting cells and a test compound to be screened under conditions suitable for the induction of a cellular response normally induced by a PRO polypeptide; and

(b) determining the induction of said cellular response to determine if the test compound is an effective agonist, wherein the induction of said cellular response is indicative of said test compound being an effective agonist.

In another embodiment, the invention concerns a method for identifying a compound capable of inhibiting the activity of a PRO polypeptide comprising contacting a candidate compound with a PRO polypeptide under conditions and for a time sufficient to allow these two components to interact and determining whether the activity of the PRO polypeptide is inhibited. In a specific aspect, either the candidate compound or the PRO polypeptide is immobilized on a solid support. In another aspect, the non-immobilized component carries a detectable label. In a preferred aspect, this method comprises the steps of:

(a) contacting cells and a test compound to be screened in the presence of a PRO polypeptide under conditions suitable for the induction of a cellular response normally induced by a PRO polypeptide; and

(b) determining the induction of said cellular response to determine if the test compound is an effective antagonist.

In another embodiment, the invention provides a method for identifying a compound that inhibits the expression of a PRO polypeptide in cells that normally express the polypeptide, wherein the method comprises contacting the cells with a test compound and determining whether the expression of the PRO polypeptide is inhibited. In a preferred aspect, this method comprises the steps of:

(a) contacting cells and a test compound to be screened under conditions suitable for allowing expression of the PRO polypeptide; and

(b) determining the inhibition of expression of said polypeptide.

In yet another embodiment, the present invention concerns a method for treating an immune-related disorder in a mammal that suffers therefrom comprising administering to the mammal a nucleic acid molecule that codes for either (a) a PRO polypeptide, (b) an agonist of a PRO polypeptide or (c) an antagonist of a PRO polypeptide, wherein said agonist or antagonist may be an anti-PRO antibody. In a preferred embodiment, the mammal is human. In another preferred embodiment, the nucleic acid is administered via *ex vivo* gene therapy. In a further preferred embodiment, the nucleic acid is comprised within a vector, more preferably an adenoviral, adeno-associated viral, lentiviral or retroviral vector.

In yet another aspect, the invention provides a recombinant viral particle comprising a viral vector consisting essentially of a promoter, nucleic acid encoding (a) a PRO polypeptide, (b) an agonist polypeptide of a PRO polypeptide, or (c) an antagonist polypeptide of a PRO polypeptide, and a signal sequence for cellular secretion of the polypeptide, wherein the viral vector is in association with viral structural proteins. Preferably, the signal sequence is from a mammal, such as from a native PRO polypeptide.

In a still further embodiment, the invention concerns an *ex vivo* producer cell comprising a nucleic acid construct that expresses retroviral structural proteins and also comprises a retroviral vector consisting essentially of a promoter, nucleic acid encoding (a) a PRO polypeptide, (b) an agonist polypeptide of a PRO polypeptide or (c) an antagonist polypeptide of a PRO polypeptide, and a signal sequence for cellular secretion of the polypeptide, wherein said producer cell packages the retroviral vector in association with the structural proteins to produce recombinant retroviral particles.

In a still further embodiment, the invention provides a method of increasing the activity of T-lymphocytes in a mammal comprising administering to said mammal (a) a PRO polypeptide, (b) an agonist of a PRO polypeptide, or (c) an antagonist of a PRO polypeptide, wherein the activity of T-lymphocytes in the mammal is increased.

5 In a still further embodiment, the invention provides a method of decreasing the activity of T-lymphocytes in a mammal comprising administering to said mammal (a) a PRO polypeptide, (b) an agonist of a PRO polypeptide, or (c) an antagonist of a PRO polypeptide, wherein the activity of T-lymphocytes in the mammal is decreased.

10 In a still further embodiment, the invention provides a method of increasing the proliferation of T-lymphocytes in a mammal comprising administering to said mammal (a) a PRO polypeptide, (b) an agonist of a PRO polypeptide, or (c) an antagonist of a PRO polypeptide, wherein the proliferation of T-lymphocytes in the mammal is increased.

15 In a still further embodiment, the invention provides a method of decreasing the proliferation of T-lymphocytes in a mammal comprising administering to said mammal (a) a PRO polypeptide, (b) an agonist of a PRO polypeptide, or (c) an antagonist of a PRO polypeptide, wherein the proliferation of T-lymphocytes in the mammal is decreased.

B. Additional Embodiments

In other embodiments of the present invention, the invention provides vectors comprising DNA encoding any of the herein described polypeptides. Host cell comprising any such vector are also provided.
20 By way of example, the host cells may be CHO cells, *E. coli*, or yeast. A process for producing any of the herein described polypeptides is further provided and comprises culturing host cells under conditions suitable for expression of the desired polypeptide and recovering the desired polypeptide from the cell culture.

In other embodiments, the invention provides chimeric molecules comprising any of the herein described polypeptides fused to a heterologous polypeptide or amino acid sequence. Example of such chimeric molecules comprise any of the herein described polypeptides fused to an epitope tag sequence or a C region of an immunoglobulin.
25

In another embodiment, the invention provides an antibody which specifically binds to any of the above or below described polypeptides. Optionally, the antibody is a monoclonal antibody, humanized antibody, antibody fragment or single-chain antibody.
30

In yet other embodiments, the invention provides oligonucleotide probes useful for isolating genomic and cDNA nucleotide sequences or as antisense probes, wherein those probes may be derived from any of the above or below described nucleotide sequences.

In other embodiments, the invention provides an isolated nucleic acid molecule comprising a nucleotide sequence that encodes a PRO polypeptide.
35

In one aspect, the isolated nucleic acid molecule comprises a nucleotide sequence having at least about 80% nucleic acid sequence identity, alternatively at least about 81% nucleic acid sequence identity, alternatively at least about 82% nucleic acid sequence identity, alternatively at least about 83% nucleic acid sequence identity, alternatively at least about 84% nucleic acid sequence identity, alternatively at least about 85% nucleic acid sequence identity, alternatively at least about 86% nucleic acid sequence identity,
40

alternatively at least about 87% nucleic acid sequence identity, alternatively at least about 88% nucleic acid sequence identity, alternatively at least about 89% nucleic acid sequence identity, alternatively at least about 90% nucleic acid sequence identity, alternatively at least about 91% nucleic acid sequence identity, alternatively at least about 92% nucleic acid sequence identity, alternatively at least about 93% nucleic acid sequence identity, alternatively at least about 94% nucleic acid sequence identity, alternatively at least about 95% nucleic acid sequence identity, alternatively at least about 96% nucleic acid sequence identity, alternatively at least about 97% nucleic acid sequence identity, alternatively at least about 98% nucleic acid sequence identity and alternatively at least about 99% nucleic acid sequence identity to (a) a DNA molecule encoding a PRO polypeptide having a full-length amino acid sequence as disclosed herein, an amino acid sequence lacking the signal peptide as disclosed herein, an extracellular domain of a transmembrane protein, with or without the signal peptide, as disclosed herein or any other specifically defined fragment of the full-length amino acid sequence as disclosed herein, or (b) the complement of the DNA molecule of (a).

In other aspects, the isolated nucleic acid molecule comprises a nucleotide sequence having at least about 80% nucleic acid sequence identity, alternatively at least about 81% nucleic acid sequence identity, alternatively at least about 82% nucleic acid sequence identity, alternatively at least about 83% nucleic acid sequence identity, alternatively at least about 84% nucleic acid sequence identity, alternatively at least about 85% nucleic acid sequence identity, alternatively at least about 86% nucleic acid sequence identity, alternatively at least about 87% nucleic acid sequence identity, alternatively at least about 88% nucleic acid sequence identity, alternatively at least about 89% nucleic acid sequence identity, alternatively at least about 90% nucleic acid sequence identity, alternatively at least about 91% nucleic acid sequence identity, alternatively at least about 92% nucleic acid sequence identity, alternatively at least about 93% nucleic acid sequence identity, alternatively at least about 94% nucleic acid sequence identity, alternatively at least about 95% nucleic acid sequence identity, alternatively at least about 96% nucleic acid sequence identity, alternatively at least about 97% nucleic acid sequence identity, alternatively at least about 98% nucleic acid sequence identity and alternatively at least about 99% nucleic acid sequence identity to (a) a DNA molecule comprising the coding sequence of a full-length PRO polypeptide cDNA as disclosed herein, the coding sequence of a PRO polypeptide lacking the signal peptide as disclosed herein, the coding sequence of an extracellular domain of a transmembrane PRO polypeptide, with or without the signal peptide, as disclosed herein or the coding sequence of any other specifically defined fragment of the full-length amino acid sequence as disclosed herein, or (b) the complement of the DNA molecule of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising a nucleotide sequence having at least about 80% nucleic acid sequence identity, alternatively at least about 81% nucleic acid sequence identity, alternatively at least about 82% nucleic acid sequence identity, alternatively at least about 83% nucleic acid sequence identity, alternatively at least about 84% nucleic acid sequence identity, alternatively at least about 85% nucleic acid sequence identity, alternatively at least about 86% nucleic acid sequence identity, alternatively at least about 87% nucleic acid sequence identity, alternatively at least about 88% nucleic acid sequence identity, alternatively at least about 89% nucleic acid sequence identity, alternatively at least about 90% nucleic acid sequence identity, alternatively at least about 91% nucleic acid sequence identity, alternatively at least about 92% nucleic acid sequence identity, alternatively at least about 93% nucleic acid sequence identity, alternatively at least about 94% nucleic acid

sequence identity, alternatively at least about 95% nucleic acid sequence identity, alternatively at least about 96% nucleic acid sequence identity, alternatively at least about 97% nucleic acid sequence identity, alternatively at least about 98% nucleic acid sequence identity and alternatively at least about 99% nucleic acid sequence identity to (a) a DNA molecule that encodes the same mature polypeptide encoded by any of the human protein cDNAs as disclosed herein, or (b) the complement of the DNA molecule of (a).

Another aspect the invention provides an isolated nucleic acid molecule comprising a nucleotide sequence encoding a PRO polypeptide which is either transmembrane domain-deleted or transmembrane domain-inactivated, or is complementary to such encoding nucleotide sequence, wherein the transmembrane domain(s) of such polypeptide are disclosed herein. Therefore, soluble extracellular domains of the herein described PRO polypeptides are contemplated.

Another embodiment is directed to fragments of a PRO polypeptide coding sequence, or the complement thereof, that may find use as, for example, hybridization probes, for encoding fragments of a PRO polypeptide that may optionally encode a polypeptide comprising a binding site for an anti-PRO antibody or as antisense oligonucleotide probes. Such nucleic acid fragments are usually at least about 20 nucleotides in length, alternatively at least about 30 nucleotides in length, alternatively at least about 40 nucleotides in length, alternatively at least about 50 nucleotides in length, alternatively at least about 60 nucleotides in length, alternatively at least about 70 nucleotides in length, alternatively at least about 80 nucleotides in length, alternatively at least about 90 nucleotides in length, alternatively at least about 100 nucleotides in length, alternatively at least about 110 nucleotides in length, alternatively at least about 120 nucleotides in length, alternatively at least about 130 nucleotides in length, alternatively at least about 140 nucleotides in length, alternatively at least about 150 nucleotides in length, alternatively at least about 160 nucleotides in length, alternatively at least about 170 nucleotides in length, alternatively at least about 180 nucleotides in length, alternatively at least about 190 nucleotides in length, alternatively at least about 200 nucleotides in length, alternatively at least about 250 nucleotides in length, alternatively at least about 300 nucleotides in length, alternatively at least about 350 nucleotides in length, alternatively at least about 400 nucleotides in length, alternatively at least about 450 nucleotides in length, alternatively at least about 500 nucleotides in length, alternatively at least about 600 nucleotides in length, alternatively at least about 700 nucleotides in length, alternatively at least about 800 nucleotides in length, alternatively at least about 900 nucleotides in length and alternatively at least about 1000 nucleotides in length, wherein in this context the term "about" means the referenced nucleotide sequence length plus or minus 10% of that referenced length. It is noted that novel fragments of a PRO polypeptide-encoding nucleotide sequence may be determined in a routine manner by aligning the PRO polypeptide-encoding nucleotide sequence with other known nucleotide sequences using any of a number of well known sequence alignment programs and determining which PRO polypeptide-encoding nucleotide sequence fragment(s) are novel. All of such PRO polypeptide-encoding nucleotide sequences are contemplated herein. Also contemplated are the PRO polypeptide fragments encoded by these nucleotide molecule fragments, preferably those PRO polypeptide fragments that comprise a binding site for an anti-PRO antibody.

In another embodiment, the invention provides isolated PRO polypeptide encoded by any of the isolated nucleic acid sequences herein above identified.

In a certain aspect, the invention concerns an isolated PRO polypeptide, comprising an amino acid sequence having at least about 80% amino acid sequence identity, alternatively at least about 81% amino acid sequence identity, alternatively at least about 82% amino acid sequence identity, alternatively at least about 83% amino acid sequence identity, alternatively at least about 84% amino acid sequence identity, alternatively at least about 85% amino acid sequence identity, alternatively at least about 86% amino acid sequence identity, alternatively at least about 87% amino acid sequence identity, alternatively at least about 88% amino acid sequence identity, alternatively at least about 89% amino acid sequence identity, alternatively at least about 90% amino acid sequence identity, alternatively at least about 91% amino acid sequence identity, alternatively at least about 92% amino acid sequence identity, alternatively at least about 93% amino acid sequence identity, alternatively at least about 94% amino acid sequence identity, alternatively at least about 95% amino acid sequence identity, alternatively at least about 96% amino acid sequence identity, alternatively at least about 97% amino acid sequence identity, alternatively at least about 98% amino acid sequence identity and alternatively at least about 99% amino acid sequence identity to a PRO polypeptide having a full-length amino acid sequence as disclosed herein, an amino acid sequence lacking the signal peptide as disclosed herein, an extracellular domain of a transmembrane protein, with or without the signal peptide, as disclosed herein or any other specifically defined fragment of the full-length amino acid sequence as disclosed herein.

In a further aspect, the invention concerns an isolated PRO polypeptide comprising an amino acid sequence having at least about 80% amino acid sequence identity, alternatively at least about 81% amino acid sequence identity, alternatively at least about 82% amino acid sequence identity, alternatively at least about 83% amino acid sequence identity, alternatively at least about 84% amino acid sequence identity, alternatively at least about 85% amino acid sequence identity, alternatively at least about 86% amino acid sequence identity, alternatively at least about 87% amino acid sequence identity, alternatively at least about 88% amino acid sequence identity, alternatively at least about 89% amino acid sequence identity, alternatively at least about 90% amino acid sequence identity, alternatively at least about 91% amino acid sequence identity, alternatively at least about 92% amino acid sequence identity, alternatively at least about 93% amino acid sequence identity, alternatively at least about 94% amino acid sequence identity, alternatively at least about 95% amino acid sequence identity, alternatively at least about 96% amino acid sequence identity, alternatively at least about 97% amino acid sequence identity, alternatively at least about 98% amino acid sequence identity and alternatively at least about 99% amino acid sequence identity to an amino acid sequence encoded by any of the human protein cDNAs as disclosed herein.

In a specific aspect, the invention provides an isolated PRO polypeptide without the N-terminal signal sequence and/or the initiating methionine and is encoded by a nucleotide sequence that encodes such an amino acid sequence as herein before described. Processes for producing the same are also herein described, wherein those processes comprise culturing a host cell comprising a vector which comprises the appropriate encoding nucleic acid molecule under conditions suitable for expression of the PRO polypeptide and recovering the PRO polypeptide from the cell culture.

Another aspect the invention provides an isolated PRO polypeptide which is either transmembrane domain-deleted or transmembrane domain-inactivated. Processes for producing the same are also herein described, wherein those processes comprise culturing a host cell comprising a vector which comprises the

appropriate encoding nucleic acid molecule under conditions suitable for expression of the PRO polypeptide and recovering the PRO polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO polypeptide as defined herein. In a particular embodiment, the agonist or antagonist is an anti-PRO antibody
5 or a small molecule.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists to a PRO polypeptide which comprise contacting the PRO polypeptide with a candidate molecule and monitoring a biological activity mediated by said PRO polypeptide. Preferably, the PRO polypeptide is a native PRO polypeptide.

10 In a still further embodiment, the invention concerns a composition of matter comprising a PRO polypeptide, or an agonist or antagonist of a PRO polypeptide as herein described, or an anti-PRO antibody, in combination with a carrier. Optionally, the carrier is a pharmaceutically acceptable carrier.

Another embodiment of the present invention is directed to the use of a PRO polypeptide, or an agonist or antagonist thereof as herein before described, or an anti-PRO antibody, for the preparation of a
15 medicament useful in the treatment of a condition which is responsive to the PRO polypeptide, an agonist or antagonist thereof or an anti-PRO antibody.

List of Figures

- Figure 1: DNA325395, NP_000973.2, 200012.x.at
 Figure 2: PRO81927
 Figure 3: DNA329897, NP_031401.1, 200020.at
 Figure 4: PRO69676
 Figure 5: DNA326769, NP_001000.2, 200024.at
 Figure 6: PRO83105
 Figure 7: DNA329898, NP_000979.1, 200025.s.at
 Figure 8: PRO10643
 Figure 9: DNA293451, NP_296374.1, 200026.at
 Figure 10: PRO70720
 Figure 11: DNA326466, NP_004530.1, 200027.at
 Figure 12: PRO60800
 Figure 13: DNA329899, NP_002785.1, 200039.s.at
 Figure 14: PRO69614
 Figure 15: DNA326953, HSPC117, 200042.at
 Figure 16: PRO83270
 Figure 17: DNA255084, NP_001081.1, 200045.at
 Figure 18: PRO50170
 Figure 19: DNA272614, NP_004506.1, 200052.s.at
 Figure 20: PRO60747
 Figure 21: DNA304680, HSPCB, 200064.at
 Figure 22: PRO71106
 Figure 23: DNA189703, NP_005539.1, 200079.s.at
 Figure 24: PRO22637
 Figure 25: DNA329900, NP_002905.1, 1053.at
 Figure 26: PRO81549
 Figure 27: DNA88189, NP_037362.1, 266.s.at
 Figure 28: PRO2690
 Figure 29: DNA272992, NP_055479.1, 32069.at
 Figure 30: PRO61064
 Figure 31A-B: DNA329901, BAA32291.2, 32091.at
 Figure 32: PRO85218
 Figure 33: DNA329902, NP_110419.2, 32502.at
 Figure 34: PRO85219
 Figure 35: DNA329903, NP_005596.2, 32541.at
 Figure 36: PRO85220
 Figure 37: DNA327521, NP_002192.2, 33304.at
 Figure 38: PRO58320
 Figure 39: DNA272223, NP_004444.1, 33494.at
 Figure 40: PRO60485
 Figure 41A-B: DNA329904, NP_066554.1, 33767.at
 Figure 42: PRO85221
 Figure 43: DNA210121, NP_001794.1, 34210.at
 Figure 44: PRO33667
 Figure 45: DNA269828, NP_006691.1, 35254.at
 Figure 46: PRO58230
 Figure 47: DNA88643, NP_000190.1, 35626.at
 Figure 48: PRO2455
 Figure 49: DNA331435, NP_006143.1, 35974.at
 Figure 50: PRO86495
 Figure 51A-B: DNA272022, NP_002607.1, 36829.at
 Figure 52: PRO60296
 Figure 53: DNA226967, NP_055145.2, 37028.at
 Figure 54: PRO37430
 Figure 55: DNA226043, NP_006424.2, 37145.at
 Figure 56: PRO36506
 Figure 57: DNA329906, MGC14258, 37577.at
 Figure 58: PRO85223
 Figure 59: DNA256295, NP_002310.1, 37796.at
 Figure 60: PRO51339
 Figure 61: DNA328354, AF237769, 37966.at
 Figure 62: PRO84215
 Figure 63A-B: DNA329907, NP_036423.1, 38158.at
 Figure 64: PRO85224
 Figure 65A-B: DNA329908, BAA13246.1, 38892.at
 Figure 66: PRO85225
 Figure 67: DNA328356, BC013566, 39248.at
 Figure 68: PRO38028
 Figure 69: DNA327523, NP_004916.1, 39249.at
 Figure 70: PRO38028
 Figure 71A-B: DNA328358, STK10, 40420.at
 Figure 72: PRO84218
 Figure 73: DNA329909, NP_077084.1, 40446.at
 Figure 74: PRO62251
 Figure 75: DNA329910, NP_003251.2, 40837.at
 Figure 76: PRO82891
 Figure 77A-B: DNA329093, NP_006631.1, 41220.at
 Figure 78: PRO84745
 Figure 79A-C: DNA331436, 7689629.6, 43427.at
 Figure 80: PRO86496
 Figure 81: DNA154653, DNA154653, 43511.s.at
 Figure 82: DNA262129, NP_079389.1, 44790.s.at
 Figure 83: PRO54740
 Figure 84: DNA326185, NP_073607.2, 45633.at
 Figure 85: PRO82602
 Figure 86: DNA329912, NP_004614.1, 46167.at
 Figure 87: PRO85227
 Figure 88: DNA329913, SSB-3, 46256.at
 Figure 89: PRO85228
 Figure 90: DNA324145, NP_060259.1, 46665.at
 Figure 91: PRO80846
 Figure 92: DNA329094, NP_077285.1, 48531.at
 Figure 93: PRO84746
 Figure 94: DNA329914, NP_079175.2, 52285.f.at
 Figure 95: PRO85229
 Figure 96: DNA328364, NP_068577.1, 52940.at
 Figure 97: PRO84223
 Figure 98: DNA329915, NP_065093.1, 56197.at
 Figure 99: PRO85230
 Figure 100A-B: DNA328966, AK024397, 57082.at
 Figure 101: PRO84670
 Figure 102A-B: DNA226870, NP_000782.1, 48808.at
 Figure 103: PRO37333
 Figure 104: DNA328366, NP_079233.1, 59375.at
 Figure 105: PRO84225
 Figure 106: DNA331437, 338326.15, 60084.at
 Figure 107: PRO86497
 Figure 108: DNA328367, NP_079108.2, 60471.at

- Figure 109: PRO84226
 Figure 110: DNA327876, NP.005081.1, 60528.at
 Figure 111: PRO83815
 Figure 112: DNA329917, NP.065174.1, 64486.at
 Figure 113: PRO85232
 Figure 114: DNA329918, BC008671, 65630.at
 Figure 115: PRO85233
 Figure 116A-B: DNA196428, BAA31649.1, 76897.s.at
 Figure 117: PRO71274
 Figure 118: DNA329919, C20orf67, 89948.at
 Figure 119: PRO85234
 Figure 120: DNA328369, BC007634, 90610.at
 Figure 121: DNA269410, NP.002725.1, 200605.s.at
 Figure 122: PRO57836
 Figure 123A-B: DNA326380, NP.004850.1, 200614.at
 Figure 124: PRO82774
 Figure 125A-B: DNA194778, NP.055545.1, 200616.s.at
 Figure 126: PRO24056
 Figure 127: DNA287245, NP.004175.1, 200628.s.at
 Figure 128: PRO69520
 Figure 129: DNA287245, WARS, 200629.at
 Figure 130: PRO69520
 Figure 131: DNA327532, GLUL, 200648.s.at
 Figure 132: PRO71134
 Figure 133: DNA97285, NP.005557.1, 200650.s.at
 Figure 134: PRO3632
 Figure 135: DNA226125, NP.003136.1, 200652.at
 Figure 136: PRO36588
 Figure 137: DNA325923, NP.008819.1, 200655.s.at
 Figure 138: PRO4904
 Figure 139: DNA227055, NP.002625.1, 200658.s.at
 Figure 140: PRO37518
 Figure 141: DNA275062, NP.006136.1, 200664.s.at
 Figure 142: PRO62782
 Figure 143: DNA275062, DNAJB1, 200666.s.at
 Figure 144: PRO62782
 Figure 145A-B: DNA328372, 105551.7, 200685.at
 Figure 146: PRO84229
 Figure 147A-B: DNA329920, NP.036558.1, 200687.s.at
 Figure 148: PRO85235
 Figure 149: DNA324633, BC000478, 200691.s.at
 Figure 150: PRO81277
 Figure 151: DNA324897, NP.006845.1, 200700.s.at
 Figure 152: PRO12468
 Figure 153: DNA275267, NP.003737.1, 200703.at
 Figure 154: PRO62952
 Figure 155: DNA328373, AB034747, 200704.at
 Figure 156: PRO84230
 Figure 157: DNA328374, NP.004853.1, 200706.s.at
 Figure 158: PRO84231
 Figure 159: DNA290260, NP.036555.1, 200715.x.at
 Figure 160: PRO70385
 Figure 161: DNA329921, 1315403.9, 200719.at
 Figure 162: PRO85236
 Figure 163: DNA329538, M11S1, 200722.s.at
 Figure 164: PRO85088
 Figure 165: DNA227618, HSGPIP137, 200723.s.at
 Figure 166: PRO38081
 Figure 167: DNA327114, NP.006004.1, 200725.x.at
 Figure 168: PRO62466
 Figure 169A-B: DNA327534, NP.003454.1, 200730.s.at
 Figure 170: PRO41180
 Figure 171A-B: DNA327534, PTP4A1, 200731.s.at
 Figure 172: PRO41180
 Figure 173: DNA331438, 402431.7, 200732.s.at
 Figure 174: PRO86498
 Figure 175: DNA327845, NP.000282.1, 200737.at
 Figure 176: PRO61271
 Figure 177: DNA327845, PGK1, 200738.s.at
 Figure 178: PRO61271
 Figure 179: DNA287207, NP.006316.1, 200750.s.at
 Figure 180: PRO39268
 Figure 181A-B: DNA274977, HSU97105, 200762.at
 Figure 182: PRO62709
 Figure 183: DNA324135, BC001854, 200768.s.at
 Figure 184: PRO80837
 Figure 185: DNA324135, NP.005902.1, 200769.s.at
 Figure 186: PRO80837
 Figure 187: DNA271608, NP.055485.1, 200777.s.at
 Figure 188: PRO59895
 Figure 189: DNA226262, NP.005554.1, 200783.s.at
 Figure 190: PRO36725
 Figure 191: DNA324060, NP.002530.1, 200790.at
 Figure 192: PRO80773
 Figure 193: DNA272928, NP.055579.1, 200794.x.at
 Figure 194: PRO61012
 Figure 195: DNA304668, NP.005336.2, 200799.at
 Figure 196: PRO71095
 Figure 197: DNA227607, NP.005337.1, 200800.s.at
 Figure 198: PRO38070
 Figure 199: DNA287211, NP.002147.1, 200806.s.at
 Figure 200: PRO69492
 Figure 201: DNA287211, HSPD1, 200807.s.at
 Figure 202: PRO69492
 Figure 203: DNA269874, NP.001271.1, 200810.s.at
 Figure 204: PRO58272
 Figure 205: DNA269874, CIRBP, 200811.at
 Figure 206: PRO58272
 Figure 207: DNA227795, NP.006420.1, 200812.at
 Figure 208: PRO38258
 Figure 209: DNA325596, NP.000356.1, 200822.x.at
 Figure 210: PRO69549
 Figure 211A-B: DNA328700, AF097514, 200831.s.at
 Figure 212: PRO84464
 Figure 213A-B: DNA328378, AB032261, 200832.s.at
 Figure 214: PRO84233
 Figure 215: DNA329922, CTSB, 200838.at
 Figure 216: PRO3344

- Figure 217: DNA88165, HUMCTSB, 200839.s.at
 Figure 218: PRO2678
 Figure 219: DNA329923, NP_057211.3, 200847.s.at
 Figure 220: PRO85237
 Figure 221: DNA324509, NP_002097.1, 200853.at
 Figure 222: PRO10297
 Figure 223A-C: DNA331439, NP_001447.1, 200859.x.at
 Figure 224: PRO86499
 Figure 225A-B: DNA228029, NP_055577.1, 200862.at
 Figure 226: PRO38492
 Figure 227: DNA226112, NP_002769.1, 200866.s.at
 Figure 228: PRO36575
 Figure 229: DNA226112, PSAP, 200871.s.at
 Figure 230: PRO36575
 Figure 231: DNA254537, NP_002957.1, 200872.at
 Figure 232: PRO49642
 Figure 233: DNA271030, NP_006383.1, 200875.s.at
 Figure 234: PRO59358
 Figure 235: DNA324107, NP_006421.1, 200877.at
 Figure 236: PRO80814
 Figure 237: DNA328379, BC015869, 200878.at
 Figure 238: PRO84234
 Figure 239: DNA329099, 1164406.9, 200880.at
 Figure 240: PRO60127
 Figure 241: DNA271847, NP_001530.1, 200881.s.at
 Figure 242: PRO60127
 Figure 243: DNA287187, NP_002620.1, 200886.s.at
 Figure 244: PRO69473
 Figure 245A-B: DNA327539, NP_009330.1, 200887.s.at
 Figure 246: PRO12211
 Figure 247: DNA326326, NP_000969.1, 200888.s.at
 Figure 248: PRO82724
 Figure 249: DNA325584, NP_002005.1, 200894.s.at
 Figure 250: PRO59262
 Figure 251: DNA325584, FKBP4, 200895.s.at
 Figure 252: PRO59262
 Figure 253: DNA328380, HSHLAEHCM, 200904.at
 Figure 254: DNA304665, NP_000995.1, 200909.s.at
 Figure 255: PRO71092
 Figure 256: DNA272695, NP_001722.1, 200920.s.at
 Figure 257: PRO60817
 Figure 258: DNA272695, BTG1, 200921.s.at
 Figure 259: PRO60817
 Figure 260: DNA227077, NP_005558.1, 200923.at
 Figure 261: PRO37540
 Figure 262: DNA327255, NP_002385.2, 200924.s.at
 Figure 263: PRO57298
 Figure 264: DNA225878, NP_004334.1, 200935.at
 Figure 265: PRO36341
 Figure 266: DNA329925, NP_001528.1, 200942.s.at
 Figure 267: PRO85239
 Figure 268A-B: DNA287217, NP_001750.1, 200951.s.at
 Figure 269: PRO36766
 Figure 270A-B: DNA287217, CCND2, 200952.s.at
 Figure 271: PRO36766
 Figure 272: DNA227491, NP_009027.1, 200960.x.at
 Figure 273: PRO37954
 Figure 274: DNA331440, NP_036380.2, 200961.at
 Figure 275: PRO86500
 Figure 276A-B: DNA331289, ABLIM1, 200965.s.at
 Figure 277: PRO86390
 Figure 278: DNA287355, NP_000025.1, 200966.x.at
 Figure 279: PRO69617
 Figure 280: DNA324110, NP_005908.1, 200978.at
 Figure 281: PRO4918
 Figure 282: DNA329928, ANXA6, 200982.s.at
 Figure 283: PRO85241
 Figure 284A-B: DNA325896, NP_001521.1, 200989.at
 Figure 285: PRO82352
 Figure 286: DNA329929, 400903.6, 200994.at
 Figure 287: PRO85242
 Figure 288: DNA325778, CKAP4, 200998.s.at
 Figure 289: PRO82248
 Figure 290: DNA331441, BC015436, 200999.s.at
 Figure 291: DNA275408, NP_001596.1, 201000.at
 Figure 292: PRO63068
 Figure 293: DNA304713, NP_006463.2, 201008.s.at
 Figure 294: PRO71139
 Figure 295: DNA304713, TXNIP, 201009.s.at
 Figure 296: PRO71139
 Figure 297: DNA304713, S73591, 201010.s.at
 Figure 298: PRO71139
 Figure 299: DNA89242, NP_000691.1, 201012.at
 Figure 300: PRO2907
 Figure 301: DNA328388, BC010273, 201013.s.at
 Figure 302: PRO84240
 Figure 303: DNA328388, NP_006443.1, 201014.s.at
 Figure 304: PRO84240
 Figure 305: DNA151697, DNA151697, 201016.at
 Figure 306: PRO11993
 Figure 307A-B: DNA329101, NP_056988.2, 201024.x.at
 Figure 308: PRO84751
 Figure 309A-B: DNA329101, IF2, 201027.s.at
 Figure 310: PRO84751
 Figure 311: DNA287372, NP_002618.1, 201037.at
 Figure 312: PRO69632
 Figure 313: DNA328391, NP_004408.1, 201041.s.at
 Figure 314: PRO84242
 Figure 315: DNA328391, DUSP1, 201044.x.at
 Figure 316: PRO84242
 Figure 317: DNA274743, NP_002850.1, 201087.at
 Figure 318: PRO62517
 Figure 319: DNA254725, NP_002257.1, 201088.at
 Figure 320: PRO49824
 Figure 321: DNA329930, ATP6V1B2, 201089.at
 Figure 322: PRO85243
 Figure 323: DNA287198, NP_006073.1, 201090.x.at
 Figure 324: PRO69484

- Figure 325A-B: DNA328395, NP_056198.1, 201104.x.at
 Figure 326: PRO84245
 Figure 327: DNA304719, NP_002296.1, 201105.at
 Figure 328: PRO71145
 Figure 329: DNA329931, AF053642, 201111.at
 Figure 330: DNA331442, NP_002783.1, 201114.x.at
 Figure 331: PRO83189
 Figure 332: DNA273865, NP_006221.1, 201115.at
 Figure 333: PRO61824
 Figure 334: DNA326273, NP_001961.1, 201123.s.at
 Figure 335: PRO82678
 Figure 336: DNA329255, NP_006267.1, 201129.at
 Figure 337: PRO84855
 Figure 338: DNA329103, NP_002112.2, 201137.s.at
 Figure 339: PRO84752
 Figure 340: DNA329104, NP_004085.1, 201144.s.at
 Figure 341: PRO69550
 Figure 342: DNA329105, NP_006109.2, 201145.at
 Figure 343: PRO84753
 Figure 344: DNA329015, NFE2L2, 201146.at
 Figure 345: PRO84691
 Figure 346: DNA329932, BC008801, 201160.s.at
 Figure 347: PRO85244
 Figure 348: DNA151802, NP_003661.1, 201169.s.at
 Figure 349: PRO12890
 Figure 350: DNA151802, BHLHB2, 201170.s.at
 Figure 351: PRO12890
 Figure 352: DNA273342, NP_005887.1, 201193.at
 Figure 353: PRO61345
 Figure 354: DNA331443, NP_003000.1, 201194.at
 Figure 355: PRO86501
 Figure 356A-B: DNA103453, HUME16GEN, 201195.s.at
 Figure 357: PRO4780
 Figure 358: DNA272251, NP_002798.1, 201198.s.at
 Figure 359: PRO60513
 Figure 360: DNA103488, NP_002583.1, 201202.at
 Figure 361: PRO4815
 Figure 362: DNA327544, NP_002865.1, 201222.s.at
 Figure 363: PRO70357
 Figure 364: DNA287173, ENO1, 201231.s.at
 Figure 365: PRO69463
 Figure 366: DNA287331, NP_002645.1, 201251.at
 Figure 367: PRO69595
 Figure 368: DNA274139, NP_006494.1, 201252.at
 Figure 369: PRO62075
 Figure 370: DNA270950, NP_003182.1, 201263.at
 Figure 371: PRO59281
 Figure 372A-B: DNA328404, NP_003321.1, 201266.at
 Figure 373: PRO84251
 Figure 374: DNA331444, NP_002781.1, 201274.at
 Figure 375: PRO60981
 Figure 376: DNA323936, NP_001995.1, 201275.at
 Figure 377: PRO80669
 Figure 378: DNA328405, NP_112556.1, 201277.s.at
 Figure 379: PRO84252
 Figure 380: DNA270526, NP_001166.1, 201288.at
 Figure 381: PRO58903
 Figure 382A-B: DNA327545, TOP2A, 201291.s.at
 Figure 383: PRO82731
 Figure 384: DNA327546, HSTOP2A10, 201292.at
 Figure 385: DNA328407, WSB1, 201294.s.at
 Figure 386: PRO84254
 Figure 387A-B: DNA226778, HSM800772, 201295.s.at
 Figure 388: PRO37241
 Figure 389: DNA327547, NP_006091.1, 201298.s.at
 Figure 390: PRO83583
 Figure 391: DNA287222, NP_055555.1, 201303.at
 Figure 392: PRO69501
 Figure 393: DNA324612, P311, 201310.s.at
 Figure 394: PRO81261
 Figure 395: DNA325595, NP_001966.1, 201313.at
 Figure 396: PRO38010
 Figure 397: DNA331445, NP_002778.1, 201317.s.at
 Figure 398: PRO71133
 Figure 399: DNA274745, NP_006815.1, 201323.at
 Figure 400: PRO62518
 Figure 401: DNA150781, NP_001414.1, 201324.at
 Figure 402: PRO12467
 Figure 403: DNA329002, AF385084, 201326.at
 Figure 404: PRO4912
 Figure 405: DNA329002, NP_001753.1, 201327.s.at
 Figure 406: PRO4912
 Figure 407: DNA269536, S80343, 201330.at
 Figure 408: PRO57952
 Figure 409: DNA273323, NP_004243.1, 201349.at
 Figure 410: PRO61330
 Figure 411: DNA103227, NP_004466.1, 201350.at
 Figure 412: PRO4557
 Figure 413: DNA329934, NP_000090.1, 201360.at
 Figure 414: PRO2721
 Figure 415: DNA329107, NP_008818.3, 201367.s.at
 Figure 416: PRO84754
 Figure 417A-B: DNA329108, 1383643.16, 201368.at
 Figure 418: PRO84755
 Figure 419: DNA329107, ZFP36L2, 201369.s.at
 Figure 420: PRO84754
 Figure 421A-E: DNA331446, NP_000436.1, 201373.at
 Figure 422: PRO86502
 Figure 423: DNA329109, NP_004957.1, 201376.s.at
 Figure 424: PRO81854
 Figure 425: DNA329111, NP_001349.1, 201385.at
 Figure 426: PRO84756
 Figure 427: DNA270979, NP_002800.1, 201388.at
 Figure 428: PRO59309
 Figure 429: DNA331447, NP_006614.1, 201397.at
 Figure 430: PRO85247
 Figure 431: DNA329937, NP_002786.2, 201400.at
 Figure 432: PRO61014
 Figure 433: DNA328412, NP_060428.1, 201411.s.at

- Figure 434: PRO84257
 Figure 435: DNA329938, 1394805.1, 201416.at
 Figure 436: PRO70544
 Figure 437: DNA329939, 1393503.1, 201417.at
 Figure 438: PRO85248
 Figure 439: DNA83109, NP_006323.1, 201422.at
 Figure 440: PRO2592
 Figure 441: DNA226600, NP_003371.1, 201426.s.at
 Figure 442: PRO37063
 Figure 443: DNA272286, NP_001743.1, 201432.at
 Figure 444: PRO60544
 Figure 445: DNA327550, NP_001959.1, 201437.s.at
 Figure 446: PRO81164
 Figure 447A-C: DNA88140, COL6A3, 201438.at
 Figure 448: PRO2670
 Figure 449: DNA150535, NP_004809.1, 201440.at
 Figure 450: PRO12078
 Figure 451: DNA325049, NP_005605.1, 201453.x.at
 Figure 452: PRO37938
 Figure 453: DNA326736, NP_006657.1, 201459.at
 Figure 454: PRO83076
 Figure 455: DNA226359, NP_002219.1, 201464.x.at
 Figure 456: PRO36822
 Figure 457: DNA226359, JUN, 201465.s.at
 Figure 458: PRO36822
 Figure 459: DNA226359, DNA226359, 201466.s.at
 Figure 460: PRO36822
 Figure 461: DNA328413, NP_004823.1, 201470.at
 Figure 462: PRO84258
 Figure 463: DNA103320, NP_002220.1, 201473.at
 Figure 464: PRO4650
 Figure 465: DNA325704, NP_004981.2, 201475.x.at
 Figure 466: PRO82188
 Figure 467: DNA327551, NP_001024.1, 201476.s.at
 Figure 468: PRO59289
 Figure 469: DNA327551, RRM1, 201477.s.at
 Figure 470: PRO59289
 Figure 471: DNA254783, NP_001354.1, 201478.s.at
 Figure 472: PRO49881
 Figure 473: DNA329940, NP_001805.1, 201487.at
 Figure 474: PRO2679
 Figure 475: DNA304459, BC005020, 201489.at
 Figure 476: PRO37073
 Figure 477: DNA304459, NP_005720.1, 201490.s.at
 Figure 478: PRO37073
 Figure 479: DNA325920, NP_036243.1, 201491.at
 Figure 480: PRO82373
 Figure 481: DNA328415, BC006997, 201503.at
 Figure 482: PRO60207
 Figure 483: DNA329941, NP_001543.1, 201508.at
 Figure 484: PRO85249
 Figure 485: DNA323741, NP_003123.1, 201516.at
 Figure 486: PRO80498
 Figure 487: DNA329942, NCBP2, 201521.s.at
 Figure 488: PRO85250
 Figure 489: DNA328418, NP_003398.1, 201531.at
 Figure 490: PRO84261
 Figure 491: DNA331292, NP_002779.1, 201532.at
 Figure 492: PRO84262
 Figure 493: DNA329943, NP_009037.1, 201534.s.at
 Figure 494: PRO85251
 Figure 495: DNA331448, UBL3, 201535.at
 Figure 496: PRO86503
 Figure 497: DNA272171, NP_002379.2, 201555.at
 Figure 498: PRO60438
 Figure 499: DNA226291, NP_055047.1, 201556.s.at
 Figure 500: PRO36754
 Figure 501: DNA226291, VAMP2, 201557.at
 Figure 502: PRO36754
 Figure 503A-B: DNA270995, NP_004721.1, 201574.at
 Figure 504: PRO59324
 Figure 505: DNA227071, NP_000260.1, 201577.at
 Figure 506: PRO37534
 Figure 507: DNA327199, NP_066979.1, 201580.s.at
 Figure 508: PRO83475
 Figure 509A-B: DNA329944, AB032988, 201581.at
 Figure 510: DNA329945, NP_006354.2, 201583.s.at
 Figure 511: PRO85252
 Figure 512A-B: DNA329946, D80000, 201589.at
 Figure 513: DNA290280, NP_004359.1, 201605.x.at
 Figure 514: PRO70425
 Figure 515: DNA329947, NP_536806.1, 201613.s.at
 Figure 516: PRO37674
 Figure 517: DNA272904, NP_006784.1, 201619.at
 Figure 518: PRO60991
 Figure 519: DNA255406, NP_005533.1, 201625.s.at
 Figure 520: PRO50473
 Figure 521: DNA255406, INSIG1, 201627.s.at
 Figure 522: PRO50473
 Figure 523: DNA329115, NP_434702.1, 201631.s.at
 Figure 524: PRO84760
 Figure 525: DNA287240, NP_004326.1, 201641.at
 Figure 526: PRO29371
 Figure 527: DNA327557, NP_004214.1, 201649.at
 Figure 528: PRO83588
 Figure 529A-B: DNA220748, NP_000201.1, 201656.at
 Figure 530: PRO34726
 Figure 531A-B: DNA328422, NP_004448.1, 201662.s.at
 Figure 532: PRO84263
 Figure 533A-B: DNA273732, NP_005487.2, 201663.s.at
 Figure 534: PRO61695
 Figure 535A-B: DNA273732, HSM801845, 201664.at
 Figure 536: PRO61695
 Figure 537: DNA273090, NP_002347.4, 201669.s.at
 Figure 538: PRO61148
 Figure 539: DNA273090, MARCKS, 201670.s.at
 Figure 540: PRO61148
 Figure 541: DNA290244, NP_000261.1, 201695.s.at
 Figure 542: PRO70353
 Figure 543: DNA329948, NP_002797.1, 201699.at

- Figure 544: PRO85253
 Figure 545: DNA324742, NP_001751.1, 201700.at
 Figure 546: PRO81367
 Figure 547: DNA270883, NP_001061.1, 201714.at
 Figure 548: PRO59218
 Figure 549A-B: DNA151806, NP_001422.1, 201719.s.at
 Figure 550: PRO12768
 Figure 551: DNA227461, NP_006753.1, 201720.s.at
 Figure 552: PRO37924
 Figure 553: DNA227461, LAPTM5, 201721.s.at
 Figure 554: PRO37924
 Figure 555: DNA329949, BC003376, 201726.at
 Figure 556: PRO85254
 Figure 557: DNA227576, NP_005618.1, 201739.at
 Figure 558: PRO38039
 Figure 559: DNA326373, NP_008855.1, 201742.x.at
 Figure 560: PRO82769
 Figure 561: DNA327559, NP_058432.1, 201752.s.at
 Figure 562: PRO83589
 Figure 563: DNA331294, ADD3, 201753.s.at
 Figure 564: PRO86393
 Figure 565: DNA227035, NP_006730.1, 201755.at
 Figure 566: PRO37498
 Figure 567: DNA329016, NP_006283.1, 201758.at
 Figure 568: PRO4887
 Figure 569: DNA328427, NP_061109.1, 201760.s.at
 Figure 570: PRO84265
 Figure 571: DNA287167, NP_006627.1, 201761.at
 Figure 572: PRO59136
 Figure 573: DNA287625, NP_002809.1, 201762.s.at
 Figure 574: PRO69491
 Figure 575: DNA329950, NP_076961.1, 201764.at
 Figure 576: PRO11558
 Figure 577A-B: DNA329951, NP_055680.1, 201774.s.at
 Figure 578: PRO85255
 Figure 579: DNA151017, NP_004835.1, 201810.s.at
 Figure 580: PRO12841
 Figure 581: DNA151017, SH3BP5, 201811.x.at
 Figure 582: PRO12841
 Figure 583: DNA227929, NP_061932.1, 201812.s.at
 Figure 584: PRO38392
 Figure 585: DNA324015, NP_006326.1, 201821.s.at
 Figure 586: PRO80735
 Figure 587: DNA329952, BC010285, 201829.at
 Figure 588: PRO85256
 Figure 589: DNA329952, NET1, 201830.s.at
 Figure 590: PRO85256
 Figure 591: DNA329954, NP_001518.1, 201833.at
 Figure 592: PRO85258
 Figure 593A-B: DNA329955, AB029551, 201845.s.at
 Figure 594: PRO85259
 Figure 595: DNA254350, NP_004043.2, 201848.s.at
 Figure 596: PRO49461
 Figure 597: DNA254350, BNIP3, 201849.at
 Figure 598: PRO49461
 Figure 599: DNA329118, NP_068660.1, 201853.s.at
 Figure 600: PRO83123
 Figure 601: DNA272066, NP_002931.1, 201872.s.at
 Figure 602: PRO60337
 Figure 603: DNA150805, NP_055703.1, 201889.at
 Figure 604: PRO11583
 Figure 605: DNA253582, DNA253582, 201890.at
 Figure 606: PRO49181
 Figure 607: DNA329956, NP_000875.1, 201892.s.at
 Figure 608: PRO85260
 Figure 609: DNA328431, NP_001817.1, 201897.s.at
 Figure 610: PRO45093
 Figure 611: DNA254978, NP_060625.1, 201917.s.at
 Figure 612: PRO50067
 Figure 613: DNA329057, NP_004116.2, 201921.at
 Figure 614: PRO84719
 Figure 615: DNA227112, NP_006397.1, 201923.at
 Figure 616: PRO37575
 Figure 617: DNA275240, NP_005906.2, 201930.at
 Figure 618: PRO62927
 Figure 619: DNA273014, NP_000117.1, 201931.at
 Figure 620: PRO61085
 Figure 621A-B: DNA329120, NP_002560.1, 201945.at
 Figure 622: PRO2752
 Figure 623: DNA274167, NP_006422.1, 201946.s.at
 Figure 624: PRO62097
 Figure 625: DNA274167, CCT2, 201947.s.at
 Figure 626: PRO62097
 Figure 627: DNA103481, NP_037417.1, 201948.at
 Figure 628: PRO4808
 Figure 629A-B: DNA327563, NP_066945.1, 201963.at
 Figure 630: PRO83592
 Figure 631: DNA275214, NP_002473.1, 201970.s.at
 Figure 632: PRO62908
 Figure 635A-B: DNA328433, ATP6V1A1, 201971.s.at
 Figure 634: PRO84268
 Figure 635A-B: DNA272191, NP_002947.1, 201975.at
 Figure 636: PRO60456
 Figure 637: DNA328809, PTPN12, 202006.at
 Figure 638: PRO4803
 Figure 639: DNA328437, AF083441, 202021.x.at
 Figure 640: PRO84271
 Figure 641: DNA329957, NP_005156.1, 202022.at
 Figure 642: PRO85261
 Figure 643A-B: DNA329958, NP_510880.1, 202039.at
 Figure 644: PRO85262
 Figure 645: DNA327017, NP_004586.2, 202043.s.at
 Figure 646: PRO61744
 Figure 647A-B: DNA227985, NP_055107.1, 202047.s.at
 Figure 648: PRO38448
 Figure 649A-B: DNA225991, NP_000518.1, 202067.s.at
 Figure 650: PRO36454

Figure 651A-B: DNA225991, LDLR, 202068.s.at
 Figure 652: PRO36454
 Figure 653: DNA327567, NP_005521.1, 202069.s.at
 Figure 654: PRO83596
 Figure 655: DNA226116, NP_002990.1, 202071.at
 Figure 656: PRO36579
 Figure 657: DNA289522, NP_004994.1, 202077.at
 Figure 658: PRO70276
 Figure 659: DNA327568, NP_002453.1, 202086.at
 Figure 660: PRO57922
 Figure 661: DNA327569, CTS1, 202087.s.at
 Figure 662: PRO2683
 Figure 663: DNA329959, 251651.5, 202094.at
 Figure 664: PRO85263
 Figure 665: DNA129504, NP_001159.1, 202095.s.at
 Figure 666: PRO7143
 Figure 667: DNA328440, NP_004517.1, 202107.s.at
 Figure 668: PRO84274
 Figure 669: DNA329960, 1381890.1, 202136.at
 Figure 670: PRO85264
 Figure 671: DNA324895, NP_006294.2, 202138.x.at
 Figure 672: PRO81501
 Figure 673: DNA227150, NP_002337.1, 202145.at
 Figure 674: PRO37613
 Figure 675: DNA329020, NP_057637.1, 202153.s.at
 Figure 676: PRO84695
 Figure 677: DNA328442, NP_006078.2, 202154.x.at
 Figure 678: PRO84275
 Figure 679A-C: DNA331449, NP_004371.1, 202160.at
 Figure 680: PRO86504
 Figure 681: DNA327573, BC007655, 202165.at
 Figure 682: PRO59301
 Figure 683: DNA329962, AASDHPPT, 202170.s.at
 Figure 684: PRO85266
 Figure 685A-B: DNA329963, NP_060700.1, 202184.s.at
 Figure 686: PRO85267
 Figure 687: DNA254570, NP_055484.1, 202188.at
 Figure 688: PRO49673
 Figure 689A-B: DNA304479, BC016556, 202194.at
 Figure 690: PRO7733
 Figure 691A-B: DNA329599, NP_003128.2, 202200.s.at
 Figure 692: PRO85131
 Figure 693A-B: DNA329964, 215949.9, 202206.at
 Figure 694: PRO85268
 Figure 695: DNA329965, BC001051, 202208.s.at
 Figure 696: PRO85269
 Figure 697: DNA325477, NP_004256.1, 202218.s.at
 Figure 698: PRO12878
 Figure 699: DNA328258, SLC16A1, 202236.s.at
 Figure 700: PRO84151
 Figure 701: DNA326133, NP_005021.2, 202240.at
 Figure 702: PRO82557
 Figure 703: DNA328444, MGC14458, 202246.s.at
 Figure 704: PRO84277
 Figure 705A-B: DNA227176, NP_056371.1, 202255.s.at
 Figure 706: PRO37639
 Figure 707: DNA326120, NP_006101.1, 202257.s.at
 Figure 708: PRO82546
 Figure 709: DNA150808, NP_002044.1, 202269.x.at
 Figure 710: PRO12478
 Figure 711: DNA150808, GBP1, 202270.at
 Figure 712: PRO12478
 Figure 713: DNA329966, NP_006295.1, 202276.at
 Figure 714: PRO22705
 Figure 715: DNA304716, NP_510867.1, 202284.s.at
 Figure 716: PRO71142
 Figure 717: DNA331450, NP_004381.1, 202295.s.at
 Figure 718: PRO2682
 Figure 719A-B: DNA329967, NP_003592.2, 202303.x.at
 Figure 720: PRO85270
 Figure 721: DNA329524, NP_000584.2, 202307.s.at
 Figure 722: PRO36996
 Figure 723A-B: DNA151108, NP_004167.3, 202308.at
 Figure 724: PRO12105
 Figure 725: DNA270142, NP_005947.2, 202309.at
 Figure 726: PRO58531
 Figure 727: DNA269842, NP_002708.1, 202313.at
 Figure 728: PRO58243
 Figure 729: DNA328448, NP_000777.1, 202314.at
 Figure 730: PRO62362
 Figure 731: DNA331451, UNG, 202330.s.at
 Figure 732: PRO86505
 Figure 733A-B: DNA329970, NP_000910.2, 202336.s.at
 Figure 734: PRO85272
 Figure 735: DNA255088, NP_003249.1, 202338.at
 Figure 736: PRO50174
 Figure 737: DNA325115, NP_001435.1, 202345.s.at
 Figure 738: PRO81689
 Figure 739: DNA270502, NP_002807.1, 202352.s.at
 Figure 740: PRO58880
 Figure 741A-B: DNA227353, NP_055637.1, 202375.at
 Figure 742: PRO37816
 Figure 743: DNA328449, NP_005462.1, 202382.s.at
 Figure 744: PRO60304
 Figure 745: DNA290234, NP_002914.1, 202388.at
 Figure 746: PRO70333
 Figure 747: DNA325417, NP_001742.1, 202402.s.at
 Figure 748: PRO69635
 Figure 749: DNA150989, NP_005523.1, 202411.at
 Figure 750: PRO12569
 Figure 751: DNA326563, NP_036421.2, 202417.at
 Figure 752: PRO82927
 Figure 753: DNA150514, NP_065203.1, 202418.at
 Figure 754: PRO12304
 Figure 755: DNA88332, NP_002026.1, 202419.at
 Figure 756: PRO2753
 Figure 757A-B: DNA329971, NP_075266.1,

202422.s.at
 Figure 758: PRO85273
 Figure 759: DNA227121, NP_066928.1, 202430.s.at
 Figure 760: PRO37584
 Figure 761: DNA66487, NP_002458.1, 202431.s.at
 Figure 762: PRO1213
 Figure 763: DNA103322, NP_005818.1, 202433.at
 Figure 764: PRO4652
 Figure 765: DNA68868, DNA68868, 202441.at
 Figure 766: PRO1460
 Figure 767: DNA227121, PLSCR1, 202446.s.at
 Figure 768: PRO37584
 Figure 769: DNA329972, BC004452, 202451.at
 Figure 770: PRO85274
 Figure 771A-B: DNA329973, NP_055461.1, 202459.s.at
 Figure 772: PRO82824
 Figure 773A-B: DNA269642, NP_004557.1, 202464.s.at
 Figure 774: PRO58054
 Figure 775: DNA227921, NP_003789.1, 202468.s.at
 Figure 776: PRO38384
 Figure 777A-B: DNA329122, NP_067675.1, 202478.at
 Figure 778: PRO84764
 Figure 779: DNA329123, NP_002873.1, 202483.s.at
 Figure 780: PRO84765
 Figure 781A-B: DNA103449, NP_008862.1, 202498.s.at
 Figure 782: PRO4776
 Figure 783: DNA329974, NP_055083.1, 202501.at
 Figure 784: PRO85275
 Figure 785: DNA234442, NP_055551.1, 202503.s.at
 Figure 786: PRO38852
 Figure 787A-B: DNA273879, NP_055753.1, 202519.at
 Figure 788: PRO61835
 Figure 789A-B: DNA277809, NP_055582.1, 202524.s.at
 Figure 790: PRO64556
 Figure 791: DNA328452, NP_000394.1, 202528.at
 Figure 792: PRO63289
 Figure 793A-B: DNA226870, DHFR, 202532.s.at
 Figure 794: PRO37333
 Figure 795: DNA331452, BC003584, 202533.s.at
 Figure 796: PRO86506
 Figure 797: DNA331453, NP_060993.1, 202534.x.at
 Figure 798: PRO69586
 Figure 799: DNA329976, NP_003815.1, 202535.at
 Figure 800: PRO4801
 Figure 801: DNA329977, BC001553, 202536.at
 Figure 802: PRO85276
 Figure 803A-B: DNA255105, NP_000850.1, 202539.s.at
 Figure 804: PRO50187
 Figure 805A-B: DNA255105, HMGR, 202540.s.at
 Figure 806: PRO50187
 Figure 807A-B: DNA274852, NP_004115.1, 202543.s.at
 Figure 808: PRO62605
 Figure 809: DNA275244, DNA275244, 202557.at
 Figure 810A-C: DNA331454, NP_068506.1, 202565.s.at
 Figure 811: PRO86507
 Figure 812A-C: DNA329978, SVIL, 202566.s.at
 Figure 813: PRO85277
 Figure 814: DNA326939, NP_004166.1, 202567.at
 Figure 815: PRO83257
 Figure 816: DNA325587, NP_068772.1, 202580.x.at
 Figure 817: PRO82083
 Figure 818: DNA227607, HSPA1B, 202581.at
 Figure 819: PRO38070
 Figure 820: DNA328456, NP_000467.1, 202587.s.at
 Figure 821: PRO84283
 Figure 822: DNA329979, NP_001062.1, 202589.at
 Figure 823: PRO82821
 Figure 824: DNA329125, NP_056159.1, 202595.s.at
 Figure 825: PRO84767
 Figure 826A-C: DNA270287, NP_003480.1, 202599.s.at
 Figure 827: PRO58675
 Figure 828A-C: DNA270287, NRIP1, 202600.s.at
 Figure 829: PRO58675
 Figure 830A-C: DNA329268, NP_004220.1, 202610.s.at
 Figure 831: PRO84864
 Figure 832: DNA274881, NP_001896.1, 202613.at
 Figure 833: PRO62626
 Figure 834A-B: DNA329980, I134366.16, 202615.at
 Figure 835: PRO85278
 Figure 836: DNA329126, NP_005025.1, 202635.s.at
 Figure 837: PRO84768
 Figure 838: DNA59763, NP_000192.1, 202637.s.at
 Figure 839: PRO160
 Figure 840: DNA59763, ICAM1, 202638.s.at
 Figure 841: PRO160
 Figure 842: DNA289528, NP_004302.1, 202641.at
 Figure 843: PRO70286
 Figure 844A-B: DNA151841, NP_006281.1, 202643.s.at
 Figure 845: PRO12904
 Figure 846A-B: DNA151841, TNFAIP3, 202644.s.at
 Figure 847: PRO12904
 Figure 848: DNA329981, NP_001155.1, 202652.at
 Figure 849: PRO49894
 Figure 850: DNA254129, NP_006001.1, 202655.at
 Figure 851: PRO49244
 Figure 852: DNA331455, NP_002792.1, 202659.at
 Figure 853: PRO58763
 Figure 854: DNA287424, NP_004292.1, 202666.s.at
 Figure 855: PRO69681
 Figure 856: DNA326896, NP_003672.1, 202671.s.at
 Figure 857: PRO69486
 Figure 858: DNA289526, ATF3, 202672.s.at

- Figure 859: PRO70282
Figure 860: DNA84130, NP_003801.1, 202687.s.at
Figure 861: PRO1096
Figure 862: DNA84130, TNFSF10, 202688.at
Figure 863: PRO1096
Figure 864: DNA329982, NP_008937.1, 202697.at
Figure 865: PRO85279
Figure 866A-B: DNA150467, NP_055513.1, 202699.s.at
Figure 867: PRO12272
Figure 868A-B: DNA150467, KIAA0792, 202700.s.at
Figure 869: PRO12272
Figure 870: DNA326000, NP_004692.1, 202705.at
Figure 871: PRO82442
Figure 872: DNA273371, NP_000364.1, 202706.s.at
Figure 873: PRO61373
Figure 874: DNA329983, BC012595, 202710.at
Figure 875: PRO85280
Figure 876: DNA43010, NP_000588.1, 202718.at
Figure 877: PRO36145
Figure 878A-B: DNA270254, NP_002006.2, 202723.s.at
Figure 879: PRO58642
Figure 880: DNA150713, NP_006570.1, 202735.at
Figure 881: PRO12082
Figure 882: DNA58828, DNA58828, 202746.at
Figure 883: PRO1189
Figure 884: DNA327192, NP_004858.1, 202747.s.at
Figure 885: PRO1189
Figure 886: DNA227133, NP_004111.1, 202748.at
Figure 887: PRO37596
Figure 888: DNA329984, NP_004618.2, 202749.at
Figure 889: PRO11656
Figure 890A-C: DNA329129, NP_009134.1, 202760.s.at
Figure 891: PRO84288
Figure 892: DNA329008, NP_004337.2, 202763.at
Figure 893: PRO12832
Figure 894A-B: DNA328464, 977954.20, 202769.at
Figure 895: PRO84290
Figure 896: DNA226578, NP_004345.1, 202770.s.at
Figure 897: PRO37041
Figure 898: DNA273346, NP_055316.1, 202779.s.at
Figure 899: PRO61349
Figure 900: DNA329985, NP_002185.1, 202794.at
Figure 901: PRO60589
Figure 902: DNA88428, NP_000202.1, 202803.s.at
Figure 903: PRO2787
Figure 904: DNA329986, NP_006454.1, 202811.at
Figure 905: PRO61895
Figure 906A-B: DNA226364, NP_001612.1, 202820.at
Figure 907: PRO36827
Figure 908: DNA328465, NP_005639.1, 202823.at
Figure 909: PRO84291
Figure 910: DNA329987, NP_000286.2, 202833.s.at
Figure 911: PRO85281
Figure 912: DNA269828, FLN29, 202837.at
Figure 913: PRO58230
Figure 914: DNA329988, NP_036460.1, 202842.s.at
Figure 915: PRO1471
Figure 916: DNA329988, DNAJB9, 202843.at
Figure 917: PRO1471
Figure 918: DNA103394, NP_004198.1, 202855.s.at
Figure 919: PRO4722
Figure 920: DNA103394, SLC16A3, 202856.s.at
Figure 921: PRO4722
Figure 922A-B: DNA272022, PER1, 202861.at
Figure 923: PRO60296
Figure 924: DNA275144, NP_000128.1, 202862.at
Figure 925: PRO62852
Figure 926: DNA328467, SP100, 202864.s.at
Figure 927: PRO84293
Figure 928: DNA287289, NP_058132.1, 202869.at
Figure 929: PRO69559
Figure 930: DNA273060, NP_001246.1, 202870.s.at
Figure 931: PRO61125
Figure 932: DNA329130, NP_004286.2, 202871.at
Figure 933: PRO20124
Figure 934: DNA328469, NP_001686.1, 202874.s.at
Figure 935: PRO84295
Figure 936: DNA271881, PSCD1, 202880.s.at
Figure 937: PRO60160
Figure 938: DNA329989, HSPP2R15, 202886.s.at
Figure 939A-B: DNA225538, NP_002476.1, 202906.s.at
Figure 940: PRO36001
Figure 941A-B: DNA225538, NBS1, 202907.s.at
Figure 942: PRO36001
Figure 943: DNA328483, NP_061163.1, 202911.at
Figure 944: PRO84309
Figure 945: DNA327584, NP_002955.2, 202917.s.at
Figure 946: PRO80649
Figure 947A-B: DNA329132, NP_002648.1, 202925.s.at
Figure 948: PRO83145
Figure 949: DNA272979, NP_003841.1, 202930.s.at
Figure 950: PRO61058
Figure 951: DNA331456, BIN1, 202931.x.at
Figure 952: PRO86508
Figure 953: DNA327585, NP_056518.1, 202937.x.at
Figure 954: PRO83605
Figure 955: DNA328471, ZMPSTE24, 202939.at
Figure 956: PRO84297
Figure 957: DNA304681, NP_066552.1, 202941.at
Figure 958: PRO71107
Figure 959: DNA269481, NP_001976.1, 202942.at
Figure 960: PRO57901
Figure 961: DNA273320, NP_008950.1, 202954.at
Figure 962: PRO61327
Figure 963: DNA273334, NP_000246.1, 202960.s.at
Figure 964: PRO61341
Figure 965A-B: DNA328473, NP_006473.1,

202968.s.at
 Figure 966: PRO84299
 Figure 967A-B: DNA227293, NP.055698.1, 202972.s.at
 Figure 968: PRO37756
 Figure 969A-B: DNA227293, KIAA0914, 202973.x.at
 Figure 970: PRO37756
 Figure 971: DNA329135, NP.002913.2, 202988.s.at
 Figure 972: PRO58102
 Figure 973: DNA274034, NP.006388.1, 203022.at
 Figure 974: PRO61977
 Figure 975: DNA329136, NP.057475.1, 203023.at
 Figure 976: PRO84772
 Figure 977A-B: DNA271865, NP.055566.1, 203037.s.at
 Figure 978: PRO60145
 Figure 979A-B: DNA304464, NP.055733.1, 203044.at
 Figure 980: PRO71042
 Figure 981A-B: DNA329991, NP.003911.1, 203046.s.at
 Figure 982: PRO85284
 Figure 983: DNA331457, AF119894, 203047.at
 Figure 984: PRO86509
 Figure 985: DNA150976, NP.071503.1, 203054.s.at
 Figure 986: PRO12565
 Figure 987: DNA326693, NP.004697.2, 203055.s.at
 Figure 988: PRO83039
 Figure 989: DNA188357, NP.000651.1, 203085.s.at
 Figure 990: PRO21897
 Figure 991: DNA324133, NP.037379.1, 203089.s.at
 Figure 992: PRO80835
 Figure 993: DNA269984, NP.055443.1, 203094.at
 Figure 994: PRO58380
 Figure 995: DNA329992, NP.002399.1, 203102.s.at
 Figure 996: PRO59267
 Figure 997: DNA329993, NP.115754.1, 203113.s.at
 Figure 998: PRO85285
 Figure 999: DNA329994, PCSK7, 203118.at
 Figure 1000: PRO85286
 Figure 1001A-B: DNA150447, NP.004854.1, 203128.at
 Figure 1002: PRO12256
 Figure 1003: DNA254543, NP.006799.1, 203133.at
 Figure 1004: PRO49648
 Figure 1005: DNA269918, NP.003633.1, 203138.at
 Figure 1006: PRO58316
 Figure 1007: DNA329001, BCL6, 203140.at
 Figure 1008: PRO26296
 Figure 1009A-B: DNA329995, NP.006452.1, 203145.at
 Figure 1010: PRO85287
 Figure 1011A-B: DNA226330, NP.001461.1, 203146.s.at
 Figure 1012: PRO36793
 Figure 1013: DNA271624, NP.001539.1, 203153.at
 Figure 1014: PRO59911
 Figure 1015: DNA269660, NP.003192.1, 203177.x.at
 Figure 1016: PRO58071
 Figure 1017: DNA304720, NP.062427.1, 203186.s.at
 Figure 1018: PRO71146
 Figure 1019A-B: DNA271744, NP.055476.1, 203206.at
 Figure 1020: PRO60028
 Figure 1021: DNA329997, BC001866, 203209.at
 Figure 1022: PRO61115
 Figure 1023: DNA329997, NP.031396.1, 203210.s.at
 Figure 1024: PRO61115
 Figure 1025A-B: DNA328481, MTMR2, 203211.s.at
 Figure 1026: PRO84307
 Figure 1027: DNA331458, 995529.4, 203213.at
 Figure 1028: PRO86510
 Figure 1029: DNA331459, CDC2, 203214.x.at
 Figure 1030: PRO70806
 Figure 1031: DNA76514, NP.000409.1, 203233.at
 Figure 1032: PRO2540
 Figure 1033: DNA325507, NP.005842.1, 203252.at
 Figure 1034: PRO69461
 Figure 1035: DNA330000, NP.036277.1, 203270.at
 Figure 1036: PRO85289
 Figure 1037: DNA302020, NP.005564.1, 203276.at
 Figure 1038: PRO70993
 Figure 1039: DNA328486, NP.000149.1, 203282.at
 Figure 1040: PRO60119
 Figure 1041A-B: DNA330001, NP.036394.1, 203285.s.at
 Figure 1042: PRO85290
 Figure 1043: DNA225675, NP.005561.1, 203293.s.at
 Figure 1044: PRO36138
 Figure 1045: DNA330002, BC007195, 203315.at
 Figure 1046: PRO80853
 Figure 1047A-B: DNA330003, NP.005532.1, 203331.s.at
 Figure 1048: PRO85291
 Figure 1049: DNA330004, NP.055785.2, 203333.at
 Figure 1050: PRO85292
 Figure 1051: DNA330005, NP.003696.2, 203340.s.at
 Figure 1052: PRO85293
 Figure 1053: DNA271959, NP.002885.1, 203344.s.at
 Figure 1054: PRO60234
 Figure 1055: DNA330006, NP.031384.1, 203347.s.at
 Figure 1056: PRO85294
 Figure 1057: DNA330007, NP.055111.1, 203357.s.at
 Figure 1058: PRO85295
 Figure 1059: DNA330008, NP.004447.2, 203358.s.at
 Figure 1060: PRO85296
 Figure 1061: DNA272449, NP.036465.1, 203360.s.at
 Figure 1062: PRO60698
 Figure 1063: DNA324514, NP.002349.1, 203362.s.at
 Figure 1064: PRO81169
 Figure 1065: DNA325749, NP.003868.1, 203372.s.at
 Figure 1066: PRO12839
 Figure 1067: DNA325749, STAT2, 203373.at

Figure 1068: PRO12839
 Figure 1069: DNA274960, NP_008856.1, 203380.x.at
 Figure 1070: PRO62694
 Figure 1071: DNA151022, NP_001336.1, 203385.at
 Figure 1072: PRO12096
 Figure 1073: DNA331460, NP_002780.1, 203396.at
 Figure 1074: PRO60499
 Figure 1075: DNA326892, NP_003711.1, 203405.at
 Figure 1076: PRO83213
 Figure 1077: DNA274778, NP_005917.1, 203406.at
 Figure 1078: PRO62545
 Figure 1079: DNA270134, NP_000098.1, 203409.at
 Figure 1080: PRO58523
 Figure 1081: DNA28759, NP_006150.1, 203413.at
 Figure 1082: PRO2520
 Figure 1083: DNA287267, NP_001228.1, 203418.at
 Figure 1084: PRO37015
 Figure 1085A-B: DNA256807, NP_057339.1, 203420.at
 Figure 1086: PRO51738
 Figure 1087: DNA326745, NP_002682.1, 203422.at
 Figure 1088: PRO83083
 Figure 1089: DNA330009, NP_054753.1, 203428.s.at
 Figure 1090: PRO85297
 Figure 1091A-B: DNA275186, DNA275186, 203432.at
 Figure 1092A-B: DNA330010, NP_005721.2, 203445.s.at
 Figure 1093: PRO85298
 Figure 1094: DNA273410, NP_004036.1, 203454.s.at
 Figure 1095: PRO61409
 Figure 1096: DNA328495, NP_055578.1, 203465.at
 Figure 1097: PRO58967
 Figure 1098A-C: DNA331461, NP_005493.2, 203504.s.at
 Figure 1099: PRO86511
 Figure 1100A-B: DNA331462, NP_003096.1, 203509.at
 Figure 1101: PRO86512
 Figure 1102: DNA272911, NP_006545.1, 203517.at
 Figure 1103: PRO60997
 Figure 1104A-D: DNA331463, NP_000072.1, 203518.at
 Figure 1105: PRO86513
 Figure 1106A-C: DNA331464, NP_055160.1, 203520.s.at
 Figure 1107: PRO86514
 Figure 1108A-C: DNA330014, HRHFR2436, 203521.s.at
 Figure 1109: PRO85302
 Figure 1110: DNA325404, NP_002330.1, 203523.at
 Figure 1111: PRO81936
 Figure 1112: DNA323910, NP_002956.1, 203535.at
 Figure 1113: PRO80648
 Figure 1114A-B: DNA272399, NP_001197.1, 203542.s.at
 Figure 1115: PRO60653
 Figure 1116A-B: DNA272399, BTEB1, 203543.s.at
 Figure 1117: PRO60653
 Figure 1118: DNA324684, NP_004210.1, 203554.x.at
 Figure 1119: PRO81319
 Figure 1120: DNA330015, NP_004620.1, 203564.at
 Figure 1121: PRO58704
 Figure 1122: DNA330016, NP_006346.1, 203567.s.at
 Figure 1123: PRO85303
 Figure 1124A-B: DNA150765, NP_003974.1, 203579.s.at
 Figure 1125: PRO12458
 Figure 1126: DNA273676, NP_055488.1, 203584.at
 Figure 1127: PRO61644
 Figure 1128: DNA271003, NP_003720.1, 203594.at
 Figure 1129: PRO59332
 Figure 1130A-B: DNA270323, NP_036552.1, 203595.s.at
 Figure 1131: PRO58710
 Figure 1132A-B: DNA270323, RI58, 203596.s.at
 Figure 1133: PRO58710
 Figure 1134: DNA330017, NP_009118.1, 203597.s.at
 Figure 1135: PRO60916
 Figure 1136: DNA329604, NP_003127.1, 203605.at
 Figure 1137: PRO85134
 Figure 1138: DNA287246, NP_004044.2, 203612.at
 Figure 1139: PRO69521
 Figure 1140: DNA330018, NP_064528.1, 203622.s.at
 Figure 1141: PRO85304
 Figure 1142: DNA331465, SKP2, 203625.x.at
 Figure 1143: PRO81225
 Figure 1144A-B: DNA327596, 345314.2, 203628.at
 Figure 1145: PRO1920
 Figure 1146A-B: DNA331466, BCL2, 203685.at
 Figure 1147: PRO86515
 Figure 1148A-B: DNA330021, NP_001940.1, 203693.s.at
 Figure 1149: PRO85306
 Figure 1150: DNA329900, RFC2, 203696.s.at
 Figure 1151: PRO81549
 Figure 1152A-C: DNA331467, NP_002213.1, 203710.at
 Figure 1153: PRO86516
 Figure 1154: DNA329144, KIAA0020, 203712.at
 Figure 1155: PRO84779
 Figure 1156: DNA326402, NP_004515.1, 203713.s.at
 Figure 1157: PRO82793
 Figure 1158: DNA324183, DPP4, 203716.s.at
 Figure 1159: PRO80881
 Figure 1160: DNA150784, NP_001974.1, 203720.s.at
 Figure 1161: PRO12800
 Figure 1162A-B: DNA269573, NP_002212.1, 203723.at
 Figure 1163: PRO57986
 Figure 1164: DNA330023, NP_001915.1, 203725.at
 Figure 1165: PRO85308

Figure 1166: DNA227020, NP_001416.1, 203729.at
 Figure 1167: PRO37483
 Figure 1168A-B: DNA325369, NP_055877.2, 203737.s.at
 Figure 1169: PRO81905
 Figure 1170A-B: DNA150748, NP_001105.1, 203741.s.at
 Figure 1171: PRO12446
 Figure 1172: DNA327523, AQP3, 203747.at
 Figure 1173: PRO38028
 Figure 1174: DNA330024, NP_058521.1, 203748.x.at
 Figure 1175: PRO85309
 Figure 1176: DNA97279, NP_005345.2, 203751.x.at
 Figure 1177: PRO3628
 Figure 1178A-B: DNA325972, BUB1B, 203755.at
 Figure 1179: PRO82417
 Figure 1180: DNA330025, NP_055565.2, 203764.at
 Figure 1181: PRO85310
 Figure 1182: DNA330026, NP_005899.1, 203778.at
 Figure 1183: PRO85311
 Figure 1184: DNA330027, NP_036578.1, 203787.at
 Figure 1185: PRO85312
 Figure 1186A-B: DNA150954, NP_055695.1, 203799.at
 Figure 1187: PRO12558
 Figure 1188: DNA331468, DGUOK, 203816.at
 Figure 1189: PRO86517
 Figure 1190: DNA274125, NP_071739.1, 203830.at
 Figure 1191: PRO62061
 Figure 1192A-B: DNA331469, 094680.4, 203845.at
 Figure 1193: PRO86518
 Figure 1194A-B: DNA325529, GAB2, 203853.s.at
 Figure 1195: PRO82037
 Figure 1196A-B: DNA275079, NP_056648.1, 203865.s.at
 Figure 1197: PRO62797
 Figure 1198: DNA275339, NP_005685.1, 203880.at
 Figure 1199: PRO63012
 Figure 1200: DNA329034, NP_006075.2, 203882.at
 Figure 1201: PRO84701
 Figure 1202A-B: DNA288692, NP_055719.1, 203884.s.at
 Figure 1203: PRO70078
 Figure 1204: DNA328513, TAF9, 203893.at
 Figure 1205: PRO37815
 Figure 1206A-B: DNA330030, NP_055684.1, 203907.s.at
 Figure 1207: PRO85315
 Figure 1208: DNA82376, NP_002407.1, 203915.at
 Figure 1209: PRO1723
 Figure 1210: DNA271676, NP_002052.1, 203925.at
 Figure 1211: PRO59961
 Figure 1212: DNA288249, NP_002940.1, 203931.s.at
 Figure 1213: PRO69507
 Figure 1214: DNA330031, NP_057210.1, 203960.s.at
 Figure 1215: PRO85316
 Figure 1216: DNA275012, NP_004679.1, 203964.at
 Figure 1217: PRO62740
 Figure 1218: DNA272338, NP_001245.1, 203967.at
 Figure 1219: PRO60595
 Figure 1220: DNA272338, CDC6, 203968.s.at
 Figure 1221: PRO60595
 Figure 1222: DNA227232, NP_001850.1, 203971.at
 Figure 1223: PRO37695
 Figure 1224: DNA271374, NP_005474.1, 203976.s.at
 Figure 1225: PRO59673
 Figure 1226: DNA226133, NP_001983.1, 203989.x.at
 Figure 1227: PRO36596
 Figure 1228: DNA225915, NP_000561.1, 204006.s.at
 Figure 1229: PRO36378
 Figure 1230: DNA330032, HUMGCRFC, 204007.at
 Figure 1231: PRO85317
 Figure 1232: DNA329145, DUSP4, 204014.at
 Figure 1233: PRO84780
 Figure 1234: DNA331470, HSU48807, 204015.s.at
 Figure 1235: PRO86519
 Figure 1236: DNA326089, NP_000508.1, 204018.x.at
 Figure 1237: PRO3629
 Figure 1238: DNA330033, NP_056492.1, 204019.s.at
 Figure 1239: PRO85318
 Figure 1240: DNA330034, NP_002907.1, 204023.at
 Figure 1241: PRO85319
 Figure 1242: DNA328271, NP_008988.2, 204026.s.at
 Figure 1243: PRO81868
 Figure 1244: DNA330035, NP_004228.1, 204033.at
 Figure 1245: PRO85320
 Figure 1246: DNA325181, CLTA, 204050.s.at
 Figure 1247: PRO81742
 Figure 1248: DNA226342, NP_000305.1, 204054.at
 Figure 1249: PRO36805
 Figure 1250A-B: DNA331471, NP_055498.1, 204063.s.at
 Figure 1251: PRO61468
 Figure 1252: DNA274783, NP_006272.1, 204068.at
 Figure 1253: PRO62549
 Figure 1254A-C: DNA331472, NP_075463.1, 204072.s.at
 Figure 1255: PRO86520
 Figure 1256: DNA270476, NP_003591.1, 204092.s.at
 Figure 1257: PRO58855
 Figure 1258: DNA216689, NP_002975.1, 204103.at
 Figure 1259: PRO34276
 Figure 1260: DNA328522, NP_001769.2, 204118.at
 Figure 1261: PRO2696
 Figure 1262: DNA150529, NP_003323.1, 204122.at
 Figure 1263: PRO12313
 Figure 1264: DNA328524, NP_057097.1, 204125.at
 Figure 1265: PRO84336
 Figure 1266: DNA304489, NP_003495.1, 204126.s.at
 Figure 1267: PRO71058
 Figure 1268: DNA330037, BC000149, 204127.at
 Figure 1269: PRO82290

Figure 1270: DNA325824, NP_002906.1, 204128.s.at
 Figure 1271: PRO82290
 Figure 1272: DNA328525, BC021224, 204131.s.at
 Figure 1273: PRO84337
 Figure 1274: DNA103532, NP_003263.1, 204137.at
 Figure 1275: PRO4859
 Figure 1276: DNA330038, BC016330, 204146.at
 Figure 1277: PRO85322
 Figure 1278: DNA330039, NP_002396.2, 204152.s.at
 Figure 1279: PRO85323
 Figure 1280: DNA330039, MFNG, 204153.s.at
 Figure 1281: PRO85323
 Figure 1282: DNA330040, NP_523240.1, 204159.at
 Figure 1283: PRO59546
 Figure 1284: DNA273694, NP_006092.1, 204162.at
 Figure 1285: PRO61661
 Figure 1286: DNA227116, NP_006738.1, 204164.at
 Figure 1287: PRO37579
 Figure 1288A-B: DNA254376, NP_055778.1, 204166.at
 Figure 1289: PRO49486
 Figure 1290: DNA272655, NP_001818.1, 204170.s.at
 Figure 1291: PRO60781
 Figure 1292: DNA330041, NP_000088.2, 204172.at
 Figure 1293: PRO85324
 Figure 1294: DNA328528, MLC1SA, 204173.at
 Figure 1295: PRO60636
 Figure 1296: DNA329148, NP_056955.1, 204175.at
 Figure 1297: PRO84782
 Figure 1298: DNA226380, NP_001765.1, 204192.at
 Figure 1299: PRO4695
 Figure 1300: DNA271778, NP_068594.1, 204205.at
 Figure 1301: PRO60062
 Figure 1302: DNA330042, HSU16307, 204221.x.at
 Figure 1303: PRO85325
 Figure 1304: DNA150812, NP_006842.1, 204222.s.at
 Figure 1305: PRO12481
 Figure 1306: DNA227514, NP_000152.1, 204224.s.at
 Figure 1307: PRO37977
 Figure 1308: DNA88308, NP_004097.1, 204232.at
 Figure 1309: PRO2739
 Figure 1310: DNA226881, NP_002008.2, 204236.at
 Figure 1311: PRO37344
 Figure 1312: DNA270434, NP_006434.1, 204238.s.at
 Figure 1313: PRO58814
 Figure 1314A-B: DNA287273, NP_006435.1, 204240.s.at
 Figure 1315: PRO69545
 Figure 1316: DNA330043, NP_001789.2, 204252.at
 Figure 1317: PRO85326
 Figure 1318A-B: DNA103527, NP_000367.1, 204253.s.at
 Figure 1319: PRO4854
 Figure 1320A-B: DNA103527, VDR, 204254.s.at
 Figure 1321: PRO4854
 Figure 1322A-B: DNA103527, HUMVDR, 204255.s.at
 Figure 1323: PRO4854
 Figure 1324: DNA228132, NP_076995.1, 204256.at
 Figure 1325: PRO38595
 Figure 1326: DNA226577, NP_071390.1, 204265.s.at
 Figure 1327: PRO37040
 Figure 1328: DNA88643, SGSH, 204293.at
 Figure 1329: PRO2455
 Figure 1330: DNA330044, GTSE1, 204318.s.at
 Figure 1331: PRO85327
 Figure 1332: DNA330045, NP_005943.1, 204326.x.at
 Figure 1333: PRO82583
 Figure 1334: DNA328530, NP_009198.2, 204328.at
 Figure 1335: PRO24118
 Figure 1336: DNA330046, 987987.10, 204334.at
 Figure 1337: PRO85328
 Figure 1338: DNA328531, NP_037542.1, 204348.s.at
 Figure 1339: PRO84338
 Figure 1340: DNA330047, BC005250, 204349.at
 Figure 1341: PRO37777
 Figure 1342A-B: DNA193847, NP_055518.1, 204377.s.at
 Figure 1343: PRO23272
 Figure 1344: DNA328533, NP_003647.1, 204392.at
 Figure 1345: PRO84340
 Figure 1346: DNA226462, NP_002241.1, 204401.at
 Figure 1347: PRO36925
 Figure 1348A-B: DNA330048, AF080255, 204407.at
 Figure 1349: PRO85329
 Figure 1350: DNA327616, NP_075011.1, 204415.at
 Figure 1351: PRO83624
 Figure 1352: DNA331473, NP_000839.1, 204418.x.at
 Figure 1353: PRO60552
 Figure 1354: DNA226286, NP_001657.1, 204425.at
 Figure 1355: PRO36749
 Figure 1356: DNA327617, NP_006811.1, 204439.at
 Figure 1357: PRO83625
 Figure 1358A-B: DNA330049, NP_004514.2, 204444.at
 Figure 1359: PRO85330
 Figure 1360: DNA329150, NP_000689.1, 204446.s.at
 Figure 1361: PRO84783
 Figure 1362: DNA270496, NP_001316.1, 204459.at
 Figure 1363: PRO58875
 Figure 1364: DNA330050, NP_056289.1, 204502.at
 Figure 1365: PRO85331
 Figure 1366: DNA273612, HSU79274, 204521.at
 Figure 1367: PRO61586
 Figure 1368: DNA330051, NP_003431.1, 204523.at
 Figure 1369: PRO85332
 Figure 1370A-B: DNA330052, NP_009227.1, 204531.s.at
 Figure 1371: PRO25103
 Figure 1372: DNA82362, NP_001556.1, 204533.at
 Figure 1373: PRO1718
 Figure 1374A-B: DNA331474, 357276.11, 204552.at

Figure 1375: PRO86521
 Figure 1376A-B: DNA329036, NP_002451.1, 204562.at
 Figure 1377: PRO84703
 Figure 1378: DNA287284, NP_060943.1, 204565.at
 Figure 1379: PRO59915
 Figure 1380: DNA151910, NP_004906.2, 204567.s.at
 Figure 1381: PRO12754
 Figure 1382A-B: DNA273627, NP_055739.1, 204568.at
 Figure 1383: PRO61599
 Figure 1384: DNA272992, N4BP1, 204601.at
 Figure 1385: PRO61064
 Figure 1386: DNA254157, NP_005245.2, 204618.s.at
 Figure 1387: PRO49271
 Figure 1388: DNA151048, NP_005177.1, 204621.s.at
 Figure 1389: PRO12850
 Figure 1390: DNA151048, NR4A2, 204622.x.at
 Figure 1391: PRO12850
 Figure 1392A-B: DNA330054, NP_004746.1, 204633.s.at
 Figure 1393: PRO85334
 Figure 1394: DNA254470, NP_002488.1, 204641.at
 Figure 1395: PRO49578
 Figure 1396: DNA226182, EDG1, 204642.at
 Figure 1397: PRO36645
 Figure 1398: DNA210121, CDW52, 204661.at
 Figure 1399: PRO33667
 Figure 1400: DNA103526, LRMP, 204674.at
 Figure 1401: PRO4853
 Figure 1402: DNA225974, NP_000864.1, 204683.at
 Figure 1403: PRO36437
 Figure 1404: DNA256295, LRN, 204692.at
 Figure 1405: PRO51339
 Figure 1406: DNA227573, NP_001780.1, 204696.s.at
 Figure 1407: PRO38036
 Figure 1408: DNA329151, NP_004280.3, 204702.s.at
 Figure 1409: PRO84784
 Figure 1410: DNA331475, KNSL5, 204709.s.at
 Figure 1411: PRO86522
 Figure 1412A-B: DNA331476, NP_000121.1, 204713.s.at
 Figure 1413: PRO86523
 Figure 1414A-B: DNA225911, F5, 204714.s.at
 Figure 1415: PRO36374
 Figure 1416A-B: DNA218283, NP_004436.1, 204718.at
 Figure 1417: PRO34335
 Figure 1418A-B: DNA256461, NP_009017.1, 204728.s.at
 Figure 1419: PRO51498
 Figure 1420A-C: DNA274487, NP_055562.1, 204730.at
 Figure 1421: PRO62389
 Figure 1422A-B: DNA83176, NP_003234.1, 204731.at
 Figure 1423: PRO2620
 Figure 1424A-B: DNA325192, NP_038203.1, 204744.s.at
 Figure 1425: PRO81753
 Figure 1426: DNA330057, NP_005941.1, 204745.x.at
 Figure 1427: PRO85337
 Figure 1428: DNA287178, NP_001540.1, 204747.at
 Figure 1429: PRO69467
 Figure 1430: DNA330058, NP_004529.2, 204749.at
 Figure 1431: PRO85338
 Figure 1432: DNA329153, NP_001259.1, 204759.at
 Figure 1433: PRO84786
 Figure 1434: DNA330059, NP_068370.1, 204760.s.at
 Figure 1435: PRO85339
 Figure 1436: DNA330060, NP_002443.2, 204766.s.at
 Figure 1437: PRO85340
 Figure 1438: DNA329154, BC000323, 204767.s.at
 Figure 1439: PRO69568
 Figure 1440: DNA325479, NP_004102.1, 204768.s.at
 Figure 1441: PRO69568
 Figure 1442: DNA328541, NP_004503.1, 204773.at
 Figure 1443: PRO4843
 Figure 1444: DNA329155, NP_000034.1, 204780.s.at
 Figure 1445: PRO1207
 Figure 1446: DNA329155, TNFRSF6, 204781.s.at
 Figure 1447: PRO1207
 Figure 1448: DNA272121, NP_005895.1, 204790.at
 Figure 1449: PRO60391
 Figure 1450A-B: DNA330061, NP_055525.1, 204793.at
 Figure 1451: PRO85341
 Figure 1452: DNA103269, NP_005366.1, 204798.at
 Figure 1453: PRO4599
 Figure 1454: DNA287168, NP_003132.2, 204804.at
 Figure 1455: PRO69460
 Figure 1456: DNA330062, NP_006017.1, 204805.s.at
 Figure 1457: PRO85342
 Figure 1458A-B: DNA329907, ESPL1, 204817.at
 Figure 1459: PRO85224
 Figure 1460: DNA331477, NP_003309.1, 204822.at
 Figure 1461: PRO58276
 Figure 1462: DNA255289, NP_055606.1, 204825.at
 Figure 1463: PRO50363
 Figure 1464A-B: DNA226387, NP_001752.1, 204826.at
 Figure 1465: PRO36850
 Figure 1466: DNA328544, NP_006673.1, 204834.at
 Figure 1467: PRO84347
 Figure 1468A-B: DNA270446, NP_058633.1, 204835.at
 Figure 1469: PRO58825
 Figure 1470: DNA330063, HUMLPTPASE, 204852.s.at
 Figure 1471: PRO85343
 Figure 1472: DNA150598, NP_003541.1, 204857.at
 Figure 1473: PRO12142
 Figure 1474: DNA225661, NP_001944.1, 204858.s.at

Figure 1475: PRO36124
 Figure 1476A-B: DNA330064, 332518.2, 204886.at
 Figure 1477: PRO85344
 Figure 1478: DNA330065, NP_055079.2, 204887.s.at
 Figure 1479: PRO85345
 Figure 1480: DNA103444, LCK, 204890.s.at
 Figure 1481: PRO4771
 Figure 1482: DNA331478, BC013200, 204891.s.at
 Figure 1483: PRO86524
 Figure 1484: DNA194139, DNA194139, 204897.at
 Figure 1485: PRO23533
 Figure 1486: DNA255326, NP_003855.1, 204900.x.at
 Figure 1487: PRO50396
 Figure 1488: DNA329157, NP_004271.1, 204905.s.at
 Figure 1489: PRO62861
 Figure 1490: DNA329011, NP_005169.1, 204908.s.at
 Figure 1491: PRO4785
 Figure 1492A-B: DNA76503, NP_001549.1, 204912.at
 Figure 1493: PRO2536
 Figure 1494: DNA330066, NP_004520.1, 204917.s.at
 Figure 1495: PRO85346
 Figure 1496: DNA228014, NP_002153.1, 204949.at
 Figure 1497: PRO38477
 Figure 1498: DNA271093, NP_004064.1, 204958.at
 Figure 1499: PRO59417
 Figure 1500: DNA103283, NP_002423.1, 204959.at
 Figure 1501: PRO4613
 Figure 1502: DNA330067, NP_001800.1, 204962.s.at
 Figure 1503: PRO60368
 Figure 1504: DNA287399, NP_058197.1, 204972.at
 Figure 1505: PRO69656
 Figure 1506: DNA269665, NP_002454.1, 204994.at
 Figure 1507: PRO58076
 Figure 1508: DNA331479, 411441.5, 204995.at
 Figure 1509: PRO86525
 Figure 1510: DNA272427, NP_004799.1, 205005.s.at
 Figure 1511: PRO60679
 Figure 1512: DNA272427, NMT2, 205006.s.at
 Figure 1513: PRO60679
 Figure 1514: DNA329534, NP_004615.2, 205019.s.at
 Figure 1515: PRO2904
 Figure 1516: DNA331480, RAD51, 205024.s.at
 Figure 1517: PRO86526
 Figure 1518: DNA329159, NP_005195.2, 205027.s.at
 Figure 1519: PRO4660
 Figure 1520: DNA325061, NP_005208.1, 205033.s.at
 Figure 1521: PRO9980
 Figure 1522: DNA328297, NP_477097.1, 205034.at
 Figure 1523: PRO59418
 Figure 1524A-C: DNA331481, NP_001804.1, 205046.at
 Figure 1525: PRO86527
 Figure 1526: DNA324991, ASNS, 205047.s.at
 Figure 1527: PRO81585
 Figure 1528: DNA271461, NP_000937.1, 205053.at
 Figure 1529: PRO59757
 Figure 1530A-B: DNA220750, NP_002199.2, 205055.at
 Figure 1531: PRO34728
 Figure 1532: DNA330071, NP_003607.1, 205063.at
 Figure 1533: PRO85350
 Figure 1534: DNA330072, NP_071801.1, 205072.s.at
 Figure 1535: PRO85351
 Figure 1536: DNA304705, NP_002634.1, 205078.at
 Figure 1537: PRO71131
 Figure 1538: DNA327632, NP_001302.1, 205081.at
 Figure 1539: PRO83635
 Figure 1540: DNA255336, NP_061332.1, 205084.at
 Figure 1541: PRO50406
 Figure 1542: DNA330073, NP_004144.1, 205085.at
 Figure 1543: PRO85352
 Figure 1544: DNA330074, HUMHMI45, 205098.at
 Figure 1545: PRO85353
 Figure 1546: DNA226177, NP_001286.1, 205099.s.at
 Figure 1547: PRO36640
 Figure 1548: DNA192060, NP_002974.1, 205114.s.at
 Figure 1549: PRO21960
 Figure 1550: DNA299899, NP_002148.1, 205133.s.at
 Figure 1551: PRO62760
 Figure 1552: DNA331482, NP_001241.1, 205153.s.at
 Figure 1553: PRO34457
 Figure 1554: DNA330075, CDC25C, 205167.s.at
 Figure 1555: PRO85354
 Figure 1556: DNA330076, NP_005410.1, 205170.at
 Figure 1557: PRO85355
 Figure 1558: DNA328810, NP_001770.1, 205173.x.at
 Figure 1559: PRO2557
 Figure 1560: DNA330077, ITGB3BP, 205176.s.at
 Figure 1561: PRO85356
 Figure 1562: DNA151804, NP_006500.1, 205205.at
 Figure 1563: PRO12188
 Figure 1564: DNA272443, NP_055531.1, 205213.s.at
 Figure 1565: PRO60693
 Figure 1566: DNA273535, NP_004217.1, 205214.at
 Figure 1567: PRO61515
 Figure 1568: DNA325255, NP_001994.2, 205237.at
 Figure 1569: PRO1910
 Figure 1570: DNA330078, NP_001648.1, 205239.at
 Figure 1571: PRO46
 Figure 1572: DNA327634, NP_005129.1, 205241.at
 Figure 1573: PRO83636
 Figure 1574: DNA188333, NP_006410.1, 205242.at
 Figure 1575: PRO21708
 Figure 1576: DNA227081, NP_000390.2, 205249.at
 Figure 1577: PRO37544
 Figure 1578: DNA227447, NP_003193.1, 205254.x.at
 Figure 1579: PRO37910
 Figure 1580: DNA227447, TCF7, 205255.x.at
 Figure 1581: PRO37910
 Figure 1582A-B: DNA226483, NP_000892.1, 205259.at
 Figure 1583: PRO36946

Figure 1584A-B: DNA330079, 341358.1, 205263.at
 Figure 1585: PRO1162
 Figure 1586A-B: DNA188301, NP_002300.1, 205266.at
 Figure 1587: PRO21834
 Figure 1588: DNA227173, NP_001456.1, 205285.s.at
 Figure 1589: PRO37636
 Figure 1590A-B: DNA331483, CDC14A, 205288.at
 Figure 1591: PRO86528
 Figure 1592A-B: DNA331484, NP_000869.1, 205291.at
 Figure 1593: PRO3276
 Figure 1594: DNA88119, NP_000617.1, 205297.s.at
 Figure 1595: PRO2663
 Figure 1596A-B: DNA330081, NP_003026.1, 205339.at
 Figure 1597: PRO85358
 Figure 1598: DNA256854, NP_000456.1, 205345.at
 Figure 1599: PRO51785
 Figure 1600: DNA270415, NP_002059.1, 205349.at
 Figure 1601: PRO58796
 Figure 1602: DNA325568, NP_001265.1, 205393.s.at
 Figure 1603: PRO12187
 Figure 1604: DNA325568, CHEK1, 205394.at
 Figure 1605: PRO12187
 Figure 1606: DNA330082, NP_005582.1, 205395.s.at
 Figure 1607: PRO60497
 Figure 1608: DNA328561, NP_004624.1, 205403.at
 Figure 1609: PRO2019
 Figure 1610: DNA329010, NP_004942.1, 205419.at
 Figure 1611: PRO23370
 Figure 1612A-B: DNA210654, NP_055726.1, 205434.s.at
 Figure 1613: PRO54603
 Figure 1614: DNA287337, NP_002096.1, 205436.s.at
 Figure 1615: PRO69600
 Figure 1616: DNA330083, NP_003073.1, 205443.at
 Figure 1617: PRO69499
 Figure 1618: DNA272221, NP_037431.1, 205449.at
 Figure 1619: PRO60483
 Figure 1620: DNA88194, NP_000724.1, 205456.at
 Figure 1621: PRO2220
 Figure 1622: DNA188355, NP_004582.1, 205476.at
 Figure 1623: PRO21885
 Figure 1624: DNA287224, NP_005092.1, 205483.s.at
 Figure 1625: PRO69503
 Figure 1626: DNA330084, NP_055265.1, 205484.at
 Figure 1627: PRO9895
 Figure 1628: DNA225959, NP_006135.1, 205488.at
 Figure 1629: PRO36422
 Figure 1630: DNA331485, GNLY, 205495.s.at
 Figure 1631: PRO86529
 Figure 1632: DNA328566, NP_060446.1, 205510.s.at
 Figure 1633: PRO84363
 Figure 1634: DNA327639, NP_001053.2, 205513.at
 Figure 1635: PRO83640
 Figure 1636: DNA330085, D86324, 205518.s.at
 Figure 1637: PRO85359
 Figure 1638: DNA330086, NP_079184.1, 205519.at
 Figure 1639: PRO85360
 Figure 1640: DNA254810, NP_056536.1, 205527.s.at
 Figure 1641: PRO49906
 Figure 1642: DNA331486, OAS1, 205552.s.at
 Figure 1643: PRO69559
 Figure 1644: DNA330087, PCSK5, 205559.s.at
 Figure 1645: PRO85361
 Figure 1646: DNA256257, NP_055213.1, 205569.at
 Figure 1647: PRO51301
 Figure 1648A-B: DNA327643, NP_055712.1, 205594.at
 Figure 1649: PRO83644
 Figure 1650: DNA329013, NP_005649.1, 205599.at
 Figure 1651: PRO20128
 Figure 1652: DNA324324, NP_000679.1, 205633.s.at
 Figure 1653: PRO81000
 Figure 1654: DNA330088, NP_003087.1, 205644.s.at
 Figure 1655: PRO61962
 Figure 1656: DNA287317, NP_003724.1, 205660.at
 Figure 1657: PRO69582
 Figure 1658: DNA328570, NP_004040.1, 205681.at
 Figure 1659: PRO37843
 Figure 1660: DNA330089, NP_004200.2, 205691.at
 Figure 1661: PRO12507
 Figure 1662: DNA226234, NP_001766.1, 205692.s.at
 Figure 1663: PRO36697
 Figure 1664: DNA330090, NP_002749.2, 205698.s.at
 Figure 1665: PRO62976
 Figure 1666: DNA220761, NP_000880.1, 205718.at
 Figure 1667: PRO34739
 Figure 1668A-B: DNA271762, NP_000048.1, 205733.at
 Figure 1669: PRO60046
 Figure 1670: DNA331318, NP_003636.1, 205768.s.at
 Figure 1671: PRO51139
 Figure 1672: DNA331318, SLC27A2, 205769.at
 Figure 1673: PRO51139
 Figure 1674: DNA330091, NP_057461.1, 205771.s.at
 Figure 1675: PRO85362
 Figure 1676: DNA330092, NP_004904.1, 205781.at
 Figure 1677: PRO85363
 Figure 1678A-B: DNA220752, NP_000623.1, 205786.s.at
 Figure 1679: PRO34730
 Figure 1680: DNA330093, NP_003717.2, 205790.at
 Figure 1681: PRO85364
 Figure 1682: DNA76517, NP_002176.1, 205798.at
 Figure 1683: PRO2541
 Figure 1684A-B: DNA271915, NP_056191.1, 205801.s.at
 Figure 1685: PRO60192
 Figure 1686: DNA194766, NP_079504.1, 205804.s.at
 Figure 1687: PRO24046

Figure 1688A-B: DNA328574, NP.004963.1, 205841.at
 Figure 1689: PRO84368
 Figure 1690A-B: DNA328574, JAK2, 205842.s.at
 Figure 1691: PRO84368
 Figure 1692: DNA330094, TREX1, 205875.s.at
 Figure 1693: PRO85365
 Figure 1694: DNA331320, HSU37122, 205882.x.at
 Figure 1695: PRO86409
 Figure 1696A-B: DNA220746, NP.000876.1, 205884.at
 Figure 1697: PRO34724
 Figure 1698A-B: DNA220746, ITGA4, 205885.s.at
 Figure 1699: PRO34724
 Figure 1700: DNA329540, NP.006389.1, 205890.s.at
 Figure 1701: PRO85090
 Figure 1702: DNA330095, NP.004732.1, 205895.s.at
 Figure 1703: PRO85366
 Figure 1704: DNA328576, HSU20350, 205898.at
 Figure 1705: PRO4940
 Figure 1706: DNA287318, NP.002683.1, 205909.at
 Figure 1707: PRO69583
 Figure 1708: DNA75525, NP.005805.1, 205929.at
 Figure 1709: PRO2524
 Figure 1710: DNA76516, NP.000556.1, 205945.at
 Figure 1711: PRO2022
 Figure 1712: DNA329047, NP.006390.1, 205965.at
 Figure 1713: PRO58425
 Figure 1714: DNA273487, NP.004785.1, 206039.at
 Figure 1715: PRO61470
 Figure 1716A-B: DNA290265, NP.003421.1, 206059.at
 Figure 1717: PRO70395
 Figure 1718: DNA330096, NP.057051.1, 206060.s.at
 Figure 1719: PRO37163
 Figure 1720: DNA271992, NP.006665.1, 206082.at
 Figure 1721: PRO60267
 Figure 1722: DNA270851, NP.006617.1, 206098.at
 Figure 1723: PRO59189
 Figure 1724: DNA226105, NP.002925.1, 206111.at
 Figure 1725: PRO36568
 Figure 1726: DNA83063, NP.004429.1, 206114.at
 Figure 1727: PRO2068
 Figure 1728A-B: DNA151420, NP.004421.1, 206115.at
 Figure 1729: PRO12876
 Figure 1730: DNA287306, NP.059993.1, 206133.at
 Figure 1731: PRO69572
 Figure 1732: DNA330097, NP.001233.1, 206150.at
 Figure 1733: PRO2024
 Figure 1734: DNA331487, GABPB2, 206173.x.at
 Figure 1735: PRO86530
 Figure 1736: DNA329005, NP.003028.1, 206181.at
 Figure 1737: PRO12612
 Figure 1738: DNA330098, NP.073619.1, 206205.at
 Figure 1739: PRO85367
 Figure 1740: DNA329168, CLC, 206207.at
 Figure 1741: PRO84794
 Figure 1742: DNA281446, NP.031394.1, 206220.s.at
 Figure 1743: PRO66285
 Figure 1744: DNA281446, GAP1IP4BP, 206221.at
 Figure 1745: PRO66285
 Figure 1746A-B: DNA331488, NP.055523.1, 206316.s.at
 Figure 1747: PRO86531
 Figure 1748: DNA327661, NP.005522.1, 206332.s.at
 Figure 1749: PRO83652
 Figure 1750: DNA218278, NP.000408.1, 206341.at
 Figure 1751: PRO34330
 Figure 1752: DNA269870, NP.005382.1, 206348.s.at
 Figure 1753: PRO58270
 Figure 1754A-B: DNA330100, NP.055690.1, 206364.at
 Figure 1755: PRO85369
 Figure 1756: DNA329169, NP.002986.1, 206366.x.at
 Figure 1757: PRO1610
 Figure 1758: DNA271310, NP.004411.1, 206374.at
 Figure 1759: PRO59617
 Figure 1760A-E: DNA331489, NP.066267.1, 206385.s.at
 Figure 1761: PRO86532
 Figure 1762: DNA326727, NP.001527.1, 206445.s.at
 Figure 1763: PRO83069
 Figure 1764A-B: DNA271891, NP.055766.1, 206448.at
 Figure 1765: PRO60170
 Figure 1766: DNA153751, NP.005942.1, 206461.x.at
 Figure 1767: PRO12925
 Figure 1768: DNA88203, NP.055022.1, 206485.at
 Figure 1769: PRO2698
 Figure 1770: DNA288243, NP.002277.3, 206486.at
 Figure 1771: PRO36451
 Figure 1772: DNA269850, NP.002003.1, 206492.at
 Figure 1773: PRO58251
 Figure 1774: DNA270444, NP.004824.1, 206513.at
 Figure 1775: PRO58823
 Figure 1776A-B: DNA188192, NP.006130.1, 206545.at
 Figure 1777: PRO21704
 Figure 1778A-B: DNA330102, NP.004289.1, 206550.s.at
 Figure 1779: PRO85371
 Figure 1780: DNA331490, OAS2, 206553.at
 Figure 1781: PRO69656
 Figure 1782: DNA227540, NP.003036.1, 206566.at
 Figure 1783: PRO38003
 Figure 1784: DNA330103, NP.056179.1, 206584.at
 Figure 1785: PRO19671
 Figure 1786: DNA329172, NP.005254.1, 206589.at
 Figure 1787: PRO84796
 Figure 1788: DNA103451, NP.003846.1, 206618.at
 Figure 1789: PRO4778

Figure 1790: DNA227709, NP_000947.1, 206631.at
 Figure 1791: PRO38172
 Figure 1792: DNA331491, NP_004891.2, 206632.s.at
 Figure 1793: PRO62308
 Figure 1794: DNA331492, BCL2L1, 206665.s.at
 Figure 1795: PRO83141
 Figure 1796: DNA88374, NP_002095.1, 206666.at
 Figure 1797: PRO2768
 Figure 1798: DNA330105, HUMNCAX, 206676.at
 Figure 1799: PRO85372
 Figure 1800: DNA328590, C6orf32, 206707.x.at
 Figure 1801: PRO84375
 Figure 1802: DNA330106, NP_003646.1, 206724.at
 Figure 1803: PRO85373
 Figure 1804A-B: DNA88191, NP_001234.1, 206729.at
 Figure 1805: PRO2691
 Figure 1806A-B: DNA88650, NP_005807.1, 206761.at
 Figure 1807: PRO2460
 Figure 1808: DNA226427, NP_002251.1, 205785.s.at
 Figure 1809: PRO36890
 Figure 1810: DNA88195, NP_000064.1, 206804.at
 Figure 1811: PRO2693
 Figure 1812: DNA256561, NP_062550.1, 206914.at
 Figure 1813: PRO51592
 Figure 1814: DNA93439, NP_006555.1, 206974.at
 Figure 1815: PRO4515
 Figure 1816: DNA35629, NP_000586.2, 206975.at
 Figure 1817: PRO7
 Figure 1818: DNA328591, NP_006635.1, 206976.s.at
 Figure 1819: PRO84376
 Figure 1820: DNA331493, CCR2, 206978.at
 Figure 1821: PRO84690
 Figure 1822: DNA188346, NP_001450.1, 206980.s.at
 Figure 1823: PRO21766
 Figure 1824A-B: DNA227659, NP_000570.1, 206991.s.at
 Figure 1825: PRO38122
 Figure 1826A-B: DNA227750, NP_001550.1, 206999.at
 Figure 1827: PRO38213
 Figure 1828: DNA329903, PPP3CC, 207000.s.at
 Figure 1829: PRO85220
 Figure 1830: DNA330108, NP_004080.1, 207001.x.at
 Figure 1831: PRO85374
 Figure 1832: DNA331494, PLAGL1, 207002.s.at
 Figure 1833: PRO62736
 Figure 1834: DNA331495, HUMBCL2B, 207005.s.at
 Figure 1835: PRO86533
 Figure 1836: DNA330110, HUMK10A, 207023.x.at
 Figure 1837: PRO85375
 Figure 1838: DNA225550, NP_003844.1, 207072.at
 Figure 1839: PRO36013
 Figure 1840: DNA273159, NP_005457.1, 207078.at
 Figure 1841: PRO61201
 Figure 1842: DNA227481, VAMP1, 207100.s.at
 Figure 1843: PRO37944
 Figure 1844: DNA218655, NP_000585.1, 207113.s.at
 Figure 1845: PRO34451
 Figure 1846: DNA330111, NP_002615.2, 207132.x.at
 Figure 1847: PRO85376
 Figure 1848: DNA330112, NP_444504.1, 207153.s.at
 Figure 1849: PRO61610
 Figure 1850: DNA103418, NP_036616.1, 207165.at
 Figure 1851: PRO4746
 Figure 1852: DNA330113, NP_203124.1, 207181.s.at
 Figure 1853: PRO85377
 Figure 1854: DNA330114, NP_006134.1, 207183.at
 Figure 1855: PRO4946
 Figure 1856: DNA331496, RBMS1, 207266.x.at
 Figure 1857: PRO86534
 Figure 1858: DNA83048, NP_001916.1, 207269.at
 Figure 1859: PRO2057
 Figure 1860A-B: DNA330115, NP_077739.1, 207324.s.at
 Figure 1861: PRO85378
 Figure 1862A-B: DNA226536, NP_003225.1, 207332.s.at
 Figure 1863: PRO36999
 Figure 1864: DNA331497, LTb, 207339.s.at
 Figure 1865: PRO11604
 Figure 1866: DNA330117, NP_003966.1, 207351.s.at
 Figure 1867: PRO85379
 Figure 1868: DNA330118, NP_036389.2, 207361.at
 Figure 1869: PRO85380
 Figure 1870: DNA226396, NP_002180.1, 207375.s.at
 Figure 1871: PRO36859
 Figure 1872: DNA227668, NP_000158.1, 207387.s.at
 Figure 1873: PRO38131
 Figure 1874A-B: DNA329093, MSF, 207425.s.at
 Figure 1875: PRO84745
 Figure 1876: DNA36718, NP_000563.1, 207433.at
 Figure 1877: PRO73
 Figure 1878A-B: DNA330119, NP_060189.2, 207474.at
 Figure 1879: PRO85381
 Figure 1880: DNA328597, NP_001680.1, 207507.s.at
 Figure 1881: PRO84381
 Figure 1882: DNA328597, ATP5G3, 207508.at
 Figure 1883: PRO84381
 Figure 1884A-B: DNA256059, NP_005164.1, 207521.s.at
 Figure 1885: PRO51107
 Figure 1886A-B: DNA256059, ATP2A3, 207522.s.at
 Figure 1887: PRO51107
 Figure 1888: DNA304473, NP_001552.2, 207536.s.at
 Figure 1889: PRO2023
 Figure 1890: DNA325454, NP_003637.1, 207556.s.at
 Figure 1891: PRO81977
 Figure 1892: DNA328601, NP_056490.1, 207574.s.at
 Figure 1893: PRO84384
 Figure 1894A-B: DNA330120, FLJ10971, 207606.s.at
 Figure 1895: PRO85382

Figure 1896: DNA255271, NP_038475.1, 207610.s.at
 Figure 1897: PRO50348
 Figure 1898: DNA331498, TANK, 207616.s.at
 Figure 1899: PRO86535
 Figure 1900: DNA226337, NP_005683.2, 207622.s.at
 Figure 1901: PRO36800
 Figure 1902: DNA227606, NP_001872.2, 207630.s.at
 Figure 1903: PRO38069
 Figure 1904: DNA196426, NP_037440.1, 207651.at
 Figure 1905: PRO24924
 Figure 1906: DNA328554, NP_038202.1, 207677.s.at
 Figure 1907: PRO84354
 Figure 1908A-B: DNA226405, NP_006525.1, 207700.s.at
 Figure 1909: PRO36868
 Figure 1910: DNA329064, NP_060301.1, 207735.at
 Figure 1911: PRO84724
 Figure 1912: DNA329020, NUP62, 207740.s.at
 Figure 1913: PRO84695
 Figure 1914: DNA325654, NP_054752.1, 207761.s.at
 Figure 1915: PRO4348
 Figure 1916A-B: DNA329179, NP_056958.1, 207785.s.at
 Figure 1917: PRO84802
 Figure 1918: DNA227494, NP_002158.1, 207826.s.at
 Figure 1919: PRO37957
 Figure 1920A-C: DNA331499, NP_057427.2, 207828.s.at
 Figure 1921: PRO86536
 Figure 1922: DNA329182, HPII, 207838.x.at
 Figure 1923: PRO84805
 Figure 1924: DNA330123, NP_008984.1, 207840.at
 Figure 1925: PRO35080
 Figure 1926: DNA227175, NP_006857.1, 207857.at
 Figure 1927: PRO37638
 Figure 1928: DNA330124, NP_002981.2, 207861.at
 Figure 1929: PRO34107
 Figure 1930: DNA217245, NP_000579.1, 207906.at
 Figure 1931: PRO34287
 Figure 1932: DNA218651, NP_003798.1, 207907.at
 Figure 1933: PRO34447
 Figure 1934: DNA330125, NP_002729.2, 207957.s.at
 Figure 1935: PRO85385
 Figure 1936A-B: DNA226290, NP_036333.1, 207966.s.at
 Figure 1937: PRO36753
 Figure 1938: DNA329183, NP_055962.1, 207971.s.at
 Figure 1939: PRO84806
 Figure 1940A-B: DNA330126, NP_008912.1, 207978.s.at
 Figure 1941: PRO85386
 Figure 1942: DNA329184, CTED2, 207980.s.at
 Figure 1943: PRO84807
 Figure 1944A-C: DNA254145, NP_004329.1, 207996.s.at
 Figure 1945: PRO49260
 Figure 1946: DNA275286, NP_009205.1, 208002.s.at
 Figure 1947: PRO62967
 Figure 1948: DNA288217, NP_002101.1, 208018.s.at
 Figure 1949: PRO69990
 Figure 1950: DNA227224, NP_060877.1, 208029.s.at
 Figure 1951: PRO37687
 Figure 1952A-B: DNA188492, NAB1, 208047.s.at
 Figure 1953: PRO22070
 Figure 1954: DNA330127, NP_006442.2, 208051.s.at
 Figure 1955: PRO85387
 Figure 1956A-B: DNA328607, NP_003639.1, 208072.s.at
 Figure 1957: PRO84390
 Figure 1958A-C: DNA331500, NP_003307.2, 208073.x.at
 Figure 1959: PRO86537
 Figure 1960A-B: DNA328312, NP_110378.1, 208078.s.at
 Figure 1961: PRO84180
 Figure 1962: DNA331501, STK6, 208079.s.at
 Figure 1963: PRO58855
 Figure 1964: DNA323896, NP_112182.1, 208103.s.at
 Figure 1965: PRO80638
 Figure 1966: DNA330129, NP_112495.1, 208119.s.at
 Figure 1967: PRO85389
 Figure 1968: DNA325329, NP_004719.1, 208152.s.at
 Figure 1969: PRO81872
 Figure 1970: DNA36717, NP_000581.1, 208193.at
 Figure 1971: PRO72
 Figure 1972A-E: DNA330130, HISTITIN, 208195.at
 Figure 1973: DNA328611, RASGRP2, 208206.s.at
 Figure 1974: PRO84393
 Figure 1975: DNA328612, NP_000166.2, 208308.s.at
 Figure 1976: PRO84394
 Figure 1977A-D: DNA331502, NP_000050.1, 208368.s.at
 Figure 1978: PRO86538
 Figure 1979: DNA324250, NP_536349.1, 208392.x.at
 Figure 1980: PRO80934
 Figure 1981A-B: DNA331503, RAD50, 208393.s.at
 Figure 1982: PRO86539
 Figure 1983: DNA327690, NP_004022.1, 208436.s.at
 Figure 1984: PRO83673
 Figure 1985: DNA103427, NP_005239.1, 208438.s.at
 Figure 1986: PRO4755
 Figure 1987A-C: DNA331504, ATM, 208442.s.at
 Figure 1988: PRO86540
 Figure 1989A-B: DNA330134, BAZ1B, 208445.s.at
 Figure 1990: PRO85394
 Figure 1991A-C: DNA331505, NP_000642.2, 208488.s.at
 Figure 1992: PRO86541
 Figure 1993: DNA330136, NP_002441.1, 208581.x.at
 Figure 1994: PRO82583
 Figure 1995A-C: DNA331506, NP_001448.1, 208614.s.at

Figure 1996: PRO86542
 Figure 1997A-B: DNA330138, PTP4A2, 208617.s.at
 Figure 1998: PRO85397
 Figure 1999A-B: DNA273567, NP_004944.1, 208624.s.at
 Figure 2000: PRO61545
 Figure 2001A-B: DNA273567, EIF4G1, 208625.s.at
 Figure 2002: PRO61545
 Figure 2003: DNA325912, NP_001093.1, 208636.at
 Figure 2004: PRO82367
 Figure 2005: DNA325912, ACTN1, 208637.x.at
 Figure 2006: PRO82367
 Figure 2007: DNA329188, BC012142, 208638.at
 Figure 2008: PRO84810
 Figure 2009: DNA324641, NP_005608.1, 208646.at
 Figure 2010: PRO10849
 Figure 2011: DNA271268, NP_009057.1, 208649.s.at
 Figure 2012: PRO59579
 Figure 2013: DNA328617, AT299343, 208653.s.at
 Figure 2014: PRO84399
 Figure 2015: DNA330139, AK022493, 208657.s.at
 Figure 2016: PRO85398
 Figure 2017A-C: DNA151898, TTC3, 208661.s.at
 Figure 2018: PRO12135
 Figure 2019A-C: DNA151898, D84294, 208662.s.at
 Figure 2020: PRO12135
 Figure 2021A-C: DNA331507, D83327, 208663.s.at
 Figure 2022: DNA304686, NP_002565.1, 208680.at
 Figure 2023: PRO71112
 Figure 2024A-B: DNA328619, BC001188, 208691.at
 Figure 2025: PRO84401
 Figure 2026: DNA287189, NP_002038.1, 208693.s.at
 Figure 2027: PRO69475
 Figure 2028: DNA330140, AF275798, 208696.at
 Figure 2029: PRO85399
 Figure 2030A-C: DNA331508, 198777.9, 208707.at
 Figure 2031: PRO86543
 Figure 2032: DNA97298, NP_003899.1, 208726.s.at
 Figure 2033: PRO3645
 Figure 2034: DNA330142, BC003564, 208737.at
 Figure 2035: PRO85401
 Figure 2036: DNA331509, 1138554.23, 208740.at
 Figure 2037: PRO86544
 Figure 2038: DNA328591, HSP105B, 208744.x.at
 Figure 2039: PRO84376
 Figure 2040: DNA287285, NP_005794.1, 208748.s.at
 Figure 2041: PRO69556
 Figure 2042: DNA324217, AIIIC, 208758.at
 Figure 2043: PRO80908
 Figure 2044: DNA327696, AF228339, 208763.s.at
 Figure 2045: PRO83679
 Figure 2046A-B: DNA331510, 1298307.1, 208776.at
 Figure 2047: PRO86545
 Figure 2048: DNA287427, NP_002806.1, 208777.s.at
 Figure 2049: PRO69684
 Figure 2050: DNA287219, NP_110379.1, 208778.s.at
 Figure 2051: PRO69498
 Figure 2052: DNA329189, NP_009139.1, 208787.at
 Figure 2053: PRO4911
 Figure 2054: DNA238565, NP_005907.2, 208795.s.at
 Figure 2055: PRO39210
 Figure 2056: DNA330145, NP_002788.1, 208799.at
 Figure 2057: PRO84403
 Figure 2058: DNA331511, HSMPIO, 208805.at
 Figure 2059A-C: DNA331512, 1397486.26, 208806.at
 Figure 2060: PRO86547
 Figure 2061A-B: DNA330147, HSU91543, 208807.s.at
 Figure 2062: PRO85405
 Figure 2063: DNA324531, NP_002120.1, 208808.s.at
 Figure 2064: PRO81185
 Figure 2065: DNA273521, NP_002070.1, 208813.at
 Figure 2066: PRO61502
 Figure 2067A-B: DNA330148, AB020636, 208838.at
 Figure 2068A-B: DNA330149, HSM801778, 208839.s.at
 Figure 2069: PRO82209
 Figure 2070: DNA227874, NP_003320.1, 208864.s.at
 Figure 2071: PRO38337
 Figure 2072: DNA328624, BC003562, 208891.at
 Figure 2073: PRO59076
 Figure 2074: DNA331513, DUSP6, 208892.s.at
 Figure 2075: PRO84404
 Figure 2076: DNA331330, BC005047, 208893.s.at
 Figure 2077: PRO82215
 Figure 2078: DNA329221, NP_061984.1, 208894.at
 Figure 2079: PRO4555
 Figure 2080A-B: DNA329007, NP_003277.1, 208900.s.at
 Figure 2081: PRO37029
 Figure 2082A-B: DNA329007, TOP1, 208901.s.at
 Figure 2083: PRO37029
 Figure 2084: DNA327700, BC015130, 208905.at
 Figure 2085: PRO83683
 Figure 2086: DNA327701, NP_001203.1, 208910.s.at
 Figure 2087: PRO82667
 Figure 2088: DNA281442, NP_149124.1, 208912.s.at
 Figure 2089: PRO66281
 Figure 2090A-B: DNA330151, AB029003, 208914.at
 Figure 2091: DNA325473, NP_006353.2, 208922.s.at
 Figure 2092: PRO81996
 Figure 2093: DNA329552, NP_063948.1, 208925.at
 Figure 2094: PRO85097
 Figure 2095: DNA326233, NP_000968.2, 208929.x.at
 Figure 2096: PRO82645
 Figure 2097: DNA327702, NP_006490.2, 208934.s.at
 Figure 2098: PRO83684
 Figure 2099: DNA330152, NP_001939.1, 208956.x.at
 Figure 2100: PRO85406
 Figure 2101: DNA290261, NP_001291.2, 208960.s.at
 Figure 2102: PRO70387
 Figure 2103A-B: DNA325478, NP_037534.2,

208962.s.at
 Figure 2104: PRO81999
 Figure 2105: DNA327661, IFI16, 208965.s.at
 Figure 2106: PRO83652
 Figure 2107A-B: DNA270277, AF208043, 208966.x.at
 Figure 2108: PRO58665
 Figure 2109: DNA326343, KPNB1, 208974.x.at
 Figure 2110: PRO82739
 Figure 2111A-B: DNA330153, HUMIMP90A, 208975.s.at
 Figure 2112: PRO82739
 Figure 2113: DNA328629, NP_006079.1, 208977.x.at
 Figure 2114: PRO84407
 Figure 2115: DNA330154, HUMPECAM27, 208981.at
 Figure 2116: DNA330155, 7692317.2, 208982.at
 Figure 2117: PRO85407
 Figure 2118: DNA330156, NP_003749.1, 208985.s.at
 Figure 2119: PRO85408
 Figure 2120: DNA331514, STAT3, 208992.s.at
 Figure 2121: PRO86548
 Figure 2122: DNA227552, NP_003346.2, 208997.s.at
 Figure 2123: PRO38015
 Figure 2124: DNA227552, UCP2, 208998.at
 Figure 2125: PRO38015
 Figure 2126: DNA328630, NP_036293.1, 209004.s.at
 Figure 2127: PRO84408
 Figure 2128: DNA331515, FBXL5, 209005.at
 Figure 2129: PRO86549
 Figure 2130: DNA328631, AKO27318, 209006.s.at
 Figure 2131: PRO84409
 Figure 2132: DNA331516, DNAJB6, 209015.s.at
 Figure 2133: PRO83680
 Figure 2134: DNA328633, NP_004784.2, 209017.s.at
 Figure 2135: PRO84411
 Figure 2136: DNA330158, NP_057554.4, 209020.at
 Figure 2137: PRO85410
 Figure 2138: DNA327851, NP_006363.2, 209024.s.at
 Figure 2139: PRO83795
 Figure 2140: DNA328635, BC020946, 209026.x.at
 Figure 2141: PRO84413
 Figure 2142: DNA331517, NP_004150.1, 209040.s.at
 Figure 2143: PRO69506
 Figure 2144A-C: DNA328637, HSA7042, 209052.s.at
 Figure 2145: PRO81109
 Figure 2146A-B: DNA331518, AF330040, 209053.s.at
 Figure 2147: PRO86550
 Figure 2148A-B: DNA226405, NCOA3, 209060.x.at
 Figure 2149: PRO36868
 Figure 2150: DNA330159, HSM801885, 209064.x.at
 Figure 2151: PRO85411
 Figure 2152: DNA330160, NP_006285.1, 209066.x.at
 Figure 2153: PRO85412
 Figure 2154: DNA329194, NP_112740.1, 209068.at
 Figure 2155: PRO84814
 Figure 2156A-B: DNA330161, NP_085059.1, 209081.s.at
 Figure 2157: PRO85413
 Figure 2158: DNA330162, NP_057093.1, 209091.s.at
 Figure 2159: PRO85414
 Figure 2160: DNA330163, NP_060308.1, 209104.s.at
 Figure 2161: PRO85415
 Figure 2162: DNA330164, NP_004752.1, 209110.s.at
 Figure 2163: PRO85416
 Figure 2164: DNA327709, NP_000509.1, 209116.x.at
 Figure 2165: PRO83690
 Figure 2166: DNA288254, NP_006000.2, 209118.s.at
 Figure 2167: PRO69536
 Figure 2168: DNA325163, NP_001113.1, 209122.at
 Figure 2169: PRO81730
 Figure 2170: DNA330165, BC015833, 209138.x.at
 Figure 2171: PRO85417
 Figure 2172: DNA327713, BC010653, 209146.at
 Figure 2173: PRO37975
 Figure 2174: DNA325285, AKR1C3, 209160.at
 Figure 2175: PRO81832
 Figure 2176: DNA330166, BC001588, 209161.at
 Figure 2177: PRO85418
 Figure 2178: DNA271722, NP_004688.1, 209162.s.at
 Figure 2179: PRO60006
 Figure 2180: DNA330167, CAB43224.1, 209177.at
 Figure 2181: PRO85419
 Figure 2182A-B: DNA328642, AF073310, 209184.s.at
 Figure 2183: PRO84418
 Figure 2184: DNA331331, AF161416, 209185.s.at
 Figure 2185A-B: DNA328643, HUMHK1A, 209186.at
 Figure 2186: PRO84419
 Figure 2187: DNA189700, NP_005243.1, 209189.at
 Figure 2188: PRO25619
 Figure 2189: DNA324766, NP_005443.2, 209196.at
 Figure 2190: PRO81387
 Figure 2191: DNA226176, NP_003458.1, 209201.x.at
 Figure 2192: PRO36639
 Figure 2193: DNA326267, NP_004861.1, 209208.at
 Figure 2194: PRO82674
 Figure 2195: DNA326891, NP_001748.1, 209213.at
 Figure 2196: PRO83212
 Figure 2197: DNA227483, NP_003120.1, 209218.at
 Figure 2198: PRO37946
 Figure 2199: DNA330168, NP_006322.1, 209233.at
 Figure 2200: PRO85420
 Figure 2201: DNA328649, NP_116093.1, 209251.x.at
 Figure 2202: PRO84424
 Figure 2203: DNA255255, NP_071437.1, 209267.s.at
 Figure 2204: PRO50332
 Figure 2205A-B: DNA188492, AF045451, 209272.at
 Figure 2206: PRO22070
 Figure 2207A-B: DNA226827, NP_001673.1,

209281.s.at
 Figure 2208: PRO37290
 Figure 2209: DNA328601, GADD45B, 209304.x.at
 Figure 2210: PRO84384
 Figure 2211: DNA328651, AF087853, 209305.s.at
 Figure 2212: PRO82889
 Figure 2213: DNA151780, NP_006611.1, 209314.s.at
 Figure 2214: PRO12057
 Figure 2215: DNA330169, NP_006709.1, 209318.x.at
 Figure 2216: PRO62736
 Figure 2217: DNA275106, HSU76248, 209339.at
 Figure 2218: PRO62821
 Figure 2219: DNA269630, NP_003281.1, 209344.at
 Figure 2220: PRO58042
 Figure 2221A-B: DNA328658, AF055376, 209348.s.at
 Figure 2222: PRO84432
 Figure 2223: DNA330170, AF109161, 209357.at
 Figure 2224: PRO84807
 Figure 2225: DNA327720, NP_001970.1, 209368.at
 Figure 2226: PRO83699
 Figure 2227: DNA330171, CAA34971.1, 209374.s.at
 Figure 2228: PRO85421
 Figure 2229: DNA330172, BC009529, 209377.s.at
 Figure 2230: PRO85422
 Figure 2231: DNA330173, HUMAUTOTAX, 209392.at
 Figure 2232: PRO85423
 Figure 2233: DNA330174, AK027512, 209404.s.at
 Figure 2234: PRO85424
 Figure 2235: DNA330175, NP_006836.1, 209408.at
 Figure 2236: PRO59681
 Figure 2237A-B: DNA271241, HSU61500, 209412.at
 Figure 2238: PRO59556
 Figure 2239: DNA330176, AAB61703.1, 209417.s.at
 Figure 2240: PRO85425
 Figure 2241: DNA225767, NP_000534.1, 209420.s.at
 Figure 2242: PRO36230
 Figure 2243: DNA330177, BC001743, 209446.s.at
 Figure 2244: PRO10283
 Figure 2245: DNA273076, HSU59863, 209451.at
 Figure 2246: PRO61137
 Figure 2247: DNA326089, HBA2, 209458.x.at
 Figure 2248: PRO3629
 Figure 2249: DNA287304, AAH00040.1, 209461.x.at
 Figure 2250: PRO69571
 Figure 2251: DNA297388, NP_004208.1, 209464.at
 Figure 2252: PRO70812
 Figure 2253: DNA330178, HSTM2CEA, 209498.at
 Figure 2254: PRO85426
 Figure 2255: DNA330179, NP_067023.1, 209504.s.at
 Figure 2256: PRO85427
 Figure 2257: DNA324899, NP_002938.1, 209507.at
 Figure 2258: PRO81503
 Figure 2259: DNA330180, NP_009149.2, 209510.at
 Figure 2260: PRO85428
 Figure 2261: DNA274027, RAB27A, 209514.s.at
 Figure 2262: PRO61971
 Figure 2263: DNA274027, HSU38654, 209515.s.at
 Figure 2264: PRO61971
 Figure 2265: DNA272213, NP_002477.1, 209520.s.at
 Figure 2266: PRO60475
 Figure 2267: DNA330181, HSM802358, 209523.at
 Figure 2268: DNA328663, NP_057157.1, 209524.at
 Figure 2269: PRO36183
 Figure 2270: DNA330182, PLAA, 209533.s.at
 Figure 2271: PRO85430
 Figure 2272: DNA330183, AF181265, 209536.s.at
 Figure 2273: DNA327724, AF323542S7, 209546.s.at
 Figure 2274: DNA257501, NP_115688.1, 209551.at
 Figure 2275: PRO52073
 Figure 2276: DNA330184, BC022475, 209566.at
 Figure 2277: PRO85432
 Figure 2278: DNA290251, NP_055207.1, 209569.x.at
 Figure 2279: PRO70367
 Figure 2280: DNA329202, BC001745, 209570.s.at
 Figure 2281: PRO70367
 Figure 2282: DNA329203, NP_003788.1, 209572.s.at
 Figure 2283: PRO84819
 Figure 2284: DNA304797, NP_005935.3, 209583.s.at
 Figure 2285: PRO71209
 Figure 2286: DNA328666, AF084943, 209585.s.at
 Figure 2287: PRO1917
 Figure 2288: DNA270689, NP_002042.1, 209604.s.at
 Figure 2289: PRO59053
 Figure 2290: DNA271823, NP_004279.2, 209606.at
 Figure 2291: PRO60104
 Figure 2292A-B: DNA328670, BC001618, 209610.s.at
 Figure 2293: PRO70011
 Figure 2294: DNA330185, NP_071415.1, 209624.s.at
 Figure 2295: PRO85433
 Figure 2296: DNA328599, HSNFKBS, 209636.at
 Figure 2297: PRO84382
 Figure 2298: DNA330186, NP_004327.1, 209642.at
 Figure 2299: PRO85434
 Figure 2300A-B: DNA330187, HSM801454, 209649.at
 Figure 2301: PRO85435
 Figure 2302: DNA330188, NP_004356.1, 209662.at
 Figure 2303: PRO85436
 Figure 2304: DNA323856, PAI-RBP1, 209669.s.at
 Figure 2305: PRO80599
 Figure 2306: DNA330189, BC000712, 209680.s.at
 Figure 2307: PRO85437
 Figure 2308: DNA193881, AAF15129.1, 209681.at
 Figure 2309: PRO23299
 Figure 2310A-B: DNA272671, HSU26710, 209682.at
 Figure 2311: PRO60796
 Figure 2312: DNA330125, HUMPKB, 209685.s.at
 Figure 2313: PRO85385
 Figure 2314: DNA331519, HMMR, 209709.s.at

- Figure 2315: PRO86551
 Figure 2316: DNA328264, NP_005183.2, 209714.s.at
 Figure 2317: PRO12087
 Figure 2318: DNA330191, NP_036249.1, 209715.at
 Figure 2319: PRO85439
 Figure 2320A-C: DNA254412, AF008915, 209717.at
 Figure 2321: PRO49522
 Figure 2322A-B: DNA330192, 234780.1, 209733.at
 Figure 2323: PRO85440
 Figure 2324: DNA330193, BC015929, 209750.at
 Figure 2325: DNA330194, HSU09087, 209754.s.at
 Figure 2326: PRO85442
 Figure 2327: DNA275195, NP_001025.1, 209773.s.at
 Figure 2328: PRO62893
 Figure 2329: DNA329205, NP_001343.1, 209782.s.at
 Figure 2330: PRO84821
 Figure 2331: DNA226436, NP_001772.1, 209795.at
 Figure 2332: PRO36899
 Figure 2333: DNA327731, NP_003302.1, 209803.s.at
 Figure 2334: PRO83707
 Figure 2335A-B: DNA271368, HUMKIAI, 209804.at
 Figure 2336: PRO59668
 Figure 2337: DNA329206, AF151103, 209813.x.at
 Figure 2338: PRO84822
 Figure 2339A-C: DNA331520, 1096711.1, 209815.at
 Figure 2340: PRO86552
 Figure 2341: DNA327732, UMPK, 209825.s.at
 Figure 2342: PRO61801
 Figure 2343: DNA328676, IL16, 209827.s.at
 Figure 2344: PRO84448
 Figure 2345A-B: DNA196499, AB002384, 209829.at
 Figure 2346: PRO24988
 Figure 2347: DNA330197, NP_112190.1, 209832.s.at
 Figure 2348: PRO85445
 Figure 2349: DNA328677, AF060511, 209836.x.at
 Figure 2350: PRO84449
 Figure 2351: DNA270180, NP_478123.1, 209849.s.at
 Figure 2352: PRO58569
 Figure 2353: DNA331521, BC018951, 209868.s.at
 Figure 2354: PRO58719
 Figure 2355A-B: DNA329536, NP_005494.2, 209870.s.at
 Figure 2356: PRO22775
 Figure 2357: DNA330198, AB014719, 209871.s.at
 Figure 2358: PRO85446
 Figure 2359: DNA324184, NP_065726.1, 209891.at
 Figure 2360: PRO80682
 Figure 2361: DNA328258, HSM802616, 209900.s.at
 Figure 2362: PRO84151
 Figure 2363: DNA330152, DUT, 209932.s.at
 Figure 2364: PRO85406
 Figure 2365: DNA150133, AAD01646.1, 209933.s.at
 Figure 2366: PRO12219
 Figure 2367: DNA329208, CFLAR, 209939.x.at
 Figure 2368: PRO84823
 Figure 2369: DNA330199, BC004357, 209944.at
 Figure 2370: PRO85447
 Figure 2371A-B: DNA329065, HSU12767, 209959.at
 Figure 2372: PRO84725
 Figure 2373: DNA154921, DNA154921, 209967.s.at
 Figure 2374: DNA327736, BC002704, 209969.s.at
 Figure 2375: PRO83711
 Figure 2376: DNA324895, JTV1, 209971.x.at
 Figure 2377: PRO81501
 Figure 2378: DNA226658, NP_003736.1, 209999.x.at
 Figure 2379: PRO37121
 Figure 2380: DNA226658, SSI-1, 210001.s.at
 Figure 2381: PRO37121
 Figure 2382: DNA330200, NP_056222.1, 210006.at
 Figure 2383: PRO85448
 Figure 2384: DNA269534, NP_002155.1, 210029.at
 Figure 2385: PRO57950
 Figure 2386: DNA326054, NP_002159.1, 210046.s.at
 Figure 2387: PRO82489
 Figure 2388: DNA326809, NP_036244.2, 210052.s.at
 Figure 2389: PRO83142
 Figure 2390: DNA150551, AAB97010.1, 210054.at
 Figure 2391: PRO12778
 Figure 2392: DNA274960, SFRS5, 210077.s.at
 Figure 2393: PRO62694
 Figure 2394: DNA324922, BC018962, 210095.s.at
 Figure 2395: PRO119
 Figure 2396A-B: DNA328685, NP_127497.1, 210113.s.at
 Figure 2397: PRO34751
 Figure 2398: DNA330201, NP_003774.1, 210121.at
 Figure 2399: PRO50625
 Figure 2400: DNA330202, NP_005400.1, 210163.at
 Figure 2401: PRO19838
 Figure 2402: DNA287620, NP_004122.1, 210164.at
 Figure 2403: PRO2081
 Figure 2404: DNA270196, HUMZFM1B, 210172.at
 Figure 2405: PRO58584
 Figure 2406: DNA330203, NP_003755.1, 210190.at
 Figure 2407: PRO85449
 Figure 2408: DNA331335, AF070576, 210201.x.at
 Figure 2409: DNA331522, AF068918, 210202.s.at
 Figure 2410: PRO86553
 Figure 2411: DNA331523, RAD1, 210216.x.at
 Figure 2412: PRO61690
 Figure 2413: DNA328467, AF056322, 210218.s.at
 Figure 2414: PRO84293
 Figure 2415: DNA217253, NP_000749.1, 210229.s.at
 Figure 2416: PRO34295
 Figure 2417: DNA331084, BC008487, 210254.at
 Figure 2418: PRO81984
 Figure 2419A-B: DNA270015, NP_003444.1, 210281.s.at
 Figure 2420: PRO58410
 Figure 2421: DNA330206, NP_005801.2, 210288.at
 Figure 2422: PRO85450

Figure 2423: DNA329945, SEC23B, 210293.s.at
 Figure 2424: PRO85252
 Figure 2425: DNA218653, NP_003799.1, 210314.x.at
 Figure 2426: PRO34449
 Figure 2427: DNA326239, NP_006752.1, 210317.s.at
 Figure 2428: PRO39530
 Figure 2429: DNA329213, NP_219491.1, 210321.at
 Figure 2430: PRO2313
 Figure 2431A-B: DNA329214, NP_001087.1, 210337.s.at
 Figure 2432: PRO84826
 Figure 2433: DNA225528, NP_000610.1, 210354.at
 Figure 2434: PRO35991
 Figure 2435: DNA196621, HUMLY9, 210370.s.at
 Figure 2436: DNA330207, BC001131, 210387.at
 Figure 2437: PRO85451
 Figure 2438: DNA226229, NP_002432.1, 210410.s.at
 Figure 2439: PRO36692
 Figure 2440A-B: DNA330208, AF164622, 210425.x.at
 Figure 2441: PRO85452
 Figure 2442: DNA329215, NP_036224.1, 210439.at
 Figure 2443: PRO7424
 Figure 2444: DNA226394, NP_002552.1, 210448.s.at
 Figure 2445: PRO36857
 Figure 2446: DNA331524, BC003388, 210458.s.at
 Figure 2447: PRO86554
 Figure 2448: DNA331525, BC002448, 210461.s.at
 Figure 2449: PRO86555
 Figure 2450: DNA329216, AF022375, 210512.s.at
 Figure 2451: PRO84827
 Figure 2452: DNA227633, NP_001156.1, 210538.s.at
 Figure 2453: PRO38096
 Figure 2454: DNA330209, BC000585, 210542.s.at
 Figure 2455: PRO85453
 Figure 2456: DNA331526, BC014563, 210559.s.at
 Figure 2457: PRO58324
 Figure 2458: DNA331527, BC001602, 210563.x.at
 Figure 2459: PRO86556
 Figure 2460: DNA331528, AF00619, 210564.x.at
 Figure 2461: PRO86557
 Figure 2462: DNA329217, BC003406, 210571.s.at
 Figure 2463: PRO84828
 Figure 2464: DNA330210, HSU03858, 210607.at
 Figure 2465: PRO126
 Figure 2466: DNA330211, NP_009092.1, 210629.x.at
 Figure 2467: PRO85454
 Figure 2468: DNA330212, HUMKRT10A, 210633.x.at
 Figure 2469: PRO85455
 Figure 2470: DNA331529, LAIR1, 210644.s.at
 Figure 2471: PRO86558
 Figure 2472A-C: DNA330214, HUMTPRD, 210645.s.at
 Figure 2473: PRO12135
 Figure 2474: DNA329218, NP_055227.1, 210691.s.at
 Figure 2475: PRO84829
 Figure 2476: DNA330215, DKFZp762A227Homo, 210692.s.at
 Figure 2477: DNA331530, AF064103, 210742.at
 Figure 2478: PRO86559
 Figure 2479: DNA237817, NP_001307.1, 210766.s.at
 Figure 2480: PRO38923
 Figure 2481A-B: DNA330216, NP_006445.1, 210778.s.at
 Figure 2482: PRO85457
 Figure 2483: DNA226881, FLI1, 210786.s.at
 Figure 2484: PRO37344
 Figure 2485: DNA255402, NP_055288.1, 210802.s.at
 Figure 2486: PRO50469
 Figure 2487: DNA330027, SSBP2, 210829.s.at
 Figure 2488: PRO85312
 Figure 2489: DNA329219, BC000385, 210844.x.at
 Figure 2490: PRO81278
 Figure 2491A-B: DNA331107, HSU26455, 210858.x.at
 Figure 2492: PRO86255
 Figure 2493: DNA188234, NP_000630.1, 210865.at
 Figure 2494: PRO21942
 Figure 2495: DNA331531, PFDN5, 210908.s.at
 Figure 2496: PRO86560
 Figure 2497: DNA330217, AF043183, 210915.x.at
 Figure 2498: PRO85458
 Figure 2499: DNA274326, NP_003079.1, 210933.s.at
 Figure 2500: PRO62244
 Figure 2501: DNA329317, NP_057353.1, 210948.s.at
 Figure 2502: PRO81157
 Figure 2503: DNA331532, AF125393, 210951.x.at
 Figure 2504: PRO86561
 Figure 2505: DNA330218, HUMTCAXA, 210972.x.at
 Figure 2506: DNA273236, NP_004306.1, 210980.s.at
 Figure 2507: PRO61263
 Figure 2508: DNA269888, NP_002073.1, 210981.s.at
 Figure 2509: PRO58286
 Figure 2510: DNA329221, HLA-DRA, 210982.s.at
 Figure 2511: PRO4555
 Figure 2512: DNA238565, MCM7, 210983.s.at
 Figure 2513: PRO39210
 Figure 2514: DNA326239, YWHAE, 210996.s.at
 Figure 2515: PRO39530
 Figure 2516A-B: DNA330219, NP_150241.1, 211013.x.at
 Figure 2517: PRO85459
 Figure 2518: DNA327699, AB023420, 211015.s.at
 Figure 2519: PRO83682
 Figure 2520: DNA288254, TUBA3, 211058.x.at
 Figure 2521: PRO69536
 Figure 2522: DNA329992, MGAT2, 211061.s.at
 Figure 2523: PRO59267
 Figure 2524: DNA324171, NP_065438.1, 211070.x.at
 Figure 2525: PRO60753

Figure 2526: DNA330220, NP_006809.1, 211071.s.at
 Figure 2527: PRO60769
 Figure 2528: DNA287198, K-ALPHA-1, 211072.x.at
 Figure 2529: PRO69484
 Figure 2530: DNA254470, NEK2, 211080.s.at
 Figure 2531: PRO49578
 Figure 2532: DNA196432, AF064804, 211106.at
 Figure 2533: PRO24928
 Figure 2534: DNA330202, CXCL11, 211122.s.at
 Figure 2535: PRO19838
 Figure 2536: DNA304765, HUMTCRGAD, 211144.x.at
 Figure 2537: PRO71178
 Figure 2538: DNA327752, HSDHACTYL, 211150.s.at
 Figure 2539A-B: DNA328700, SCD, 211162.x.at
 Figure 2540: PRO84464
 Figure 2541: DNA330221, NP_056071.1, 211207.s.at
 Figure 2542: PRO85460
 Figure 2543: DNA330222, NP_003848.1, 211226.at
 Figure 2544: PRO45958
 Figure 2545: DNA218278, IL2RA, 211269.s.at
 Figure 2546: PRO34330
 Figure 2547: DNA151022, DGKA, 211272.s.at
 Figure 2548: PRO12096
 Figure 2549: DNA330223, NP_001790.1, 211297.s.at
 Figure 2550: PRO49730
 Figure 2551A-C: DNA328811, ITPR1, 211323.s.at
 Figure 2552: PRO84551
 Figure 2553: DNA188234, TNFSF6, 211333.s.at
 Figure 2554: PRO21942
 Figure 2555: DNA103395, HSU80737, 211352.s.at
 Figure 2556: PRO4723
 Figure 2557A-B: DNA275066, NP_000170.1, 211450.s.at
 Figure 2558: PRO62786
 Figure 2559: DNA327755, NP_115957.1, 211458.s.at
 Figure 2560: PRO83725
 Figure 2561: DNA93439, CXCR6, 211469.s.at
 Figure 2562: PRO4515
 Figure 2563: DNA330175, KNSL6, 211519.s.at
 Figure 2564: PRO59681
 Figure 2565: DNA327756, NP_068814.2, 211538.s.at
 Figure 2566: PRO83726
 Figure 2567: DNA269888, GPRK6, 211543.s.at
 Figure 2568: PRO58286
 Figure 2569: DNA226255, NP_003047.1, 211576.s.at
 Figure 2570: PRO36718
 Figure 2571: DNA330211, LST1, 211581.x.at
 Figure 2572: PRO85454
 Figure 2573: DNA330224, HUMNCA, 211657.at
 Figure 2574: PRO85461
 Figure 2575: DNA327709, HBB, 211696.x.at
 Figure 2576: PRO83690
 Figure 2577: DNA331533, PPARG, 211699.x.at
 Figure 2578: PRO86562
 Figure 2579: DNA331534, AF116616, 211708.s.at
 Figure 2580: DNA226342, PTEN, 211711.s.at
 Figure 2581: PRO36805
 Figure 2582: DNA328706, BC021909, 211714.x.at
 Figure 2583: PRO10347
 Figure 2584: DNA88307, NP_001992.1, 211734.s.at
 Figure 2585: PRO2280
 Figure 2586: DNA329225, EVI2B, 211742.s.at
 Figure 2587: PRO84833
 Figure 2588: DNA331535, AF105974, 211745.x.at
 Figure 2589: PRO3629
 Figure 2590: DNA328649, TUBA6, 211750.x.at
 Figure 2591: PRO84424
 Figure 2592: DNA254725, KPNA2, 211762.s.at
 Figure 2593: PRO49824
 Figure 2594: DNA330225, NP_115712.1, 211767.at
 Figure 2595: PRO85462
 Figure 2596A-B: DNA329226, BC006181, 211784.s.at
 Figure 2597: PRO60388
 Figure 2598: DNA304473, BC006196, 211786.at
 Figure 2599: PRO2023
 Figure 2600: DNA330226, AF198052, 211794.at
 Figure 2601: PRO85463
 Figure 2602: DNA227173, FYB, 211795.s.at
 Figure 2603: PRO37636
 Figure 2604: DNA331536, AAA60662.1, 211796.s.at
 Figure 2605: PRO86563
 Figure 2606: DNA331537, CCNE2, 211814.s.at
 Figure 2607: PRO59418
 Figure 2608A-B: DNA331342, DEFCAR, 211822.s.at
 Figure 2609: PRO86422
 Figure 2610: DNA331343, AK026398, 211824.x.at
 Figure 2611: PRO86423
 Figure 2612: DNA331538, AF327066, 211825.s.at
 Figure 2613: PRO86564
 Figure 2614A-B: DNA331539, BRCA1, 211851.x.at
 Figure 2615: PRO86565
 Figure 2616A-B: DNA188192, CD28, 211856.x.at
 Figure 2617: PRO21704
 Figure 2618: DNA331540, AF222343, 211861.x.at
 Figure 2619: PRO86566
 Figure 2620: DNA330228, HUMTCRAZ, 211902.x.at
 Figure 2621: PRO85465
 Figure 2622: DNA226176, CXCR4, 211919.s.at
 Figure 2623: PRO36639
 Figure 2624: DNA272286, CAT, 211922.s.at
 Figure 2625: PRO60544
 Figure 2626: DNA330229, BC011915, 211926.s.at
 Figure 2627: PRO85466
 Figure 2628: DNA226254, NP_001408.1, 211937.at
 Figure 2629: PRO36717
 Figure 2630: DNA330230, NP_060977.1, 211938.at
 Figure 2631: PRO85467
 Figure 2632A-B: DNA325306, ITGB1, 211945.s.at
 Figure 2633: PRO81851

Figure 2634A-B: DNA272195, HUMORFGA, 211951.at
 Figure 2635: DNA328437, NP.005792.1, 211956.s.at
 Figure 2636: PRO84271
 Figure 2637: DNA325941, NP.005339.1, 211969.at
 Figure 2638: PRO82388
 Figure 2639: DNA287194, AAA60258.1, 211974.x.at
 Figure 2640: PRO69480
 Figure 2641A-C: DNA331541, 1390535.1, 211986.at
 Figure 2642: PRO86567
 Figure 2643: DNA330232, NP.291032.1, 211991.s.at
 Figure 2644: PRO85469
 Figure 2645: DNA330233, AF218029, 211999.at
 Figure 2646: PRO11403
 Figure 2647: DNA287433, NP.006810.1, 212009.s.at
 Figure 2648: PRO69690
 Figure 2649A-D: DNA103461, MKI67, 212020.s.at
 Figure 2650: PRO4788
 Figure 2651A-D: DNA226463, HSMKI67A, 212021.s.at
 Figure 2652: PRO36926
 Figure 2653A-D: DNA103461, HSMKI67, 212022.s.at
 Figure 2654: PRO4788
 Figure 2655A-D: DNA226463, DNA226463, 212023.s.at
 Figure 2656: PRO36926
 Figure 2657: DNA275447, HSMEMA, 212037.at
 Figure 2658: PRO63095
 Figure 2659: DNA103380, NP.003365.1, 212038.s.at
 Figure 2660: PRO4710
 Figure 2661A-B: DNA330234, 215138.24, 212045.at
 Figure 2662: PRO85470
 Figure 2663: DNA328709, BC004151, 212048.s.at
 Figure 2664: PRO37676
 Figure 2665A-B: DNA330235, BAA20790.1, 212061.at
 Figure 2666: PRO85471
 Figure 2667: DNA330236, 228447.20, 212071.s.at
 Figure 2668: PRO85472
 Figure 2669: DNA154139, DNA154139, 212099.at
 Figure 2670A-B: DNA331542, BAA74910.1, 212108.at
 Figure 2671: PRO86568
 Figure 2672A-B: DNA150956, BAA06685.1, 212110.at
 Figure 2673: PRO12560
 Figure 2674: DNA328711, AK023154, 212115.at
 Figure 2675: PRO84468
 Figure 2676: DNA219225, NP.002874.1, 212125.at
 Figure 2677: PRO34531
 Figure 2678: DNA330238, BC019676, 212127.at
 Figure 2679: DNA328713, AF100737, 212130.x.at
 Figure 2680: PRO84470
 Figure 2681: DNA330239, AK027643, 212131.at
 Figure 2682: PRO85474
 Figure 2683: DNA330240, CAA52801.1, 212141.at
 Figure 2684: PRO85475
 Figure 2685: DNA330240, HSP1CDC21, 212142.at
 Figure 2686A-B: DNA150829, AB014568, 212144.at
 Figure 2687: DNA329602, AK2, 212175.s.at
 Figure 2688: PRO85133
 Figure 2689: DNA330241, AF314185, 212176.at
 Figure 2690: DNA328716, HSM800707, 212179.at
 Figure 2691: DNA330242, BC007034, 212185.x.at
 Figure 2692: PRO85477
 Figure 2693: DNA330243, BC015663, 212190.at
 Figure 2694: PRO2584
 Figure 2695: DNA326233, RPI.13, 212191.x.at
 Figure 2696: PRO82645
 Figure 2697A-C: DNA330244, 253946.17, 212196.at
 Figure 2698: PRO85478
 Figure 2699A-B: DNA330245, 230497.7, 212206.s.at
 Figure 2700: PRO85479
 Figure 2701: DNA331543, BC008710, 212227.x.at
 Figure 2702: PRO84271
 Figure 2703: DNA327770, 1384008.4, 212239.at
 Figure 2704: PRO83736
 Figure 2705: DNA151120, DNA151120, 212240.s.at
 Figure 2706: PRO12179
 Figure 2707: DNA330246, AF326773, 212241.at
 Figure 2708A-B: DNA329229, 1345070.7, 212249.at
 Figure 2709: PRO84835
 Figure 2710: DNA329182, BC016852, 212259.s.at
 Figure 2711: PRO84805
 Figure 2712: DNA331544, BC018823, 212266.s.at
 Figure 2713: PRO86569
 Figure 2714: DNA327771, NP.109591.1, 212268.at
 Figure 2715: PRO83737
 Figure 2716: DNA326463, NP.000976.1, 212270.x.at
 Figure 2717: PRO82846
 Figure 2718: DNA150980, HUMMAC30X, 212279.at
 Figure 2719: DNA150980, DNA150980, 212281.s.at
 Figure 2720: PRO12566
 Figure 2721: DNA253017, DNA253017, 212282.at
 Figure 2722: PRO48926
 Figure 2723: DNA328719, BC012895, 212295.s.at
 Figure 2724: PRO84475
 Figure 2725: DNA271103, NP.005796.1, 212296.at
 Figure 2726: PRO59425
 Figure 2727: DNA207620, DNA207620, 212300.at
 Figure 2728: DNA330247, BC019110, 212313.at
 Figure 2729: PRO85481
 Figure 2730: DNA330248, BC019924, 212320.at
 Figure 2731: PRO10347
 Figure 2732A-B: DNA124122, HSP130K, 212331.at
 Figure 2733: PRO6323
 Figure 2734A-B: DNA124122, NP.005602.2, 212332.at
 Figure 2735: PRO6323
 Figure 2736: DNA287190, CAB43217.1, 212333.at
 Figure 2737: PRO69476

Figure 2738A-B: DNA330216, MAD4, 212347.x.at
 Figure 2739: PRO85457
 Figure 2740A-B: DNA327773, BAA25456.1, 212366.at
 Figure 2741: PRO83739
 Figure 2742A-C: DNA330249, AAA99177.1, 212372.at
 Figure 2743: PRO85482
 Figure 2744: DNA329231, NP.000810.1, 212378.at
 Figure 2745: PRO84837
 Figure 2746: DNA329231, GART, 212379.at
 Figure 2747: PRO84837
 Figure 2748A-B: DNA150950, HUMKIAAH, 212396.s.at
 Figure 2749A-B: DNA328549, NP.002897.1, 212397.at
 Figure 2750: PRO84350
 Figure 2751A-B: DNA328549, RDX, 212398.at
 Figure 2752: PRO84350
 Figure 2753: DNA151330, DNA151330, 212400.at
 Figure 2754: PRO11708
 Figure 2755A-B: DNA330250, NP.060727.1, 212406.s.at
 Figure 2756: PRO85483
 Figure 2757: DNA254828, AK023204, 212408.at
 Figure 2758: PRO49923
 Figure 2759: DNA330251, NP.059965.1, 212430.at
 Figure 2760: PRO85484
 Figure 2761: DNA327774, BC016808, 212460.at
 Figure 2762: PRO83740
 Figure 2763A-B: DNA330252, NP.055447.1, 212473.s.at
 Figure 2764: PRO85485
 Figure 2765: DNA269630, TPM4, 212481.s.at
 Figure 2766: PRO58042
 Figure 2767: DNA330253, BC007665, 212493.s.at
 Figure 2768: PRO85486
 Figure 2769: DNA330254, AK024029, 212508.at
 Figure 2770: PRO85487
 Figure 2771A-B: DNA254192, BAA07648.1, 212510.at
 Figure 2772: PRO49304
 Figure 2773: DNA329233, 383512.16, 212527.at
 Figure 2774: PRO84839
 Figure 2775: DNA226041, NP.005555.1, 212531.at
 Figure 2776: PRO36504
 Figure 2777: DNA269882, HSWLE1HU, 212533.at
 Figure 2778: PRO58280
 Figure 2779A-D: DNA328737, 148650.1, 212560.at
 Figure 2780: PRO84490
 Figure 2781A-B: DNA330255, AK025499, 212561.at
 Figure 2782: PRO85488
 Figure 2783: DNA225632, NP.002037.2, 212581.x.at
 Figure 2784: PRO36095
 Figure 2785A-C: DNA329236, AF392452, 212582.at
 Figure 2786: PRO84841
 Figure 2787A-B: DNA331545, AB040884, 212585.at
 Figure 2788: DNA275100, DNA275100, 212589.at
 Figure 2789: DNA330256, BC020889, 212592.at
 Figure 2790: PRO81145
 Figure 2791: DNA330257, 441179.4, 212605.s.at
 Figure 2792: PRO85489
 Figure 2793A-B: DNA330258, BAA22955.2, 212619.at
 Figure 2794: PRO85490
 Figure 2795A-B: DNA330258, AB006624, 212621.at
 Figure 2796: DNA330259, NP.008944.1, 212638.s.at
 Figure 2797: PRO49366
 Figure 2798: DNA331357, BC010494, 212639.x.at
 Figure 2799: PRO38556
 Figure 2800A-D: DNA327777, HSILIRECA, 212657.s.at
 Figure 2801A-B: DNA327778, AB011154, 212675.s.at
 Figure 2802: DNA273465, DNA273465, 212677.s.at
 Figure 2803: DNA328744, AF318364, 212680.x.at
 Figure 2804: PRO84496
 Figure 2805A-B: DNA329901, AB007915, 212683.at
 Figure 2806A-B: DNA269508, AB011110, 212706.at
 Figure 2807A-B: DNA331546, 332730.12, 212714.at
 Figure 2808: PRO86570
 Figure 2809: DNA331547, BC010994, 212734.x.at
 Figure 2810: PRO82645
 Figure 2811: DNA329906, BC007848, 212738.at
 Figure 2812: PRO85223
 Figure 2813: DNA330261, NP.110383.1, 212762.s.at
 Figure 2814: PRO85492
 Figure 2815: DNA330262, NP.006409.2, 212768.s.at
 Figure 2816: PRO85493
 Figure 2817A-B: DNA254149, BAA06224.1, 212789.at
 Figure 2818: PRO49264
 Figure 2819: DNA331548, BC017356, 212827.at
 Figure 2820: PRO86571
 Figure 2821A-B: DNA150452, BAA32470.1, 212830.at
 Figure 2822: PRO12260
 Figure 2823A-B: DNA331549, BAA07892.2, 212832.s.at
 Figure 2824: PRO86572
 Figure 2825: DNA271714, BAA05039.1, 212836.at
 Figure 2826: PRO59998
 Figure 2827: DNA331550, AAA59587.1, 212859.x.at
 Figure 2828: PRO6386
 Figure 2829A-B: DNA328753, BAA13212.1, 212873.at
 Figure 2830: PRO84502
 Figure 2831: DNA330265, NP.056436.1, 212886.at
 Figure 2832: PRO85495
 Figure 2833A-B: DNA271215, BAA24380.1, 212892.at
 Figure 2834: PRO59530

Figure 2835A-B: DNA330266, CAA10334.1, 212902.at
 Figure 2836: PRO85496
 Figure 2837A-B: DNA271137, AB014589, 212905.at
 Figure 2838: DNA271630, DNA271630, 212907.at
 Figure 2839: DNA330267, 235076.14, 212914.at
 Figure 2840: PRO85497
 Figure 2841: DNA330268, BC009116, 212928.at
 Figure 2842: PRO85498
 Figure 2843: DNA331551, BC013078, 212933.x.at
 Figure 2844: PRO82645
 Figure 2845A-B: DNA330269, BC020584, 212936.at
 Figure 2846: PRO23868
 Figure 2847: DNA330270, HUMORF007, 212949.at
 Figure 2848A-B: DNA331552, PAM, 212958.x.at
 Figure 2849: PRO86573
 Figure 2850: DNA273283, HUMCYSTRNA, 212971.at
 Figure 2851: DNA330271, 399773.20, 212980.at
 Figure 2852: PRO85500
 Figure 2853: DNA330272, AF119896, 212981.s.at
 Figure 2854: DNA330273, AK027564, 213007.at
 Figure 2855: PRO85502
 Figure 2856: DNA254940, BAA91770.1, 213008.at
 Figure 2857: PRO50030
 Figure 2858: DNA325596, TPII, 213011.s.at
 Figure 2859: PRO69549
 Figure 2860: DNA331553, 228519.3, 213021.at
 Figure 2861: PRO86574
 Figure 2862A-B: DNA253815, BAA20833.2, 213035.at
 Figure 2863: PRO49218
 Figure 2864A-B: DNA329240, NP.056133.1, 213039.at
 Figure 2865: PRO84845
 Figure 2866A-B: DNA330275, BAA25487.1, 213045.at
 Figure 2867: PRO85504
 Figure 2868A-B: DNA329242, BAA76857.1, 213056.at
 Figure 2869: PRO84847
 Figure 2870: DNA323869, NP.000960.2, 213080.x.at
 Figure 2871: PRO80612
 Figure 2872: DNA270466, HUMG6PD, 213093.at
 Figure 2873: DNA330276, NP.001614.3, 213095.x.at
 Figure 2874: PRO85505
 Figure 2875: DNA331554, AF118070, 213113.s.at
 Figure 2876: PRO86575
 Figure 2877: DNA287230, AAA36325.1, 213138.at
 Figure 2878: PRO69509
 Figure 2879: DNA330277, CAB45152.1, 213142.x.at
 Figure 2880: PRO85506
 Figure 2881: DNA228053, DNA228053, 213156.at
 Figure 2882: DNA151370, DNA151370, 213158.at
 Figure 2883: PRO11747
 Figure 2884: DNA106374, DNA106374, 213164.at
 Figure 2885A-B: DNA330278, BAA13216.1, 213174.at
 Figure 2886: PRO85507
 Figure 2887: DNA330279, AF043182, 213193.x.at
 Figure 2888: PRO85508
 Figure 2889: DNA227909, NP.005024.1, 213226.at
 Figure 2890: PRO38372
 Figure 2891A-B: DNA330280, BAA83045.2, 213254.at
 Figure 2892: PRO85509
 Figure 2893A-B: DNA328761, BAA82991.1, 213280.at
 Figure 2894: PRO84509
 Figure 2895: DNA331555, BC009874, 213281.at
 Figure 2896A-B: DNA274945, HSACKI10, 213287.s.at
 Figure 2897: DNA260974, NP.006065.1, 213293.s.at
 Figure 2898: PRO54720
 Figure 2899: DNA328357, 1452321.2, 213295.at
 Figure 2900: PRO84217
 Figure 2901A-B: DNA329248, BAA20816.1, 213302.at
 Figure 2902: PRO84850
 Figure 2903A-B: DNA255273, BAA83044.1, 213309.at
 Figure 2904: PRO50349
 Figure 2905: DNA155418, DNA155418, 213326.at
 Figure 2906A-B: DNA331355, AAG24545.1, 213330.s.at
 Figure 2907: PRO86431
 Figure 2908A-B: DNA330281, AB058688, 213341.at
 Figure 2909: DNA327789, 1449824.5, 213348.at
 Figure 2910: PRO83753
 Figure 2911: DNA287176, AB025254, 213361.at
 Figure 2912: DNA327790, 1448999.3, 213364.s.at
 Figure 2913: PRO83754
 Figure 2914A-B: DNA330282, 217860.13, 213376.at
 Figure 2915: PRO85510
 Figure 2916: DNA330283, BC020225, 213408.s.at
 Figure 2917: PRO85511
 Figure 2918: DNA330284, 235806.16, 213434.at
 Figure 2919: PRO85512
 Figure 2920: DNA225632, GAPD, 213453.x.at
 Figure 2921: PRO36095
 Figure 2922A-B: DNA330285, 241020.1, 213469.at
 Figure 2923: PRO85513
 Figure 2924: DNA328766, NP.006077.1, 213476.x.at
 Figure 2925: PRO84514
 Figure 2926: DNA330286, BC018130, 213506.at
 Figure 2927: PRO85514
 Figure 2928: DNA326639, NP.001229.1, 213523.at
 Figure 2929: PRO82992
 Figure 2930A-C: DNA330287, AF380180, 213538.at
 Figure 2931: PRO85515
 Figure 2932: DNA227483, SQLE, 213562.s.at
 Figure 2933: PRO37946

Figure 2934: DNA330288, NP_005506.1, 213566.at
 Figure 2935: PRO2869
 Figure 2936: DNA330289, 197444.1, 213567.at
 Figure 2937: PRO85516
 Figure 2938: DNA159560, DNA159560, 213577.at
 Figure 2939: DNA330290, 1398807.8, 213581.at
 Figure 2940: PRO85517
 Figure 2941: DNA327799, HSRP26AA, 213587.s.at
 Figure 2942: PRO40011
 Figure 2943: DNA273753, AAC39561.1, 213599.at
 Figure 2944: PRO61716
 Figure 2945: DNA330291, 1500175.9, 213616.at
 Figure 2946: PRO85518
 Figure 2947A-C: DNA330292, NP_056045.2, 213618.at
 Figure 2948: PRO85519
 Figure 2949: DNA225974, ICAM2, 213620.s.at
 Figure 2950: PRO36437
 Figure 2951: DNA331556, BC009513, 213646.x.at
 Figure 2952: PRO38556
 Figure 2953A-B: DNA273985, BAA07647.1, 213647.at
 Figure 2954: PRO61932
 Figure 2955: DNA270758, HSU54778, 213655.at
 Figure 2956: PRO59117
 Figure 2957: DNA330293, BC011922, 213666.at
 Figure 2958: PRO85520
 Figure 2959: DNA325704, MARS, 213671.s.at
 Figure 2960: PRO82188
 Figure 2961: DNA304796, NP_443109.1, 213696.s.at
 Figure 2962: PRO71208
 Figure 2963: DNA273236, ASAH1, 213702.x.at
 Figure 2964: PRO61263
 Figure 2965: DNA255913, DNA255913, 213725.x.at
 Figure 2966: DNA328629, TUBB2, 213726.x.at
 Figure 2967: PRO84407
 Figure 2968: DNA328771, HSMYOSTIE, 213733.at
 Figure 2969A-C: DNA151167, FLNA, 213746.s.at
 Figure 2970: PRO12867
 Figure 2971: DNA326273, BC001832, 213757.at
 Figure 2972: PRO82678
 Figure 2973A-B: DNA274483, NP_000126.1, 213778.x.at
 Figure 2974: PRO62385
 Figure 2975: DNA328774, NP_004263.1, 213793.s.at
 Figure 2976: PRO60536
 Figure 2977: DNA327804, AF442151, 213797.at
 Figure 2978: PRO69493
 Figure 2979A-B: DNA329967, SMARCA5, 213859.x.at
 Figure 2980: PRO85270
 Figure 2981: DNA151041, HSAMYB2, 213906.at
 Figure 2982: DNA330294, 426625.1, 213908.at
 Figure 2983: PRO85521
 Figure 2984: DNA330295, NP_037515.1, 213951.s.at
 Figure 2985: PRO85522
 Figure 2986: DNA327807, NP_115613.1, 213975.s.at
 Figure 2987: PRO83768
 Figure 2988: DNA327808, NP_002961.1, 213988.s.at
 Figure 2989: PRO83769
 Figure 2990: DNA329136, HSPC111, 214011.s.at
 Figure 2991: PRO84772
 Figure 2992: DNA196110, DNA196110, 214016.s.at
 Figure 2993: PRO24635
 Figure 2994: DNA227224, LC27, 214039.s.at
 Figure 2995: PRO37687
 Figure 2996: DNA330296, 206955.3, 214054.at
 Figure 2997: PRO85523
 Figure 2998: DNA273696, DNA273696, 214060.at
 Figure 2999A-B: DNA330297, AF378753, 214081.at
 Figure 3000: PRO85524
 Figure 3001: DNA227091, NP_000256.1, 214084.x.at
 Figure 3002: PRO37554
 Figure 3003: DNA331557, BC016778, 214085.x.at
 Figure 3004: PRO86576
 Figure 3005: DNA254686, NP_005475.1, 214086.s.at
 Figure 3006: PRO49786
 Figure 3007: DNA330298, BC011911, 214095.at
 Figure 3008: PRO83772
 Figure 3009: DNA329254, BC004215, 214096.s.at
 Figure 3010: PRO84854
 Figure 3011: DNA330299, AK023737, 214102.at
 Figure 3012: PRO85525
 Figure 3013: DNA331360, AK022497, 214177.s.at
 Figure 3014: PRO86435
 Figure 3015A-B: DNA269826, NP_003195.1, 214179.s.at
 Figure 3016: PRO58228
 Figure 3017: DNA331558, AF000424, 214181.x.at
 Figure 3018: PRO86577
 Figure 3019: DNA290295, NP_055203.1, 214193.s.at
 Figure 3020: PRO70455
 Figure 3021: DNA327701, C1QBP, 214214.s.at
 Figure 3022: PRO82667
 Figure 3023: DNA331361, NP_003318.1, 214228.x.at
 Figure 3024: PRO2398
 Figure 3025: DNA154914, DNA154914, 214230.at
 Figure 3026: DNA330300, NP_004883.1, 214257.s.at
 Figure 3027: PRO41086
 Figure 3028: DNA273940, DNA273940, 214272.at
 Figure 3029: DNA97279, JUNB, 214326.x.at
 Figure 3030: PRO3628
 Figure 3031: DNA84130, HSU37518, 214329.x.at
 Figure 3032: PRO1096
 Figure 3033: DNA272928, DAZAP2, 214334.x.at
 Figure 3034: PRO61012
 Figure 3035: DNA331362, AF275719, 214359.s.at
 Figure 3036: PRO86436
 Figure 3037: DNA331559, AF043723, 214368.at
 Figure 3038: PRO85114
 Figure 3039: DNA328611, AF043722, 214369.s.at
 Figure 3040: PRO84393

Figure 3041: DNA273138, NP_005495.1, 214390.s.at
 Figure 3042: PRO61182
 Figure 3043: DNA273174, NP_001951.1, 214394.x.at
 Figure 3044: PRO61211
 Figure 3045: DNA328782, 337794.1, 214405.at
 Figure 3046: PRO84528
 Figure 3047: DNA326090, NP_000549.1, 214414.x.at
 Figure 3048: PRO3629
 Figure 3049: DNA271374, CHAF1A, 214426.x.at
 Figure 3050: PRO59673
 Figure 3051: DNA287630, NP_000160.1, 214430.at
 Figure 3052: PRO2154
 Figure 3053: DNA327811, SHMT2, 214437.s.at
 Figure 3054: PRO83772
 Figure 3055: DNA331363, AF001383, 214439.x.at
 Figure 3056: PRO86437
 Figure 3057: DNA331560, NP_001326.1, 214450.at
 Figure 3058: PRO85081
 Figure 3059: DNA273138, BCAT1, 214452.at
 Figure 3060: PRO61182
 Figure 3061: DNA327812, NP_006408.2, 214453.s.at
 Figure 3062: PRO83773
 Figure 3063: DNA150971, NP_002249.1, 214470.at
 Figure 3064: PRO12564
 Figure 3065: DNA330301, NP_008908.1, 214482.at
 Figure 3066: PRO85526
 Figure 3067: DNA325246, RRP4, 214507.s.at
 Figure 3068: PRO81800
 Figure 3069: DNA331561, CREM, 214508.x.at
 Figure 3070: PRO86578
 Figure 3071: DNA331562, NP_003090.1, 214531.s.at
 Figure 3072: PRO85654
 Figure 3073: DNA216515, NP_003166.1, 214567.s.at
 Figure 3074: PRO34267
 Figure 3075: DNA331223, HUMPRF1M, 214617.at
 Figure 3076: DNA331563, BC004101, 214643.x.at
 Figure 3077: PRO86579
 Figure 3078: DNA150552, AAB97011.1, 214661.s.at
 Figure 3079: PRO12326
 Figure 3080: DNA330303, BAA05499.1, 214662.at
 Figure 3081: PRO85528
 Figure 3082: DNA330304, HSIGVL026, 214677.x.at
 Figure 3083: PRO85529
 Figure 3084: DNA287355, ALDOA, 214687.x.at
 Figure 3085: PRO69617
 Figure 3086: DNA330305, HSU79263, 214700.x.at
 Figure 3087: DNA288259, NP_114172.1, 214710.s.at
 Figure 3088: PRO4676
 Figure 3089: DNA324984, NP_115540.1, 214714.at
 Figure 3090: PRO81578
 Figure 3091: DNA330306, 407311.1, 214743.at
 Figure 3092: PRO85531
 Figure 3093: DNA331564, BC014654, 214752.x.at
 Figure 3094: PRO86580
 Figure 3095: DNA254338, AAA60119.1, 214765.s.at
 Figure 3096: PRO49449
 Figure 3097: DNA275473, DNA275473, 214787.at
 Figure 3098A-B: DNA272353, AB007958, 214833.at
 Figure 3099: DNA226577, C6orf9, 214847.s.at
 Figure 3100: PRO37040
 Figure 3101A-B: DNA331565, BAA34472.1, 214945.at
 Figure 3102: PRO86581
 Figure 3103: DNA328530, LAK-4P, 214958.s.at
 Figure 3104: PRO24118
 Figure 3105A-B: DNA271654, AB020704, 214978.s.at
 Figure 3106A-B: DNA329261, HSM802517, 215001.s.at
 Figure 3107: PRO84859
 Figure 3108: DNA330308, 307914.1, 215029.at
 Figure 3109: PRO85533
 Figure 3110: DNA196372, HSBCLXL, 215037.s.at
 Figure 3111: PRO24874
 Figure 3112: DNA331566, AIF1, 215051.x.at
 Figure 3113: PRO86582
 Figure 3114: DNA330309, NP_003503.1, 215071.s.at
 Figure 3115: PRO85534
 Figure 3116A-B: DNA330307, AB018295, 215133.s.at
 Figure 3117: DNA331567, 333089.1, 215147.at
 Figure 3118: PRO86583
 Figure 3119: DNA273371, UMPS, 215165.x.at
 Figure 3120: PRO61373
 Figure 3121A-B: DNA150496, AB023212, 215175.at
 Figure 3122A-B: DNA220748, ITGA6, 215177.s.at
 Figure 3123: PRO34726
 Figure 3124: DNA330311, 405318.1, 215221.at
 Figure 3125: PRO85536
 Figure 3126: DNA227597, NP_000627.1, 215223.s.at
 Figure 3127: PRO38060
 Figure 3128A-B: DNA330312, 406407.1, 215262.at
 Figure 3129: PRO85537
 Figure 3130: DNA331568, TADA3L, 215273.s.at
 Figure 3131: PRO80953
 Figure 3132: DNA330314, 026641.5, 215275.at
 Figure 3133: PRO85538
 Figure 3134: DNA330315, 1500205.1, 215283.at
 Figure 3135: PRO85539
 Figure 3136: DNA330316, 1448781.1, 215284.at
 Figure 3137: PRO85540
 Figure 3138: DNA330317, 228133.1, 215330.at
 Figure 3139: PRO85541
 Figure 3140: DNA331569, NP_000552.1, 215333.x.at
 Figure 3141: PRO85542
 Figure 3142: DNA327831, NP_076956.1, 215380.s.at
 Figure 3143: PRO83783
 Figure 3144: DNA328801, 407831.1, 215392.at
 Figure 3145: PRO84543
 Figure 3146: DNA325174, NP_038470.1, 215416.s.at
 Figure 3147: PRO9819
 Figure 3148: DNA275385, NP_002085.1, 215438.x.at

Figure 3149: PRO63048
 Figure 3150: DNA331570, BC015794, 215440.s.at
 Figure 3151: PRO84545
 Figure 3152: DNA330319, AF247727, 215483.at
 Figure 3153: DNA331571, MAP2K3, 215498.s.at
 Figure 3154: PRO86584
 Figure 3155: DNA330186, BUB1, 215509.s.at
 Figure 3156: PRO85434
 Figure 3157: DNA330321, 315726.1, 215605.at
 Figure 3158: PRO85545
 Figure 3159: DNA331572, AF000426, 215633.x.at
 Figure 3160: PRO86585
 Figure 3161: DNA330031, LOC51668, 215691.x.at
 Figure 3162: PRO85316
 Figure 3163: DNA331573, HSAPT1, 215719.x.at
 Figure 3164A-B: DNA254376, KIAA0963, 215760.s.at
 Figure 3165: PRO49486
 Figure 3166A-B: DNA328805, BAA86482.1, 215785.s.at
 Figure 3167: PRO84547
 Figure 3168: DNA331574, HUMTCGCH, 215806.x.at
 Figure 3169: DNA330322, 234025.21, 215855.s.at
 Figure 3170: PRO85546
 Figure 3171: DNA330323, 335053.1, 215908.at
 Figure 3172: PRO85547
 Figure 3173: DNA330324, HHEX, 215933.s.at
 Figure 3174: PRO58034
 Figure 3175: DNA331575, AF223408, 215942.s.at
 Figure 3176: PRO86587
 Figure 3177: DNA330325, NP_055057.1, 215948.x.at
 Figure 3178: PRO85548
 Figure 3179: DNA227668, GK, 215966.x.at
 Figure 3180: PRO38131
 Figure 3181: DNA330326, AY007142, 215967.s.at
 Figure 3182: PRO85549
 Figure 3183: DNA331576, HSRNAGLK, 215977.x.at
 Figure 3184: DNA188736, U00115, 215990.s.at
 Figure 3185: PRO26296
 Figure 3186: DNA331577, 208045.1, 216109.at
 Figure 3187: PRO86588
 Figure 3188: DNA331578, HSTCELD, 216133.at
 Figure 3189: PRO86589
 Figure 3190: DNA254783, DKC1, 216212.s.at
 Figure 3191: PRO49881
 Figure 3192A-B: DNA255273, AB029015, 216218.s.at
 Figure 3193A-B: DNA256461, AND-1, 216228.s.at
 Figure 3194: PRO51498
 Figure 3195: DNA329266, BC000142, 216237.s.at
 Figure 3196: PRO12845
 Figure 3197: DNA151048, HSNOT, 216248.s.at
 Figure 3198: PRO12850
 Figure 3199: DNA329155, BC012479, 216252.x.at
 Figure 3200: PRO1207
 Figure 3201: DNA331579, HSCLCA, 216295.s.at
 Figure 3202: DNA88189, CD24, 216379.x.at
 Figure 3203: PRO2690
 Figure 3204: DNA330329, IR1875335, 216483.s.at
 Figure 3205: DNA287243, NP_004452.1, 216602.s.at
 Figure 3206: PRO69518
 Figure 3207: DNA331580, 1099517.2, 216607.s.at
 Figure 3208: PRO86590
 Figure 3209: DNA227874, TXN, 216609.at
 Figure 3210: PRO38337
 Figure 3211: DNA88296, NP_005733.1, 216640.s.at
 Figure 3212: PRO2274
 Figure 3213: DNA269692, S59049, 216834.at
 Figure 3214: PRO58102
 Figure 3215: DNA227597, SOD2, 216841.s.at
 Figure 3216: PRO38060
 Figure 3217A-B: DNA330331, BAA86451.1, 216873.s.at
 Figure 3218: PRO85554
 Figure 3219: DNA188275, NP_002181.1, 216876.s.at
 Figure 3220: PRO21800
 Figure 3221A-B: DNA150987, NP_006051.1, 216901.s.at
 Figure 3222: PRO12163
 Figure 3223: DNA329267, HUMTCRGAAC, 216920.s.at
 Figure 3224A-C: DNA328811, HUMINSP3R1, 216944.s.at
 Figure 3225: PRO84551
 Figure 3226A-B: DNA151027, AAA80979.1, 216952.s.at
 Figure 3227: PRO12843
 Figure 3228A-E: DNA269650, PLEC1, 216971.s.at
 Figure 3229A-B: PRO58061
 Figure 3230: DNA328812, BAA86575.1, 216997.x.at
 Figure 3231: PRO84552
 Figure 3232: DNA331581, AAB59396.1, 217022.s.at
 Figure 3233: PRO86591
 Figure 3234: DNA331366, HUMGPCR, 217028.at
 Figure 3235: PRO4516
 Figure 3236A-B: DNA227293, AB020721, 217047.s.at
 Figure 3237: PRO37756
 Figure 3238A-B: DNA329269, BAA32292.2, 217122.s.at
 Figure 3239: PRO84865
 Figure 3240: DNA331582, AAA59588.1, 217165.x.at
 Figure 3241: PRO86592
 Figure 3242: DNA331583, S70123, 217173.s.at
 Figure 3243: DNA331584, AF105973, 217232.x.at
 Figure 3244: PRO86593
 Figure 3245: DNA330334, NP_114402.1, 217286.s.at
 Figure 3246: PRO85557
 Figure 3247: DNA331369, HSU88968, 217294.s.at
 Figure 3248A-B: DNA331585, AF051334, 217299.s.at
 Figure 3249: PRO86594

Figure 3250: DNA331586, S81916, 217356.s.at
 Figure 3251: DNA331587, HSNMGMRNA, 217398.x.at
 Figure 3252: PRO86595
 Figure 3253: DNA330335, NP_054765.1, 217408.at
 Figure 3254: PRO62166
 Figure 3255: DNA331588, AF097635, 217414.x.at
 Figure 3256: PRO3629
 Figure 3257: DNA329539, HLA-DMA, 217478.s.at
 Figure 3258: PRO85089
 Figure 3259: DNA331589, 243999.2, 217502.at
 Figure 3260: PRO86596
 Figure 3261: DNA329271, 406848.1, 217591.at
 Figure 3262: PRO84867
 Figure 3263: DNA330337, 1447003.1, 217616.at
 Figure 3264: PRO85559
 Figure 3265: DNA331590, 368556.1, 217655.at
 Figure 3266: PRO86597
 Figure 3267: DNA330339, HSA012375, 217672.x.at
 Figure 3268: DNA323856, HSM800628, 217725.x.at
 Figure 3269: PRO80599
 Figure 3270: DNA326523, NP_001121.2, 217729.s.at
 Figure 3271: PRO71126
 Figure 3272: DNA325832, NP_068839.1, 217731.s.at
 Figure 3273: PRO1869
 Figure 3274A-B: DNA327847, 142131.14, 217738.at
 Figure 3275: PRO2834
 Figure 3276: DNA88541, NP_005737.1, 217739.s.at
 Figure 3277: PRO2834
 Figure 3278: DNA327935, NP_079422.1, 217745.s.at
 Figure 3279: PRO83866
 Figure 3280: DNA327849, NP_057269.1, 217755.at
 Figure 3281: PRO83794
 Figure 3282A-B: DNA274131, AF183421, 217762.s.at
 Figure 3283: PRO62067
 Figure 3284: DNA330340, NP_006859.1, 217763.s.at
 Figure 3285: PRO85562
 Figure 3286A-B: DNA274131, DNA274131, 217764.s.at
 Figure 3287: PRO62067
 Figure 3288: DNA325821, NP_057016.1, 217769.s.at
 Figure 3289: PRO82287
 Figure 3290: DNA325910, AF167438, 217776.at
 Figure 3291: PRO82365
 Figure 3292: DNA227358, NP_057479.1, 217777.s.at
 Figure 3293: PRO37821
 Figure 3294: DNA328819, NP_057145.1, 217783.s.at
 Figure 3295: PRO84557
 Figure 3296: DNA325873, SKB1, 217786.at
 Figure 3297: PRO82331
 Figure 3298: DNA331591, NP_055241.1, 217792.at
 Figure 3299: PRO69560
 Figure 3300: DNA328303, NP_056525.1, 217807.s.at
 Figure 3301: PRO84173
 Figure 3302: DNA227223, NP_064583.1, 217814.at
 Figure 3303: PRO37686
 Figure 3304: DNA327851, NSAP1, 217834.s.at
 Figure 3305: PRO83795
 Figure 3306: DNA328823, NP_057421.1, 217838.s.at
 Figure 3307: PRO84561
 Figure 3308: DNA330341, NP_006061.2, 217839.at
 Figure 3309: PRO85563
 Figure 3310: DNA254773, NP_057231.1, 217841.s.at
 Figure 3311: PRO49871
 Figure 3312: DNA330342, NP_067021.1, 217844.at
 Figure 3313: PRO85564
 Figure 3314: DNA329272, NP_055181.1, 217850.at
 Figure 3315: PRO84868
 Figure 3316A-B: DNA330343, AF403012, 217857.s.at
 Figure 3317: DNA330344, NP_057392.1, 217870.s.at
 Figure 3318: PRO85565
 Figure 3319: DNA326937, NP_002406.1, 217871.s.at
 Figure 3320: PRO83255
 Figure 3321: DNA330345, NP_055130.1, 217906.at
 Figure 3322: PRO85566
 Figure 3323: DNA330346, NP_054880.2, 217907.at
 Figure 3324: PRO85567
 Figure 3325: DNA325780, NP_060371.1, 217914.at
 Figure 3326: PRO82250
 Figure 3327: DNA327853, NP_054769.1, 217919.s.at
 Figure 3328: PRO82223
 Figure 3329: DNA330347, 255559.4, 217922.at
 Figure 3330: PRO85568
 Figure 3331: DNA330348, NP_079150.1, 217929.s.at
 Figure 3332: PRO85569
 Figure 3333: DNA330349, BC022093, 217931.at
 Figure 3334: DNA287241, NP_056991.1, 217933.s.at
 Figure 3335: PRO69516
 Figure 3336A-B: DNA225648, NP_061165.1, 217941.s.at
 Figure 3337: PRO36111
 Figure 3338: DNA326730, NP_057037.1, 217950.at
 Figure 3339: PRO83072
 Figure 3340: DNA329273, NP_037374.1, 217957.at
 Figure 3341: PRO84869
 Figure 3342: DNA328829, NP_057230.1, 217959.s.at
 Figure 3343: PRO84566
 Figure 3344: DNA328830, NP_061118.1, 217962.at
 Figure 3345: PRO84567
 Figure 3346: DNA329274, NP_055195.1, 217963.s.at
 Figure 3347: PRO84870
 Figure 3348: DNA325496, NP_037397.2, 217969.at
 Figure 3349: PRO82013
 Figure 3350: DNA327855, NP_057387.1, 217975.at
 Figure 3351: PRO83367
 Figure 3352: DNA227218, NP_003721.2, 217983.s.at
 Figure 3353: PRO37681
 Figure 3354: DNA227218, RNASE6PL, 217984.at
 Figure 3355: PRO37681
 Figure 3356A-B: DNA227238, NP_038476.1, 217985.s.at

Figure 3357: PRO37701
 Figure 3358A-B: DNA227238, BAZ1A, 217986.s.at
 Figure 3359: PRO37701
 Figure 3360: DNA328831, NP.057329.1, 217989.at
 Figure 3361: PRO233
 Figure 3362: DNA328832, NP.067022.1, 217995.at
 Figure 3363: PRO84568
 Figure 3364: DNA328833, BC018929, 217996.at
 Figure 3365: PRO84569
 Figure 3366: DNA328834, AF220656, 217997.at
 Figure 3367: DNA287364, NP.031376.1, 218000.s.at
 Figure 3368: PRO69625
 Figure 3369: DNA273008, NP.003972.1, 218009.s.at
 Figure 3370: PRO61079
 Figure 3371: DNA330350, NP.006108.1, 218025.s.at
 Figure 3372: PRO85570
 Figure 3373: DNA328836, NP.054894.1, 218027.at
 Figure 3374: PRO84572
 Figure 3375: DNA329275, AF070673, 218032.at
 Figure 3376: PRO12342
 Figure 3377: DNA331592, ANKT, 218039.at
 Figure 3378: PRO82424
 Figure 3379: DNA328838, NP.054797.2, 218049.s.at
 Figure 3380: PRO70319
 Figure 3381: DNA330352, NP.075059.1, 218051.s.at
 Figure 3382: PRO85571
 Figure 3383: DNA329276, NP.077001.1, 218069.at
 Figure 3384: PRO12104
 Figure 3385: DNA328841, NP.060557.2, 218073.s.at
 Figure 3386: PRO84575
 Figure 3387: DNA329277, NP.054883.3, 218084.x.at
 Figure 3388: PRO6241
 Figure 3389: DNA330353, BC020796, 218085.at
 Figure 3390: PRO69464
 Figure 3391: DNA329278, NP.004495.1, 218092.s.at
 Figure 3392: PRO84871
 Figure 3393: DNA227313, NP.060945.1, 218095.s.at
 Figure 3394: PRO37776
 Figure 3395: DNA331593, MRPL4, 218105.s.at
 Figure 3396: PRO86598
 Figure 3397: DNA326596, NP.060624.1, 218115.at
 Figure 3398: PRO82954
 Figure 3399: DNA330355, NP.055063.1, 218117.at
 Figure 3400: PRO83289
 Figure 3401: DNA330356, NP.006318.1, 218118.s.at
 Figure 3402: PRO85572
 Figure 3403: DNA330357, NP.078786.2, 218130.at
 Figure 3404: PRO85573
 Figure 3405: DNA227155, NP.057654.1, 218135.at
 Figure 3406: PRO37618
 Figure 3407: DNA254496, NP.060076.1, 218149.s.at
 Figure 3408: PRO49604
 Figure 3409: DNA330358, NP.079012.1, 218154.at
 Figure 3410: PRO85574
 Figure 3411: DNA254739, NP.068766.1, 218156.s.at
 Figure 3412: PRO49837
 Figure 3413: DNA304470, PRO2577, 218172.s.at
 Figure 3414: PRO2577
 Figure 3415: DNA330359, NP.065145.1, 218178.s.at
 Figure 3416: PRO85575
 Figure 3417: DNA304495, NP.057156.1, 218193.s.at
 Figure 3418: PRO793
 Figure 3419A-C: DNA330360, NP.078789.1, 218204.s.at
 Figure 3420: PRO85576
 Figure 3421: DNA327858, NP.036473.1, 218238.at
 Figure 3422: PRO83800
 Figure 3423: DNA327858, CRFG, 218239.s.at
 Figure 3424: PRO83800
 Figure 3425A-B: DNA330361, CKAP2, 218252.at
 Figure 3426: PRO85577
 Figure 3427: DNA328850, NP.057187.1, 218254.s.at
 Figure 3428: PRO84581
 Figure 3429: DNA331594, MRPL24, 218270.at
 Figure 3430: PRO11652
 Figure 3431: DNA273230, NP.060914.1, 218273.s.at
 Figure 3432: PRO61257
 Figure 3433: DNA324444, NP.006333.1, 218308.at
 Figure 3434: PRO81108
 Figure 3435: DNA330363, NP.060252.1, 218331.s.at
 Figure 3436: PRO85578
 Figure 3437: DNA329281, NP.036526.2, 218336.at
 Figure 3438: PRO84874
 Figure 3439A-B: DNA330364, NP.004417.1, 218338.at
 Figure 3440: PRO85579
 Figure 3441: DNA272918, NP.055269.1, 218346.s.at
 Figure 3442: PRO61003
 Figure 3443: DNA327862, NP.060445.1, 218349.s.at
 Figure 3444: PRO83803
 Figure 3445: DNA328854, NP.056979.1, 218350.s.at
 Figure 3446: PRO84585
 Figure 3447A-B: DNA273415, KIF4A, 218355.at
 Figure 3448: PRO61414
 Figure 3449: DNA324890, NP.037525.1, 218356.at
 Figure 3450: PRO81496
 Figure 3451: DNA330365, NP.036591.1, 218357.s.at
 Figure 3452: PRO85580
 Figure 3453A-B: DNA331595, NP.073602.2, 218376.s.at
 Figure 3454: PRO86599
 Figure 3455: DNA330367, NP.057174.1, 218379.at
 Figure 3456: PRO85582
 Figure 3457: DNA328856, NP.068376.1, 218380.at
 Figure 3458: PRO84586
 Figure 3459: DNA227248, NP.006287.1, 218397.at
 Figure 3460: PRO37711
 Figure 3461A-B: DNA287192, NP.006178.1, 218400.at
 Figure 3462: PRO69478
 Figure 3463: DNA329912, TTC4, 218442.at
 Figure 3464: PRO85227

Figure 3465: DNA150661, NP_057162.1, 218446.s.at
 Figure 3466: PRO12398
 Figure 3467: DNA304781, NP_057385.2, 218461.at
 Figure 3468: PRO71191
 Figure 3469: DNA328861, NP_057030.2, 218472.s.at
 Figure 3470: PRO84589
 Figure 3471: DNA330368, NP_064446.1, 218494.s.at
 Figure 3472: PRO85583
 Figure 3473: DNA150648, NP_037464.1, 218507.at
 Figure 3474: PRO11576
 Figure 3475: DNA328864, NP_060726.2, 218512.at
 Figure 3476: PRO84592
 Figure 3477: DNA330369, NP_060822.1, 218513.at
 Figure 3478: PRO85584
 Figure 3479: DNA330370, NP_060415.1, 218519.at
 Figure 3480: PRO190
 Figure 3481: DNA327867, NP_061873.2, 218532.s.at
 Figure 3482: PRO83808
 Figure 3483: DNA330371, NP_060813.1, 218535.s.at
 Figure 3484: PRO85585
 Figure 3485: DNA327868, NP_060601.2, 218542.at
 Figure 3486: PRO83809
 Figure 3487: DNA255113, NP_073587.1, 218543.s.at
 Figure 3488: PRO50195
 Figure 3489: DNA330372, NP_057117.1, 218549.s.at
 Figure 3490: PRO85586
 Figure 3491: DNA330373, NP_060751.1, 218552.at
 Figure 3492: PRO85587
 Figure 3493: DNA330374, NP_054901.1, 218556.at
 Figure 3494: PRO23321
 Figure 3495: DNA330375, NP_059142.1, 218558.s.at
 Figure 3496: PRO85588
 Figure 3497: DNA329587, NP_036256.1, 218566.s.at
 Figure 3498: PRO85121
 Figure 3499: DNA329286, NP_005691.2, 218567.x.at
 Figure 3500: PRO69644
 Figure 3501: DNA329054, NP_078805.2, 218578.at
 Figure 3502: PRO84716
 Figure 3503A-B: DNA273435, NP_057532.1, 218585.s.at
 Figure 3504: PRO61430
 Figure 3505: DNA227327, NP_060547.1, 218593.at
 Figure 3506: PRO37790
 Figure 3507: DNA328628, NP_060542.2, 218594.at
 Figure 3508: PRO84406
 Figure 3509: DNA287642, NP_060934.1, 218597.s.at
 Figure 3510: PRO9902
 Figure 3511A-B: DNA254789, NP_057301.1, 218603.at
 Figure 3512: PRO49887
 Figure 3513: DNA330376, NP_076962.1, 218622.at
 Figure 3514: PRO85589
 Figure 3515: DNA327869, NP_057672.1, 218625.at
 Figure 3516: PRO1898
 Figure 3517: DNA330377, NP_036577.1, 218638.s.at
 Figure 3518: PRO85590
 Figure 3519: DNA330378, NP_071741.2, 218662.s.at
 Figure 3520: PRO81126
 Figure 3521: DNA330378, HCAP-G, 218663.at
 Figure 3522: PRO81126
 Figure 3523: DNA287291, NP_067036.1, 218676.s.at
 Figure 3524: PRO69561
 Figure 3525: DNA304835, NP_071327.1, 218681.s.at
 Figure 3526: PRO71242
 Figure 3527: DNA330379, NP_073562.1, 218689.at
 Figure 3528: PRO85591
 Figure 3529: DNA329288, NP_061910.1, 218695.at
 Figure 3530: PRO84880
 Figure 3531: DNA287378, NP_060898.1, 218715.at
 Figure 3532: PRO69637
 Figure 3533: DNA327202, NP_057289.1, 218718.at
 Figure 3534: PRO200
 Figure 3535: DNA330380, NP_078937.2, 218722.s.at
 Figure 3536: PRO85592
 Figure 3537: DNA324251, NP_060880.2, 218726.at
 Figure 3538: PRO80935
 Figure 3539: DNA227617, NP_057161.1, 218732.at
 Figure 3540: PRO38080
 Figure 3541: DNA330381, NP_076958.1, 218741.at
 Figure 3542: PRO38668
 Figure 3543: DNA330382, NP_005724.1, 218755.at
 Figure 3544: PRO61907
 Figure 3545: DNA330383, NP_054828.1, 218782.s.at
 Figure 3546: PRO85593
 Figure 3547: DNA330384, NP_060388.1, 218802.at
 Figure 3548: PRO51129
 Figure 3549: DNA88315, NP_004098.1, 218831.s.at
 Figure 3550: PRO2743
 Figure 3551: DNA330385, NP_057733.2, 218859.s.at
 Figure 3552: PRO85594
 Figure 3553: DNA330386, NP_057394.1, 218866.s.at
 Figure 3554: PRO85595
 Figure 3555: DNA330387, NP_036309.1, 218875.s.at
 Figure 3556: PRO85596
 Figure 3557: DNA327874, BC022791, 218880.at
 Figure 3558: PRO4805
 Figure 3559A-B: DNA271829, NP_006775.1, 218882.s.at
 Figure 3560: PRO60109
 Figure 3561: DNA330388, NP_078905.1, 218883.s.at
 Figure 3562: PRO85597
 Figure 3563: DNA226633, NP_060376.1, 218886.at
 Figure 3564: PRO37096
 Figure 3565: DNA304780, NP_060562.2, 218888.s.at
 Figure 3566: PRO69889
 Figure 3567: DNA256762, AK022882, 218889.at
 Figure 3568: PRO51695
 Figure 3569: DNA328881, NP_057706.2, 218890.x.at
 Figure 3570: PRO49469
 Figure 3571: DNA325622, NP_060518.1, 218894.s.at
 Figure 3572: PRO82113
 Figure 3573: DNA225694, NP_060087.1, 218902.at

Figure 3574: PRO36157
 Figure 3575: DNA325690, NP_076973.1, 218903.s.at
 Figure 3576: PRO82179
 Figure 3577: DNA328364, SIGIRR, 218921.at
 Figure 3578: PRO84223
 Figure 3579: DNA287166, NP_055129.1, 218943.s.at
 Figure 3580: PRO69459
 Figure 3581: DNA330389, NP_079221.1, 218979.at
 Figure 3582: PRO85598
 Figure 3583: DNA329050, NP_057053.1, 218982.s.at
 Figure 3584: PRO84712
 Figure 3585: DNA330390, NP_057630.1, 218983.at
 Figure 3586: PRO85599
 Figure 3587: DNA288277, NP_061915.1, 218984.at
 Figure 3588: PRO70034
 Figure 3589: DNA256265, NP_060101.1, 218986.s.at
 Figure 3590: PRO51309
 Figure 3591: DNA227194, FLJ11000, 218999.at
 Figure 3592: PRO37657
 Figure 3593: DNA330391, NP_076999.1, 219000.s.at
 Figure 3594: PRO34008
 Figure 3595: DNA330392, NP_078923.2, 219007.at
 Figure 3596: PRO85600
 Figure 3597: DNA328885, NP_061108.2, 219017.at
 Figure 3598: PRO50294
 Figure 3599: DNA330393, NP_067635.1, 219024.at
 Figure 3600: PRO85601
 Figure 3601: DNA329292, NP_057185.1, 219031.s.at
 Figure 3602: PRO84882
 Figure 3603: DNA330394, NP_079402.1, 219035.s.at
 Figure 3604: PRO85602
 Figure 3605: DNA329293, NP_057136.1, 219037.at
 Figure 3606: PRO84883
 Figure 3607: DNA328886, NP_078811.1, 219040.at
 Figure 3608: PRO84610
 Figure 3609: DNA331596, NP_060841.1, 219049.at
 Figure 3610: PRO84884
 Figure 3611: DNA330395, NP_060212.1, 219062.s.at
 Figure 3612: PRO85603
 Figure 3613: DNA330396, NP_077303.1, 219088.s.at
 Figure 3614: PRO85604
 Figure 3615: DNA330397, NP_054873.1, 219094.at
 Figure 3616: PRO85605
 Figure 3617: DNA331597, PLA2G4B, 219095.at
 Figure 3618: PRO86600
 Figure 3619: DNA330398, NP_060367.1, 219133.at
 Figure 3620: PRO85606
 Figure 3621: DNA297191, NP_060962.2, 219148.at
 Figure 3622: PRO70808
 Figure 3623: DNA329295, NP_036549.1, 219155.at
 Figure 3624: PRO84885
 Figure 3625A-B: DNA329438, NP_476516.1, 219158.s.at
 Figure 3626: PRO85008
 Figure 3627: DNA328892, NP_067643.2, 219165.at
 Figure 3628: PRO84616
 Figure 3629: DNA330399, NP_060609.1, 219166.at
 Figure 3630: PRO85607
 Figure 3631: DNA330400, NP_078796.1, 219176.at
 Figure 3632: PRO85608
 Figure 3633: DNA271455, NP_057735.1, 219179.at
 Figure 3634: PRO59751
 Figure 3635: DNA330401, NP_057377.1, 219191.s.at
 Figure 3636: PRO85609
 Figure 3637: DNA330402, NP_076996.1, 219200.at
 Figure 3638: PRO85610
 Figure 3639: DNA287235, NP_060598.1, 219204.s.at
 Figure 3640: PRO69514
 Figure 3641: DNA327879, NP_071451.1, 219209.at
 Figure 3642: PRO83818
 Figure 3643: DNA330403, NP_059110.1, 219211.at
 Figure 3644: PRO85611
 Figure 3645: DNA330404, ZNF361, 219228.at
 Figure 3646: PRO85612
 Figure 3647: DNA225594, NP_037404.1, 219229.at
 Figure 3648: PRO36057
 Figure 3649: DNA328894, NP_060796.1, 219243.at
 Figure 3650: PRO84617
 Figure 3651: DNA329296, NP_060328.1, 219258.at
 Figure 3652: PRO84886
 Figure 3653: DNA3304461, NP_054877.1, 219283.at
 Figure 3654: PRO71039
 Figure 3655: DNA330405, RBM15, 219286.s.at
 Figure 3656: PRO85613
 Figure 3657A-B: DNA329076, NP_064627.1, 219306.at
 Figure 3658: PRO84733
 Figure 3659: DNA329914, FLJ12542, 219311.at
 Figure 3660: PRO85229
 Figure 3661: DNA255939, NP_078876.1, 219315.s.at
 Figure 3662: PRO50991
 Figure 3663: DNA287404, NP_073748.1, 219334.s.at
 Figure 3664: PRO69661
 Figure 3665: DNA254710, NP_060382.1, 219352.at
 Figure 3666: PRO49810
 Figure 3667: DNA325169, HSPC177, 219356.s.at
 Figure 3668: PRO81734
 Figure 3669: DNA330406, NP_079368.1, 219359.at
 Figure 3670: PRO85614
 Figure 3671: DNA330407, NP_057026.2, 219363.s.at
 Figure 3672: PRO85615
 Figure 3673: DNA330408, NP_077024.1, 219364.at
 Figure 3674: PRO85616
 Figure 3675: DNA254518, NP_057354.1, 219371.s.at
 Figure 3676: PRO49625
 Figure 3677: DNA327886, NP_060832.1, 219399.at
 Figure 3678: PRO41077
 Figure 3679: DNA256417, NP_077271.1, 219402.s.at
 Figure 3680: PRO51457
 Figure 3681A-B: DNA327887, NP_006656.1, 219403.s.at
 Figure 3682: PRO83823

Figure 3683: DNA271811, NP_036514.1, 219421.at
 Figure 3684: PRO60092
 Figure 3685: DNA329014, NP_005746.2, 219424.at
 Figure 3686: PRO9998
 Figure 3687: DNA328901, FLJ20533, 219449.s.at
 Figure 3688: PRO84622
 Figure 3689: DNA328902, NP_071750.1, 219452.at
 Figure 3690: PRO84623
 Figure 3691: DNA328367, RIN3, 219456.s.at
 Figure 3692: PRO84226
 Figure 3693: DNA331598, AK026092, 219457.s.at
 Figure 3694: PRO86601
 Figure 3695: DNA327890, NP_079021.1, 219493.at
 Figure 3696: PRO83826
 Figure 3697A-B: DNA227179, NP_059120.1, 219505.at
 Figure 3698: PRO37642
 Figure 3699A-C: DNA331599, BCL11B, 219528.s.at
 Figure 3700: PRO86602
 Figure 3701: DNA329300, GEMIN6, 219539.at
 Figure 3702: PRO84889
 Figure 3703: DNA328908, 7691567.2, 219540.at
 Figure 3704: PRO84629
 Figure 3705: DNA256737, NP_060276.1, 219541.at
 Figure 3706: PRO51671
 Figure 3707: DNA330410, NP_060925.1, 219555.s.at
 Figure 3708: PRO85618
 Figure 3709A-B: DNA331600, NP_061985.1, 219577.s.at
 Figure 3710: PRO86603
 Figure 3711: DNA325053, NP_060230.2, 219588.s.at
 Figure 3712: PRO81637
 Figure 3713: DNA330412, NP_057617.1, 219594.at
 Figure 3714: PRO23600
 Figure 3715: DNA331601, NP_071915.1, 219628.at
 Figure 3716: PRO85620
 Figure 3717: DNA330414, NP_057615.1, 219657.s.at
 Figure 3718: PRO81138
 Figure 3719A-B: DNA274044, HSM801565, 219671.at
 Figure 3720: PRO61987
 Figure 3721: DNA293243, RCP, 219681.s.at
 Figure 3722: PRO70699
 Figure 3723: DNA255161, NP_071430.1, 219684.at
 Figure 3724: PRO50241
 Figure 3725: DNA287206, NP_060124.1, 219691.at
 Figure 3726: PRO69488
 Figure 3727A-B: DNA330297, NP_065138.2, 219700.at
 Figure 3728: PRO85524
 Figure 3729: DNA330416, TDP1, 219715.s.at
 Figure 3730: PRO85622
 Figure 3731: DNA330417, NP_085144.1, 219716.at
 Figure 3732: PRO21341
 Figure 3733A-B: DNA227255, NP_036579.1, 219753.at
 Figure 3734: PRO37718
 Figure 3735: DNA328919, NP_078987.1, 219777.at
 Figure 3736: PRO84637
 Figure 3737A-B: DNA331602, NP_060568.3, 219787.s.at
 Figure 3738: PRO86604
 Figure 3739: DNA255822, NP_036346.1, 219797.at
 Figure 3740: PRO50877
 Figure 3741: DNA227305, NP_064564.1, 219806.s.at
 Figure 3742: PRO37768
 Figure 3743: DNA329303, NP_054737.1, 219819.s.at
 Figure 3744: PRO84892
 Figure 3745: DNA287295, NP_078784.1, 219836.at
 Figure 3746: PRO69564
 Figure 3747: DNA287234, NP_114174.1, 219862.s.at
 Figure 3748: PRO69513
 Figure 3749: DNA287221, NP_057407.1, 219863.at
 Figure 3750: PRO69500
 Figure 3751: DNA330419, NP_038469.1, 219864.s.at
 Figure 3752: PRO85624
 Figure 3753: DNA255255, LOC64116, 219869.s.at
 Figure 3754: PRO50332
 Figure 3755: DNA330420, NP_078890.1, 219871.at
 Figure 3756: PRO85625
 Figure 3757: DNA256325, NP_005470.1, 219889.at
 Figure 3758: PRO51367
 Figure 3759: DNA330421, NP_057438.2, 219911.s.at
 Figure 3760: PRO85626
 Figure 3761A-B: DNA330422, NP_057736.2, 219913.s.at
 Figure 3762: PRO85627
 Figure 3763: DNA227787, NP_060606.1, 219918.s.at
 Figure 3764: PRO38250
 Figure 3765: DNA330423, NP_037466.2, 219920.s.at
 Figure 3766: PRO85628
 Figure 3767A-B: DNA330424, LTBP3, 219922.s.at
 Figure 3768: PRO85629
 Figure 3769: DNA328924, NP_057150.2, 219933.at
 Figure 3770: PRO84641
 Figure 3771: DNA218280, NP_068570.1, 219971.at
 Figure 3772: PRO34332
 Figure 3773: DNA325979, NP_060924.4, 219978.s.at
 Figure 3774: PRO82424
 Figure 3775: DNA330425, NP_078956.1, 219990.at
 Figure 3776: PRO85630
 Figure 3777A-B: DNA330426, SGK1, 220038.at
 Figure 3778: PRO85631
 Figure 3779: DNA328926, NP_064703.1, 220046.s.at
 Figure 3780: PRO84643
 Figure 3781A-B: DNA218680, NP_071731.1, 220048.at
 Figure 3782: PRO21724
 Figure 3783: DNA330427, NP_036593.1, 220052.s.at
 Figure 3784: PRO85632
 Figure 3785: DNA330428, NP_060385.1, 220060.s.at
 Figure 3786: PRO85633

Figure 3787: DNA330537, NP_060533.2, 220085.at
 Figure 3788: PRO81892
 Figure 3789: DNA256091, NP_071385.1, 220094.s.at
 Figure 3790: PRO51141
 Figure 3791: DNA330430, NP_078945.1, 220112.at
 Figure 3792: PRO85634
 Figure 3793: DNA330431, NP_055198.1, 220118.at
 Figure 3794: PRO85635
 Figure 3795: DNA227302, NP_037401.1, 220132.s.at
 Figure 3796: PRO37765
 Figure 3797: DNA330432, NP_079219.1, 220169.at
 Figure 3798: PRO85636
 Figure 3799: DNA331603, TMPRSS3, 220177.s.at
 Figure 3800: PRO83482
 Figure 3801: DNA256291, NP_079182.1, 220232.at
 Figure 3802: PRO51335
 Figure 3803: DNA330434, NP_060842.1, 220235.s.at
 Figure 3804: PRO85637
 Figure 3805: DNA330435, NP_060179.1, 220306.at
 Figure 3806: PRO85638
 Figure 3807: DNA330436, NP_037394.1, 220319.s.at
 Figure 3808: PRO85639
 Figure 3809: DNA327904, NP_071419.2, 220330.s.at
 Figure 3810: PRO83839
 Figure 3811: DNA287186, NP_061134.1, 220358.at
 Figure 3812: PRO69472
 Figure 3813A-B: DNA330437, NP_079366.1, 220370.s.at
 Figure 3814: PRO85640
 Figure 3815: DNA330438, NP_061026.1, 220485.s.at
 Figure 3816: PRO50795
 Figure 3817: DNA327214, NP_078991.2, 220495.s.at
 Figure 3818: PRO83483
 Figure 3819: DNA324252, NP_060444.1, 220521.s.at
 Figure 3820: PRO80936
 Figure 3821: DNA331604, PHEMX, 220558.x.at
 Figure 3822: PRO86605
 Figure 3823: DNA256363, NP_057686.1, 220565.at
 Figure 3824: PRO51405
 Figure 3825: DNA255798, NP_079265.1, 220576.at
 Figure 3826: PRO50853
 Figure 3827: DNA330440, NP_079098.1, 220591.s.at
 Figure 3828: PRO85642
 Figure 3829: DNA255734, NP_057607.1, 220646.s.at
 Figure 3830: PRO50791
 Figure 3831A-B: DNA327908, MCM10, 220651.s.at
 Figure 3832: PRO83843
 Figure 3833: DNA329306, NP_079149.2, 220655.at
 Figure 3834: PRO84895
 Figure 3835A-B: DNA327909, ARNTL2, 220658.s.at
 Figure 3836: PRO83844
 Figure 3837: DNA329307, NP_037483.1, 220684.at
 Figure 3838: PRO84896
 Figure 3839: DNA323756, NP_057267.2, 220688.s.at
 Figure 3840: PRO80512
 Figure 3841: DNA331380, DKFZp566O084Homo, 220690.s.at
 Figure 3842: DNA330442, NP_054866.1, 220692.at
 Figure 3843: PRO85643
 Figure 3844: DNA330443, NP_061086.1, 220702.at
 Figure 3845: PRO85644
 Figure 3846: DNA288247, NP_478059.1, 220892.s.at
 Figure 3847: PRO70011
 Figure 3848: DNA327916, NP_079466.1, 220940.at
 Figure 3849: PRO83851
 Figure 3850: DNA327953, NP_055182.2, 220942.x.at
 Figure 3851: PRO83878
 Figure 3852: DNA327917, NP_112240.1, 220966.x.at
 Figure 3853: PRO83852
 Figure 3854: DNA329078, VMP1, 220990.s.at
 Figure 3855: PRO23253
 Figure 3856A-B: DNA254516, NP_112196.1, 220992.s.at
 Figure 3857: PRO49623
 Figure 3858: DNA330444, NP_110405.1, 220999.s.at
 Figure 3859: PRO85645
 Figure 3860: DNA324246, NP_112188.1, 221004.s.at
 Figure 3861: PRO80930
 Figure 3862: DNA330445, NP_112174.1, 221012.s.at
 Figure 3863: PRO85646
 Figure 3864A-B: DNA254816, NP_110444.1, 221031.s.at
 Figure 3865: PRO49912
 Figure 3866: DNA330446, NP_054889.1, 221046.s.at
 Figure 3867: PRO85647
 Figure 3868: DNA330447, NP_079174.1, 221080.s.at
 Figure 3869: PRO85648
 Figure 3870: DNA226227, NP_060872.1, 221111.at
 Figure 3871: PRO36690
 Figure 3872: DNA227267, NP_061130.1, 221123.x.at
 Figure 3873: PRO37730
 Figure 3874: DNA217256, NP_065386.1, 221165.s.at
 Figure 3875: PRO34298
 Figure 3876: DNA329310, AK027224, 221185.s.at
 Figure 3877: PRO84899
 Figure 3878: DNA324408, NP_060493.2, 221203.s.at
 Figure 3879: PRO81072
 Figure 3880A-B: DNA330448, NP_059111.1, 221221.s.at
 Figure 3881: PRO85649
 Figure 3882: DNA331605, CISH, 221223.x.at
 Figure 3883: PRO86458
 Figure 3884: DNA330450, AK025947, 221235.s.at
 Figure 3885: PRO85651
 Figure 3886: DNA330451, NP_110429.1, 221249.s.at
 Figure 3887: PRO85652
 Figure 3888: DNA330452, NP_112494.2, 221258.s.at
 Figure 3889: PRO85653
 Figure 3890: DNA295327, NP_068575.1, 221271.at
 Figure 3891: PRO70773
 Figure 3892: DNA330453, NP_112597.1, 221277.s.at
 Figure 3893: PRO85654

Figure 3894: DNA329312, NP.005205.2, 221331.x.at
 Figure 3895: PRO84901
 Figure 3896: DNA288250, NP.112487.1, 221434.s.at
 Figure 3897: PRO70013
 Figure 3898: DNA330454, NP.112589.1, 221436.s.at
 Figure 3899: PRO85655
 Figure 3900: DNA330455, 1097190.16, 221477.s.at
 Figure 3901: PRO85656
 Figure 3902: DNA150865, NP.057005.1, 221488.s.at
 Figure 3903: PRO11587
 Figure 3904: DNA272972, NP.057356.1, 221496.s.at
 Figure 3905: PRO61052
 Figure 3906A-B: DNA329316, AF158555, 221510.s.at
 Figure 3907: PRO84904
 Figure 3908: DNA330456, NP.060571.1, 221520.s.at
 Figure 3909: PRO85657
 Figure 3910: DNA326221, NP.057179.1, 221521.s.at
 Figure 3911: PRO82634
 Figure 3912: DNA328953, NP.004086.1, 221539.at
 Figure 3913: PRO70296
 Figure 3914: DNA329317, AF288571, 221558.s.at
 Figure 3915: PRO81157
 Figure 3916: DNA330457, NP.076944.1, 221559.s.at
 Figure 3917: PRO85658
 Figure 3918: DNA329319, BC006401, 221601.s.at
 Figure 3919: PRO1607
 Figure 3920: DNA329319, NP.005440.1, 221602.s.at
 Figure 3921: PRO1607
 Figure 3922: DNA254308, NP.060950.1, 221622.s.at
 Figure 3923: PRO49419
 Figure 3924: DNA287254, NP.077004.1, 221637.s.at
 Figure 3925: PRO69528
 Figure 3926: DNA330458, NP.060634.1, 221652.s.at
 Figure 3927: PRO85659
 Figure 3928: DNA218280, IL21R, 221658.s.at
 Figure 3929: PRO34332
 Figure 3930: DNA327927, NP.037390.2, 221666.s.at
 Figure 3931: PRO57311
 Figure 3932: DNA254777, NP.055140.1, 221676.s.at
 Figure 3933: PRO49875
 Figure 3934: DNA330459, NP.060083.1, 221677.s.at
 Figure 3935: PRO50083
 Figure 3936: DNA330460, NP.060255.2, 221685.s.at
 Figure 3937: PRO85660
 Figure 3938: DNA273185, DNA273185, 221727.at
 Figure 3939: DNA330461, BC005104, 221732.at
 Figure 3940: DNA328961, NP.443112.1, 221756.at
 Figure 3941: PRO84667
 Figure 3942: DNA328961, MGC17330, 221757.at
 Figure 3943: PRO84667
 Figure 3944: DNA330462, NP.060103.1, 221766.s.at
 Figure 3945: PRO85661
 Figure 3946: DNA193901, DNA193901, 221768.at
 Figure 3947: PRO23319
 Figure 3948: DNA328964, AK056028, 221770.at
 Figure 3949: PRO84669
 Figure 3950: DNA330463, HSM801191, 221790.s.at
 Figure 3951A-B: DNA151745, DNA151745, 221805.at
 Figure 3952: PRO12033
 Figure 3953: DNA274058, NP.057203.1, 221816.s.at
 Figure 3954: PRO61999
 Figure 3955: DNA325039, NP.004902.1, 221824.s.at
 Figure 3956: PRO2733
 Figure 3957: DNA273311, NP.003022.1, 221833.at
 Figure 3958: PRO61319
 Figure 3959: DNA272419, AF105036, 221841.s.at
 Figure 3960: PRO60672
 Figure 3961: DNA330464, NP.067082.1, 221882.s.at
 Figure 3962: PRO85663
 Figure 3963A-B: DNA330465, 253695.2, 221916.at
 Figure 3964: PRO85664
 Figure 3965A-B: DNA330466, AB018304, 221922.at
 Figure 3966: DNA329321, NP.112493.1, 221931.s.at
 Figure 3967: PRO84906
 Figure 3968: DNA330467, NP.060114.1, 221986.s.at
 Figure 3969: PRO85665
 Figure 3970: DNA287235, FLJ10534, 221987.s.at
 Figure 3971: PRO69514
 Figure 3972: DNA327114, RPL10, 221989.at
 Figure 3973: PRO62466
 Figure 3974: DNA331606, BC018529, 222017.x.at
 Figure 3975: PRO86606
 Figure 3976: DNA257797, DNA257797, 222036.s.at
 Figure 3977: DNA257798, DNA257798, 222037.at
 Figure 3978: DNA330468, 1454101.4, 222044.at
 Figure 3979: PRO85666
 Figure 3980: DNA329919, BC013365, 222045.s.at
 Figure 3981: PRO85234
 Figure 3982: DNA304466, NP.004834.1, 222062.at
 Figure 3983: PRO34336
 Figure 3984: DNA325648, NP.037409.2, 222077.s.at
 Figure 3985: PRO82139
 Figure 3986: DNA331386, HST000012, 222150.s.at
 Figure 3987: DNA287209, NP.056350.1, 222154.s.at
 Figure 3988: PRO69490
 Figure 3989: DNA256784, NP.075069.1, 222209.s.at
 Figure 3990: PRO51716
 Figure 3991: DNA328977, NP.071344.1, 222216.s.at
 Figure 3992: PRO84678
 Figure 3993: DNA330469, NP.056249.1, 222250.s.at
 Figure 3994: PRO85667
 Figure 3995: DNA328885, EK11, 222262.s.at
 Figure 3996: PRO50294
 Figure 3997: DNA330470, 096828.1, 222307.at
 Figure 3998: PRO85668
 Figure 3999: DNA330471, 027307.1, 222309.at
 Figure 4000: PRO85669
 Figure 4001: DNA330472, 128864.1, 222326.at
 Figure 4002: PRO85670
 Figure 4003: DNA330473, NP.060676.2, 222387.s.at

Figure 4004: PRO85671
 Figure 4005: DNA330474, AF186382, 222388.s.at
 Figure 4006: PRO85672
 Figure 4007: DNA331607, HSA251830, 222392.x.at
 Figure 4008: PRO86607
 Figure 4009A-B: DNA270901, NP.004238.1, 222398.s.at
 Figure 4010: PRO59235
 Figure 4011: DNA325821, BC014334, 222402.at
 Figure 4012: PRO82287
 Figure 4013: DNA227358, HSPC121, 222404.x.at
 Figure 4014: PRO37821
 Figure 4015: DNA330476, AK027421, 222405.at
 Figure 4016: PRO85674
 Figure 4017: DNA328819, CGI-127, 222408.s.at
 Figure 4018: PRO84557
 Figure 4019: DNA331608, SNX5, 222417.s.at
 Figure 4020: PRO69560
 Figure 4021: DNA326307, NP.056399.1, 222425.s.at
 Figure 4022: PRO82707
 Figure 4023: DNA227223, GK001, 222432.s.at
 Figure 4024: PRO37686
 Figure 4025A-B: DNA329326, NP.005110.1, 222439.s.at
 Figure 4026: PRO84910
 Figure 4027: DNA327939, NP.060654.1, 222442.s.at
 Figure 4028: PRO83869
 Figure 4029: DNA329327, AF198620, 222443.s.at
 Figure 4030: PRO84911
 Figure 4031A-B: DNA256489, NP.079110.1, 222464.s.at
 Figure 4032: PRO51526
 Figure 4033A-B: DNA225648, ERBB2IP, 222473.s.at
 Figure 4034: PRO36111
 Figure 4035: DNA304460, BC003048, 222500.at
 Figure 4036: PRO4984
 Figure 4037: DNA330477, NP.036227.1, 222516.at
 Figure 4038: PRO37979
 Figure 4039: DNA329328, NP.067026.2, 222532.at
 Figure 4040: PRO81912
 Figure 4041: DNA16435, DNA16435, 222543.at
 Figure 4042: PRO276
 Figure 4043: DNA330478, NP.056978.2, 222557.at
 Figure 4044: PRO85675
 Figure 4045A-B: DNA330479, 900264.1, 222572.at
 Figure 4046: PRO85676
 Figure 4047: DNA330480, NP.060697.2, 222600.s.at
 Figure 4048: PRO85677
 Figure 4049A-B: DNA330481, AB058718, 222603.at
 Figure 4050: DNA330482, AK027468, 222606.at
 Figure 4051: PRO85678
 Figure 4052: DNA330483, AK001472, 222608.s.at
 Figure 4053: PRO85679
 Figure 4054: DNA329330, NP.057130.1, 222609.s.at
 Figure 4055: PRO84914
 Figure 4056A-B: DNA331609, 402471.3, 222613.at
 Figure 4057: PRO86608
 Figure 4058: DNA330485, NP.057415.1, 222624.s.at
 Figure 4059: PRO85681
 Figure 4060: DNA327942, NP.060596.1, 222642.s.at
 Figure 4061: PRO83870
 Figure 4062: DNA327943, NP.055399.1, 222646.s.at
 Figure 4063: PRO865
 Figure 4064A-B: DNA273435, RAMP, 222680.s.at
 Figure 4065: PRO61430
 Figure 4066: DNA330486, HSM802473, 222692.s.at
 Figure 4067: DNA330487, AB052751, 222696.at
 Figure 4068: DNA330488, AK025568, 222704.at
 Figure 4069: PRO85682
 Figure 4070: DNA272874, NP.057111.1, 222714.s.at
 Figure 4071: PRO60967
 Figure 4072: DNA275116, DNA275116, 222726.s.at
 Figure 4073: DNA330489, BC019909, 222740.at
 Figure 4074: PRO85683
 Figure 4075: DNA330490, 399171.38, 222754.at
 Figure 4076: PRO85684
 Figure 4077: DNA330491, BC002522, 222759.at
 Figure 4078: PRO85685
 Figure 4079A-B: DNA330492, FLJ11294, 222763.s.at
 Figure 4080: PRO85686
 Figure 4081: DNA329332, LOC51605, 222768.s.at
 Figure 4082: PRO84916
 Figure 4083: DNA330493, AK025248, 222770.s.at
 Figure 4084: PRO85687
 Figure 4085: DNA3304780, NETO2, 222774.s.at
 Figure 4086: PRO69889
 Figure 4087: DNA330494, BC020651, 222775.s.at
 Figure 4088: PRO85688
 Figure 4089: DNA330495, NP.060468.1, 222781.s.at
 Figure 4090: PRO85689
 Figure 4091: DNA330496, HSM802366, 222793.at
 Figure 4092: DNA330395, FLJ20281, 222816.s.at
 Figure 4093: PRO85603
 Figure 4094A-B: DNA331610, TBDN100, 222837.s.at
 Figure 4095: PRO86609
 Figure 4096: DNA330881, AB027233, 222838.at
 Figure 4097: PRO1138
 Figure 4098: DNA329335, AK023411, 222843.at
 Figure 4099: PRO84919
 Figure 4100: DNA273489, NP.055210.1, 222858.s.at
 Figure 4101: PRO61472
 Figure 4102: DNA273489, DAPP1, 222859.s.at
 Figure 4103: PRO61472
 Figure 4104: DNA330498, NP.036225.1, 222862.s.at
 Figure 4105: PRO85691
 Figure 4106: DNA329336, NP.057144.1, 222867.s.at
 Figure 4107: PRO84920
 Figure 4108: DNA287404, FLJ22833, 222872.x.at
 Figure 4109: PRO69661
 Figure 4110: DNA330499, AK026944, 222875.at
 Figure 4111: PRO85692

Figure 4112: DNA330500, AK022872, 222889.at
 Figure 4113: PRO85693
 Figure 4114A-C: DNA330409, HSA404614, 222895.s.at
 Figure 4115: PRO85617
 Figure 4116: DNA330501, AK022792, 222958.s.at
 Figure 4117: PRO85694
 Figure 4118A-B: DNA330502, AB042719, 222962.s.at
 Figure 4119: PRO85695
 Figure 4120: DNA329337, AF279437, 222974.at
 Figure 4121: PRO10096
 Figure 4122: DNA329338, 459502.10, 222977.at
 Figure 4123: PRO84921
 Figure 4124A-B: DNA329339, 459502.5, 222978.at
 Figure 4125: PRO84922
 Figure 4126: DNA329340, AF078866, 222979.s.at
 Figure 4127: PRO81805
 Figure 4128: DNA152786, NP_057215.1, 222980.at
 Figure 4129: PRO10928
 Figure 4130: DNA152786, RAB10, 222981.s.at
 Figure 4131: PRO10928
 Figure 4132A-B: DNA287236, AB024334, 222985.at
 Figure 4133: PRO10607
 Figure 4134: DNA330503, NP_038466.2, 222989.s.at
 Figure 4135: PRO85696
 Figure 4136: DNA331611, UBQLN1, 222991.s.at
 Figure 4137: PRO86610
 Figure 4138: DNA330504, NP_057575.2, 222993.at
 Figure 4139: PRO84923
 Figure 4140: DNA329371, NP_057547.3, 222996.s.at
 Figure 4141: PRO51662
 Figure 4142: DNA326195, NP_054781.1, 223018.at
 Figure 4143: PRO82611
 Figure 4144: DNA330505, BC005937, 223021.x.at
 Figure 4145: PRO85697
 Figure 4146A-B: DNA329342, AF172847, 223027.at
 Figure 4147: PRO84924
 Figure 4148: DNA329344, FRSB, 223035.s.at
 Figure 4149: PRO84926
 Figure 4150: DNA330506, NP_067061.1, 223038.s.at
 Figure 4151: PRO82123
 Figure 4152: DNA330507, AK054681, 223039.at
 Figure 4153: PRO85698
 Figure 4154: DNA287260, NP_057184.1, 223040.at
 Figure 4155: PRO69532
 Figure 4156: DNA324198, HSM801908, 223044.at
 Figure 4157: PRO37675
 Figure 4158: DNA330508, AF116694, 223047.at
 Figure 4159: PRO85699
 Figure 4160: DNA189412, NP_057390.1, 223054.at
 Figure 4161: PRO25349
 Figure 4162A-B: DNA256347, AF298880, 223055.s.at
 Figure 4163: PRO51389
 Figure 4164A-B: DNA329345, AB033117, 223056.s.at
 Figure 4165: DNA327948, NP_060394.1, 223060.at
 Figure 4166: PRO69660
 Figure 4167: DNA288247, PSA, 223062.s.at
 Figure 4168: PRO70011
 Figure 4169: DNA330509, AK024555, 223066.at
 Figure 4170: PRO80652
 Figure 4171: DNA227294, NP_060225.1, 223076.s.at
 Figure 4172: PRO37757
 Figure 4173: DNA331612, AF097492, 223079.s.at
 Figure 4174: PRO86611
 Figure 4175: DNA326258, NP_077273.1, 223081.at
 Figure 4176: PRO82665
 Figure 4177: DNA329346, AK027070, 223085.at
 Figure 4178: PRO84928
 Figure 4179: DNA327949, NP_057581.2, 223086.x.at
 Figure 4180: PRO83874
 Figure 4181: DNA331613, 238178.17, 223087.at
 Figure 4182: PRO86612
 Figure 4183: DNA329347, NP_060949.1, 223088.x.at
 Figure 4184: PRO84929
 Figure 4185: DNA330511, AK001338, 223090.x.at
 Figure 4186: PRO85701
 Figure 4187: DNA324209, NP_057018.1, 223096.at
 Figure 4188: PRO80902
 Figure 4189: DNA329349, NP_054861.1, 223100.s.at
 Figure 4190: PRO84931
 Figure 4191: DNA327917, MGC3038, 223101.s.at
 Figure 4192: PRO83852
 Figure 4193: DNA330512, NP_056494.1, 223109.at
 Figure 4194: PRO85702
 Figure 4195: DNA330436, MIR, 223129.x.at
 Figure 4196: PRO85639
 Figure 4197: DNA330513, AF212221, 223130.s.at
 Figure 4198: PRO85703
 Figure 4199A-C: DNA330514, DDX36, 223138.s.at
 Figure 4200: PRO85704
 Figure 4201A-C: DNA330514, AF217190, 223139.s.at
 Figure 4202: PRO85704
 Figure 4203: DNA325557, NP_115675.1, 223151.at
 Figure 4204: PRO82060
 Figure 4205: DNA329352, NP_057154.2, 223156.at
 Figure 4206: PRO84932
 Figure 4207: DNA329353, NP_113665.1, 223179.at
 Figure 4208: PRO84933
 Figure 4209: DNA254276, NP_054896.1, 223180.s.at
 Figure 4210: PRO49387
 Figure 4211: DNA327953, E2IG5, 223193.x.at
 Figure 4212: PRO83878
 Figure 4213A-B: DNA281444, NP_064544.1, 223197.s.at
 Figure 4214: PRO66283
 Figure 4215: DNA304467, NP_115703.1, 223212.at
 Figure 4216: PRO71043
 Figure 4217: DNA227267, LOC55893, 223216.x.at
 Figure 4218: PRO37730

Figure 4219: DNA327954, NP_113646.1, 223220.s.at
 Figure 4220: PRO83879
 Figure 4221: DNA330515, NP_004580.1, 223221.at
 Figure 4222: PRO85705
 Figure 4223: DNA329321, SEC13L, 223225.s.at
 Figure 4224: PRO84906
 Figure 4225: DNA247474, NP_054895.1, 223229.at
 Figure 4226: PRO44999
 Figure 4227: DNA330516, AK000796, 223239.at
 Figure 4228: PRO85706
 Figure 4229: DNA287171, NP_036312.1, 223240.at
 Figure 4230: PRO69462
 Figure 4231: DNA324046, NP_115700.1, 223272.s.at
 Figure 4232: PRO80763
 Figure 4233: DNA330517, NP_115879.1, 223273.at
 Figure 4234: PRO85707
 Figure 4235: DNA330518, BC002493, 223274.at
 Figure 4236: PRO85708
 Figure 4237: DNA330519, NP_060607.1, 223275.at
 Figure 4238: PRO85709
 Figure 4239: DNA330520, NP_005777.2, 223283.s.at
 Figure 4240: PRO85710
 Figure 4241: DNA330521, BC002762, 223286.at
 Figure 4242: PRO85711
 Figure 4243A-B: DNA330522, AF250920, 223287.s.at
 Figure 4244: PRO85712
 Figure 4245: DNA330523, BC001220, 223294.at
 Figure 4246: PRO85713
 Figure 4247: DNA330524, MGC4268, 223297.at
 Figure 4248: PRO85714
 Figure 4249: DNA329356, NP_115671.1, 223304.at
 Figure 4250: PRO84935
 Figure 4251: DNA330454, BC002551, 223307.at
 Figure 4252: PRO85655
 Figure 4253: DNA330526, NP_115682.1, 223318.s.at
 Figure 4254: PRO34564
 Figure 4255A-B: DNA330527, AF272663, 223319.at
 Figure 4256: PRO85716
 Figure 4257: DNA329358, NP_115649.1, 223334.at
 Figure 4258: PRO84937
 Figure 4259: DNA330528, AF151063, 223335.at
 Figure 4260: PRO50764
 Figure 4261: DNA330529, 241399.1, 223343.at
 Figure 4262: PRO85717
 Figure 4263A-B: DNA255756, HUMPDE7A, 223358.s.at
 Figure 4264: PRO50812
 Figure 4265: DNA227125, AF132297, 223377.x.at
 Figure 4266: PRO37588
 Figure 4267: DNA331614, CDCA1, 223381.at
 Figure 4268: PRO38881
 Figure 4269A-B: DNA329360, NP_115644.1, 223382.s.at
 Figure 4270: PRO84939
 Figure 4271A-B: DNA329360, NIN283, 223383.at
 Figure 4272: PRO84939
 Figure 4273: DNA330531, NP_037508.1, 223394.at
 Figure 4274: PRO85718
 Figure 4275: DNA329361, AF161528, 223397.s.at
 Figure 4276: PRO84940
 Figure 4277: DNA324156, NP_115588.1, 223403.s.at
 Figure 4278: PRO80856
 Figure 4279A-B: DNA254516, C1orf25, 223404.s.at
 Figure 4280: PRO49623
 Figure 4281: DNA256407, NP_055188.1, 223423.at
 Figure 4282: PRO51448
 Figure 4283: DNA255676, HSM801648, 223434.at
 Figure 4284: PRO50738
 Figure 4285: DNA330532, NP_078804.1, 223439.at
 Figure 4286: PRO85719
 Figure 4287: DNA330533, NP_058647.1, 223451.s.at
 Figure 4288: PRO772
 Figure 4289: DNA329365, CAB56010.1, 223452.s.at
 Figure 4290: PRO84944
 Figure 4291: DNA327958, NP_115789.1, 223484.at
 Figure 4292: PRO23554
 Figure 4293: DNA329456, NP_057126.1, 223489.x.at
 Figure 4294: PRO85023
 Figure 4295: DNA329456, RRP40, 223490.s.at
 Figure 4296: PRO85023
 Figure 4297: DNA330534, AF307332, 223494.at
 Figure 4298: PRO85720
 Figure 4299: DNA304784, NP_006564.1, 223502.s.at
 Figure 4300: PRO738
 Figure 4301: DNA330535, NP_115883.1, 223506.at
 Figure 4302: PRO85721
 Figure 4303: DNA330536, NP_115666.1, 223542.at
 Figure 4304: PRO85722
 Figure 4305: DNA330537, AF155827, 223556.at
 Figure 4306: PRO81892
 Figure 4307A-B: DNA327908, HSM801808, 223570.at
 Figure 4308: PRO83843
 Figure 4309: DNA330538, AF262027, 223598.at
 Figure 4310: PRO85723
 Figure 4311: DNA330539, NP_055411.1, 223639.s.at
 Figure 4312: PRO85724
 Figure 4313: DNA330540, NP_055081.1, 223640.at
 Figure 4314: PRO85725
 Figure 4315: DNA330541, AF277625, 223675.s.at
 Figure 4316: PRO85726
 Figure 4317: DNA330542, NP_115493.1, 223700.at
 Figure 4318: PRO85727
 Figure 4319: DNA330543, NAG73, 223725.at
 Figure 4320: PRO85728
 Figure 4321: DNA329367, ITYH2, 223741.s.at
 Figure 4322: PRO84946
 Figure 4323: DNA331615, AB049635, 223743.s.at
 Figure 4324: PRO62669
 Figure 4325: DNA188735, NP_001506.1, 223758.s.at
 Figure 4326: PRO26224

Figure 4327: DNA287253, LOC85028, 223774.at
 Figure 4328: PRO69527
 Figure 4329: DNA331616, BC004277, 223785.at
 Figure 4330: PRO86613
 Figure 4331: DNA330544, NP_277049.1, 223800.s.at
 Figure 4332: PRO85729
 Figure 4333: DNA256005, NP_004842.1, 223806.s.at
 Figure 4334: PRO51056
 Figure 4335: DNA330545, AF233516, 223834.at
 Figure 4336: PRO70906
 Figure 4337: DNA327200, NP_114156.1, 223836.at
 Figure 4338: PRO1065
 Figure 4339: DNA330546, AF132203, 223839.s.at
 Figure 4340: PRO85730
 Figure 4341: DNA330547, NP_066014.1, 223849.s.at
 Figure 4342: PRO85731
 Figure 4343: DNA331392, NP_004186.1, 223851.s.at
 Figure 4344: PRO364
 Figure 4345: DNA330548, NP_115590.1, 223880.x.at
 Figure 4346: PRO85732
 Figure 4347A-B: DNA330522, FOXP1, 223936.s.at
 Figure 4348: PRO85712
 Figure 4349A-B: DNA330550, HSM801744, 223946.at
 Figure 4350: PRO85734
 Figure 4351: DNA331393, D83532, 223961.s.at
 Figure 4352: PRO86458
 Figure 4353: DNA324248, SP110, 223980.s.at
 Figure 4354: PRO80932
 Figure 4355: DNA330551, BC009946, 223983.s.at
 Figure 4356: PRO85735
 Figure 4357: DNA330552, BC001104, 223984.s.at
 Figure 4358: PRO85736
 Figure 4359: DNA328847, NP_056338.1, 223989.s.at
 Figure 4360: PRO84579
 Figure 4361: DNA331617, AF332652, 224046.s.at
 Figure 4362: PRO86614
 Figure 4363: DNA329369, AF293026, 224130.s.at
 Figure 4364: PRO84948
 Figure 4365: DNA330553, AF116653, 224148.at
 Figure 4366: DNA331618, AF231339, 224204.x.at
 Figure 4367: PRO86615
 Figure 4368: DNA330554, AF277993, 224211.at
 Figure 4369: PRO85737
 Figure 4370A-C: DNA227619, NP_054831.1, 224218.s.at
 Figure 4371: PRO38082
 Figure 4372: DNA324707, NP_037369.1, 224232.s.at
 Figure 4373: PRO81339
 Figure 4374: DNA323935, NP_060586.1, 224233.s.at
 Figure 4375: PRO80668
 Figure 4376: DNA329370, NP_060611.2, 224247.s.at
 Figure 4377: PRO84949
 Figure 4378A-B: DNA330555, HSM801768, 224308.s.at
 Figure 4379: PRO85738
 Figure 4380: DNA330556, NP_061881.2, 224319.s.at
 Figure 4381: PRO85739
 Figure 4382: DNA330557, C20orf154, 224320.s.at
 Figure 4383: PRO85740
 Figure 4384: DNA330558, NP_057588.1, 224330.s.at
 Figure 4385: PRO84950
 Figure 4386: DNA327949, MRP64, 224334.s.at
 Figure 4387: PRO83874
 Figure 4388A-B: DNA330559, BAB21791.1, 224336.s.at
 Figure 4389: PRO85741
 Figure 4390: DNA331619, BC010896, 224345.x.at
 Figure 4391: PRO86616
 Figure 4392: DNA331620, NDRG3, 224368.s.at
 Figure 4393: PRO86617
 Figure 4394: DNA272626, RIP5, 224376.s.at
 Figure 4395: PRO60759
 Figure 4396: DNA330560, NP_510882.1, 224413.s.at
 Figure 4397: PRO85742
 Figure 4398: DNA330561, AF321617, 224416.s.at
 Figure 4399: PRO85743
 Figure 4400: DNA328323, NP_114148.2, 224428.s.at
 Figure 4401: PRO69531
 Figure 4402: DNA331621, AF060225, 224437.s.at
 Figure 4403: PRO86618
 Figure 4404: DNA330562, NP_115716.1, 224448.s.at
 Figure 4405: PRO85744
 Figure 4406: DNA330563, NP_113668.1, 224450.s.at
 Figure 4407: PRO85745
 Figure 4408: DNA330564, NP_115885.1, 224451.x.at
 Figure 4409: PRO85746
 Figure 4410: DNA330565, BC006111, 224454.at
 Figure 4411: PRO85747
 Figure 4412: DNA330566, NP_115720.1, 224464.s.at
 Figure 4413: PRO85748
 Figure 4414: DNA329373, NP_115722.1, 224467.s.at
 Figure 4415: PRO84952
 Figure 4416: DNA330567, NP_116114.1, 224504.s.at
 Figure 4417: PRO85749
 Figure 4418: DNA327976, NP_116120.1, 224511.s.at
 Figure 4419: PRO69574
 Figure 4420: DNA330568, BC006428, 224516.s.at
 Figure 4421: PRO85750
 Figure 4422: DNA329374, NP_115735.1, 224523.s.at
 Figure 4423: PRO84953
 Figure 4424: DNA331622, TNFRSF18, 224553.s.at
 Figure 4425: PRO86619
 Figure 4426: DNA330569, BC020516, 224572.s.at
 Figure 4427A-B: DNA330570, AB040903, 224578.at
 Figure 4428: DNA330571, AK027320, 224607.s.at
 Figure 4429: PRO85752
 Figure 4430: DNA327980, BC008959, 224615.x.at
 Figure 4431: PRO83900
 Figure 4432: DNA329376, BAA91036.1, 224632.at
 Figure 4433: PRO84954
 Figure 4434: DNA330572, CAB82324.1, 224648.at

Figure 4435: PRO85753
 Figure 4436A-B: DNA327981, 344095.3, 224654.at
 Figure 4437: PRO83901
 Figure 4438: DNA330573, C20orf108, 224690.at
 Figure 4439: PRO85754
 Figure 4440A-B: DNA330574, AB033054, 224698.at
 Figure 4441: DNA330575, AK022542, 224701.at
 Figure 4442: PRO85756
 Figure 4443: DNA331623, BC014138, 224711.at
 Figure 4444: PRO86620
 Figure 4445: DNA329378, BC022990, 224713.at
 Figure 4446: PRO84956
 Figure 4447: DNA324173, NP_115766.2, 224714.at
 Figure 4448: PRO80871
 Figure 4449: DNA330577, NP_443076.1, 224715.at
 Figure 4450: PRO85758
 Figure 4451A-B: DNA330578, 1353105.1, 224718.at
 Figure 4452: PRO85759
 Figure 4453: DNA330579, BC009925, 224719.s.at
 Figure 4454: PRO85760
 Figure 4455: DNA287382, 1383817.3, 224738.x.at
 Figure 4456: PRO69641
 Figure 4457: DNA257352, DNA257352, 224739.at
 Figure 4458: PRO51940
 Figure 4459: DNA331624, BC014242, 224740.at
 Figure 4460: PRO86621
 Figure 4461: DNA330581, MGC16386, 224753.at
 Figure 4462: PRO82014
 Figure 4463: DNA330582, 1454377.6, 224755.at
 Figure 4464: PRO85762
 Figure 4465: DNA330583, BC020522, 224759.s.at
 Figure 4466: PRO85763
 Figure 4467A-B: DNA287330, BAA86479.1, 224799.at
 Figure 4468: PRO69594
 Figure 4469A-B: DNA330584, FENS-1, 224800.at
 Figure 4470: PRO85764
 Figure 4471: DNA331397, AK001723, 224802.at
 Figure 4472: PRO23259
 Figure 4473: DNA330585, 206983.10, 224806.at
 Figure 4474: PRO85765
 Figure 4475: DNA330586, NP_443183.1, 224825.at
 Figure 4476: PRO85766
 Figure 4477A-B: DNA330559, AB051487, 224832.at
 Figure 4478A-B: DNA330809, 336997.1, 224838.at
 Figure 4479: PRO85973
 Figure 4480A-B: DNA330587, 1045521.4, 224839.s.at
 Figure 4481: PRO85767
 Figure 4482: DNA329380, BC014868, 224855.at
 Figure 4483: PRO80743
 Figure 4484: DNA330588, BC019034, 224871.at
 Figure 4485: PRO85768
 Figure 4486: DNA196374, DNA196374, 224880.at
 Figure 4487A-B: DNA331625, 411236.19, 224897.at
 Figure 4488: PRO86622
 Figure 4489: DNA329382, BC009072, 224913.s.at
 Figure 4490: DNA330590, CIP29, 224914.s.at
 Figure 4491: PRO85770
 Figure 4492A-B: DNA169523, DNA169523, 224917.at
 Figure 4493: PRO23253
 Figure 4494: DNA330591, NP_115865.1, 224919.at
 Figure 4495: PRO85771
 Figure 4496: DNA330592, AB014733, 224953.at
 Figure 4497: DNA287258, C20orf52, 224972.at
 Figure 4498: PRO52174
 Figure 4499: DNA151170, DNA151170, 224989.at
 Figure 4500: PRO12626
 Figure 4501: DNA330593, HS125A53, 225005.at
 Figure 4502A-B: DNA329385, 330826.1, 225010.at
 Figure 4503: PRO84961
 Figure 4504: DNA161646, DNA161646, 225036.at
 Figure 4505: DNA330594, BC005148, 225039.at
 Figure 4506: DNA331626, 412293.2, 225047.at
 Figure 4507: PRO86623
 Figure 4508: DNA195755, DNA195755, 225051.at
 Figure 4509A-B: DNA330596, 998535.1, 225070.at
 Figure 4510: PRO85774
 Figure 4511A-C: DNA271612, BAA92642.1, 225076.s.at
 Figure 4512: PRO59899
 Figure 4513: DNA330597, NP_057291.1, 225082.at
 Figure 4514: PRO85775
 Figure 4515: DNA330598, 1384569.2, 225086.at
 Figure 4516: PRO85776
 Figure 4517: DNA330599, 898528.3, 225095.at
 Figure 4518: PRO85777
 Figure 4519: DNA330600, HSA272196, 225096.at
 Figure 4520: PRO85778
 Figure 4521: DNA330601, 1322727.6, 225098.at
 Figure 4522: PRO85779
 Figure 4523: DNA331627, BC013920, 225105.at
 Figure 4524: PRO86624
 Figure 4525: DNA225597, NP_060703.1, 225106.s.at
 Figure 4526: PRO36060
 Figure 4527A-B: DNA331628, 245994.3, 225113.at
 Figure 4528: PRO86625
 Figure 4529A-B: DNA327993, 898436.7, 225133.at
 Figure 4530: PRO81138
 Figure 4531: DNA155396, DNA155396, 225143.at
 Figure 4532: DNA330603, 235138.16, 225157.at
 Figure 4533: PRO85781
 Figure 4534: DNA329393, NP_079272.4, 225158.at
 Figure 4535: PRO84969
 Figure 4536: DNA329393, EFG1, 225161.at
 Figure 4537: PRO84969
 Figure 4538: DNA330604, NP_277050.1, 225171.at
 Figure 4539: PRO85782
 Figure 4540: DNA327996, BC010181, 225195.at
 Figure 4541: PRO83915
 Figure 4542: DNA199601, DNA199601, 225199.at

Figure 4543: DNA329394, BC010416, 225201.s.at
 Figure 4544: DNA329396, NP_060866.1, 225253.s.at
 Figure 4545: PRO84972
 Figure 4546: DNA329397, NP_114109.1, 225260.s.at
 Figure 4547: PRO84973
 Figure 4548A-B: DNA329398, 411135.13, 225262.at
 Figure 4549: PRO4805
 Figure 4550A-B: DNA258863, DNA258863, 225266.at
 Figure 4551A-B: DNA331629, 233102.7, 225269.s.at
 Figure 4552: PRO86626
 Figure 4553A-B: DNA330606, 475590.1, 225290.at
 Figure 4554: PRO85784
 Figure 4555: DNA329400, BC005986, 225291.at
 Figure 4556: DNA326458, BC014003, 225297.at
 Figure 4557: PRO82841
 Figure 4558: DNA330607, 167391.12, 225300.at
 Figure 4559: PRO85785
 Figure 4560: DNA330608, BC016880, 225323.at
 Figure 4561: PRO85786
 Figure 4562A-B: DNA169918, DNA169918, 225340.s.at
 Figure 4563: PRO23256
 Figure 4564: DNA330609, AF419331, 225348.at
 Figure 4565: PRO22196
 Figure 4566: DNA327965, NP_060760.1, 225367.at
 Figure 4567: PRO83888
 Figure 4568: DNA273635, HSM801117, 225371.at
 Figure 4569A-B: DNA330610, BAB15739.1, 225372.at
 Figure 4570: PRO85787
 Figure 4571: DNA331630, BC020568, 225373.at
 Figure 4572: PRO86627
 Figure 4573A-B: DNA331631, 1383781.5, 225385.s.at
 Figure 4574: PRO86628
 Figure 4575: DNA329401, BC017480, 225386.s.at
 Figure 4576: PRO84976
 Figure 4577: DNA329402, 198708.7, 225387.at
 Figure 4578: PRO4845
 Figure 4579: DNA329403, AF288394, 225399.at
 Figure 4580: DNA331632, BC022030, 225400.at
 Figure 4581: PRO86629
 Figure 4582: DNA330612, C20orf64, 225402.at
 Figure 4583: PRO85789
 Figure 4584A-B: DNA328893, BC020490, 225406.at
 Figure 4585: PRO9914
 Figure 4586: DNA330613, BC019355, 225414.at
 Figure 4587A-B: DNA331633, 1449606.5, 225433.at
 Figure 4588: PRO86630
 Figure 4589: DNA304802, AAH00967.1, 225439.at
 Figure 4590: PRO71212
 Figure 4591: DNA328005, BC004413, 225440.at
 Figure 4592: DNA330615, NP_115732.1, 225441.x.at
 Figure 4593: PRO85791
 Figure 4594: DNA330616, 429555.1, 225443.at
 Figure 4595: PRO85792
 Figure 4596A-B: DNA330617, 336147.2, 225447.at
 Figure 4597: PRO59923
 Figure 4598: DNA329404, BC013949, 225454.at
 Figure 4599: PRO82972
 Figure 4600: DNA330618, CAB55990.1, 225457.s.at
 Figure 4601: PRO85793
 Figure 4602: DNA330618, HSM801081, 225458.at
 Figure 4603: DNA196561, DNA196561, 225470.at
 Figure 4604: DNA329405, HSM800962, 225520.at
 Figure 4605A-B: DNA330619, BC013128, 225527.at
 Figure 4606: PRO12186
 Figure 4607A-B: DNA330620, CAB55950.1, 225533.at
 Figure 4608: PRO85794
 Figure 4609: DNA330621, AF116628, 225535.s.at
 Figure 4610: DNA328008, 240051.4, 225541.at
 Figure 4611: PRO83926
 Figure 4612A-B: DNA330622, 233388.8, 225543.at
 Figure 4613: PRO85796
 Figure 4614: DNA330623, 1502854.5, 225549.at
 Figure 4615: PRO85797
 Figure 4616: DNA329406, 1503139.10, 225562.at
 Figure 4617: PRO84979
 Figure 4618: DNA330624, AK000500, 225580.at
 Figure 4619: PRO85798
 Figure 4620: DNA330625, AK025643, 225581.s.at
 Figure 4621: PRO85799
 Figure 4622: DNA304469, NP_149078.1, 225621.at
 Figure 4623: PRO71045
 Figure 4624: DNA151667, DNA151667, 225634.at
 Figure 4625: PRO11970
 Figure 4626: DNA330626, 1398905.1, 225638.at
 Figure 4627: PRO85800
 Figure 4628: DNA331634, CTSC, 225647.s.at
 Figure 4629: PRO86631
 Figure 4630A-B: DNA288261, NP_037414.2, 225655.at
 Figure 4631: PRO70021
 Figure 4632: DNA329408, NP_056235.2, 225676.s.at
 Figure 4633: PRO38893
 Figure 4634A-B: DNA330627, 987725.3, 225679.at
 Figure 4635: PRO85801
 Figure 4636: DNA329409, BC017248, 225682.s.at
 Figure 4637: PRO64981
 Figure 4638: DNA325272, NP_054891.1, 225683.x.at
 Figure 4639: PRO81822
 Figure 4640: DNA328012, BC017873, 225686.at
 Figure 4641: PRO83930
 Figure 4642: DNA328013, AAH01068.1, 225687.at
 Figure 4643: PRO83931
 Figure 4644A-C: DNA330628, 1400234.13, 225690.at
 Figure 4645: PRO85802
 Figure 4646A-B: DNA330629, BAA74856.2, 225692.at
 Figure 4647: PRO50227

Figure 4543: DNA329394, BC010416, 225201.s.at
 Figure 4544: DNA329396, NP_060866.1, 225253.s.at
 Figure 4545: PRO84972
 Figure 4546: DNA329397, NP_114109.1, 225260.s.at
 Figure 4547: PRO84973
 Figure 4548A-B: DNA329398, 411135.13, 225262.at
 Figure 4549: PRO4805
 Figure 4550A-B: DNA258863, DNA258863, 225266.at
 Figure 4551A-B: DNA331629, 233102.7, 225269.s.at
 Figure 4552: PRO86626
 Figure 4553A-B: DNA330606, 475590.1, 225290.at
 Figure 4554: PRO85784
 Figure 4555: DNA329400, BC005986, 225291.at
 Figure 4556: DNA326458, BC014003, 225297.at
 Figure 4557: PRO82841
 Figure 4558: DNA330607, 167391.12, 225300.at
 Figure 4559: PRO85785
 Figure 4560: DNA330608, BC016880, 225323.at
 Figure 4561: PRO85786
 Figure 4562A-B: DNA169918, DNA169918, 225340.s.at
 Figure 4563: PRO23256
 Figure 4564: DNA330609, AF419331, 225348.at
 Figure 4565: PRO22196
 Figure 4566: DNA327965, NP_060760.1, 225367.at
 Figure 4567: PRO83888
 Figure 4568: DNA273635, HSM801117, 225371.at
 Figure 4569A-B: DNA330610, BAB15739.1, 225372.at
 Figure 4570: PRO85787
 Figure 4571: DNA331630, BC020568, 225373.at
 Figure 4572: PRO86627
 Figure 4573A-B: DNA331631, 1383781.5, 225385.s.at
 Figure 4574: PRO86628
 Figure 4575: DNA329401, BC017480, 225386.s.at
 Figure 4576: PRO84976
 Figure 4577: DNA329402, 198708.7, 225387.at
 Figure 4578: PRO4845
 Figure 4579: DNA329403, AF288394, 225399.at
 Figure 4580: DNA331632, BC022030, 225400.at
 Figure 4581: PRO86629
 Figure 4582: DNA330612, C20orf64, 225402.at
 Figure 4583: PRO85789
 Figure 4584A-B: DNA328893, BC020490, 225406.at
 Figure 4585: PRO9914
 Figure 4586: DNA330613, BC019355, 225414.at
 Figure 4587A-B: DNA331633, 1449606.5, 225433.at
 Figure 4588: PRO86630
 Figure 4589: DNA304802, AAH00967.1, 225439.at
 Figure 4590: PRO71212
 Figure 4591: DNA328005, BC004413, 225440.at
 Figure 4592: DNA330615, NP_115732.1, 225441.x.at
 Figure 4593: PRO85791
 Figure 4594: DNA330616, 429555.1, 225443.at
 Figure 4595: PRO85792
 Figure 4596A-B: DNA330617, 336147.2, 225447.at
 Figure 4597: PRO59923
 Figure 4598: DNA329404, BC013949, 225454.at
 Figure 4599: PRO82972
 Figure 4600: DNA330618, CAB55990.1, 225457.s.at
 Figure 4601: PRO85793
 Figure 4602: DNA330618, HSM801081, 225458.at
 Figure 4603: DNA196561, DNA196561, 225470.at
 Figure 4604: DNA329405, HSM800962, 225520.at
 Figure 4605A-B: DNA330619, BC013128, 225527.at
 Figure 4606: PRO12186
 Figure 4607A-B: DNA330620, CAB55950.1, 225533.at
 Figure 4608: PRO85794
 Figure 4609: DNA330621, AF116628, 225535.s.at
 Figure 4610: DNA328008, 240051.4, 225541.at
 Figure 4611: PRO83926
 Figure 4612A-B: DNA330622, 233388.8, 225543.at
 Figure 4613: PRO85796
 Figure 4614: DNA330623, 1502854.5, 225549.at
 Figure 4615: PRO85797
 Figure 4616: DNA329406, 1503139.10, 225562.at
 Figure 4617: PRO84979
 Figure 4618: DNA330624, AK000500, 225580.at
 Figure 4619: PRO85798
 Figure 4620: DNA330625, AK025643, 225581.s.at
 Figure 4621: PRO85799
 Figure 4622: DNA304469, NP_149078.1, 225621.at
 Figure 4623: PRO71045
 Figure 4624: DNA151667, DNA151667, 225634.at
 Figure 4625: PRO11970
 Figure 4626: DNA330626, 1398905.1, 225638.at
 Figure 4627: PRO85800
 Figure 4628: DNA331634, CTSC, 225647.s.at
 Figure 4629: PRO86631
 Figure 4630A-B: DNA288261, NP_037414.2, 225655.at
 Figure 4631: PRO70021
 Figure 4632: DNA329408, NP_056235.2, 225676.s.at
 Figure 4633: PRO38893
 Figure 4634A-B: DNA330627, 987725.3, 225679.at
 Figure 4635: PRO85801
 Figure 4636: DNA329409, BC017248, 225682.s.at
 Figure 4637: PRO84981
 Figure 4638: DNA325272, NP_054891.1, 225683.x.at
 Figure 4639: PRO81822
 Figure 4640: DNA328012, BC017873, 225686.at
 Figure 4641: PRO83930
 Figure 4642: DNA328013, AAH01068.1, 225687.at
 Figure 4643: PRO83931
 Figure 4644A-C: DNA330628, 1400234.13, 225690.at
 Figure 4645: PRO85802
 Figure 4646A-B: DNA330629, BAA74856.2, 225692.at
 Figure 4647: PRO50227

Figure 4648: DNA273623, AY037153, 225693.s.at
 Figure 4649: PRO61596
 Figure 4650: DNA330630, TIGA1, 225698.at
 Figure 4651: PRO85803
 Figure 4652A-B: DNA331635, BAB13371.1, 225704.at
 Figure 4653: PRO86632
 Figure 4654: DNA331636, 221395.1, 225716.at
 Figure 4655: PRO86633
 Figure 4656: DNA330633, BC003515, 225723.at
 Figure 4657A-B: DNA330634, 243208.1, 225725.at
 Figure 4658: PRO85806
 Figure 4659A-B: DNA330635, 233691.4, 225736.at
 Figure 4660: PRO85807
 Figure 4661: DNA324266, NP_056268.1, 225741.at
 Figure 4662: PRO80949
 Figure 4663: DNA323970, MGC21854, 225763.at
 Figure 4664: PRO80699
 Figure 4665: DNA331637, 7693984.1, 225768.at
 Figure 4666: PRO86634
 Figure 4667: DNA330636, NP_201575.2, 225794.s.at
 Figure 4668: PRO85808
 Figure 4669: DNA330636, LOC91689, 225795.at
 Figure 4670: PRO85808
 Figure 4671: DNA329414, MGC4677, 225799.at
 Figure 4672: PRO84986
 Figure 4673: DNA330637, NP_478136.1, 225803.at
 Figure 4674: PRO85809
 Figure 4675A-C: DNA330638, CAB63749.1, 225814.at
 Figure 4676: PRO85810
 Figure 4677: DNA330639, 420605.8, 225834.at
 Figure 4678: PRO85811
 Figure 4679: DNA329417, 411336.1, 225842.at
 Figure 4680: PRO84989
 Figure 4681: DNA287622, AF041429, 225849.s.at
 Figure 4682: DNA329418, BC018969, 225850.at
 Figure 4683: PRO19906
 Figure 4684: DNA287370, BAB14983.1, 225866.at
 Figure 4685: PRO69630
 Figure 4686A-B: DNA331638, 1097910.3, 225886.at
 Figure 4687: PRO86635
 Figure 4688A-B: DNA331639, 1391157.25, 225888.at
 Figure 4689: PRO86636
 Figure 4690: DNA330642, NP_115494.1, 225898.at
 Figure 4691: PRO85814
 Figure 4692A-B: DNA331640, 481415.9, 225927.at
 Figure 4693: PRO86637
 Figure 4694A-B: DNA255887, BAB13380.1, 225929.s.at
 Figure 4695: PRO50940
 Figure 4696A-B: DNA255887, AB046774, 225931.s.at
 Figure 4697A-B: DNA330644, 236657.4, 225935.at
 Figure 4698: PRO85816
 Figure 4699: DNA331641, AK027752, 225959.s.at
 Figure 4700: PRO86638
 Figure 4701A-B: DNA329360, AF378524, 225962.at
 Figure 4702: PRO84939
 Figure 4703: DNA329420, BC018014, 225970.at
 Figure 4704A-B: DNA330645, 350385.2, 225973.at
 Figure 4705: PRO85817
 Figure 4706A-B: DNA329421, 343552.1, 225974.at
 Figure 4707: PRO84992
 Figure 4708A-B: DNA331642, BAB15719.1, 225979.at
 Figure 4709: PRO86639
 Figure 4710: DNA330647, AK002174, 226001.at
 Figure 4711: PRO85819
 Figure 4712: DNA330648, 1399123.1, 226005.at
 Figure 4713: PRO85820
 Figure 4714: DNA330649, AK056957, 226008.at
 Figure 4715: PRO85821
 Figure 4716A-B: DNA331643, 246054.6, 226021.at
 Figure 4717: PRO86640
 Figure 4718: DNA331644, 027830.2, 226034.at
 Figure 4719: PRO86641
 Figure 4720: DNA328021, BC004538, 226038.at
 Figure 4721: DNA273736, DNA273736, 226040.at
 Figure 4722: DNA330652, CLONE24945, 226055.at
 Figure 4723: PRO85824
 Figure 4724: DNA330653, 7687670.2, 226068.at
 Figure 4725: PRO85825
 Figure 4726: DNA304795, AK056513, 226077.at
 Figure 4727: PRO71207
 Figure 4728A-B: DNA331645, AAD09327.1, 226082.s.at
 Figure 4729: PRO86642
 Figure 4730: DNA287271, NP_116188.2, 226088.at
 Figure 4731: PRO69542
 Figure 4732: DNA330655, AF114264, 226103.at
 Figure 4733: PRO85827
 Figure 4734A-B: DNA330656, AK023825, 226109.at
 Figure 4735: PRO85828
 Figure 4736: DNA329425, BC008294, 226117.at
 Figure 4737: DNA330657, 198409.1, 226140.s.at
 Figure 4738: PRO85829
 Figure 4739: DNA330658, 204262.3, 226157.at
 Figure 4740: PRO85830
 Figure 4741: DNA330659, AF289605, 226175.at
 Figure 4742: PRO85831
 Figure 4743A-B: DNA330660, 979126.7, 226178.at
 Figure 4744: PRO85832
 Figure 4745A-B: DNA259025, DNA259025, 226180.at
 Figure 4746: PRO52958
 Figure 4747: DNA56350, DNA56350, 226181.at
 Figure 4748: PRO956
 Figure 4749: DNA330661, BAB47431.1, 226194.at
 Figure 4750: PRO85833
 Figure 4751A-B: DNA329428, 1446144.8, 226218.at
 Figure 4752: PRO84999

Figure 4753: DNA195822, DNA195822, 226241.s.at
 Figure 4754A-B: DNA330662, 334156.1, 226252.at
 Figure 4755: PRO85834
 Figure 4756: DNA331646, 956845.3, 226261.at
 Figure 4757: PRO86643
 Figure 4758A-B: DNA330664, 400637.4, 226265.at
 Figure 4759: PRO85836
 Figure 4760A-B: DNA330665, 233070.3, 226270.at
 Figure 4761: PRO85837
 Figure 4762: DNA330665, 199829.14, 226272.at
 Figure 4763: PRO85838
 Figure 4764: DNA193896, DNA193896, 226276.at
 Figure 4765: PRO23314
 Figure 4766: DNA330667, AF301222, 226287.at
 Figure 4767: DNA330668, BC010176, 226308.at
 Figure 4768: PRO85840
 Figure 4769: DNA328028, NP.005773.1, 226319.s.at
 Figure 4770: PRO83945
 Figure 4771: DNA328028, ALY, 226320.at
 Figure 4772: PRO83945
 Figure 4773: DNA330669, 236903.4, 226321.at
 Figure 4774: PRO85841
 Figure 4775: DNA330670, BC018453, 226329.s.at
 Figure 4776: PRO85842
 Figure 4777A-B: DNA330671, 228447.18, 226342.at
 Figure 4778: PRO85843
 Figure 4779: DNA330672, 255309.4, 226347.at
 Figure 4780: PRO85844
 Figure 4781: DNA330673, 236879.2, 226348.at
 Figure 4782: PRO85845
 Figure 4783: DNA329430, NP.116191.2, 226353.at
 Figure 4784: PRO38524
 Figure 4785: DNA331647, 236137.11, 226354.at
 Figure 4786: PRO86644
 Figure 4787A-B: DNA330675, 177663.2, 226368.at
 Figure 4788: PRO85847
 Figure 4789: DNA330676, CAA11393.1, 226388.at
 Figure 4790: PRO85848
 Figure 4791: DNA330677, 1384190.6, 226390.at
 Figure 4792: PRO85849
 Figure 4793: DNA151740, DNA151740, 226419.s.at
 Figure 4794: PRO12029
 Figure 4795: DNA329433, NP.115937.1, 226442.at
 Figure 4796: PRO85003
 Figure 4797: DNA330678, 401430.1, 226444.at
 Figure 4798: PRO85850
 Figure 4799: DNA287657, BC009447, 226448.at
 Figure 4800: PRO69688
 Figure 4801: DNA330679, BC013040, 226456.at
 Figure 4802A-B: DNA330680, BC022792, 226477.at
 Figure 4803: PRO85852
 Figure 4804: DNA326066, NP.291022.1, 226488.at
 Figure 4805: PRO82501
 Figure 4806A-B: DNA330681, 971066.5, 226503.at
 Figure 4807: PRO85853
 Figure 4808: DNA330682, HSM801031, 226510.at
 Figure 4809: DNA304794, NP.115521.2, 226541.at
 Figure 4810: PRO71206
 Figure 4811: DNA330683, 1446727.8, 226546.at
 Figure 4812: PRO85854
 Figure 4813: DNA330684, 984114.1, 226548.at
 Figure 4814: PRO85855
 Figure 4815A-B: DNA328031, 331264.1, 226587.at
 Figure 4816: PRO83948
 Figure 4817: DNA330685, BAB13430.1, 226588.at
 Figure 4818: PRO85856
 Figure 4819A-B: DNA330686, 1502531.18, 226602.s.at
 Figure 4820: PRO85857
 Figure 4821: DNA328033, 1446419.1, 226625.at
 Figure 4822: PRO83949
 Figure 4823: DNA330687, 215158.5, 226650.at
 Figure 4824: PRO85858
 Figure 4825: DNA258913, DNA258913, 226661.at
 Figure 4826: PRO52846
 Figure 4827A-C: DNA328462, HSA303079, 226694.at
 Figure 4828: PRO84288
 Figure 4829: DNA328037, BC016969, 226702.at
 Figure 4830: DNA330688, 240121.1, 226725.at
 Figure 4831: PRO85859
 Figure 4832A-C: DNA330689, 978733.6, 226732.at
 Figure 4833: PRO85860
 Figure 4834: DNA257914, DNA257914, 226743.at
 Figure 4835: PRO52447
 Figure 4836: DNA330690, 245065.1, 226745.at
 Figure 4837: PRO85861
 Figure 4838: DNA330691, BC022075, 226748.at
 Figure 4839: PRO85862
 Figure 4840: DNA329435, 347092.10, 226750.at
 Figure 4841: PRO85005
 Figure 4842: DNA331648, 243999.3, 226757.at
 Figure 4843: PRO86645
 Figure 4844: DNA330692, 1446140.1, 226758.at
 Figure 4845: PRO85863
 Figure 4846A-B: DNA330331, AB032963, 226771.at
 Figure 4847: DNA330693, HSBRN1H12, 226773.at
 Figure 4848A-B: DNA330694, 481455.4, 226810.at
 Figure 4849: PRO85865
 Figure 4850: DNA330695, 404167.9, 226818.at
 Figure 4851: PRO85866
 Figure 4852A-C: DNA330696, 404167.10, 226841.at
 Figure 4853: PRO85867
 Figure 4854: DNA330697, BC011808, 226858.at
 Figure 4855: PRO85868
 Figure 4856A-B: DNA329436, 236863.1, 226869.at
 Figure 4857: PRO85006
 Figure 4858: DNA330698, BC020852, 226896.at
 Figure 4859: PRO85869
 Figure 4860: DNA329437, 156503.10, 226901.at
 Figure 4861: PRO85007
 Figure 4862: DNA330699, BC014203, 226905.at

- Figure 4863: DNA330564, ARHGAP9, 226906.s.at
 Figure 4864: PRO85746
 Figure 4865: DNA327917, BC000798, 226915.s.at
 Figure 4866: PRO83852
 Figure 4867A-C: DNA331649, 201042.4, 226921.at
 Figure 4868: PRO86646
 Figure 4869: DNA328044, 039170.3, 226936.at
 Figure 4870: PRO83958
 Figure 4871: DNA151713, DNA151713, 226943.at
 Figure 4872: PRO12003
 Figure 4873: DNA330701, NP.115652.1, 226945.at
 Figure 4874: PRO85872
 Figure 4875: DNA330702, 023085.2, 226965.at
 Figure 4876: PRO85873
 Figure 4877: DNA330703, 201413.1, 226970.at
 Figure 4878: PRO85874
 Figure 4879: DNA154627, DNA154627, 226976.at
 Figure 4880: DNA330704, BC019075, 226980.at
 Figure 4881: PRO85875
 Figure 4882A-B: DNA331650, HSA314788, 226998.at
 Figure 4883: PRO85008
 Figure 4884: DNA329439, HSM802614, 227014.at
 Figure 4885A-B: DNA330705, 198782.1, 227020.at
 Figure 4886: PRO85876
 Figure 4887A-B: DNA330706, AF445027, 227027.at
 Figure 4888: PRO85877
 Figure 4889: DNA330707, 028375.3, 227044.at
 Figure 4890: PRO85878
 Figure 4891: DNA330708, 1101317.1, 227066.at
 Figure 4892: PRO85879
 Figure 4893: DNA329440, 7691797.1, 227068.at
 Figure 4894: PRO85009
 Figure 4895: DNA330709, 7692923.1, 227117.at
 Figure 4896: PRO85880
 Figure 4897: DNA323785, NP.116261.1, 227134.at
 Figure 4898: PRO80537
 Figure 4899: DNA330710, 331040.11, 227135.at
 Figure 4900: PRO85881
 Figure 4901A-B: DNA330711, 425448.18, 227150.at
 Figure 4902: PRO85882
 Figure 4903: DNA330712, 1452648.12, 227167.s.at
 Figure 4904: PRO85883
 Figure 4905: DNA328281, BC000282, 227172.at
 Figure 4906: DNA330713, 334485.4, 227187.at
 Figure 4907: PRO85884
 Figure 4908: DNA330714, 034544.1, 227198.at
 Figure 4909: PRO85885
 Figure 4910: DNA330715, BC022374, 227211.at
 Figure 4911: PRO85886
 Figure 4912A-B: DNA330620, HSM800990, 227212.s.at
 Figure 4913: DNA330716, BC021675, 227236.at
 Figure 4914: PRO85887
 Figure 4915: DNA251633, AK023151, 227245.at
 Figure 4916: PRO47694
 Figure 4917: DNA327206, AY037161, 227262.at
 Figure 4918: PRO271
 Figure 4919A-B: DNA329442, AH007300S2, 227265.at
 Figure 4920A-B: DNA331651, 099572.12, 227266.s.at
 Figure 4921: PRO86647
 Figure 4922: DNA330717, 232831.10, 227290.at
 Figure 4923: PRO85888
 Figure 4924: DNA329445, 001839.3, 227291.s.at
 Figure 4925: PRO85013
 Figure 4926: DNA330718, 025465.3, 227295.at
 Figure 4927: PRO85889
 Figure 4928: DNA330719, 7697121.1, 227307.at
 Figure 4929: PRO85890
 Figure 4930: DNA330720, 186766.12, 227337.at
 Figure 4931: PRO85891
 Figure 4932: DNA35664, DNA35664, 227345.at
 Figure 4933: PRO34697
 Figure 4934A-B: DNA330721, 198680.1, 227350.at
 Figure 4935: PRO85892
 Figure 4936: DNA226872, NP.001955.1, 227404.s.at
 Figure 4937: PRO37335
 Figure 4938A-B: DNA330722, AB058729, 227418.at
 Figure 4939: DNA330723, AB040960, 227438.at
 Figure 4940: DNA329447, BC016981, 227449.at
 Figure 4941: PRO85015
 Figure 4942: DNA330724, AK056677, 227450.at
 Figure 4943: PRO1575
 Figure 4944A-B: DNA328054, 233014.1, 227458.at
 Figure 4945: PRO83968
 Figure 4946A-B: DNA258781, DNA258781, 227466.at
 Figure 4947: PRO52715
 Figure 4948: DNA329448, BC012948, 227477.at
 Figure 4949: PRO85016
 Figure 4950: DNA329053, LOC51105, 227523.s.at
 Figure 4951: PRO84715
 Figure 4952: DNA330725, 337360.7, 227545.at
 Figure 4953: PRO85894
 Figure 4954: DNA330726, BC014967, 227558.at
 Figure 4955: PRO85895
 Figure 4956A-B: DNA331652, 1447357.3, 227572.at
 Figure 4957: PRO86648
 Figure 4958: DNA330728, HSM801012, 227580.s.at
 Figure 4959: PRO85897
 Figure 4960: DNA330729, 031130.2, 227600.at
 Figure 4961: PRO85898
 Figure 4962A-B: DNA287193, AB037794, 227606.s.at
 Figure 4963: DNA330730, BC010846, 227607.at
 Figure 4964: PRO85899
 Figure 4965: DNA257714, NP.150280.1, 227609.at
 Figure 4966: PRO52268
 Figure 4967: DNA330731, BC012337, 227614.at
 Figure 4968: DNA196237, DNA196237, 227616.at

Figure 4969A-B: DNA330426, AF085233, 227627.at
 Figure 4970: PRO85631
 Figure 4971A-B: DNA330733, BAA92631.1, 227653.at
 Figure 4972: PRO85902
 Figure 4973: DNA329449, 979180.1, 227682.at
 Figure 4974: PRO85017
 Figure 4975: DNA330734, BC008322, 227686.at
 Figure 4976: PRO85903
 Figure 4977: DNA273987, DNA273987, 227708.at
 Figure 4978: DNA330735, 1400830.3, 227722.at
 Figure 4979: PRO85904
 Figure 4980: DNA329450, BC017226, 227726.at
 Figure 4981: PRO85018
 Figure 4982A-B: DNA330736, BAA86532.1, 227732.at
 Figure 4983: PRO85905
 Figure 4984A-B: DNA330737, 331100.8, 227766.at
 Figure 4985: PRO85906
 Figure 4986: DNA331653, 212641.1, 227792.at
 Figure 4987: PRO86649
 Figure 4988: DNA151733, DNA151733, 227807.at
 Figure 4989: PRO12022
 Figure 4990A-B: DNA330739, AK000004, 227811.at
 Figure 4991: DNA329454, BC022534, 227856.at
 Figure 4992: PRO85022
 Figure 4993: DNA260485, DNA260485, 227867.at
 Figure 4994: PRO54411
 Figure 4995: DNA327214, AK056512, 227873.at
 Figure 4996: PRO83483
 Figure 4997: DNA151503, DNA151503, 227877.at
 Figure 4998: PRO11849
 Figure 4999: DNA329481, NP_057234.2, 227915.at
 Figure 5000: PRO60949
 Figure 5001: DNA329456, AF151860, 227916.x.at
 Figure 5002: PRO85023
 Figure 5003A-B: DNA330740, AY028320S2, 227928.at
 Figure 5004: DNA151580, DNA151580, 227930.at
 Figure 5005: PRO11901
 Figure 5006: DNA330741, 350868.1, 227952.at
 Figure 5007: PRO85909
 Figure 5008A-B: DNA331654, 476805.1, 228006.at
 Figure 5009: PRO86650
 Figure 5010: DNA330539, ZNRD1, 228009.x.at
 Figure 5011: PRO85724
 Figure 5012: DNA150660, NP_057151.1, 228019.s.at
 Figure 5013: PRO12397
 Figure 5014A-B: DNA328432, NP_005768.1, 228030.at
 Figure 5015: PRO61793
 Figure 5016: DNA331655, 1449874.3, 228053.s.at
 Figure 5017: PRO86651
 Figure 5018: DNA330743, AK054689, 228062.at
 Figure 5019: PRO85911
 Figure 5020: DNA331656, 244771.1, 228063.s.at
 Figure 5021: PRO86652
 Figure 5022: DNA331657, BLR1, 228065.at
 Figure 5023: PRO23970
 Figure 5024: DNA329459, 230998.1, 228066.at
 Figure 5025: PRO85026
 Figure 5026: DNA330745, BC011716, 228069.at
 Figure 5027: PRO85913
 Figure 5028: DNA196216, DNA196216, 228071.at
 Figure 5029: DNA329460, BC017117, 228092.at
 Figure 5030: PRO85027
 Figure 5031: DNA330746, 346395.7, 228097.at
 Figure 5032: PRO85914
 Figure 5033: DNA330436, AF187016, 228098.s.at
 Figure 5034: PRO85639
 Figure 5035A-C: DNA331658, 200650.1, 228109.at
 Figure 5036: PRO86653
 Figure 5037: DNA329461, BC016615, 228113.at
 Figure 5038: PRO85028
 Figure 5039: DNA330748, 224725.3, 228159.at
 Figure 5040: PRO85916
 Figure 5041: DNA330749, 337382.1, 228174.at
 Figure 5042: PRO85917
 Figure 5043: DNA330750, 984920.1, 228180.at
 Figure 5044: PRO85918
 Figure 5045: DNA153924, DNA153924, 228188.at
 Figure 5046: DNA330751, 334282.2, 228189.at
 Figure 5047: PRO85919
 Figure 5048: DNA330752, 7694335.3, 228191.at
 Figure 5049: PRO85920
 Figure 5050A-B: DNA331659, 198497.1, 228201.at
 Figure 5051: PRO86654
 Figure 5052A-C: DNA328072, AB051556, 228230.at
 Figure 5053: DNA330754, 349978.1, 228242.at
 Figure 5054: PRO85922
 Figure 5055: DNA328663, CGI-142, 228266.s.at
 Figure 5056: PRO36183
 Figure 5057: DNA260948, DNA260948, 228273.at
 Figure 5058: PRO54700
 Figure 5059: DNA330755, BC020784, 228280.at
 Figure 5060: PRO85923
 Figure 5061: DNA331660, 230589.4, 228281.at
 Figure 5062: PRO86655
 Figure 5063A-B: DNA330757, AB046790, 228323.at
 Figure 5064: DNA304814, BC016879, 228330.at
 Figure 5065: PRO52650
 Figure 5066: DNA194202, DNA194202, 228370.at
 Figure 5067: PRO23594
 Figure 5068: DNA330758, 238545.7, 228381.at
 Figure 5069: PRO85925
 Figure 5070: DNA330759, 337444.1, 228390.at
 Figure 5071: PRO85926
 Figure 5072A-B: DNA330760, 330900.8, 228401.at
 Figure 5073: PRO85927
 Figure 5074: DNA228118, DNA228118, 228456.s.at
 Figure 5075: DNA297188, NP_116233.1, 228468.at
 Figure 5076: PRO70805

Figure 5077A-C: DNA331661, 388991.1, 228487.s.at
 Figure 5078: PRO86656
 Figure 5079: DNA330762, BC010269, 228499.at
 Figure 5080: PRO80989
 Figure 5081: DNA195938, DNA195938, 228531.at
 Figure 5082: DNA329463, 412954.5, 228532.at
 Figure 5083: PRO85030
 Figure 5084: DNA330763, 1306177.32, 228549.at
 Figure 5085: PRO85929
 Figure 5086: DNA331662, 1450017.11, 228559.at
 Figure 5087: PRO86657
 Figure 5088A-C: DNA331663, 475198.1, 228562.at
 Figure 5089: PRO86658
 Figure 5090: DNA330766, 977419.7, 228597.at
 Figure 5091: PRO85932
 Figure 5092A-B: DNA331664, 201954.14, 228603.at
 Figure 5093: PRO86659
 Figure 5094: DNA328079, 239903.1, 228617.at
 Figure 5095: PRO83991
 Figure 5096: DNA330768, NP_003681.1, 228620.at
 Figure 5097: PRO60565
 Figure 5098A-B: DNA271477, NP_055774.1, 228641.at
 Figure 5099: PRO59770
 Figure 5100: DNA330769, 230457.1, 228664.at
 Figure 5101: PRO85934
 Figure 5102: DNA330770, 1447329.13, 228702.at
 Figure 5103: PRO85935
 Figure 5104: DNA330771, 1447928.4, 228710.at
 Figure 5105: PRO85936
 Figure 5106: DNA330772, 286623.2, 228729.at
 Figure 5107: PRO85937
 Figure 5108: DNA330773, 027401.1, 228758.at
 Figure 5109: PRO85938
 Figure 5110: DNA330774, 024160.1, 228760.at
 Figure 5111: PRO85939
 Figure 5112: DNA273232, DNA273232, 228785.at
 Figure 5113: DNA330775, 407523.3, 228806.at
 Figure 5114: PRO85940
 Figure 5115: DNA330776, NP_005740.1, 228834.at
 Figure 5116: PRO58014
 Figure 5117: DNA256483, IISM802155, 228859.at
 Figure 5118: PRO51520
 Figure 5119: DNA331665, 330848.1, 228869.at
 Figure 5120: PRO86660
 Figure 5121: DNA330778, 998621.10, 228891.at
 Figure 5122: PRO85942
 Figure 5123: DNA328084, 236591.7, 228905.at
 Figure 5124: PRO83996
 Figure 5125: DNA330779, 244243.1, 228953.at
 Figure 5126: PRO85943
 Figure 5127: DNA330780, 335374.1, 228955.at
 Figure 5128: PRO85944
 Figure 5129: DNA330781, 289775.9, 228960.at
 Figure 5130: PRO85945
 Figure 5131A-B: DNA331666, 7684887.1, 228964.at
 Figure 5132: PRO86661
 Figure 5133: DNA330783, 239601.22, 228987.at
 Figure 5134: PRO85947
 Figure 5135: DNA330784, 233595.21, 228990.at
 Figure 5136: PRO85948
 Figure 5137: DNA330785, 475283.24, 228999.at
 Figure 5138: PRO85949
 Figure 5139: DNA330786, 233085.1, 229029.at
 Figure 5140: PRO85950
 Figure 5141: DNA330787, 349981.7, 229040.at
 Figure 5142: PRO85951
 Figure 5143: DNA330788, AF305195, 229060.at
 Figure 5144: PRO85952
 Figure 5145: DNA330789, 199829.13, 229064.s.at
 Figure 5146: PRO85953
 Figure 5147: DNA330790, NP_116133.1, 229070.at
 Figure 5148: PRO85954
 Figure 5149: DNA330791, 7697349.2, 229072.at
 Figure 5150: PRO85955
 Figure 5151: DNA330792, 983946.2, 229097.at
 Figure 5152: PRO85956
 Figure 5153: DNA155281, DNA155281, 229111.at
 Figure 5154: DNA330793, 215114.2, 229145.at
 Figure 5155: PRO85957
 Figure 5156: DNA330794, 481414.8, 229202.at
 Figure 5157: PRO85958
 Figure 5158: DNA330795, BC017339, 229253.at
 Figure 5159: PRO85959
 Figure 5160: DNA265865, DNA265865, 229274.at
 Figure 5161: DNA151375, DNA151375, 229327.s.at
 Figure 5162: PRO11752
 Figure 5163: DNA328919, FLJ22690, 229367.s.at
 Figure 5164: PRO84637
 Figure 5165: DNA257575, DNA257575, 229374.at
 Figure 5166: DNA268708, DNA268708, 229391.s.at
 Figure 5167A-C: DNA331667, 198342.3, 229394.s.at
 Figure 5168: PRO86662
 Figure 5169: DNA287421, 234832.1, 229437.at
 Figure 5170: PRO69678
 Figure 5171: DNA330797, 211332.1, 229442.at
 Figure 5172: PRO85961
 Figure 5173: DNA328090, 007911.2, 229450.at
 Figure 5174: PRO84001
 Figure 5175: DNA330798, 984597.1, 229483.at
 Figure 5176: PRO85962
 Figure 5177: DNA330799, 481875.1, 229551.x.at
 Figure 5178: PRO85963
 Figure 5179: DNA330800, AK056271, 229595.at
 Figure 5180: PRO85964
 Figure 5181: DNA330801, 199864.1, 229610.at
 Figure 5182: PRO85965
 Figure 5183: DNA327205, NP_443174.1, 229625.at
 Figure 5184: PRO83478
 Figure 5185A-B: DNA226321, NP_006021.1, 229636.at
 Figure 5186: PRO36784

Figure 5187A-B: DNA330802, 7694410.1, 229686.at
 Figure 5188: PRO85966
 Figure 5189: DNA331668, 403448.4, 229699.at
 Figure 5190: PRO86663
 Figure 5191A-C: DNA330804, NP_055847.1, 229704.at
 Figure 5192: PRO85968
 Figure 5193: DNA331669, 1466538.1, 229718.at
 Figure 5194: PRO86664
 Figure 5195A-B: DNA227985, CBX6, 229733.s.at
 Figure 5196: PRO38448
 Figure 5197: DNA330806, 200298.1, 229809.at
 Figure 5198: PRO85970
 Figure 5199: DNA330807, 334422.1, 229814.at
 Figure 5200: PRO85971
 Figure 5201: DNA328092, NP_002598.2, 229830.at
 Figure 5202: PRO84003
 Figure 5203: DNA330808, 1397087.3, 229838.at
 Figure 5204: PRO85972
 Figure 5205: DNA328972, BC009950, 229872.s.at
 Figure 5206A-C: DNA330810, AF330041, 229881.at
 Figure 5207: PRO85974
 Figure 5208: DNA287290, AK001793, 229980.s.at
 Figure 5209: PRO69560
 Figure 5210: DNA330811, 1382987.2, 230000.at
 Figure 5211: PRO85975
 Figure 5212A-B: DNA330812, 000264.19, 230021.at
 Figure 5213: PRO85976
 Figure 5214: DNA330813, 246201.1, 230036.at
 Figure 5215: PRO85977
 Figure 5216: DNA258657, DNA258657, 230060.at
 Figure 5217: PRO52596
 Figure 5218: DNA330814, 309641.1, 230097.at
 Figure 5219: PRO85978
 Figure 5220: DNA329467, 029236.1, 230110.at
 Figure 5221: PRO85033
 Figure 5222: DNA330815, AK057940, 230165.at
 Figure 5223: PRO85979
 Figure 5224: DNA329468, BC011589, 230170.at
 Figure 5225: PRO88
 Figure 5226: DNA330816, 980409.1, 230192.at
 Figure 5227: PRO85980
 Figure 5228A-B: DNA194784, DNA194784, 230218.at
 Figure 5229: PRO24061
 Figure 5230: DNA331670, 373719.30, 230257.s.at
 Figure 5231: PRO86665
 Figure 5232A-C: DNA330817, AB020335, 230265.at
 Figure 5233: PRO85981
 Figure 5234: DNA330818, 212282.1, 230304.at
 Figure 5235: PRO85982
 Figure 5236: DNA330819, 982802.1, 230337.at
 Figure 5237: PRO85983
 Figure 5238: DNA330820, 230585.2, 230345.at
 Figure 5239: PRO85984
 Figure 5240: DNA329470, NP_002756.1, 230352.at
 Figure 5241: PRO85035
 Figure 5242: DNA331671, 277648.15, 230375.at
 Figure 5243: PRO86666
 Figure 5244: DNA331672, 332195.1, 230391.at
 Figure 5245: PRO86667
 Figure 5246: DNA257756, DNA257756, 230405.at
 Figure 5247: DNA330823, 010867.1, 230449.x.at
 Figure 5248: PRO85987
 Figure 5249A-B: DNA331673, 333480.5, 230489.at
 Figure 5250: PRO86668
 Figure 5251A-B: DNA330825, 406864.4, 230526.at
 Figure 5252: PRO85989
 Figure 5253: DNA331674, 059446.1, 230529.at
 Figure 5254: PRO86669
 Figure 5255: DNA330827, NP_079521.1, 230536.at
 Figure 5256: PRO85991
 Figure 5257: DNA330828, 233615.1, 230566.at
 Figure 5258: PRO85992
 Figure 5259: DNA330829, 007717.1, 230580.at
 Figure 5260: PRO85993
 Figure 5261: DNA257789, NP_116219.1, 230656.s.at
 Figure 5262: PRO52338
 Figure 5263: DNA330830, 216899.1, 230703.at
 Figure 5264: PRO85994
 Figure 5265A-B: DNA328499, SORL1, 230707.at
 Figure 5266: PRO84321
 Figure 5267A-B: DNA328099, 335889.1, 230779.at
 Figure 5268: PRO84009
 Figure 5269: DNA194391, HSM800477, 230848.s.at
 Figure 5270: DNA330831, 208876.1, 230913.at
 Figure 5271: PRO85995
 Figure 5272: DNA330832, 253831.5, 230930.at
 Figure 5273: PRO85996
 Figure 5274: DNA304827, AF293462, 230966.at
 Figure 5275: PRO1265
 Figure 5276: DNA330833, 984179.1, 230970.at
 Figure 5277: PRO85997
 Figure 5278: DNA331675, BC017477, 231094.s.at
 Figure 5279: PRO86670
 Figure 5280: DNA331676, 980781.1, 231109.at
 Figure 5281: PRO86671
 Figure 5282: DNA329473, 370473.13, 231124.x.at
 Figure 5283: PRO85038
 Figure 5284: DNA330835, 399441.1, 231166.at
 Figure 5285: PRO85999
 Figure 5286A-B: DNA330836, 242968.17, 231169.at
 Figure 5287: PRO86000
 Figure 5288: DNA330837, 429490.1, 231182.at
 Figure 5289: PRO86001
 Figure 5290: DNA150808, HUMGBP1, 231577.s.at
 Figure 5291: PRO12478
 Figure 5292: DNA155700, DNA155700, 231579.s.at
 Figure 5293: DNA330838, NP_037460.2, 231715.s.at
 Figure 5294: PRO80743
 Figure 5295: DNA330839, NP_060908.1, 231769.at
 Figure 5296: PRO86002

Figure 5297: DNA330840, BC015355, 231772.x.at
 Figure 5298: PRO86003
 Figure 5299: DNA208647, DNA208647, 231775.at
 Figure 5300: PRO1206
 Figure 5301: DNA330841, 983019.1, 231776.at
 Figure 5302: PRO86004
 Figure 5303: DNA329474, AK001874, 231784.s.at
 Figure 5304: PRO38893
 Figure 5305: DNA330842, 242234.14, 231793.s.at
 Figure 5306: PRO86005
 Figure 5307: DNA329312, AF414120, 231794.at
 Figure 5308: PRO84901
 Figure 5309: DNA330843, 201388.1, 231832.at
 Figure 5310: PRO86006
 Figure 5311A-B: DNA330844, 243553.2, 231852.at
 Figure 5312: PRO86007
 Figure 5313: DNA330845, BC009777, 231863.at
 Figure 5314: PRO86008
 Figure 5315A-B: DNA330846, BC005847, 231876.at
 Figure 5316: DNA331677, 981573.1, 231890.at
 Figure 5317: PRO86672
 Figure 5318: DNA330848, 1447268.2, 231904.at
 Figure 5319: PRO86011
 Figure 5320: DNA330849, EFG2, 231918.s.at
 Figure 5321: PRO86012
 Figure 5322A-B: DNA256267, BAB13444.1, 231956.at
 Figure 5323: PRO51311
 Figure 5324A-B: DNA271768, AB037834, 231996.at
 Figure 5325A-C: DNA330850, 152462.1, 232044.at
 Figure 5326: PRO86013
 Figure 5327: DNA330851, 337679.3, 232081.at
 Figure 5328: PRO86014
 Figure 5329: DNA330852, 1383611.1, 232138.at
 Figure 5330: PRO86015
 Figure 5331: DNA330853, 255956.19, 232141.at
 Figure 5332: PRO86016
 Figure 5333: DNA328113, 218535.1, 232150.at
 Figure 5334: PRO84020
 Figure 5335: DNA330854, AK023113, 232155.at
 Figure 5336: PRO86017
 Figure 5337: DNA331678, ABIN-2, 232160.s.at
 Figure 5338: PRO86673
 Figure 5339A-E: DNA331679, NP_112598.1, 232164.s.at
 Figure 5340: PRO86674
 Figure 5341: DNA330856, HSM802268, 232165.at
 Figure 5342: DNA330857, 271071.1, 232175.at
 Figure 5343: PRO86020
 Figure 5344: DNA330858, 252659.1, 232213.at
 Figure 5345: PRO86021
 Figure 5346: DNA330859, 016890.1, 232216.at
 Figure 5347: PRO86022
 Figure 5348: DNA331680, 393520.1, 232238.at
 Figure 5349: PRO86675
 Figure 5350: DNA330861, AK000490, 232278.s.at
 Figure 5351: PRO86024
 Figure 5352: DNA287658, 199168.2, 232291.at
 Figure 5353: PRO69902
 Figure 5354: DNA331681, 339154.9, 232304.at
 Figure 5355: PRO86676
 Figure 5356: DNA330863, 295041.1, 232365.at
 Figure 5357: PRO86026
 Figure 5358: DNA331682, 1384413.5, 232369.at
 Figure 5359: PRO86677
 Figure 5360: DNA287182, 424693.25, 232375.at
 Figure 5361: PRO69470
 Figure 5362: DNA330865, 066613.1, 232412.at
 Figure 5363: PRO86028
 Figure 5364: DNA331683, 422960.1, 232504.at
 Figure 5365: PRO86678
 Figure 5366: DNA330867, 333565.1, 232527.at
 Figure 5367: PRO86030
 Figure 5368: DNA331684, AF161339, 232543.x.at
 Figure 5369: DNA330868, 337037.1, 232584.at
 Figure 5370: PRO86031
 Figure 5371: DNA330869, 406591.1, 232687.at
 Figure 5372: PRO86032
 Figure 5373: DNA330870, 227719.1, 232883.at
 Figure 5374: PRO86033
 Figure 5375: DNA330871, 419923.1, 233019.at
 Figure 5376: PRO86034
 Figure 5377: DNA287404, AK026486, 233085.s.at
 Figure 5378: PRO69661
 Figure 5379: DNA330872, 056107.1, 233127.at
 Figure 5380: PRO86035
 Figure 5381A-B: DNA329422, BAA92605.1, 233208.x.at
 Figure 5382: PRO84993
 Figure 5383A-B: DNA330873, AB040885, 233458.at
 Figure 5384: DNA330874, NP_057528.1, 233461.x.at
 Figure 5385: PRO86037
 Figure 5386: DNA331423, AF176071, 233467.s.at
 Figure 5387: DNA330875, 006221.2, 233506.at
 Figure 5388: PRO86038
 Figure 5389: DNA330876, AK055587, 233528.s.at
 Figure 5390: PRO86039
 Figure 5391: DNA328812, AB033087, 233575.s.at
 Figure 5392: DNA330877, NP_055075.1, 233588.x.at
 Figure 5393: PRO86040
 Figure 5394A-C: DNA330638, HSM801490, 233632.s.at
 Figure 5395: DNA329287, NP_057484.2, 233746.x.at
 Figure 5396: PRO84879
 Figure 5397: DNA329481, ASB2, 233857.s.at
 Figure 5398: PRO60949
 Figure 5399: DNA326800, XRN2, 233878.s.at
 Figure 5400: PRO83133
 Figure 5401: DNA330547, MOV10, 233917.s.at
 Figure 5402: PRO85731
 Figure 5403: DNA330878, NP_079111.1, 233937.at
 Figure 5404: PRO86041

Figure 5405: DNA329571, HSPC195, 233955.x.at
 Figure 5406: PRO51662
 Figure 5407: DNA329332, BC001262, 233970.s.at
 Figure 5408: PRO84916
 Figure 5409: DNA331685, AK026111, 233986.s.at
 Figure 5410: PRO86680
 Figure 5411: DNA331686, HSA271091, 234000.s.at
 Figure 5412: PRO86681
 Figure 5413: DNA331687, HUMVA25A, 234013.at
 Figure 5414: PRO86682
 Figure 5415: DNA330880, NP_150283.1, 234284.at
 Figure 5416: PRO86043
 Figure 5417: DNA330881, CRACC, 234306.s.at
 Figure 5418: PRO1138
 Figure 5419: DNA329312, CTLA4, 234362.s.at
 Figure 5420: PRO84901
 Figure 5421: DNA329483, NP_443104.1, 234408.at
 Figure 5422: PRO20110
 Figure 5423: DNA287425, NP_060979.1, 234464.s.at
 Figure 5424: PRO69682
 Figure 5425: DNA330387, FBXO5, 234863.x.at
 Figure 5426: PRO85596
 Figure 5427: DNA304813, NP_277053.1, 234973.at
 Figure 5428: PRO71222
 Figure 5429: DNA330882, 406739.1, 234974.at
 Figure 5430: PRO86044
 Figure 5431: DNA330883, 1384547.1, 234986.at
 Figure 5432: PRO86045
 Figure 5433A-B: DNA330884, 267153.16, 234987.at
 Figure 5434: PRO86046
 Figure 5435: DNA257389, NP_116248.1, 234993.at
 Figure 5436: PRO51974
 Figure 5437: DNA330885, AK055618, 235022.at
 Figure 5438: PRO86047
 Figure 5439: DNA331688, 404157.1, 235052.at
 Figure 5440: PRO86683
 Figure 5441: DNA331689, 996962.6, 235056.at
 Figure 5442: PRO86684
 Figure 5443: DNA328143, AK054678, 235061.at
 Figure 5444: PRO84018
 Figure 5445: DNA330888, 7687712.2, 235088.at
 Figure 5446: PRO69581
 Figure 5447: DNA330889, AK055762, 235096.at
 Figure 5448: PRO86050
 Figure 5449: DNA193891, DNA193891, 235099.at
 Figure 5450: PRO23309
 Figure 5451A-B: DNA330890, AB058722, 235106.at
 Figure 5452: DNA330891, AK027315, 235113.at
 Figure 5453: PRO86052
 Figure 5454: DNA328146, BC019239, 235117.at
 Figure 5455: PRO84051
 Figure 5456: DNA330892, 198067.4, 235136.at
 Figure 5457: PRO86053
 Figure 5458: DNA330893, 337392.1, 235157.at
 Figure 5459: PRO86054
 Figure 5460: DNA329486, 1058246.1, 235175.at
 Figure 5461: PRO85047
 Figure 5462: DNA330894, AF455817, 235177.at
 Figure 5463: PRO86055
 Figure 5464: DNA331690, 200228.1, 235199.at
 Figure 5465: PRO86685
 Figure 5466: DNA330896, 250896.1, 235213.at
 Figure 5467: PRO86057
 Figure 5468: DNA329488, 1501300.6, 235244.at
 Figure 5469: PRO85049
 Figure 5470A-C: DNA330897, 332999.23, 235252.at
 Figure 5471: PRO86058
 Figure 5472: DNA324093, BC019263, 235256.s.at
 Figure 5473: PRO80802
 Figure 5474: DNA260946, NP_115741.1, 235266.at
 Figure 5475: PRO54699
 Figure 5476A-C: DNA329379, 010205.2, 235287.at
 Figure 5477: PRO84957
 Figure 5478: DNA330898, 227608.1, 235299.at
 Figure 5479: PRO86059
 Figure 5480A-B: DNA330899, 7690822.1, 235306.at
 Figure 5481: PRO86060
 Figure 5482A-B: DNA330900, 199492.10, 235331.x.at
 Figure 5483: PRO86061
 Figure 5484: DNA330901, 400258.1, 235360.at
 Figure 5485: PRO86062
 Figure 5486: DNA330902, 481462.4, 235389.at
 Figure 5487: PRO86063
 Figure 5488: DNA331691, 405045.1, 235412.at
 Figure 5489: PRO86686
 Figure 5490: DNA330904, 1446121.1, 235415.at
 Figure 5491: PRO86065
 Figure 5492: DNA331692, 979330.2, 235425.at
 Figure 5493: PRO86687
 Figure 5494: DNA257872, DNA257872, 235457.at
 Figure 5495: DNA330906, NP_116171.2, 235458.at
 Figure 5496: PRO86067
 Figure 5497: DNA257302, DNA257302, 235463.s.at
 Figure 5498: DNA330907, 7692322.1, 235469.at
 Figure 5499: PRO86068
 Figure 5500: DNA331693, 203586.1, 235508.at
 Figure 5501: PRO86688
 Figure 5502: DNA330909, 229234.17, 235523.at
 Figure 5503: PRO86070
 Figure 5504: DNA304793, NP_443173.1, 235574.at
 Figure 5505: PRO71205
 Figure 5506: DNA330910, 032253.1, 235581.at
 Figure 5507: PRO86071
 Figure 5508: DNA330911, 1446080.1, 235607.at
 Figure 5509: PRO86072
 Figure 5510: DNA330912, 984873.1, 235609.at
 Figure 5511: PRO86073
 Figure 5512: DNA331694, 222666.9, 235643.at
 Figure 5513: PRO86689
 Figure 5514: DNA331695, 350462.1, 235652.at
 Figure 5515: PRO86690

Figure 5516: DNA330915, 238456.7, 235662.at
 Figure 5517: PRO86076
 Figure 5518: DNA330916, 234580.1, 235670.at
 Figure 5519: PRO86077
 Figure 5520: DNA330917, 238496.1, 235696.at
 Figure 5521: PRO86078
 Figure 5522: DNA330918, 250552.1, 235699.at
 Figure 5523: PRO86079
 Figure 5524: DNA330919, 423261.6, 235739.at
 Figure 5525: PRO86080
 Figure 5526: DNA330920, 249518.17, 235783.at
 Figure 5527: PRO86081
 Figure 5528: DNA330921, 246858.18, 235816.s.at
 Figure 5529: PRO86082
 Figure 5530: DNA330922, 1447139.1, 235907.at
 Figure 5531: PRO86083
 Figure 5532: DNA330923, 981520.1, 235940.at
 Figure 5533: PRO86084
 Figure 5534: DNA330924, 237828.3, 235984.at
 Figure 5535: PRO86085
 Figure 5536: DNA330925, 257787.1, 235985.at
 Figure 5537: PRO86086
 Figure 5538: DNA330926, 1446421.2, 236079.at
 Figure 5539: PRO86087
 Figure 5540: DNA330927, 1499766.1, 236156.at
 Figure 5541: PRO86088
 Figure 5542A-E: DNA328165, 327340.35, 236172.at
 Figure 5543: PRO38220
 Figure 5544: DNA330928, 227714.1, 236180.at
 Figure 5545: PRO86089
 Figure 5546: DNA329489, 338163.1, 236280.at
 Figure 5547: PRO85050
 Figure 5548: DNA257767, DNA257767, 236285.at
 Figure 5549: DNA288255, 236339.1, 236295.s.at
 Figure 5550: PRO70016
 Figure 5551: DNA331696, 215451.1, 236338.at
 Figure 5552: PRO86691
 Figure 5553: DNA329490, 267918.1, 236347.at
 Figure 5554: PRO85051
 Figure 5555: DNA330930, 407665.1, 236379.at
 Figure 5556: PRO86091
 Figure 5557: DNA331697, 342862.1, 236419.at
 Figure 5558: PRO86692
 Figure 5559: DNA330932, 231907.4, 236470.at
 Figure 5560: PRO86093
 Figure 5561: DNA330933, 407881.1, 236506.at
 Figure 5562: PRO86094
 Figure 5563: DNA330934, 406491.1, 236595.at
 Figure 5564: PRO86095
 Figure 5565: DNA330935, 229915.1, 236610.at
 Figure 5566: PRO86096
 Figure 5567A-C: DNA330936, 351043.1, 236641.at
 Figure 5568: PRO86097
 Figure 5569: DNA330937, 205124.1, 236645.at
 Figure 5570: PRO86098
 Figure 5571: DNA330938, 7688127.1, 236668.at
 Figure 5572: PRO86099
 Figure 5573: DNA259749, DNA259749, 236782.at
 Figure 5574: DNA329491, 211743.1, 236787.at
 Figure 5575: PRO85052
 Figure 5576: DNA330939, 214517.1, 236796.at
 Figure 5577: PRO86100
 Figure 5578: DNA330940, 211136.19, 236832.at
 Figure 5579: PRO86101
 Figure 5580: DNA330941, 399601.2, 236836.at
 Figure 5581: PRO86102
 Figure 5582: DNA330942, 337215.1, 236907.at
 Figure 5583: PRO86103
 Figure 5584: DNA330943, 1042935.2, 237009.at
 Figure 5585: PRO86104
 Figure 5586: DNA330944, 218030.2, 237180.at
 Figure 5587: PRO86105
 Figure 5588: DNA330945, 334209.1, 237181.at
 Figure 5589: PRO86106
 Figure 5590A-B: DNA226536, TFRC.237215.s.at
 Figure 5591: PRO36999
 Figure 5592: DNA330946, 023719.1, 237626.at
 Figure 5593: PRO86107
 Figure 5594: DNA331698, 341647.1, 237741.at
 Figure 5595: PRO86693
 Figure 5596: DNA330948, 305319.1, 237746.at
 Figure 5597: PRO86109
 Figure 5598: DNA330949, 089765.7, 237759.at
 Figure 5599: PRO86110
 Figure 5600: DNA331699, 983684.2, 237953.at
 Figure 5601: PRO86694
 Figure 5602: DNA330951, 253376.3, 238012.at
 Figure 5603: PRO86112
 Figure 5604A-B: DNA330952, 333610.10, 238021.s.at
 Figure 5605: PRO86113
 Figure 5606: DNA330953, BC019600, 238063.at
 Figure 5607: DNA331700, 983399.1, 238082.at
 Figure 5608: PRO86695
 Figure 5609: DNA330955, 311471.1, 238303.at
 Figure 5610: PRO86115
 Figure 5611: DNA330956, 329762.1, 238311.at
 Figure 5612: PRO86116
 Figure 5613: DNA329493, 337072.5, 238423.at
 Figure 5614: PRO85054
 Figure 5615: DNA108695, DNA108695, 238508.at
 Figure 5616: PRO9743
 Figure 5617: DNA330957, 003538.1, 238509.at
 Figure 5618: PRO86117
 Figure 5619: DNA330958, 370339.1, 238541.at
 Figure 5620: PRO86118
 Figure 5621: DNA330959, 358161.17, 238545.at
 Figure 5622: PRO86119
 Figure 5623: DNA260158, DNA260158, 238551.at
 Figure 5624: DNA329495, 1447201.1, 238581.at
 Figure 5625: PRO85056
 Figure 5626: DNA329496, AK056126, 238600.at

Figure 5627: PRO85057
 Figure 5628: DNA329497, 232064.1, 238619.at
 Figure 5629: PRO85058
 Figure 5630: DNA330960, 001782.1, 238633.at
 Figure 5631: PRO86120
 Figure 5632: DNA330961, 903323.1, 238651.at
 Figure 5633: PRO86121
 Figure 5634A-B: DNA329499, 332504.1, 238778.at
 Figure 5635: PRO85060
 Figure 5636: DNA330962, 336371.2, 238893.at
 Figure 5637: PRO86122
 Figure 5638A-B: DNA330963, 241110.10, 238910.at
 Figure 5639: PRO86123
 Figure 5640: DNA331701, 337114.1, 238913.at
 Figure 5641: PRO86696
 Figure 5642: DNA330965, NP_443111.2, 238960.s.at
 Figure 5643: PRO86125
 Figure 5644: DNA330966, 213271.1, 238987.at
 Figure 5645: PRO86126
 Figure 5646: DNA330967, 1499563.1, 238996.x.at
 Figure 5647: PRO86127
 Figure 5648: DNA330968, 005876.1, 239002.at
 Figure 5649: PRO86128
 Figure 5650: DNA328194, 998827.1, 239049.at
 Figure 5651: PRO84097
 Figure 5652: DNA331702, 406864.3, 239062.at
 Figure 5653: PRO86697
 Figure 5654: DNA330970, 026912.1, 239081.at
 Figure 5655: PRO86130
 Figure 5656: DNA330971, 413731.1, 239096.at
 Figure 5657: PRO86131
 Figure 5658A-B: DNA330972, 141588.42, 239133.at
 Figure 5659: PRO86132
 Figure 5660: DNA330973, NP_003328.1, 239163.at
 Figure 5661: PRO10751
 Figure 5662: DNA330974, 348211.8, 239219.at
 Figure 5663: PRO86133
 Figure 5664: DNA330975, 207267.3, 239278.at
 Figure 5665: PRO86134
 Figure 5666: DNA330976, 023223.1, 239328.at
 Figure 5667: PRO86135
 Figure 5668: DNA329501, 205323.1, 239331.at
 Figure 5669: PRO85062
 Figure 5670: DNA330977, 996962.2, 239364.at
 Figure 5671: PRO86136
 Figure 5672: DNA330978, 039840.1, 239376.at
 Figure 5673: PRO86137
 Figure 5674: DNA330979, 407730.7, 239388.at
 Figure 5675: PRO86138
 Figure 5676: DNA330980, 1134871.2, 239401.at
 Figure 5677: PRO86139
 Figure 5678: DNA330981, 406409.1, 239404.at
 Figure 5679: PRO86140
 Figure 5680: DNA330982, 980479.1, 239413.at
 Figure 5681: PRO86141
 Figure 5682: DNA328200, 405394.1, 239442.at
 Figure 5683: PRO84103
 Figure 5684: DNA330983, 305289.1, 239448.at
 Figure 5685: PRO86142
 Figure 5686: DNA330984, 015432.1, 239476.at
 Figure 5687: PRO86143
 Figure 5688: DNA330985, 317098.1, 239494.at
 Figure 5689: PRO86144
 Figure 5690: DNA330986, 215812.1, 239533.at
 Figure 5691: PRO86145
 Figure 5692: DNA330987, 116344.1, 239655.at
 Figure 5693: PRO86146
 Figure 5694: DNA330988, 333476.1, 239680.at
 Figure 5695: PRO86147
 Figure 5696: DNA330989, 298825.1, 239695.at
 Figure 5697: PRO86148
 Figure 5698: DNA330990, 004652.1, 239721.at
 Figure 5699: PRO86149
 Figure 5700: DNA330991, 017874.1, 239757.at
 Figure 5701: PRO86150
 Figure 5702: DNA330992, AK027783, 239771.at
 Figure 5703: PRO86151
 Figure 5704: DNA330993, 1439890.1, 239803.at
 Figure 5705: PRO86152
 Figure 5706: DNA330994, NP_115730.1, 239824.s.at
 Figure 5707: PRO86153
 Figure 5708A-C: DNA330995, 233142.9, 239897.at
 Figure 5709: PRO84857
 Figure 5710: DNA258952, DNA258952, 239901.at
 Figure 5711: DNA257698, DNA257698, 240070.at
 Figure 5712: DNA328206, 1384214.3, 240277.at
 Figure 5713: PRO84109
 Figure 5714: DNA330996, 144353.1, 240347.at
 Figure 5715: PRO86154
 Figure 5716: DNA331703, 314831.10, 240452.at
 Figure 5717: PRO86698
 Figure 5718: DNA330998, 979930.1, 240665.at
 Figure 5719: PRO86156
 Figure 5720: DNA330999, 1454193.1, 240830.at
 Figure 5721: PRO86157
 Figure 5722: DNA331000, 7693121.3, 240890.at
 Figure 5723: PRO86158
 Figure 5724: DNA331704, CARS, 240983.s.at
 Figure 5725: PRO86699
 Figure 5726: DNA329504, 197187.1, 241365.at
 Figure 5727: PRO85065
 Figure 5728: DNA331001, 1499887.1, 241370.at
 Figure 5729: PRO86159
 Figure 5730: DNA331002, 231340.1, 241435.at
 Figure 5731: PRO86160
 Figure 5732: DNA331003, 391185.30, 241495.at
 Figure 5733: PRO86161
 Figure 5734: DNA331004, 314498.1, 241505.at
 Figure 5735: PRO86162
 Figure 5736: DNA331005, 197725.1, 241722.x.at
 Figure 5737: PRO86163
 Figure 5738: DNA329505, BC017102, 241734.at

Figure 5739: DNA331006, 193718.1, 241740.at
 Figure 5740: PRO86164
 Figure 5741: DNA331007, 405858.1, 241756.at
 Figure 5742: PRO86165
 Figure 5743: DNA331705, 428179.1, 241775.at
 Figure 5744: PRO86700
 Figure 5745: DNA195721, DNA195721, 241819.at
 Figure 5746: DNA331009, 222011.1, 241824.at
 Figure 5747: PRO86167
 Figure 5748: DNA331010, 218800.1, 241843.at
 Figure 5749: PRO86168
 Figure 5750: DNA331011, 979953.1, 241859.at
 Figure 5751: PRO86169
 Figure 5752: DNA331012, 030070.1, 241869.at
 Figure 5753: PRO86170
 Figure 5754: DNA331013, 406509.1, 241924.at
 Figure 5755: PRO86171
 Figure 5756: DNA329506, NP_387510.1, 241937.s.at
 Figure 5757: PRO85067
 Figure 5758: DNA331014, 1447958.2, 241985.at
 Figure 5759: PRO86172
 Figure 5760: DNA331015, 109159.1, 242031.at
 Figure 5761: PRO86173
 Figure 5762: DNA331016, 229438.1, 242051.at
 Figure 5763: PRO86174
 Figure 5764: DNA328213, 419856.5, 242059.at
 Figure 5765: PRO84116
 Figure 5766: DNA331017, 409906.7, 242060.x.at
 Figure 5767: PRO86175
 Figure 5768: DNA331018, 355930.1, 242110.at
 Figure 5769: PRO86176
 Figure 5770: DNA331019, 234788.2, 242245.at
 Figure 5771: PRO86177
 Figure 5772: DNA331020, 403459.1, 242261.at
 Figure 5773: PRO86178
 Figure 5774: DNA331021, 017309.1, 242268.at
 Figure 5775: PRO86179
 Figure 5776: DNA331022, BC009627, 242304.at
 Figure 5777: DNA331023, 119753.1, 242362.at
 Figure 5778: PRO86181
 Figure 5779: DNA331024, 028992.1, 242388.x.at
 Figure 5780: PRO86182
 Figure 5781: DNA328220, 239839.1, 242405.at
 Figure 5782: PRO84123
 Figure 5783: DNA331025, 127891.1, 242457.at
 Figure 5784: PRO86183
 Figure 5785: DNA328221, 221374.1, 242471.at
 Figure 5786: PRO84124
 Figure 5787: DNA257874, DNA257874, 242517.at
 Figure 5788: DNA331026, 014632.1, 242518.at
 Figure 5789: PRO86184
 Figure 5790: DNA331027, 053796.1, 242560.at
 Figure 5791: PRO86185
 Figure 5792: DNA331028, 7693434.1, 242606.at
 Figure 5793: PRO86186
 Figure 5794: DNA331706, 351474.1, 242617.at
 Figure 5795: PRO86701
 Figure 5796: DNA331707, 330870.5, 242625.at
 Figure 5797: PRO86702
 Figure 5798: DNA331030, 407930.2, 242648.at
 Figure 5799: PRO86188
 Figure 5800: DNA331031, 405967.1, 242669.at
 Figure 5801: PRO86189
 Figure 5802A-C: DNA331708, NP_006258.2, 242712.x.at
 Figure 5803: PRO86703
 Figure 5804A-C: DNA331033, AF330045, 242722.at
 Figure 5805: PRO86191
 Figure 5806: DNA331034, 7689086.1, 242735.x.at
 Figure 5807: PRO86192
 Figure 5808: DNA331035, 210512.1, 242783.at
 Figure 5809: PRO86193
 Figure 5810: DNA331036, 360991.1, 242836.at
 Figure 5811: PRO86194
 Figure 5812: DNA328224, 028975.1, 242859.at
 Figure 5813: PRO84127
 Figure 5814: DNA331037, 206873.1, 242890.at
 Figure 5815: PRO86195
 Figure 5816: DNA331709, 017276.1, 242903.at
 Figure 5817: PRO86704
 Figure 5818: DNA331710, 227540.15, 242960.at
 Figure 5819: PRO86705
 Figure 5820: DNA331711, 427600.1, 243006.at
 Figure 5821: PRO86706
 Figure 5822: DNA331041, 982079.2, 243030.at
 Figure 5823: PRO86199
 Figure 5824: DNA331042, 019764.1, 243037.at
 Figure 5825: PRO86200
 Figure 5826: DNA331043, 005042.1, 243134.at
 Figure 5827: PRO86201
 Figure 5828: DNA331044, 226264.10, 243154.at
 Figure 5829: PRO86202
 Figure 5830: DNA331045, 066434.1, 243222.at
 Figure 5831: PRO86203
 Figure 5832: DNA331712, 005752.1, 243271.at
 Figure 5833: PRO86707
 Figure 5834: DNA331047, BC020624, 243362.s.at
 Figure 5835: DNA331048, 7688599.1, 243366.s.at
 Figure 5836: PRO86206
 Figure 5837: DNA331049, 402027.4, 243395.at
 Figure 5838: PRO86207
 Figure 5839: DNA331713, 982999.2, 243423.at
 Figure 5840: PRO86708
 Figure 5841: DNA331051, 306804.1, 243469.at
 Figure 5842: PRO86209
 Figure 5843: DNA331714, 332965.1, 243496.at
 Figure 5844: PRO86709
 Figure 5845: DNA331053, 243689.1, 243509.at
 Figure 5846: PRO86211
 Figure 5847: DNA331715, 7683458.1, 243514.at
 Figure 5848: PRO86710
 Figure 5849: DNA331055, 1512996.3, 243561.at

Figure 5850: PRO86213
 Figure 5851: DNA258957, DNA258957, 243631.at
 Figure 5852: DNA331056, 218946.1, 243759.at
 Figure 5853: PRO86214
 Figure 5854: DNA194184, DNA194184, 243764.at
 Figure 5855: PRO23576
 Figure 5856: DNA331057, 031316.1, 243888.at
 Figure 5857: PRO86215
 Figure 5858: DNA331058, 400813.1, 243918.at
 Figure 5859: PRO86216
 Figure 5860: DNA331059, 035870.32, 243934.at
 Figure 5861: PRO86217
 Figure 5862: DNA210271, DNA210271, 243999.at
 Figure 5863: PRO33803
 Figure 5864A-B: DNA331060, 406931.1, 244008.at
 Figure 5865: PRO86218
 Figure 5866: DNA331061, 198683.4, 244026.at
 Figure 5867: PRO86219
 Figure 5868: DNA331062, BC021973, 244052.at
 Figure 5869: PRO23771
 Figure 5870: DNA331716, 212607.1, 244267.at
 Figure 5871: PRO86711
 Figure 5872: DNA331064, 006039.1, 244313.at
 Figure 5873: PRO86221
 Figure 5874: DNA108738, DNA108738, 244321.at
 Figure 5875: PRO9822
 Figure 5876: DNA331065, 341348.1, 244382.at
 Figure 5877: PRO86222
 Figure 5878: DNA331066, 207228.1, 244443.at
 Figure 5879: PRO86223
 Figure 5880: DNA328239, 331922.4, 244450.at
 Figure 5881: PRO84142
 Figure 5882: DNA331067, 164869.1, 244599.at
 Figure 5883: PRO86224
 Figure 5884: DNA331068, 337465.1, 244677.at
 Figure 5885: PRO86225
 Figure 5886: DNA329512, 336575.1, 244780.at
 Figure 5887: PRO85073
 Figure 5888: DNA331069, 008651.1, 244798.at
 Figure 5889: PRO86226
 Figure 5890: DNA331070, 393412.1, 244801.at
 Figure 5891: PRO86227
 Figure 5892: DNA331071, 343563.1, 244869.at
 Figure 5893: PRO86228
 Figure 5894A-B: DNA254566, BAA11502.1, D80007.at
 Figure 5895: PRO49669
 Figure 5896: DNA328961, BC011049, DNA36995.at
 Figure 5897: PRO84667
 Figure 5898A-B: DNA331072, AB046821, DNA53991.at
 Figure 5899: DNA327200, KSP37, DNA59602.at
 Figure 5900: PRO1065
 Figure 5901: DNA327205, GBP5, DNA61875.at
 Figure 5902: PRO83478
 Figure 5903: DNA331717, BC020203, DNA71289.at
 Figure 5904: PRO86712
 Figure 5905: DNA331718, AK024409, DNA92232.at
 Figure 5906: PRO86713
 Figure 5907: DNA96866, DNA96866, DNA96866.at
 Figure 5908: PRO6015
 Figure 5909: DNA331073, BC011775, DNA101926.at
 Figure 5910: PRO86229
 Figure 5911: DNA108670, DNA108670, DNA108670.at
 Figure 5912: PRO7171
 Figure 5913: DNA304467, BC004535, DNA108688.at
 Figure 5914: PRO71043
 Figure 5915A-B: DNA108728, DNA108728, DNA108728.at
 Figure 5916: PRO9741
 Figure 5917: DNA329215, ICOS, DNA108917.at
 Figure 5918: PRO7424
 Figure 5919: DNA331719, BC002424, DNA143288.at
 Figure 5920: PRO12705
 Figure 5921A-B: DNA150956, HUMORFKG1P, DNA150956.at
 Figure 5922: DNA330417, APOL6, DNA164989.at
 Figure 5923: PRO21341
 Figure 5924: DNA329483, AF384857, DNA166819.at
 Figure 5925: PRO20110
 Figure 5926: DNA26842, DNA26842, P.Z64949.at
 Figure 5927: PRO180
 Figure 5928: DNA304468, NP.077300.1, P.Z93700.at
 Figure 5929: PRO71044
 Figure 5930: DNA39423, DNA39423, P.X52252.at
 Figure 5931: PRO271
 Figure 5932: DNA330262, GW112, P.Z64962.at
 Figure 5933: PRO85493
 Figure 5934: DNA331074, AF252257, P.A37030.at
 Figure 5935: DNA60764, DNA60764, P.A46906.at
 Figure 5936: PRO1265
 Figure 5937: DNA331720, AF289594, P.A37063.at
 Figure 5938: PRO86714
 Figure 5939: DNA331721, BC017876, P.A37079.at
 Figure 5940: PRO71045
 Figure 5941: DNA76401, DNA76401, P.A37126.at
 Figure 5942: PRO1575
 Figure 5943: DNA304475, NP.116246.1, P.A37128.at
 Figure 5944: PRO71049
 Figure 5945: DNA66480, HSAPO1, NM.000043.at
 Figure 5946: PRO1207
 Figure 5947: DNA88195, CD3G, NM.000073.at
 Figure 5948: PRO2693
 Figure 5949: DNA325712, CDK4, NM.000075.at
 Figure 5950: PRO82194
 Figure 5951: DNA329934, BC013083, NM.000099.at
 Figure 5952: PRO2721
 Figure 5953A-B: DNA331722, HUMFVA, NM.000130.at
 Figure 5954: PRO36374
 Figure 5955: DNA331723, U66095, NM.000161.at

Figure 5956: PRO86715
 Figure 5957: DNA227668, HUMGLYKINB, NM.000167.at
 Figure 5958: PRO38131
 Figure 5959A-D: DNA331724, HSGLA, NM.000169.at
 Figure 5960: DNA331725, BC006342, NM.000175.at
 Figure 5961: DNA150823, NP.000185.1, NM.000194.at
 Figure 5962: PRO12810
 Figure 5963: DNA331726, HUMICAMA1A, NM.000201.at
 Figure 5964: PRO86716
 Figure 5965A-B: DNA88419, HSINTA6R, NM.000210.at
 Figure 5966: PRO2339
 Figure 5967: DNA88428, HUMLAP, NM.000211.at
 Figure 5968: PRO2787
 Figure 5969: DNA226014, NP.000230.1, NM.000239.at
 Figure 5970: PRO36477
 Figure 5971: DNA97287, NP.000240.1, NM.000249.at
 Figure 5972: PRO3634
 Figure 5973: DNA88554, NP.000241.1, NM.000250.at
 Figure 5974: PRO2839
 Figure 5975: DNA331727, BC008015, NM.000269.at
 Figure 5976: PRO37534
 Figure 5977A-E: DNA331728, PTEN4, NM.000314.at
 Figure 5978: DNA83020, NP.000349.1, NM.000358.at
 Figure 5979: PRO2561
 Figure 5980: DNA227081, EGR2, NM.000399.at
 Figure 5981: PRO37544
 Figure 5982: DNA76512, HSIL2REC, NM.000417.at
 Figure 5983: PRO2020
 Figure 5984: DNA76514, HSIL4R, NM.000418.at
 Figure 5985: PRO2540
 Figure 5986: DNA329522, NP.000433.2, NM.000442.at
 Figure 5987: PRO85080
 Figure 5988: DNA188732, NP.000475.1, NM.000484.at
 Figure 5989: PRO25302
 Figure 5990: DNA331729, AF281258, NM.000517.at
 Figure 5991: DNA331730, BC014514, NM.000527.at
 Figure 5992: PRO2915
 Figure 5993: DNA331731, HSASM2MR, NM.000543.at
 Figure 5994: DNA76516, IL6R, NM.000565.at
 Figure 5995: PRO2022
 Figure 5996: DNA36718, HUMIL10, NM.000572.at
 Figure 5997: PRO73
 Figure 5998: DNA324158, NP.000567.1, NM.000576.at
 Figure 5999: PRO65
 Figure 6000A-B: DNA331732, HSCCR5AB2, NM.000579.at
 Figure 6001: PRO25194
 Figure 6002: DNA290585, NP.000573.1, NM.000582.f.at
 Figure 6003: PRO70536
 Figure 6004: DNA216500, NP.000575.1, NM.000584.at
 Figure 6005: PRO34252
 Figure 6006: DNA36712, HUMIL3, NM.000588.at
 Figure 6007: PRO67
 Figure 6008A-B: DNA331733, AF361105, NM.000590.at
 Figure 6009: DNA331734, BC014081, NM.000593.at
 Figure 6010: PRO36996
 Figure 6011A-B: DNA331735, AY066019, NM.000594.at
 Figure 6012A-B: DNA331736, AY070490, NM.000595.at
 Figure 6013: DNA331737, BC009902, NM.000597.at
 Figure 6014: PRO2587
 Figure 6015: DNA217246, NP.000591.1, NM.000600.at
 Figure 6016: PRO34288
 Figure 6017: DNA331075, NP.000601.2, NM.000610.at
 Figure 6018: PRO86231
 Figure 6019A-C: DNA331738, AF375790, NM.000619.at
 Figure 6020A-B: DNA220752, TTGAM, NM.000632.at
 Figure 6021: PRO34730
 Figure 6022A-B: DNA97288, HUMBCL2C, NM.000633.at
 Figure 6023: PRO3635
 Figure 6024: DNA331739, A12178, NM.000636.at
 Figure 6025: PRO86720
 Figure 6026: DNA331740, HUMHPC, NM.000639.at
 Figure 6027: PRO1208
 Figure 6028: DNA329000, HSU03905, NM.000647.at
 Figure 6029: PRO84690
 Figure 6030: DNA328253, NP.0004029.1, NM.000699.at
 Figure 6031: PRO84149
 Figure 6032: DNA89242, ANXA1, NM.000700.at
 Figure 6033: PRO2907
 Figure 6034: DNA88194, CD3E, NM.000733.at
 Figure 6035: PRO2220
 Figure 6036: DNA329975, PRO2325, NM.000791.at
 Figure 6037: DNA331741, BC003097, NM.000873.at
 Figure 6038: PRO86721
 Figure 6039: DNA331076, HSIIFNABR, NM.000874.at
 Figure 6040: PRO86232
 Figure 6041A-B: DNA83101, NP.000868.1,

NM_000877.at
 Figure 6042: PRO2590
 Figure 6043A-B: DNA76508, A07795, NM_000878.at
 Figure 6044: PRO2538
 Figure 6045: DNA36714, NP_000870.1, NM_000879.at
 Figure 6046: PRO69
 Figure 6047A-B: DNA88417, HSINTAL4, NM_000885.at
 Figure 6048: PRO2337
 Figure 6049: DNA88433, HUMINTB7A, NM_000889.at
 Figure 6050: PRO2346
 Figure 6051: DNA226053, NP_000908.1, NM_000917.at
 Figure 6052: PRO36516
 Figure 6053A-B: DNA331742, BC018127, NM_000919.at
 Figure 6054: PRO86722
 Figure 6055: DNA227709, PTGER2, NM_000956.at
 Figure 6056: PRO38172
 Figure 6057: DNA226195, NP_000949.1, NM_000958.at
 Figure 6058: PRO36658
 Figure 6059: DNA327639, TCN1, NM_001062.at
 Figure 6060: PRO83640
 Figure 6061A-B: DNA150748, ADCY7, NM_001114.at
 Figure 6062: PRO12446
 Figure 6063: DNA171404, IISU45878, NM_001165.at
 Figure 6064: PRO20132
 Figure 6065: DNA331743, AAA19687.1, NM_001168.at
 Figure 6066: PRO12242
 Figure 6067A-B: DNA325972, BC018739, NM_001211.at
 Figure 6068: PRO82417
 Figure 6069: DNA287267, CCNA2, NM_001237.at
 Figure 6070: PRO37015
 Figure 6071: DNA196674, D86042, NM_001243.at
 Figure 6072: PRO2938
 Figure 6073: DNA325568, BC017575, NM_001274.at
 Figure 6074: PRO12187
 Figure 6075: DNA226177, CCR1, NM_001295.at
 Figure 6076: PRO36640
 Figure 6077: DNA331744, CTSW, NM_001335.at
 Figure 6078: PRO1574
 Figure 6079: DNA93466, HUMEDG, NM_001400.at
 Figure 6080: PRO4936
 Figure 6081: DNA331745, HSU77085, NM_001423.at
 Figure 6082: PRO12467
 Figure 6083A-C: DNA151167, HSABP280, NM_001456.at
 Figure 6084: PRO12867
 Figure 6085A-C: DNA331746, AF043045, NM_001457.at
 Figure 6086: PRO86723
 Figure 6087: DNA188346, FLT3LG, NM_001459.at
 Figure 6088: PRO21766
 Figure 6089: DNA227173, HSU93049, NM_001465.at
 Figure 6090: PRO37636
 Figure 6091A-B: DNA331747, GABBR1, NM_001470.at
 Figure 6092: PRO86724
 Figure 6093A-B: DNA76503, IL10RA, NM_001558.at
 Figure 6094: PRO2536
 Figure 6095A-B: DNA227750, IL12RB2, NM_001559.at
 Figure 6096: PRO38213
 Figure 6097: DNA76556, HSU03397, NM_001561.at
 Figure 6098: PRO2023
 Figure 6099: DNA82362, CXCL10, NM_001565.at
 Figure 6100: PRO1718
 Figure 6101: DNA227013, NP_001560.1, NM_001569.at
 Figure 6102: PRO37476
 Figure 6103: DNA331748, BC009799, NM_001657.at
 Figure 6104: PRO46
 Figure 6105: DNA150716, HSZNFNPRA, NM_001706.at
 Figure 6106: PRO12790
 Figure 6107: DNA331077, HUMBGPAB, NM_001712.at
 Figure 6108: PRO86233
 Figure 6109: DNA150718, NP_001727.1, NM_001736.at
 Figure 6110: PRO12435
 Figure 6111A-B: DNA226387, HSCYCLF, NM_001761.at
 Figure 6112: PRO36850
 Figure 6113: DNA329002, CCT6A, NM_001762.at
 Figure 6114: PRO4912
 Figure 6115: DNA226380, HSCD37, NM_001774.at
 Figure 6116: PRO4695
 Figure 6117: DNA331749, D84277, NM_001775.at
 Figure 6118: PRO86725
 Figure 6119: DNA88199, HUMMEMGL1, NM_001778.at
 Figure 6120: PRO2696
 Figure 6121: DNA226436, CD69, NM_001781.at
 Figure 6122: PRO36899
 Figure 6123: DNA331750, A23013, NM_001803.at
 Figure 6124: PRO2496
 Figure 6125: DNA151798, NP_001797.1, NM_001806.at
 Figure 6126: PRO12186
 Figure 6127: DNA227232, SLC31A1, NM_001859.at
 Figure 6128: PRO37695
 Figure 6129: DNA331751, S68134, NM_001881.at
 Figure 6130: PRO86726
 Figure 6131: DNA331078, NP_001894.1, NM_001903.at

Figure 6132: PRO86234
 Figure 6133: DNA331752, BC010240, NM_001908.at
 Figure 6134: PRO86727
 Figure 6135: DNA225810, HSCATHL, NM_001912.at
 Figure 6136: PRO36273
 Figure 6137: DNA83048, DEFA4, NM_001925.at
 Figure 6138: PRO2057
 Figure 6139: DNA88215, NP_001919.1, NM_001928.at
 Figure 6140: PRO2703
 Figure 6141: DNA196562, HSPCHDP7, NM_001935.at
 Figure 6142: PRO25042
 Figure 6143: DNA226871, NP_001942.1, NM_001951.at
 Figure 6144: PRO37334
 Figure 6145: DNA227332, NP_001943.1, NM_001952.at
 Figure 6146: PRO37795
 Figure 6147: DNA225661, ECGF1, NM_001953.at
 Figure 6148: PRO36124
 Figure 6149: DNA273174, HSEF1DELA, NM_001960.at
 Figure 6150: PRO61211
 Figure 6151: DNA150779, HUMFTR103, NM_001964.at
 Figure 6152: PRO12798
 Figure 6153: DNA331753, HUMENOG, NM_001975.at
 Figure 6154: PRO38010
 Figure 6155: DNA331754, BC002464, NM_001992.at
 Figure 6156: PRO86728
 Figure 6157: DNA331755, D83920, NM_002003.at
 Figure 6158: PRO86729
 Figure 6159: DNA226881, HUMERGBFLI, NM_002017.at
 Figure 6160: PRO37344
 Figure 6161: DNA88332, FVT1, NM_002035.at
 Figure 6162: PRO2753
 Figure 6163: DNA225979, G1P3, NM_002038.at
 Figure 6164: PRO36442
 Figure 6165: DNA331756, BC002666, NM_002053.at
 Figure 6166: PRO12478
 Figure 6167: DNA88374, GZMK, NM_002104.at
 Figure 6168: PRO2768
 Figure 6169: DNA228014, ICAM3, NM_002162.at
 Figure 6170: PRO38477
 Figure 6171: DNA331757, A17548, NM_002167.at
 Figure 6172: PRO86730
 Figure 6173: DNA76517, IL7R, NM_002185.at
 Figure 6174: PRO2541
 Figure 6175: DNA188271, NP_002179.1, NM_002188.at
 Figure 6176: PRO21795
 Figure 6177: DNA226396, IL15RA, NM_002189.at
 Figure 6178: PRO36859
 Figure 6179: DNA227014, NP_002190.1, NM_002199.at
 Figure 6180: PRO37477
 Figure 6181A-B: DNA88427, HSFNRB, NM_002211.at
 Figure 6182: PRO2786
 Figure 6183: DNA103215, NP_002210.1, NM_002219.at
 Figure 6184: PRO4545
 Figure 6185: DNA331758, S82269, NM_002222.at
 Figure 6186: PRO86731
 Figure 6187: DNA331759, BC002646, NM_002228.at
 Figure 6188: PRO4671
 Figure 6189: DNA331760, BC009466, NM_002229.at
 Figure 6190: PRO4650
 Figure 6191A-B: DNA331761, AF305731S5, NM_002250.at
 Figure 6192: DNA150971, KLRB1, NM_002258.at
 Figure 6193: PRO12564
 Figure 6194: DNA326343, BC003572, NM_002265.at
 Figure 6195: PRO82739
 Figure 6196: DNA288243, LAG3, NM_002286.at
 Figure 6197: PRO36451
 Figure 6198A-B: DNA188301, LIF, NM_002309.at
 Figure 6199: PRO21834
 Figure 6200A-B: DNA331762, HUMLYTOXBB, NM_002341.at
 Figure 6201: DNA88666, NP_002334.1, NM_002343.at
 Figure 6202: PRO2892
 Figure 6203: DNA227150, LY6E, NM_002346.at
 Figure 6204: PRO37613
 Figure 6205: DNA327255, BC001061, NM_002394.at
 Figure 6206: PRO57298
 Figure 6207: DNA150937, HSU94352, NM_002405.at
 Figure 6208: PRO11598
 Figure 6209: DNA82376, CXCL9, NM_002416.at
 Figure 6210: PRO1723
 Figure 6211: DNA103283, MINDA, NM_002432.at
 Figure 6212: PRO4613
 Figure 6213: DNA103525, NP_002457.1, NM_002466.at
 Figure 6214: PRO4852
 Figure 6215A-B: DNA331763, AF058696, NM_002485.at
 Figure 6216: PRO36001
 Figure 6217: DNA103382, HSU49395, NM_002561.at
 Figure 6218: PRO4711
 Figure 6219A-B: DNA88331, HSFUR, NM_002569.at
 Figure 6220: PRO2752
 Figure 6221: DNA103488, PCNA, NM_002592.at
 Figure 6222: PRO4815
 Figure 6223: DNA328587, NP_002612.1, NM_002621.at
 Figure 6224: PRO2854
 Figure 6225: DNA331764, NP_071438.1,

NM.002624.at
 Figure 6226: PRO86732
 Figure 6227: DNA227067, IISPKCB1A,
 NM.002738.at
 Figure 6228: PRO37530
 Figure 6229: DNA227090, NP.002750.1,
 NM.002759.at
 Figure 6230: PRO37553
 Figure 6231: DNA88626, HUMSAPABCD,
 NM.002778.at
 Figure 6232: PRO2875
 Figure 6233: DNA329098, BC007897, NM.002808.at
 Figure 6234: PRO84749
 Figure 6235: DNA326853, NP.002818.1,
 NM.002827.at
 Figure 6236: PRO38066
 Figure 6237: DNA88607, NP.002892.1,
 NM.002901.at
 Figure 6238: PRO2863
 Figure 6239: DNA331765, AF294009, NM.002934.at
 Figure 6240: PRO2444
 Figure 6241: DNA331766, AF043339, NM.002983.at
 Figure 6242: DNA51778, HSHC21, NM.002984.at
 Figure 6243: PRO80
 Figure 6244: DNA330124, CCL22, NM.002990.at
 Figure 6245: PRO34107
 Figure 6246: DNA227788, NP.002995.1,
 NM.003004.at
 Figure 6247: PRO38251
 Figure 6248: DNA329095, IISPKCB1A, NM.003037.at
 Figure 6249: PRO12612
 Figure 6250: DNA196489, HUMMCT, NM.003051.at
 Figure 6251: PRO24980
 Figure 6252A-B: DNA103542, HSLR11,
 NM.003105.at
 Figure 6253: PRO4869
 Figure 6254: DNA331767, D78130, NM.003129.at
 Figure 6255: PRO37946
 Figure 6256: DNA328259, AF029311, NM.003150.at
 Figure 6257: DNA227447, HSTCF1C, NM.003202.at
 Figure 6258: PRO37910
 Figure 6259A-B: DNA226536, HSTRR,
 NM.003234.at
 Figure 6260: PRO36999
 Figure 6261A-B: DNA83176, TGFBR3,
 NM.003243.at
 Figure 6262: PRO2620
 Figure 6263: DNA103532, TM7SF1, NM.003272.at
 Figure 6264: PRO4859
 Figure 6265A-B: DNA103585, HUMTOPI,
 NM.003286.at
 Figure 6266: PRO4909
 Figure 6267: DNA331768, BC007935, NM.003316.at
 Figure 6268: PRO22907
 Figure 6269: DNA331769, AF065241, NM.003329.at
 Figure 6270A-B: DNA331770, AF019563,
 NM.003332.at
 Figure 6271: DNA331771, HSU76367, NM.003355.at
 Figure 6272: PRO86733
 Figure 6273: DNA151906, HSUNG, NM.003362.f.at
 Figure 6274: PRO12214
 Figure 6275: DNA103380, HUMVDAC1X,
 NM.003374.at
 Figure 6276: PRO4710
 Figure 6277: DNA225992, NP.003374.1,
 NM.003383.at
 Figure 6278: PRO36455
 Figure 6279: DNA227330, NP.003443.1,
 NM.003452.at
 Figure 6280: PRO37793
 Figure 6281: DNA93449, AF025375, NM.003467.at
 Figure 6282: PRO4516
 Figure 6283: DNA331772, BC010022, NM.003504.at
 Figure 6284: PRO71058
 Figure 6285: DNA331773, AF123318, NM.003550.at
 Figure 6286: PRO86734
 Figure 6287: DNA331079, AF036342, NM.003650.at
 Figure 6288: PRO1191
 Figure 6289: DNA338260, AF305428, NM.003661.at
 Figure 6290: PRO84152
 Figure 6291: DNA151802, AB004066, NM.003670.at
 Figure 6292: PRO12890
 Figure 6293: DNA227213, NP.003671.1,
 NM.003680.at
 Figure 6294: PRO37676
 Figure 6295: DNA331774, AK001769, NM.003730.at
 Figure 6296: PRO86735
 Figure 6297: DNA150433, AB005043, NM.003745.at
 Figure 6298: PRO12771
 Figure 6299: DNA328377, NP.003759.1,
 NM.003768.at
 Figure 6300: PRO84232
 Figure 6301: DNA194746, HSM800355,
 NM.003798.at
 Figure 6302: DNA196431, AF064090, NM.003807.at
 Figure 6303: PRO5810
 Figure 6304: DNA61870, HSU57059, NM.003810.at
 Figure 6305: PRO1096
 Figure 6306A-B: DNA200236, NP.003807.1,
 NM.003816.at
 Figure 6307: PRO34137
 Figure 6308: DNA331775, BC000334, NM.003824.at
 Figure 6309: PRO4801
 Figure 6310: DNA331080, NP.003835.2,
 NM.003844.at
 Figure 6311: PRO86235
 Figure 6312: DNA225550, IL18RAP, NM.003853.at
 Figure 6313: PRO36013
 Figure 6314: DNA103451, IL18R1, NM.003855.at
 Figure 6315: PRO4778
 Figure 6316: DNA151011, AF037989, NM.003877.at
 Figure 6317: PRO12839

Figure 6318: DNA331776, IER3, NM.003897.at
 Figure 6319: PRO84760
 Figure 6320A-B: DNA150765, SLC7A6, NM.003983.at
 Figure 6321: PRO12458
 Figure 6322: DNA88308, HUMFCREA, NM.004106.at
 Figure 6323: PRO2739
 Figure 6324A-B: DNA331777, AF200219S2, NM.004107.at
 Figure 6325: DNA227133, GBP2, NM.004120.at
 Figure 6326: PRO37596
 Figure 6327: DNA83091, HUMSP13E, NM.004131.at
 Figure 6328: PRO2081
 Figure 6329A-B: DNA151108, SREBF1, NM.004176.at
 Figure 6330: PRO12105
 Figure 6331: DNA218676, AF125304, NM.004195.at
 Figure 6332: PRO34454
 Figure 6333: DNA103394, HSU81800, NM.004207.at
 Figure 6334: PRO4722
 Figure 6335: DNA329533, BC018782, NM.004221.at
 Figure 6336: PRO85085
 Figure 6337: DNA331778, AK027513, NM.004265.at
 Figure 6338: PRO86736
 Figure 6339: DNA151142, NP.004321.1, NM.004330.at
 Figure 6340: PRO12110
 Figure 6341: DNA227303, NP.004322.1, NM.004331.at
 Figure 6342: PRO37766
 Figure 6343: DNA287240, BST2, NM.004335.at
 Figure 6344: PRO29371
 Figure 6345: DNA225910, NP.004336.1, NM.004345.at
 Figure 6346: PRO36373
 Figure 6347: DNA331779, CASP3, NM.004346.at
 Figure 6348: PRO12832
 Figure 6349A-B: DNA326191, NP.004351.1, NM.004360.at
 Figure 6350: PRO2672
 Figure 6351A-C: DNA150729, IISU47741, NM.004380.at
 Figure 6352: PRO12147
 Figure 6353A-B: DNA151420, S40832, NM.004430.at
 Figure 6354: PRO12876
 Figure 6355A-B: DNA218283, EPHB6, NM.004445.at
 Figure 6356: PRO34335
 Figure 6357: DNA331780, BC003110, NM.004512.at
 Figure 6358: PRO4843
 Figure 6359: DNA150935, NP.004547.1, NM.004556.at
 Figure 6360: PRO12155
 Figure 6361A-B: DNA151831, NP.004564.1, NM.004573.at
 Figure 6362: PRO12198
 Figure 6363: DNA328262, HSU57094, NM.004580.at
 Figure 6364: PRO84153
 Figure 6365: DNA331781, HSU77035, NM.004591.at
 Figure 6366: PRO1724
 Figure 6367: DNA331782, HUMVAIPR, NM.004624.at
 Figure 6368: DNA329984, WRB, NM.004627.at
 Figure 6369: PRO11656
 Figure 6370: DNA329119, NP.004633.1, NM.004642.at
 Figure 6371: PRO4550
 Figure 6372: DNA328578, NP.004656.2, NM.004665.at
 Figure 6373: PRO7426
 Figure 6374: DNA331783, BC011726, NM.004706.at
 Figure 6375: PRO86737
 Figure 6376: DNA218284, AF053004, NM.004843.at
 Figure 6377: PRO34336
 Figure 6378: DNA151017, AB005047, NM.004844.at
 Figure 6379: PRO12841
 Figure 6380A-B: DNA150447, AB011098, NM.004863.at
 Figure 6381: PRO12256
 Figure 6382: DNA88295, HUMERP72H, NM.004911.at
 Figure 6383: PRO2733
 Figure 6384: DNA331784, AB001325, NM.004925.at
 Figure 6385: PRO38028
 Figure 6386A-B: DNA331785, DSC1, NM.004948.at
 Figure 6387: PRO36355
 Figure 6388: DNA227563, NP.004946.1, NM.004955.at
 Figure 6389: PRO38026
 Figure 6390: DNA331786, HUMSTPK13, NM.005030.at
 Figure 6391: PRO86738
 Figure 6392: DNA329011, BCL3, NM.005178.at
 Figure 6393: PRO4785
 Figure 6394: DNA331787, AF213050, NM.005192.at
 Figure 6395: PRO86739
 Figure 6396: DNA103330, HUMPOPSTK, NM.005204.at
 Figure 6397: PRO4660
 Figure 6398: DNA331788, HUMIGCTL3, NM.005214.at
 Figure 6399: DNA325060, NP.004075.1, NM.005217.at
 Figure 6400: PRO2570
 Figure 6401: DNA331789, HSCFOS, NM.005252.at
 Figure 6402: DNA304668, HSPA1A, NM.005346.at
 Figure 6403: PRO71095
 Figure 6404: DNA331790, HUMCMYBA, NM.005375.at
 Figure 6405: DNA227376, NP.005393.1,

NM.005402.at
 Figure 6406: PRO37839
 Figure 6407: DNA331791, BC005292, NM.005409.at
 Figure 6408: PRO19838
 Figure 6409: DNA329319, TOSO, NM.005449.at
 Figure 6410: PRO1607
 Figure 6411A-B: DNA189702, AF047348, NM.005503.at
 Figure 6412: PRO22775
 Figure 6413: DNA150989, HSP27, NM.005532.at
 Figure 6414: PRO12569
 Figure 6415A-C: DNA331792, HUMOP18A, NM.005563.at
 Figure 6416: DNA97285, LDHA, NM.005566.at
 Figure 6417: PRO3632
 Figure 6418: DNA225675, LMAN1, NM.005570.at
 Figure 6419: PRO36138
 Figure 6420: DNA331793, AF148645, NM.005614.at
 Figure 6421: PRO37938
 Figure 6422: DNA331794, BC001263, NM.005627.at
 Figure 6423: PRO86741
 Figure 6424: DNA226500, NP.005619.1, NM.005628.at
 Figure 6425: PRO36963
 Figure 6426A-B: DNA227206, NP.005648.1, NM.005657.at
 Figure 6427: PRO37669
 Figure 6428: DNA323937, NP.005689.2, NM.005698.at
 Figure 6429: PRO80670
 Figure 6430: DNA331081, NP.005714.2, NM.005723.at
 Figure 6431: PRO4845
 Figure 6432: DNA304459, PPIF, NM.005729.at
 Figure 6433: PRO37073
 Figure 6434A-B: DNA331082, AF057299, NM.005732.at
 Figure 6435: PRO86236
 Figure 6436: DNA88541, PBEF, NM.005746.at
 Figure 6437: PRO2834
 Figure 6438: DNA329014, EBI3, NM.005755.at
 Figure 6439: PRO9998
 Figure 6440: DNA93548, NP.005758.1, NM.005767.at
 Figure 6441: PRO4929
 Figure 6442: DNA331083, NP.005759.2, NM.005768.at
 Figure 6443: PRO86237
 Figure 6444: DNA193866, AF081675, NM.005810.at
 Figure 6445: PRO23288
 Figure 6446: DNA75525, GPA33, NM.005814.at
 Figure 6447: PRO2524
 Figure 6448A-B: DNA88650, TACTILE, NM.005816.at
 Figure 6449: PRO2460
 Figure 6450: DNA150959, NP.005813.1, NM.005822.at
 Figure 6451: PRO11599
 Figure 6452: DNA329538, BC001731, NM.005898.at
 Figure 6453: PRO85088
 Figure 6454: DNA324110, MDH1, NM.005917.at
 Figure 6455: PRO4918
 Figure 6456: DNA328266, NP.005993.1, NM.006002.at
 Figure 6457: PRO12125
 Figure 6458: DNA150941, NP.006012.1, NM.006021.at
 Figure 6459: PRO12548
 Figure 6460: DNA227138, NP.006045.1, NM.006054.at
 Figure 6461: PRO37601
 Figure 6462: DNA88614, HSRING6, NM.006120.at
 Figure 6463: PRO2867
 Figure 6464: DNA331795, NP.006129.2, NM.006138.at
 Figure 6465: PRO81984
 Figure 6466: DNA331796, HUMCD284, NM.006139.at
 Figure 6467: DNA330114, GPR19, NM.006143.at
 Figure 6468: PRO4946
 Figure 6469: DNA88372, HUMHSP, NM.006144.at
 Figure 6470: PRO2312
 Figure 6471: DNA103526, HSU10485, NM.006152.at
 Figure 6472: PRO4853
 Figure 6473: DNA331797, BC020544, NM.006159.at
 Figure 6474: PRO2520
 Figure 6475: DNA151049, S74017, NM.006164.at
 Figure 6476: PRO12170
 Figure 6477A-B: DNA151841, HUMA20, NM.006290.at
 Figure 6478: PRO12904
 Figure 6479: DNA331798, TSG101, NM.006292.at
 Figure 6480: PRO86742
 Figure 6481: DNA83109, HUMIIP, NM.006332.at
 Figure 6482: PRO2592
 Figure 6483: DNA331799, AY034481, NM.006372.at
 Figure 6484: PRO83688
 Figure 6485: DNA329540, UBD, NM.006398.at
 Figure 6486: PRO85090
 Figure 6487: DNA331800, BC007107, NM.006406.at
 Figure 6488: PRO12111
 Figure 6489: DNA331801, BC012589, NM.006419.at
 Figure 6490: PRO21708
 Figure 6491: DNA227795, CCT7, NM.006429.at
 Figure 6492: PRO38258
 Figure 6493: DNA329225, BC005926, NM.006495.at
 Figure 6494: PRO84833
 Figure 6495: DNA327702, AF074002, NM.006499.at
 Figure 6496: PRO83684
 Figure 6497: DNA151804, RELB, NM.006509.at
 Figure 6498: PRO12188
 Figure 6499A-B: DNA331802, AF012108,

NM.006534.at
 Figure 6500: PRO86743
 Figure 6501: DNA93439, HSY13248, NM.006564.at
 Figure 6502: PRO4515
 Figure 6503: DNA227751, NP.006557.1, NM.006566.at
 Figure 6504: PRO38214
 Figure 6505: DNA227126, NP.006559.1, NM.006568.at
 Figure 6506: PRO37589
 Figure 6507: DNA331803, AF116456, NM.006573.at
 Figure 6508: PRO738
 Figure 6509: DNA331804, BC001572, NM.006579.at
 Figure 6510: PRO12082
 Figure 6511: DNA324740, NP.006577.1, NM.006586.at
 Figure 6512: PRO81365
 Figure 6513: DNA331805, HSM801976, NM.006620.at
 Figure 6514: PRO86744
 Figure 6515: DNA328544, HSFIBLP, NM.006682.at
 Figure 6516: PRO84347
 Figure 6517: DNA227035, HUMHUMCM5, NM.006739.at
 Figure 6518: PRO37498
 Figure 6519: DNA227512, NP.006736.1, NM.006745.at
 Figure 6520: PRO37975
 Figure 6521A-B: DNA331806, AB005666, NM.006747.at
 Figure 6522: PRO86745
 Figure 6523: DNA227416, NP.006745.1, NM.006754.at
 Figure 6524: PRO37879
 Figure 6525: DNA331807, HSU30498, NM.006762.at
 Figure 6526: PRO86746
 Figure 6527: DNA227190, NP.006830.1, NM.006839.at
 Figure 6528: PRO37653
 Figure 6529: DNA150812, RTVP1, NM.006851.at
 Figure 6530: PRO12481
 Figure 6531: DNA331808, HSU82278, NM.006866.at
 Figure 6532: PRO86747
 Figure 6533: DNA103221, NP.006866.1, NM.006875.at
 Figure 6534: PRO4551
 Figure 6535: DNA328271, ZWINT, NM.007057.at
 Figure 6536: PRO81868
 Figure 6537: DNA331809, NP.009046.1, NM.007115.at
 Figure 6538: PRO86748
 Figure 6539: DNA103587, HSMRL3R, NM.007208.at
 Figure 6540: PRO4911
 Figure 6541: DNA330180, TRC8, NM.007218.at
 Figure 6542: PRO85428
 Figure 6543: DNA331810, HSU64805, NM.007295.at
 Figure 6544: PRO23937
 Figure 6545: DNA331086, AB027467, NM.012112.at
 Figure 6546: PRO86239
 Figure 6547A-B: DNA226290, HSU28811, NM.012201.at
 Figure 6548: PRO36753
 Figure 6549: DNA227143, NP.036400.1, NM.012268.at
 Figure 6550: PRO37606
 Figure 6551A-B: DNA150955, NP.036420.1, NM.012288.at
 Figure 6552: PRO12559
 Figure 6553: DNA331811, AF083247, NM.012328.at
 Figure 6554: PRO1471
 Figure 6555A-B: DNA227255, STAG3, NM.012447.at
 Figure 6556: PRO37718
 Figure 6557: DNA304476, NP.036585.1, NM.012453.at
 Figure 6558: PRO1125
 Figure 6559: DNA88510, HSNKG5, NM.012483.at
 Figure 6560: PRO2822
 Figure 6561: DNA103418, AF032862, NM.012484.at
 Figure 6562: PRO4746
 Figure 6563: DNA88189, HUMCD24B, NM.013230.at
 Figure 6564: PRO2690
 Figure 6565: DNA331812, BC019883, NM.013269.at
 Figure 6566: PRO86749
 Figure 6567: DNA103481, HUMAUANTIG, NM.013285.at
 Figure 6568: PRO4808
 Figure 6569: DNA196426, H963, NM.013308.at
 Figure 6570: PRO24924
 Figure 6571A-B: DNA329017, AF035947, NM.013324.at
 Figure 6572: PRO84692
 Figure 6573: DNA150648, HIG2, NM.013332.at
 Figure 6574: PRO11576
 Figure 6575A-B: DNA331813, AF213467, NM.013448.at
 Figure 6576: PRO86750
 Figure 6577: DNA304461, HSPC067, NM.014158.at
 Figure 6578: PRO71039
 Figure 6579: DNA331814, BC009642, NM.014164.at
 Figure 6580: PRO86751
 Figure 6581: DNA330374, ORMDL2, NM.014182.at
 Figure 6582: PRO23321
 Figure 6583: DNA88203, CD5, NM.014207.at
 Figure 6584: PRO2698
 Figure 6585A-B: DNA331815, AF135372, NM.014232.at
 Figure 6586: DNA331816, BC003067, NM.014330.at
 Figure 6587: PRO12543
 Figure 6588: DNA331817, NP.055154.2, NM.014339.at

Figure 6589: PRO86240
 Figure 6590: DNA227233, NP_055157.1, NM_014342.at
 Figure 6591: PRO37696
 Figure 6592: DNA227351, AF191020, NM_014367.at
 Figure 6593: PRO37814
 Figure 6594: DNA331088, NP_055252.2, NM_014437.at
 Figure 6595: PRO80674
 Figure 6596: DNA330084, SIT, NM_014450.at
 Figure 6597: PRO9895
 Figure 6598: DNA324198, NP_055400.1, NM_014585.at
 Figure 6599: PRO37675
 Figure 6600A-B: DNA151879, NP_055463.1, NM_014648.at
 Figure 6601: PRO12743
 Figure 6602: DNA194805, NP_055500.1, NM_014685.at
 Figure 6603: PRO24075
 Figure 6604A-B: DNA150467, AB018335, NM_014698.at
 Figure 6605: PRO12272
 Figure 6606A-B: DNA194778, KIAA0152, NM_014730.at
 Figure 6607: PRO24056
 Figure 6608A-B: DNA277809, KIAA0275, NM_014767.at
 Figure 6609: PRO64556
 Figure 6610A-B: DNA227353, SEC24D, NM_014822.at
 Figure 6611: PRO37816
 Figure 6612: DNA93507, NP_055694.1, NM_014879.at
 Figure 6613: PRO4948
 Figure 6614A-B: DNA150954, KIAA0022, NM_014880.at
 Figure 6615: PRO12558
 Figure 6616A-B: DNA227293, DNA227293, NM_014883.at
 Figure 6617: PRO37756
 Figure 6618: DNA150805, FAM3C, NM_014888.at
 Figure 6619: PRO11583
 Figure 6620A-B: DNA194837, NP_055714.1, NM_014899.at
 Figure 6621: PRO24100
 Figure 6622A-B: DNA304464, CHSY1, NM_014918.at
 Figure 6623: PRO71042
 Figure 6624: DNA330103, MD-2, NM_015364.at
 Figure 6625: PRO19671
 Figure 6626: DNA150872, NP_056202.1, NM_015387.at
 Figure 6627: PRO12814
 Figure 6628: DNA328590, BC001232, NM_015864.at
 Figure 6629: PRO84375
 Figure 6630: DNA196569, NP_056957.1, NM_015873.at
 Figure 6631: PRO19859
 Figure 6632: DNA150865, LOC51596, NM_015921.at
 Figure 6633: PRO11587
 Figure 6634: DNA150832, NP_057019.2, NM_015935.at
 Figure 6635: PRO12491
 Figure 6636: DNA331089, NP_057143.1, NM_016059.at
 Figure 6637: PRO4984
 Figure 6638: DNA331818, AF151899, NM_016072.at
 Figure 6639: PRO793
 Figure 6640: DNA328663, AK001280, NM_016073.at
 Figure 6641: PRO36183
 Figure 6642: DNA331819, BC006807, NM_016077.at
 Figure 6643: PRO38080
 Figure 6644: DNA150661, LOC51030, NM_016078.at
 Figure 6645: PRO12398
 Figure 6646: DNA329292, AF085360, NM_016101.at
 Figure 6647: PRO84882
 Figure 6648: DNA329923, HSPC035, NM_016127.at
 Figure 6649: PRO85237
 Figure 6650: DNA304832, NP_057327.1, NM_016243.at
 Figure 6651: PRO71239
 Figure 6652: DNA328831, AF126780, NM_016245.at
 Figure 6653: PRO233
 Figure 6654: DNA328513, AF151895, NM_016283.at
 Figure 6655: PRO37815
 Figure 6656: DNA304781, LOC51184, NM_016301.at
 Figure 6657: PRO71191
 Figure 6658: DNA331820, BC001144, NM_016306.at
 Figure 6659: PRO1080
 Figure 6660: DNA331821, AK023410, NM_016354.at
 Figure 6661: PRO86752
 Figure 6662: DNA330390, AF178985, NM_016546.at
 Figure 6663: PRO85599
 Figure 6664: DNA331822, AF318357, NM_016553.at
 Figure 6665: PRO86753
 Figure 6666: DNA227298, NP_057649.1, NM_016565.at
 Figure 6667: PRO37761
 Figure 6668: DNA327869, NRN1, NM_016588.at
 Figure 6669: PRO1898
 Figure 6670: DNA331823, AK027682, NM_017424.at
 Figure 6671: PRO86754
 Figure 6672: DNA225694, FLJ20005, NM_017617.at
 Figure 6673: PRO36157
 Figure 6674: DNA326385, NP_060117.2, NM_017647.at
 Figure 6675: PRO82778
 Figure 6676: DNA287206, FLJ20073, NM_017654.at
 Figure 6677: PRO69488
 Figure 6678: DNA227294, FLJ20303, NM_017755.at
 Figure 6679: PRO37757

Figure 6680: DNA226646, NP_060352.1,
NM_017882.at

Figure 6681: PRO37109

Figure 6682: DNA331824, BC010907, NM_017906.at

Figure 6683: PRO86755

Figure 6684: DNA330537, HELLS, NM_018063.at

Figure 6685: PRO81892

Figure 6686: DNA328628, BC011983, NM_018072.at

Figure 6687: PRO84406

Figure 6688: DNA328841, BC003082, NM_018087.at

Figure 6689: PRO84575

Figure 6730: DNA327199, DJ971N18.2,
NM_021156.at

Figure 6731: PRO83475

Figure 6732: DNA227276, NP_005702.1,
NM_021618.at

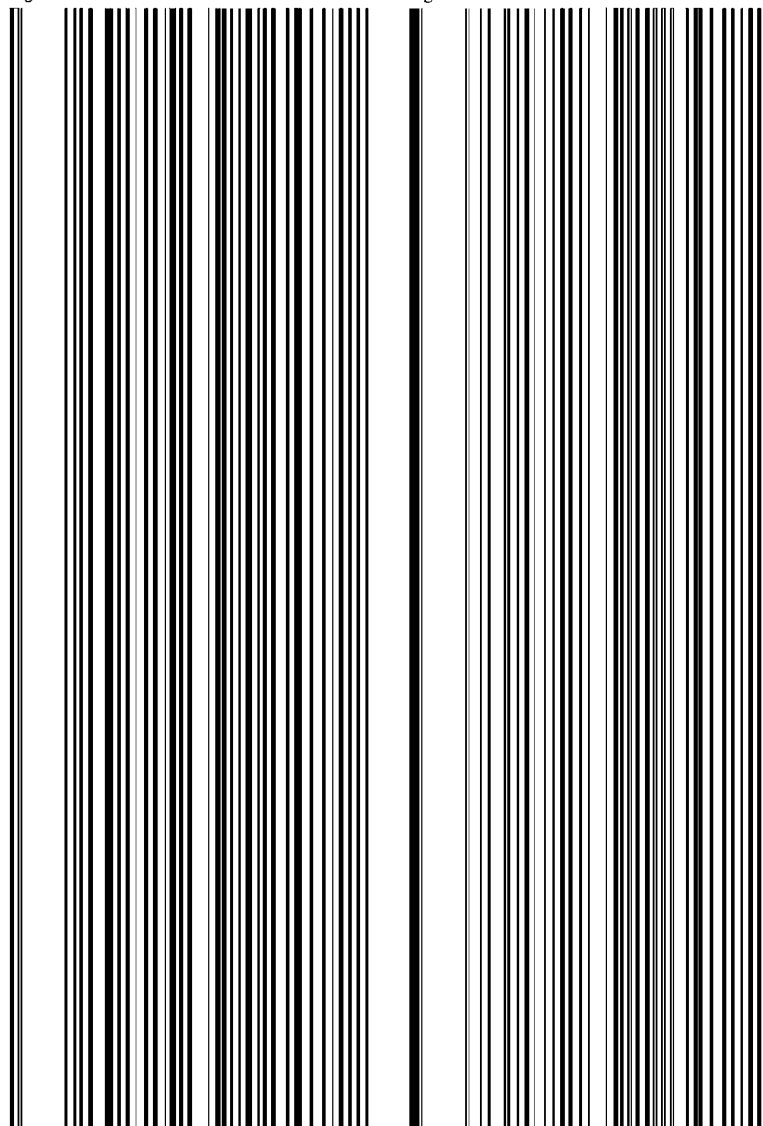
Figure 6733: PRO37739

Figure 6734A-B: DNA331832, AF051850,
NM_021738.at

Figure 6735: PRO86758

Figure 6736: DNA331833, AF269133, NM_021798.at

Figure 6737: PRO86759



HUMKG1BB.at
 Figure 6776: PRO86762
 Figure 6777A-B: DNA331842, BC004375, AF261758.at
 Figure 6778: PRO38492
 Figure 6779: DNA331095, NP_005216.1, HUME2F.at
 Figure 6780: PRO86245
 Figure 6781: DNA331843, AF202723, AB014568.at
 Figure 6782: DNA159542, DNA159542, HUMMAC30X.at
 Figure 6783: DNA331844, BC009267, HUMLAMBBA.at
 Figure 6784: PRO82888
 Figure 6785: DNA331096, S75881, P_V84330.at
 Figure 6786: PRO86246
 Figure 6787: DNA287239, AF212242, AK024843.at
 Figure 6788: PRO38497
 Figure 6789: DNA154390, DNA154390, HUMPI3KIN.at
 Figure 6790: DNA151247, DNA151247, P_V43601.at
 Figure 6791: PRO11643
 Figure 6792: DNA329950, MGC5576, P_V43613.at
 Figure 6793: PRO11558
 Figure 6794: DNA161927, DNA161927, P_Z29229.at
 Figure 6795: DNA155316, DNA155316, P_A09058.at
 Figure 6796: DNA329026, AF230200, AK021966.at
 Figure 6797A-B: DNA228052, DNA228052, AB006624.at
 Figure 6798: PRO38515
 Figure 6799: DNA161913, DNA161913, HSM800208.at
 Figure 6800: DNA331845, AK027432, HSM800284.at
 Figure 6801: PRO86763
 Figure 6802: DNA329430, SPPL2A, AX027882.at
 Figure 6803: PRO38524
 Figure 6804: DNA151422, DNA151422, P_X04312.at
 Figure 6805: PRO11792
 Figure 6806: DNA228066, NP_079431.1, AK021910.at
 Figure 6807: PRO38529
 Figure 6808A-C: DNA330360, FYCO1, AK023397.at
 Figure 6809: PRO85576
 Figure 6810: DNA287185, DNA287185, P_V84564.at
 Figure 6811: PRO37492
 Figure 6812: DNA331846, AF272741, HUMTCBYY.at
 Figure 6813: DNA331097, AK027322, AX041977.at
 Figure 6814: PRO86247
 Figure 6815: DNA151756, DNA151756, P_X84947.at
 Figure 6816: PRO12037
 Figure 6817: DNA151761, DNA151761, P_X84970.at
 Figure 6818: PRO12039
 Figure 6819: DNA331847, BC008330, AK026632.at
 Figure 6820: PRO38556
 Figure 6821: DNA326258, MGC2941, AK026537.at
 Figure 6822: PRO82665
 Figure 6823A-B: DNA287330, AB032991, AB032991.at
 Figure 6824: DNA331848, I510819.1, P_X99863.at
 Figure 6825: PRO86764
 Figure 6826: DNA331849, HSINSP4BP, HSINSP4BP.at
 Figure 6827: PRO66285
 Figure 6828A-B: DNA331850, HSA237724, HSA237724.at
 Figure 6829: DNA328049, 981676.1, HSM800856.at
 Figure 6830: PRO83963
 Figure 6831: DNA331851, AK027334, P_A51904.at
 Figure 6832: PRO23392
 Figure 6833: DNA193996, DNA193996, P_A40502.at
 Figure 6834: PRO23400
 Figure 6835: DNA194019, DNA194019, AK000004.at
 Figure 6836: PRO23421
 Figure 6837: DNA194063, DNA194063, P_V84608.at
 Figure 6838: PRO23460
 Figure 6839: DNA83046, NP_000565.1, P_X30170.at
 Figure 6840: PRO2569
 Figure 6841: DNA331852, 985629.1, P_Z59467.at
 Figure 6842: PRO86765
 Figure 6843: DNA195915, DNA195915, P_X85020.at
 Figure 6844: DNA331853, BC001305, AK027031.at
 Figure 6845: PRO23769
 Figure 6846A-B: DNA328720, NP_078800.2, P_X35729.at
 Figure 6847: PRO84476
 Figure 6848: DNA194679, BAA05062.1, HUMORFT.at
 Figure 6849: PRO23989
 Figure 6850: DNA331854, AF244129, AF244129.at
 Figure 6851: PRO86766
 Figure 6852: DNA194766, DJ434014.3, HS4340143.at
 Figure 6853: PRO24046
 Figure 6854: DNA331855, BLP1, P_Z98236.at
 Figure 6855: PRO85742
 Figure 6856: DNA330358, BC008904, AX011617.at
 Figure 6857: PRO85574
 Figure 6858: DNA330380, FLJ12436, AK022498.at
 Figure 6859: PRO85592
 Figure 6860: DNA328288, NP_073591.1, AK022938.at
 Figure 6861: PRO69876
 Figure 6862: DNA196036, DNA196036, AI471699_RC.at
 Figure 6863: DNA331098, AY052405, AX047348.at
 Figure 6864: PRO86248
 Figure 6865A-B: DNA331099, AB058685, AX048187.at
 Figure 6866: DNA331100, BC021238, P_X84987.at
 Figure 6867: PRO86249
 Figure 6868: DNA331101, NP_114143.1, 250446.2.at

Figure 6869: PRO86250
 Figure 6870: DNA331856, BC022522, 237658.8.at
 Figure 6871: PRO71209
 Figure 6872: DNA106360, DNA106360, 164869.1.at
 Figure 6873: DNA155526, DNA155526, 251178.1.at
 Figure 6874: DNA331102, NP_116052.1, 481267.1.at
 Figure 6875: PRO86251
 Figure 6876: DNA196289, DNA196289, 230230.2.at
 Figure 6877: DNA323696, BC015160, 428335.22.at
 Figure 6878: DNA326749, NP_116101.1, DNA167237.at
 Figure 6879: PRO23238
 Figure 6880: DNA210391, DNA210391, P_X85039.at
 Figure 6881: PRO34886
 Figure 6882: DNA331103, NP_009125.1, NM_007194.at
 Figure 6883: PRO34956
 Figure 6884: DNA331857, SIRPB2, NM_018556.at
 Figure 6885: PRO86767
 Figure 6886: DNA254406, NP_060854.1, NM_018384.at
 Figure 6887: PRO49516
 Figure 6888A-B: DNA331858, ABCA7, NM_019112.at
 Figure 6889: PRO86768
 Figure 6890: DNA255704, NP_057570.1, NM_016486.at
 Figure 6891: PRO50764
 Figure 6892: DNA331859, AF267245, NM_016523.at
 Figure 6893: PRO86769
 Figure 6894: DNA254470, HSU11050, NM_002497.at
 Figure 6895: PRO49578
 Figure 6896A-B: DNA256461, HSAJ6266, NM_007086.at
 Figure 6897: PRO51498
 Figure 6898: DNA330480, FLJ10808, NM_018227.at
 Figure 6899: PRO85677
 Figure 6900: DNA328669, NP_005882.1, NM_005891.at
 Figure 6901: PRO84441
 Figure 6902: DNA254777, CORO1C, NM_014325.at
 Figure 6903: PRO49875
 Figure 6904A-B: DNA329991, TIMELESS, NM_003920.at
 Figure 6905: PRO85284
 Figure 6906: DNA255161, IFRG28, NM_022147.at
 Figure 6907: PRO50241
 Figure 6908: DNA327812, IFI44, NM_006417.at
 Figure 6909: PRO83773
 Figure 6910: DNA304716, CDKN1A, NM_000389.at
 Figure 6911: PRO71142
 Figure 6912: DNA328431, HSCKSHS1, NM_001826.at
 Figure 6913: PRO45093
 Figure 6914: DNA269926, HSCDC2R, NM_001786.at
 Figure 6915: PRO58324
 Figure 6916: DNA331104, NP_066280.1, NM_021000.f.at
 Figure 6917: PRO86252
 Figure 6918A-B: DNA274893, NP_006282.1, NM_006291.at
 Figure 6919: PRO62634
 Figure 6920: DNA271455, LOC51339, NM_016651.at
 Figure 6921: PRO59751
 Figure 6922: DNA329172, GFT1, NM_005263.at
 Figure 6923: PRO84796
 Figure 6924: DNA331860, BC010940, NM_004833.at
 Figure 6925: PRO86770
 Figure 6926: DNA329274, AF187064, NM_014380.at
 Figure 6927: PRO84870
 Figure 6928A-B: DNA328535, NP_009147.2, NM_007216.at
 Figure 6929: PRO60044
 Figure 6930: DNA331861, MAP2K6, NM_002758.at
 Figure 6931: PRO86771
 Figure 6932: DNA331105, NP_009012.1, NM_007081.at
 Figure 6933: PRO86253
 Figure 6934: DNA256257, LAMP3, NM_014398.at
 Figure 6935: PRO51301
 Figure 6936: DNA256033, NP_060164.1, NM_017694.at
 Figure 6937: PRO51081
 Figure 6938A-B: DNA331106, NP_065107.1, NM_020374.at
 Figure 6939: PRO86254
 Figure 6940A-B: DNA254789, LOC51696, NM_016217.at
 Figure 6941: PRO49887
 Figure 6942A-B: DNA254376, AB023180, NM_014963.at
 Figure 6943: PRO49486
 Figure 6944: DNA254129, ARME1, NM_006010.at
 Figure 6945: PRO49244
 Figure 6946: DNA331862, AX008892, NM_005484.at
 Figure 6947: PRO86772
 Figure 6948: DNA256407, HSA249248, NM_014373.at
 Figure 6949: PRO51448
 Figure 6950A-C: DNA256495, HSU33841, NM_000051.at
 Figure 6951: PRO51531
 Figure 6952: DNA330384, FLJ20647, NM_017918.at
 Figure 6953: PRO51129
 Figure 6954: DNA331863, AK000318, NM_017760.at
 Figure 6955: PRO86773
 Figure 6956: DNA256533, NP_006105.1, NM_006114.at
 Figure 6957: PRO51565
 Figure 6958A-B: DNA287273, AF092563, NM_006444.at
 Figure 6959: PRO69545

Figure 6960: DNA256295, DNA256295, NM.002319.at
 Figure 6961: PRO51339
 Figure 6962A-C: DNA331864, HSA303086, NM.002266.at
 Figure 6963: DNA254350, AF002697, NM.004052.at
 Figure 6964: PRO49461
 Figure 6965: DNA255010, NP.061869.1, NM.018996.at
 Figure 6966: PRO50099
 Figure 6967: DNA329900, HUMA1SBU, NM.002914.at
 Figure 6968: PRO81549
 Figure 6969: DNA323838, CDKN2C, NM.001262.at
 Figure 6970: PRO59546
 Figure 6971: DNA271093, CNK, NM.004073.at
 Figure 6972: PRO59417
 Figure 6973: DNA331108, NP.005265.1, NM.005274.at
 Figure 6974: PRO10780
 Figure 6975: DNA290234, RGS2, NM.002923.at
 Figure 6976: PRO70333
 Figure 6977: DNA275015, HSU31383, NM.004125.at
 Figure 6978: PRO62743
 Figure 6979: DNA256854, HSU76638, NM.000465.at
 Figure 6980: PRO51785
 Figure 6981: DNA331865, IRF7, NM.004031.at
 Figure 6982: PRO86774
 Figure 6983: DNA255271, EMR2, NM.013447.at
 Figure 6984: PRO50348
 Figure 6985: DNA331866, AB020970, NM.022154.at
 Figure 6986: DNA331867, AF058762, NM.003857.at
 Figure 6987A-B: DNA331109, NP.005155.1, NM.005164.at
 Figure 6988: PRO50662
 Figure 6989: DNA331110, NP.057563.3, NM.016479.at
 Figure 6990: PRO86256
 Figure 6991: DNA254276, HSPC154, NM.014177.at
 Figure 6992: PRO49387
 Figure 6993: DNA287241, LAP3, NM.015907.at
 Figure 6994: PRO69516
 Figure 6995A-B: DNA331111, NP.004229.1, NM.004238.at
 Figure 6996: PRO86257
 Figure 6997: DNA255261, NP.060262.1, NM.017792.at
 Figure 6998: PRO50338
 Figure 6999A-B: DNA331868, HSM802180, NM.017631.at
 Figure 7000: DNA331869, NP.067024.1, NM.021201.at
 Figure 7001: PRO50191
 Figure 7002A-B: DNA255846, NP.057424.1, NM.016340.at
 Figure 7003: PRO50900
 Figure 7004: DNA331870, AK001274, NM.017613.at
 Figure 7005: PRO86776
 Figure 7006: DNA287221, LOC51191, NM.016323.at
 Figure 7007: PRO69500
 Figure 7008: DNA331871, BC017842, NM.004851.at
 Figure 7009: PRO86777
 Figure 7010: DNA260982, NP.060819.1, NM.018349.at
 Figure 7011: PRO54728
 Figure 7012: DNA329033, NP.005375.1, NM.005384.at
 Figure 7013: PRO84700
 Figure 7014: DNA271095, AF091433, NM.004702.at
 Figure 7015: PRO59418
 Figure 7016: DNA297387, NP.003494.1, NM.003503.at
 Figure 7017: PRO58394
 Figure 7018: DNA331872, AF099644, NM.001255.at
 Figure 7019: PRO86778
 Figure 7020: DNA331873, PTPN7, NM.002832.at
 Figure 7021: PRO69609
 Figure 7022: DNA269750, NP.002919.1, NM.002928.at
 Figure 7023: PRO58159
 Figure 7024: DNA268036, AB023416, NM.013258.at
 Figure 7025: PRO57311
 Figure 7026: DNA270522, NP.006013.1, NM.006022.at
 Figure 7027: PRO58899
 Figure 7028: DNA330057, MT1G, NM.005950.at
 Figure 7029: PRO85337
 Figure 7030A-B: DNA331113, NP.005914.1, NM.005923.at
 Figure 7031: PRO60244
 Figure 7032: DNA331874, BC002847, NM.016103.at
 Figure 7033: PRO84581
 Figure 7034: DNA269791, NP.001168.1, NM.001177.at
 Figure 7035: PRO58197
 Figure 7036: DNA331114, AF291719, NM.007182.at
 Figure 7037: PRO86258
 Figure 7038: DNA329580, HSU78170, NM.005825.at
 Figure 7039: PRO85114
 Figure 7040: DNA281436, NP.003286.1, NM.017627.at
 Figure 7041: PRO66275
 Figure 7042: DNA331875, CDC25B, NM.021874.at
 Figure 7043: PRO83123
 Figure 7044: DNA331876, BC005912, NM.002001.at
 Figure 7045: PRO2280
 Figure 7046: DNA256737, FLJ20406, NM.017806.at
 Figure 7047: PRO51671
 Figure 7048: DNA255432, NP.060283.1, NM.017813.at
 Figure 7049: PRO50499
 Figure 7050A-B: DNA254262, NP.055197.1,

NM.014382.at
 Figure 7051: PRO49373
 Figure 7052: DNA331877, HUMHMGAB,
 NM.000859.at
 Figure 7053: DNA328901, BC002748, NM.017866.at
 Figure 7054: PRO84622
 Figure 7055: DNA254416, NP.060915.1,
 NM.018445.at
 Figure 7056: PRO49526
 Figure 7057: DNA331115, AF221521, NM.020524.at
 Figure 7058: PRO86259
 Figure 7059: DNA255326, AF055993, NM.003864.at
 Figure 7060: PRO50396
 Figure 7061A-C: DNA328498, AF285167,
 NM.005502.at
 Figure 7062: PRO84320
 Figure 7063: DNA331878, AF246240, NM.018480.at
 Figure 7064: PRO86779
 Figure 7065: DNA331879, AK021999, NM.022765.at
 Figure 7066: PRO86780
 Figure 7067: DNA255135, AB016068, NM.005857.at
 Figure 7068: PRO50216
 Figure 7069: DNA331116, NP.060656.1,
 NM.018186.at
 Figure 7070: PRO86260
 Figure 7071: DNA237817, HSU33286, NM.001316.at
 Figure 7072: PRO38923
 Figure 7073A-B: DNA329904, AF203032,
 NM.021076.at
 Figure 7074: PRO85221
 Figure 7075: DNA329583, AD24, NM.022451.at
 Figure 7076: PRO85117
 Figure 7077: DNA331117, NP.065170.1,
 NM.020437.at
 Figure 7078: PRO86261
 Figure 7079: DNA254710, FLJ20637, NM.017912.at
 Figure 7080: PRO49810
 Figure 7081: DNA331880, HSIFI56R, NM.001548.at
 Figure 7082: PRO59911
 Figure 7083A-B: DNA270323, HSU34605,
 NM.012420.at
 Figure 7084: PRO58710
 Figure 7085: DNA287224, ISG15, NM.005101.at
 Figure 7086: PRO69503
 Figure 7087: DNA269922, HSISG20GN,
 NM.002201.at
 Figure 7088: PRO58320
 Figure 7089: DNA331118, NP.201569.1,
 NM.003672.at
 Figure 7090: PRO86262
 Figure 7091: DNA272655, HSCKSHS2,
 NM.001827.at
 Figure 7092: PRO60781
 Figure 7093A-B: DNA329160, NP.002821.1,
 NM.002830.at
 Figure 7094: PRO84789
 Figure 7095: DNA270415, GNA15, NM.002068.at
 Figure 7096: PRO58796
 Figure 7097: DNA331881, AK023223, NM.016131.at
 Figure 7098: PRO10928
 Figure 7099: DNA270059, NP.003920.1,
 NM.003929.at
 Figure 7100: PRO58452
 Figure 7101: DNA273487, RAB33A, NM.004794.at
 Figure 7102: PRO61470
 Figure 7103: DNA326306, NP.066960.1,
 NM.021137.at
 Figure 7104: PRO62566
 Figure 7105: DNA287378, AF244135, NM.018428.at
 Figure 7106: PRO69637
 Figure 7107: DNA327879, MDA5, NM.022168.at
 Figure 7108: PRO83818
 Figure 7109A-B: DNA327674, NP.002739.1,
 NM.002748.at
 Figure 7110: PRO83661
 Figure 7111: DNA331882, AB030251, NM.013277.at
 Figure 7112: PRO86781
 Figure 7113: DNA254518, LOC51713, NM.016270.at
 Figure 7114: PRO49625
 Figure 7115: DNA256561, CRTAM, NM.019604.at
 Figure 7116: PRO51592
 Figure 7117: DNA331883, AF096290, NM.003645.at
 Figure 7118: PRO51139
 Figure 7119: DNA255215, AF207600, NM.018638.at
 Figure 7120: PRO50294
 Figure 7121A-B: DNA256807, FAM8A1,
 NM.016255.at
 Figure 7122: PRO51738
 Figure 7123: DNA260974, TRIM22, NM.006074.at
 Figure 7124: PRO54720
 Figure 7125: DNA330443, PRO2037, NM.018616.at
 Figure 7126: PRO2037
 Figure 7127: DNA331119, NP.005433.2,
 NM.005442.at
 Figure 7128: PRO50745
 Figure 7129: DNA254274, NP.073573.1,
 NM.022736.at
 Figure 7130: PRO49385
 Figure 7131: DNA255088, HUMTK, NM.003258.at
 Figure 7132: PRO50174
 Figure 7133: DNA255113, FLJ22693, NM.022750.at
 Figure 7134: PRO50195
 Figure 7135: DNA331884, BC008870, NM.017606.at
 Figure 7136: PRO49604
 Figure 7137: DNA331885, MRPL35, NM.016622.at
 Figure 7138: PRO86782
 Figure 7139: DNA272245, NP.055301.1,
 NM.014486.f.at
 Figure 7140: PRO60507
 Figure 7141A-D: DNA331886, AF051160,
 NM.003463.at
 Figure 7142: DNA330877, HKE2, NM.014260.at

Figure 7143: PRO86040
 Figure 7144: DNA295327, IL21, NM_021803.at
 Figure 7145: PRO70773
 Figure 7146: DNA287178, HSU52513, NM_001549.at
 Figure 7147: PRO69467
 Figure 7148: DNA327661, HUMIFI6A, NM_005531.at
 Figure 7149: PRO83652
 Figure 7150A-B: DNA329036, HSU63738, NM_002460.at
 Figure 7151: PRO84703
 Figure 7152: DNA273523, NP_002154.1, NM_002163.at
 Figure 7153: PRO61504
 Figure 7154: DNA331887, AF002822, NM_004701.at
 Figure 7155: PRO82442
 Figure 7156: DNA331888, AF022109, NM_001254.at
 Figure 7157: PRO60595
 Figure 7158: DNA273535, AB011421, NM_004226.at
 Figure 7159: PRO61515
 Figure 7160: DNA275012, NMI, NM_004688.at
 Figure 7161: PRO62740
 Figure 7162: DNA331120, NP_008976.1, NM_007045.at
 Figure 7163: PRO86263
 Figure 7164: DNA331889, AF182076, NM_015710.at
 Figure 7165: PRO84173
 Figure 7166: DNA331890, AF095287, NM_004219.f.at
 Figure 7167: PRO81319
 Figure 7168: DNA331121, AF175306, NM_014288.at
 Figure 7169: PRO86264
 Figure 7170: DNA327858, AF120334, NM_012341.at
 Figure 7171: PRO83800
 Figure 7172: DNA331122, NP_005728.2, NM_005737.at
 Figure 7173: PRO86265
 Figure 7174: DNA289528, ARL3, NM_004311.at
 Figure 7175: PRO70286
 Figure 7176: DNA270526, HUMLYGDI, NM_001175.at
 Figure 7177: PRO58903
 Figure 7178: DNA271931, NP_005745.1, NM_005754.at
 Figure 7179: PRO60207
 Figure 7180: DNA329123, RANBP1, NM_002882.at
 Figure 7181: PRO84765
 Figure 7182A-B: DNA331891, HSM800983, NM_014922.at
 Figure 7183: DNA331892, BC019255, NM_006452.at
 Figure 7184: PRO84240
 Figure 7185: DNA329587, AF192466, NM_012124.at
 Figure 7186: PRO85121
 Figure 7187A-B: DNA329248, AB002359, AB002359.at
 Figure 7188: DNA254668, AB002437, AB002437.at
 Figure 7189: DNA256233, DNA256233, AB017268.f.at
 Figure 7190: PRO51278
 Figure 7191A-B: DNA255448, BAA92554.1, AB037737.at
 Figure 7192: PRO50515
 Figure 7193A-B: DNA255619, AF054589, AF054589.at
 Figure 7194: PRO50682
 Figure 7195: DNA331123, AF062649, AF062649.f.at
 Figure 7196: PRO86266
 Figure 7197A-B: DNA331893, AB058697, AK001581.at
 Figure 7198: DNA331894, HSM802273, AB032963.at
 Figure 7199: DNA331895, HUMTLEIV, AB033087.at
 Figure 7200: PRO86785
 Figure 7201A-B: DNA329039, DORFIN, AK027070.at
 Figure 7202: PRO84706
 Figure 7203: DNA255040, CAB55998.1, HSM801103.at
 Figure 7204: PRO50128
 Figure 7205: DNA328509, NP_006739.1, HSU44403.at
 Figure 7206: PRO57996
 Figure 7207: DNA254338, HUMPLT, HUMPLT.at
 Figure 7208: PRO49449
 Figure 7209: DNA331896, AF067008, NM_001363.at
 Figure 7210: PRO49881
 Figure 7211: DNA331897, BC008843, AB007915.at
 Figure 7212: PRO86786
 Figure 7213: DNA331124, NP_079430.1, AB018353.at
 Figure 7214: PRO86267
 Figure 7215A-B: DNA330736, AB033044, AB033044.at
 Figure 7216A-B: DNA331125, AB037815, AB037815.at
 Figure 7217A-B: DNA331898, AF058925, AF058925.at
 Figure 7218: PRO86787
 Figure 7219: DNA331126, AF078867, AF078866.at
 Figure 7220: PRO86269
 Figure 7221: DNA254836, BAA91233.1, AK000529.at
 Figure 7222: PRO49931
 Figure 7223: DNA88277, NP_006721.1, AK027197.at
 Figure 7224: PRO2724
 Figure 7225: DNA331899, 1399286.1, AW290940_RC.at
 Figure 7226: PRO86788
 Figure 7227: DNA256872, HSM801990, HSM801990.at
 Figure 7228A-B: DNA254192, HUMKIAAK, HUMKIAAK.at
 Figure 7229: DNA331900, BIN2, NM_016293.at

Figure 7230: PRO86789
 Figure 7231A-B: DNA256731, BAA83028.1, AB028999.at
 Figure 7232: PRO51665
 Figure 7233: DNA331901, HSM801036, AB029015.at
 Figure 7234A-B: DNA331127, BAA86477.1, AB032989.at
 Figure 7235: PRO86270
 Figure 7236A-B: DNA254672, BAA92652.1, AB037835.at
 Figure 7237: PRO49773
 Figure 7238A-C: DNA331128, NP_065892.1, AB040884.at
 Figure 7239: PRO84841
 Figure 7240: DNA269976, AAC14260.1, AF039023.at
 Figure 7241: PRO58372
 Figure 7242: DNA331129, HSA227869, HSA227869.t.at
 Figure 7243: DNA256422, HSA227900, HSA227900.at
 Figure 7244: DNA331902, BC014522, HSSOM172M.at
 Figure 7245: PRO86790
 Figure 7246: DNA329040, BC001356, HSU72882.at
 Figure 7247: PRO84707
 Figure 7248: DNA331130, AAK50430.1, HUMT1227HC.at
 Figure 7249: PRO86272
 Figure 7250A-B: DNA331131, HSA223948, AY013288.at
 Figure 7251: DNA326056, NP_072088.1, AY007810.at
 Figure 7252: PRO82491
 Figure 7253: DNA329041, HSM800399, AF132199.at
 Figure 7254: DNA255780, AK022209, AK022209.at
 Figure 7255: PRO50835
 Figure 7256: DNA254922, AK022604, AK022604.at
 Figure 7257: PRO50012
 Figure 7258: DNA330432, FLJ23235, AK026888.at
 Figure 7259: PRO85636
 Figure 7260A-B: DNA256299, AB051489, AB051489.at
 Figure 7261: DNA331903, BC015380, HSM801707.at
 Figure 7262: DNA255626, HSM802849, HSM802849.at
 Figure 7263: PRO50690
 Figure 7264: DNA331132, NP_115524.1, HSM801796.at
 Figure 7265: PRO86273
 Figure 7266: DNA255964, NP_079113.1, AK025125.at
 Figure 7267: PRO51015
 Figure 7268: DNA255465, AK024313, AK024313.at
 Figure 7269: PRO50532
 Figure 7270: DNA329597, AK022178, AK022178.at
 Figure 7271: PRO85129
 Figure 7272: DNA254228, NP_079236.1, AK021791.at
 Figure 7273: PRO49340
 Figure 7274: DNA331904, AK023431, AF298880.at
 Figure 7275: PRO86791
 Figure 7276: DNA329078, AF214006, HSM801679.at
 Figure 7277: PRO23253
 Figure 7278: DNA256784, FLJ22104, AK025757.at
 Figure 7279: PRO51716
 Figure 7280: DNA331905, AK001823, HSM801648.at
 Figure 7281: PRO86792
 Figure 7282: DNA329044, NP_064562.1, AK025265.at
 Figure 7283: PRO84709
 Figure 7284: DNA331906, HSA227916, NM_001530.at
 Figure 7285: DNA330023, GADD45A, NM_001924.at
 Figure 7286: PRO85308
 Figure 7287A-B: DNA272191, RSN, NM_002956.at
 Figure 7288: PRO60456
 Figure 7289: DNA328418, HUMG0S24A, NM_003407.at
 Figure 7290: PRO84261
 Figure 7291: DNA331133, HSU63830, NM_004180.at
 Figure 7292: PRO86274
 Figure 7293: DNA271310, DUSP8, NM_004420.at
 Figure 7294: PRO59617
 Figure 7295: DNA331907, AKAP7, NM_004842.at
 Figure 7296: PRO63228
 Figure 7297: DNA287203, NP_006182.1, NM_006191.at
 Figure 7298: PRO69487
 Figure 7299: DNA274783, HSU26424, NM_006281.at
 Figure 7300: PRO62549
 Figure 7301A-B: DNA255281, NP_006380.1, NM_006389.at
 Figure 7302: PRO50357
 Figure 7303: DNA328712, NP_006501.1, NM_006510.at
 Figure 7304: PRO84469
 Figure 7305: DNA331908, AF161440, NM_012111.at
 Figure 7306: DNA330065, STK18, NM_014264.at
 Figure 7307: PRO85345
 Figure 7308: DNA152148, DNA152148, HSP1CDC21.at
 Figure 7309: PRO10290
 Figure 7310: DNA329925, HSBP1, NM_001537.at
 Figure 7311: PRO85239
 Figure 7312: DNA331909, HSCFANT, NM_002964.at
 Figure 7313: PRO86795
 Figure 7314: DNA329139, NP_003893.2, NM_003902.at
 Figure 7315: PRO84774
 Figure 7316: DNA331910, HSSEC232, NM_006363.at

- Figure 7317: PRO86796
 Figure 7318: DNA329047, BATF, NM.006399.at
 Figure 7319: PRO58425
 Figure 7320: DNA274167, AF026166, NM.006431.at
 Figure 7321: PRO62097
 Figure 7322: DNA254572, NP.006576.1, NM.006585.at
 Figure 7323: PRO49675
 Figure 7324A-B: DNA331911, AB003334, NM.006644.at
 Figure 7325: PRO86797
 Figure 7326: DNA331912, BC009405, NM.013411.at
 Figure 7327: PRO86798
 Figure 7328: DNA255289, MELK, NM.014791.at
 Figure 7329: PRO50363
 Figure 7330A-B: DNA331913, BAB21784.1, NM.015383.at
 Figure 7331: PRO86799
 Figure 7332: DNA329148, LOC51042, NM.015871.at
 Figure 7333: PRO84782
 Figure 7334: DNA326221, AF125098, NM.016095.at
 Figure 7335: PRO82634
 Figure 7336: DNA331914, BC009398, HUMPICDC47.at
 Figure 7337: PRO86800
 Figure 7338A-B: DNA328312, HUMAREB6, HUMAREB6.at
 Figure 7339: PRO84180
 Figure 7340: DNA325941, HSPCA, IISISP90R.at
 Figure 7341: PRO82388
 Figure 7342: DNA328483, VIT1, NM.000179.at
 Figure 7343: PRO84309
 Figure 7344: DNA271847, HUMDNAJHOM, NM.001539.at
 Figure 7345: PRO60127
 Figure 7346: DNA331915, BC001786, NM.002014.at
 Figure 7347: PRO59262
 Figure 7348: DNA331916, HUMMIF, NM.002415.at
 Figure 7349: DNA331917, PHF1, NM.002636.at
 Figure 7350: PRO86802
 Figure 7351: DNA329604, SRP54, NM.003136.at
 Figure 7352: PRO85134
 Figure 7353A-B: DNA331134, NP.003381.1, NM.003390.at
 Figure 7354: PRO86275
 Figure 7355A-B: DNA290265, ZNF91, NM.003430.f.at
 Figure 7356: PRO70395
 Figure 7357A-C: DNA331918, AF009425, NM.004338.at
 Figure 7358: PRO86803
 Figure 7359: DNA254582, NP.004626.1, NM.004635.at
 Figure 7360: PRO49685
 Figure 7361A-B: DNA275334, NP.112162.1, NM.004749.at
 Figure 7362: PRO63009
 Figure 7363: DNA254157, HSU13045, NM.005254.at
 Figure 7364: PRO49271
 Figure 7365A-B: DNA124122, RBL2, NM.005611.at
 Figure 7366: PRO6323
 Figure 7367: DNA330776, TOB1, NM.005749.at
 Figure 7368: PRO58014
 Figure 7369: DNA326980, AF140598, NM.014248.at
 Figure 7370: PRO83289
 Figure 7371: DNA271608, HUMRSC419, NM.014670.at
 Figure 7372: PRO59895
 Figure 7373: DNA272928, HUMORFKG1F, NM.014764.at
 Figure 7374: PRO61012
 Figure 7375: DNA290235, NP.057121.1, NM.016037.at
 Figure 7376: PRO70335
 Figure 7377: DNA331135, HUMKG1DD, HUMKG1DD.at
 Figure 7378A-B: DNA330119, AF226044, HUMKIAAQ.at
 Figure 7379: PRO85381
 Figure 7380: DNA331137, HS24P52, HUMHSP70H.at
 Figure 7381: PRO86278
 Figure 7382A-B: DNA269805, NP.001263.1, NM.001272.at
 Figure 7383: PRO58209
 Figure 7384: DNA270689, HSGATA3R, NM.002051.at
 Figure 7385: PRO59053
 Figure 7386: DNA331919, HUMCFA, NM.002965.at
 Figure 7387: PRO80648
 Figure 7388A-B: DNA304800, NP.004146.1, NM.004155.at
 Figure 7389: PRO69458
 Figure 7390: DNA273418, AAG01157.1, NM.004301.at
 Figure 7391: PRO61417
 Figure 7392: DNA330066, MLLT3, NM.004529.at
 Figure 7393: PRO85346
 Figure 7394: DNA270733, S46622, NM.005605.at
 Figure 7395: PRO59094
 Figure 7396: DNA331138, NP.005997.2, NM.006006.at
 Figure 7397: PRO86279
 Figure 7398: DNA331139, NP.006865.1, NM.006874.at
 Figure 7399: PRO81172
 Figure 7400: DNA331920, AF090950, NM.015675.at
 Figure 7401: PRO84384
 Figure 7402: DNA329050, MRPS17, NM.015969.at
 Figure 7403: PRO84712
 Figure 7404A-B: DNA329122, GS3955, NM.021643.at

Figure 7405: PRO84764
 Figure 7406: DNA331921, 244055.1, AF320911.at
 Figure 7407: PRO86804
 Figure 7408: DNA331922, AK026275, AK026275.at
 Figure 7409: PRO86805
 Figure 7410A-B: DNA254516, AF288399, AF288399.at
 Figure 7411: PRO49623
 Figure 7412: DNA328313, NP.115579.1, AK025076.at
 Figure 7413: PRO84181
 Figure 7414: DNA327865, NP.079105.1, AK026315.at
 Figure 7415: PRO83806
 Figure 7416: DNA294813, NP.444283.1, P.T67134.at
 Figure 7417: PRO70763
 Figure 7418A-B: DNA254706, AB046851, AB046851.at
 Figure 7419: DNA329052, NP.078801.1, AK026237.at
 Figure 7420: PRO84714
 Figure 7421: DNA256890, BC008988, P.Z00467.at
 Figure 7422: PRO51824
 Figure 7423: DNA256291, FLJ1032, AK024685.f.at
 Figure 7424: PRO51335
 Figure 7425: DNA331923, HSUCP2X12, P.C69111.at
 Figure 7426: DNA213665, DNA213665, P.X30166.at
 Figure 7427: PRO35126
 Figure 7428: DNA331140, 332752.10, AK023798.at
 Figure 7429: PRO86280
 Figure 7430A-B: DNA331141, BAB13420.1, AB046814.at
 Figure 7431: PRO86281
 Figure 7432: DNA331924, BC004932, AK024551.at
 Figure 7433: PRO21434
 Figure 7434A-B: DNA256267, AB046838, AB046838.at
 Figure 7435: DNA327954, BAL, P.D00629.at
 Figure 7436: PRO83879
 Figure 7437: DNA255798, FLJ12377, AK022439.at
 Figure 7438: PRO50853
 Figure 7439: DNA330389, FLJ12888, AK022950.at
 Figure 7440: PRO85598
 Figure 7441: DNA330086, FLJ12973, AK023035.at
 Figure 7442: PRO85360
 Figure 7443: DNA331142, NP.116325.1, P.Z98137.at
 Figure 7444: PRO51781
 Figure 7445: DNA329384, BC008502, P.Z33372.at
 Figure 7446: PRO84960
 Figure 7447A-B: DNA331143, NP.149075.2, AK022613.at
 Figure 7448: PRO86282
 Figure 7449: DNA331925, 424693.10, AK022231.at
 Figure 7450: PRO86806
 Figure 7451: DNA331144, NP.078834.1, AK023982.at
 Figure 7452: PRO86283
 Figure 7453A-B: DNA331926, BAB13449.1, AB046843.at
 Figure 7454: PRO51258
 Figure 7455: DNA255197, DNA255197, P.Z50392.at
 Figure 7456: PRO50276
 Figure 7457: DNA328010, NP.149016.1, IISM801092.at
 Figure 7458: PRO83928
 Figure 7459: DNA262805, DNA262805, HSM800425.at
 Figure 7460: DNA331146, 1400830.1, HUMINT.tra.at
 Figure 7461: PRO86284
 Figure 7462: DNA328317, cig5, AF026941.at
 Figure 7463: PRO69493
 Figure 7464: DNA331147, NP.079104.1, AF131768.at
 Figure 7465: PRO86285
 Figure 7466: DNA255770, DNA255770, AK022106.at
 Figure 7467A-C: DNA254412, EV15, AF008915.at
 Figure 7468: PRO49522
 Figure 7469: DNA331148, 978273.10, AK023244.at
 Figure 7470: PRO86286
 Figure 7471: DNA330532, AK026279, AK026279.at
 Figure 7472: PRO85719
 Figure 7473: DNA330388, FLJ23468, AK027121.at
 Figure 7474: PRO85597
 Figure 7475: DNA331927, AK026969, AK026969.at
 Figure 7476: PRO86807
 Figure 7477: DNA330447, FLJ22757, AK026410.at
 Figure 7478: PRO85648
 Figure 7479: DNA324984, FLJ12298, AK022360.at
 Figure 7480: PRO81578
 Figure 7481: DNA331149, 7697327.1, HSM802839.at
 Figure 7482: PRO86287
 Figure 7483A-B: DNA256267, DNA256267, AK023113.at
 Figure 7484: PRO51311
 Figure 7485: DNA331150, BC017725, I387341.2.at
 Figure 7486: PRO86288
 Figure 7487: DNA257606, DNA257606, 428093.1.at
 Figure 7488: DNA258375, AF283301, 413231.5.at
 Figure 7489: PRO52516
 Figure 7490: DNA331928, AK027419, 154551.10.at
 Figure 7491: PRO86808
 Figure 7492: DNA328319, BC019562, 411364.2.at
 Figure 7493: DNA290812, DNA290812, 220495.3.CON.at
 Figure 7494: PRO70559
 Figure 7495: DNA304799, BC022410, 337588.1.at
 Figure 7496: PRO52633
 Figure 7497: DNA257403, DNA257403, 012814.1.at
 Figure 7498: DNA304820, NP.115940.1, 317557.1.at
 Figure 7499: PRO47351
 Figure 7500: DNA331929, BC019246,

441855.8.CON.at
 Figure 7501: PRO83338
 Figure 7502: DNA260581, DNA260581, 127987.6.at
 Figure 7503: PRO54507
 Figure 7504: DNA257576, DNA257576, 334945.2.at
 Figure 7505: DNA304819, BC004398, 202113.2.at
 Figure 7506: DNA304794, FBXO30, 222128.1.at
 Figure 7507: PRO71206
 Figure 7508: DNA259323, DNA259323, 022997.1.at
 Figure 7509: PRO53256
 Figure 7510: DNA304796, MED8, 237428.13.at
 Figure 7511: PRO71208
 Figure 7512: DNA259615, DNA259615, 1000203.1.at
 Figure 7513: DNA304805, AK027628, 475113.7.at
 Figure 7514: PRO69531
 Figure 7515: DNA304793, GBP4, 206425.2.at
 Figure 7516: PRO71205
 Figure 7517: DNA331151, 018033.1,
 018033.1.CON.at
 Figure 7518: PRO86289
 Figure 7519: DNA304068, AK057631, 1091656.1.at
 Figure 7520: PRO71035
 Figure 7521: DNA257714, EPSTI1, 337352.17.at
 Figure 7522: PRO52268
 Figure 7523: DNA304798, NP.443097.1, 246119.7.at
 Figure 7524: PRO71210
 Figure 7525: DNA258721, DNA258721, 197627.1.at
 Figure 7526A-B: DNA257461, NP.113607.1,
 086533.1.at
 Figure 7527: PRO52040
 Figure 7528: DNA331152, 1042156.3, 1042156.3.at
 Figure 7529: PRO86290
 Figure 7530: DNA331153, 004052.1, 004052.1.at
 Figure 7531: PRO86291
 Figure 7532: DNA331930, AK054582, 978231.1.at
 Figure 7533: PRO86809
 Figure 7534: DNA259587, DNA259587, 220866.1.at
 Figure 7535: DNA106195, DNA106195, 359193.13.at
 Figure 7536: DNA331154, 212376.1, 212376.1.at
 Figure 7537: PRO86292
 Figure 7538: DNA331155, 112652.1, 112652.1.at
 Figure 7539: PRO86293
 Figure 7540: DNA304806, BC019022, 983343.1.at
 Figure 7541: PRO71215
 Figure 7542: DNA262708, DNA262708,
 118516.1.LRC.at
 Figure 7543: DNA259475, DNA259475, 239162.1.at
 Figure 7544: DNA269148, DNA269148, 411192.2.at
 Figure 7545: DNA304817, BC015532, 211436.3.at
 Figure 7546: PRO71224
 Figure 7547: DNA260313, DNA260313, 1098929.1.at
 Figure 7548: PRO54242
 Figure 7549A-B: DNA328325, NP.061142.1,
 445188.4.at
 Figure 7550: PRO84190
 Figure 7551A-B: DNA304800, SERPINB9,
 354740.1.at
 Figure 7552: PRO69458
 Figure 7553: DNA331156, 118180.1, 118180.1.at
 Figure 7554: PRO86294
 Figure 7555: DNA287659, AK027790, 406833.1.at
 Figure 7556: PRO69903
 Figure 7557: DNA331931, 092555.3, 092555.4.at
 Figure 7558: PRO86810
 Figure 7559: DNA331157, NP.439896.1, 022541.5.at
 Figure 7560: PRO86295
 Figure 7561: DNA260573, DNA260573, 899597.1.at
 Figure 7562: PRO54499
 Figure 7563: DNA260157, DNA260157, 236833.1.at
 Figure 7564: PRO54086
 Figure 7565: DNA174145, DNA174145, 100083.2.at
 Figure 7566: PRO35770
 Figure 7567: DNA260167, DNA260167, 264556.1.at
 Figure 7568A-B: DNA331932, 239260.1, 239260.1.at
 Figure 7569: PRO86811
 Figure 7570: DNA260031, DNA260031, 161526.1.at
 Figure 7571: DNA258907, DNA258907, 347940.2.at
 Figure 7572: PRO52840
 Figure 7573: DNA257455, DNA257455, 977723.3.at
 Figure 7574: PRO52035
 Figure 7575: DNA304807, BC014978, 005415.2.at
 Figure 7576: PRO71216
 Figure 7577: DNA258864, DNA258864, 331965.1.at
 Figure 7578: DNA304811, 428051.2, 428051.2.at
 Figure 7579: PRO71220
 Figure 7580: DNA257389, FLJ14906, 987098.1.at
 Figure 7581: PRO51974
 Figure 7582: DNA331158, 130352.1, 130352.1.at
 Figure 7583: PRO86296
 Figure 7584: DNA258951, DNA258951, 222361.1.at
 Figure 7585: DNA331159, NP.077291.1,
 411426.29.at
 Figure 7586: PRO86297
 Figure 7587: DNA257784, DNA257784, 481853.1.at
 Figure 7588: DNA331933, AF272148, 074299.1.at
 Figure 7589: PRO86812

BRIEF DESCRIPTION OF THE DRAWINGS

In the list of figures for the present application, specific cDNA sequences which are differentially expressed in differentiated macrophages as compared to normal undifferentiated monocytes are individually identified with a specific alphanumeric designation. These cDNA sequences are differentially expressed in monocytes that are specifically treated as described in Example 1 below. If start and/or stop codons have been identified in a cDNA sequence shown in the attached figures, they are shown in bold and underlined font, and the encoded polypeptide is shown in the next consecutive figure.

The Figures 1-7589 show the nucleic acids of the invention and their encoded PRO polypeptides. Also included, for convenience is a List of Figures, which gives the figure number and the corresponding DNA or PRO number.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTSI. Definitions

The terms "PRO polypeptide" and "PRO" as used herein and when immediately followed by a numerical designation refer to various polypeptides, wherein the complete designation (i.e., PRO/number) refers to specific polypeptide sequences as described herein. The terms "PRO/number polypeptide" and "PRO/number" wherein the term "number" is provided as an actual numerical designation as used herein encompass native sequence polypeptides and polypeptide variants (which are further defined herein). The PRO polypeptides described herein may be isolated from a variety of sources, such as from human tissue types or from another source, or prepared by recombinant or synthetic methods. The term "PRO polypeptide" refers to each individual PRO/number polypeptide disclosed herein. All disclosures in this specification which refer to the "PRO polypeptide" refer to each of the polypeptides individually as well as jointly. For example, descriptions of the preparation of, purification of, derivation of, formation of, antibodies to or against, administration of, compositions containing, treatment of a disease with, etc., pertain to each polypeptide of the invention individually. The term "PRO polypeptide" also includes variants of the PRO/number polypeptides disclosed herein.

A "native sequence PRO polypeptide" comprises a polypeptide having the same amino acid sequence as the corresponding PRO polypeptide derived from nature. Such native sequence PRO polypeptides can be isolated from nature or can be produced by recombinant or synthetic means. The term "native sequence PRO polypeptide" specifically encompasses naturally-occurring truncated or secreted forms of the specific PRO polypeptide (e.g., an extracellular domain sequence), naturally-occurring variant forms (e.g., alternatively spliced forms) and naturally-occurring allelic variants of the polypeptide. In various embodiments of the invention, the native sequence PRO polypeptides disclosed herein are mature or full-length native sequence polypeptides comprising the full-length amino acids sequences shown in the accompanying figures. Start and stop codons are shown in bold font and underlined in the figures. However, while the PRO polypeptide disclosed in the accompanying figures are shown to begin with methionine residues designated herein as amino acid position 1 in the figures, it is conceivable and possible that other methionine residues located either upstream or downstream from the amino acid position 1 in the figures may be employed as the starting amino acid residue for the PRO polypeptides.

The PRO polypeptide "extracellular domain" or "ECD" refers to a form of the PRO polypeptide which is essentially free of the transmembrane and cytoplasmic domains. Ordinarily, a PRO polypeptide

ECD will have less than 1% of such transmembrane and/or cytoplasmic domains and preferably, will have less than 0.5% of such domains. It will be understood that any transmembrane domains identified for the PRO polypeptides of the present invention are identified pursuant to criteria routinely employed in the art for identifying that type of hydrophobic domain. The exact boundaries of a transmembrane domain may vary but most likely by no more than about 5 amino acids at either end of the domain as initially identified herein.

Optionally, therefore, an extracellular domain of a PRO polypeptide may contain from about 5 or fewer amino acids on either side of the transmembrane domain/extracellular domain boundary as identified in the Examples or specification and such polypeptides, with or without the associated signal peptide, and nucleic acid encoding them, are contemplated by the present invention.

The approximate location of the "signal peptides" of the various PRO polypeptides disclosed herein are shown in the present specification and/or the accompanying figures. It is noted, however, that the C-terminal boundary of a signal peptide may vary, but most likely by no more than about 5 amino acids on either side of the signal peptide C-terminal boundary as initially identified herein, wherein the C-terminal boundary of the signal peptide may be identified pursuant to criteria routinely employed in the art for identifying that type of amino acid sequence element (e.g., Nielsen et al., *Prot. Eng.* 10:1-6 (1997) and Heinje et al., *Nucl. Acids. Res.* 14:4683-4690 (1986)). Moreover, it is also recognized that, in some cases, cleavage of a signal sequence from a secreted polypeptide is not entirely uniform, resulting in more than one secreted species. These mature polypeptides, where the signal peptide is cleaved within no more than about 5 amino acids on either side of the C-terminal boundary of the signal peptide as identified herein, and the polynucleotides encoding them, are contemplated by the present invention.

"PRO polypeptide variant" means an active PRO polypeptide as defined above or below having at least about 80% amino acid sequence identity with a full-length native sequence PRO polypeptide sequence as disclosed herein, a PRO polypeptide sequence lacking the signal peptide as disclosed herein, an extracellular domain of a PRO polypeptide, with or without the signal peptide, as disclosed herein or any other fragment of a full-length PRO polypeptide sequence as disclosed herein. Such PRO polypeptide variants include, for instance, PRO polypeptides wherein one or more amino acid residues are added, or deleted, at the N- or C-terminus of the full-length native amino acid sequence. Ordinarily, a PRO polypeptide variant will have at least about 80% amino acid sequence identity, alternatively at least about 81% amino acid sequence identity, alternatively at least about 82% amino acid sequence identity, alternatively at least about 83% amino acid sequence identity, alternatively at least about 84% amino acid sequence identity, alternatively at least about 85% amino acid sequence identity, alternatively at least about 86% amino acid sequence identity, alternatively at least about 87% amino acid sequence identity, alternatively at least about 88% amino acid sequence identity, alternatively at least about 89% amino acid sequence identity, alternatively at least about 90% amino acid sequence identity, alternatively at least about 91% amino acid sequence identity, alternatively at least about 92% amino acid sequence identity, alternatively at least about 93% amino acid sequence identity, alternatively at least about 94% amino acid sequence identity, alternatively at least about 95% amino acid sequence identity, alternatively at least about 96% amino acid sequence identity, alternatively at least about 97% amino acid sequence identity, alternatively at least about 98% amino acid sequence identity and alternatively at least about 99% amino acid sequence identity to a full-length native sequence PRO polypeptide sequence as disclosed herein, a

PRO polypeptide sequence lacking the signal peptide as disclosed herein, an extracellular domain of a PRO polypeptide, with or without the signal peptide, as disclosed herein or any other specifically defined fragment of a full-length PRO polypeptide sequence as disclosed herein. Ordinarily, PRO variant polypeptides are at least about 10 amino acids in length, alternatively at least about 20 amino acids in length, alternatively at least about 30 amino acids in length, alternatively at least about 40 amino acids in length, alternatively at least about 50 amino acids in length, alternatively at least about 60 amino acids in length, alternatively at least about 70 amino acids in length, alternatively at least about 80 amino acids in length, alternatively at least about 90 amino acids in length, alternatively at least about 100 amino acids in length, alternatively at least about 150 amino acids in length, alternatively at least about 200 amino acids in length, alternatively at least about 300 amino acids in length, or more.

"Percent (%) amino acid sequence identity" with respect to the PRO polypeptide sequences identified herein is defined as the percentage of amino acid residues in a candidate sequence that are identical with the amino acid residues in the specific PRO polypeptide sequence, after aligning the sequences and introducing gaps, if necessary, to achieve the maximum percent sequence identity, and not considering any conservative substitutions as part of the sequence identity. Alignment for purposes of determining percent amino acid sequence identity can be achieved in various ways that are within the skill in the art, for instance, using publicly available computer software such as BLAST, BLAST-2, ALIGN or Megalign (DNASTAR) software. Those skilled in the art can determine appropriate parameters for measuring alignment, including any algorithms needed to achieve maximal alignment over the full length of the sequences being compared. For purposes herein, however, % amino acid sequence identity values are generated using the sequence comparison computer program ALIGN-2, wherein the complete source code for the ALIGN-2 program is provided in Table 1 below. The ALIGN-2 sequence comparison computer program was authored by Genentech, Inc. and the source code shown in Table 1 below has been filed with user documentation in the U.S. Copyright Office, Washington D.C., 20559, where it is registered under U.S. Copyright Registration No. TXU510087. The ALIGN-2 program is publicly available through Genentech, Inc., South San Francisco, California or may be compiled from the source code provided in Table 1 below. The ALIGN-2 program should be compiled for use on a UNIX operating system, preferably digital UNIX V4.0D. All sequence comparison parameters are set by the ALIGN-2 program and do not vary.

In situations where ALIGN-2 is employed for amino acid sequence comparisons, the % amino acid sequence identity of a given amino acid sequence A to, with, or against a given amino acid sequence B (which can alternatively be phrased as a given amino acid sequence A that has or comprises a certain % amino acid sequence identity to, with, or against a given amino acid sequence B) is calculated as follows:

$$100 \text{ times the fraction } X/Y$$

where X is the number of amino acid residues scored as identical matches by the sequence alignment program ALIGN-2 in that program's alignment of A and B, and where Y is the total number of amino acid residues in B. It will be appreciated that where the length of amino acid sequence A is not equal to the length of amino acid sequence B, the % amino acid sequence identity of A to B will not equal the % amino acid sequence identity of B to A. As examples of % amino acid sequence identity calculations using this

method, Tables 2 and 3 demonstrate how to calculate the % amino acid sequence identity of the amino acid sequence designated "Comparison Protein" to the amino acid sequence designated "PRO", wherein "PRO" represents the amino acid sequence of a hypothetical PRO polypeptide of interest, "Comparison Protein" represents the amino acid sequence of a polypeptide against which the "PRO" polypeptide of interest is being compared, and "X", "Y" and "Z" each represent different hypothetical amino acid residues.

Unless specifically stated otherwise, all % amino acid sequence identity values used herein are obtained as described in the immediately preceding paragraph using the ALIGN-2 computer program. However, % amino acid sequence identity values may also be obtained as described below by using the WU-BLAST-2 computer program (Altschul et al., *Methods in Enzymology* 266:460-480 (1996)). Most of the WU-BLAST-2 search parameters are set to the default values. Those not set to default values, i.e., the adjustable parameters, are set with the following values: overlap span = 1, overlap fraction = 0.125, word threshold (T) = 11, and scoring matrix = BLOSUM62. When WU-BLAST-2 is employed, a % amino acid sequence identity value is determined by dividing (a) the number of matching identical amino acid residues between the amino acid sequence of the PRO polypeptide of interest having a sequence derived from the native PRO polypeptide and the comparison amino acid sequence of interest (i.e., the sequence against which the PRO polypeptide of interest is being compared which may be a PRO variant polypeptide) as determined by WU-BLAST-2 by (b) the total number of amino acid residues of the PRO polypeptide of interest. For example, in the statement "a polypeptide comprising an the amino acid sequence A which has or having at least 80% amino acid sequence identity to the amino acid sequence B", the amino acid sequence A is the comparison amino acid sequence of interest and the amino acid sequence B is the amino acid sequence of the PRO polypeptide of interest.

Percent amino acid sequence identity may also be determined using the sequence comparison program NCBI-BLAST2 (Altschul et al., *Nucleic Acids Res.* 25:3389-3402 (1997)). The NCBI-BLAST2 sequence comparison program may be downloaded from <http://www.ncbi.nlm.nih.gov> or otherwise obtained from the National Institute of Health, Bethesda, MD. NCBI-BLAST2 uses several search parameters, wherein all of those search parameters are set to default values including, for example, unmask = yes, strand = all, expected occurrences = 10, minimum low complexity length = 15/5, multi-pass e-value = 0.01, constant for multi-pass = 25, dropoff for final gapped alignment = 25 and scoring matrix = BLOSUM62.

In situations where NCBI-BLAST2 is employed for amino acid sequence comparisons, the % amino acid sequence identity of a given amino acid sequence A to, with, or against a given amino acid sequence B (which can alternatively be phrased as a given amino acid sequence A that has or comprises a certain % amino acid sequence identity to, with, or against a given amino acid sequence B) is calculated as follows:

$$100 \text{ times the fraction } X/Y$$

where X is the number of amino acid residues scored as identical matches by the sequence alignment program NCBI-BLAST2 in that program's alignment of A and B, and where Y is the total number of amino acid residues in B. It will be appreciated that where the length of amino acid sequence A is not equal to the

length of amino acid sequence B, the % amino acid sequence identity of A to B will not equal the % amino acid sequence identity of B to A.

"PRO variant polynucleotide" or "PRO variant nucleic acid sequence" means a nucleic acid molecule which encodes an active PRO polypeptide as defined below and which has at least about 80% nucleic acid sequence identity with a nucleotide acid sequence encoding a full-length native sequence PRO polypeptide sequence as disclosed herein, a full-length native sequence PRO polypeptide sequence lacking the signal peptide as disclosed herein, an extracellular domain of a PRO polypeptide, with or without the signal peptide, as disclosed herein or any other fragment of a full-length PRO polypeptide sequence as disclosed herein. Ordinarily, a PRO variant polynucleotide will have at least about 80% nucleic acid sequence identity, alternatively at least about 81% nucleic acid sequence identity, alternatively at least about 82% nucleic acid sequence identity, alternatively at least about 83% nucleic acid sequence identity, alternatively at least about 84% nucleic acid sequence identity, alternatively at least about 85% nucleic acid sequence identity, alternatively at least about 86% nucleic acid sequence identity, alternatively at least about 87% nucleic acid sequence identity, alternatively at least about 88% nucleic acid sequence identity, alternatively at least about 89% nucleic acid sequence identity, alternatively at least about 90% nucleic acid sequence identity, alternatively at least about 91% nucleic acid sequence identity, alternatively at least about 92% nucleic acid sequence identity, alternatively at least about 93% nucleic acid sequence identity, alternatively at least about 94% nucleic acid sequence identity, alternatively at least about 95% nucleic acid sequence identity, alternatively at least about 96% nucleic acid sequence identity, alternatively at least about 97% nucleic acid sequence identity, alternatively at least about 98% nucleic acid sequence identity and alternatively at least about 99% nucleic acid sequence identity with a nucleic acid sequence encoding a full-length native sequence PRO polypeptide sequence as disclosed herein, a full-length native sequence PRO polypeptide sequence lacking the signal peptide as disclosed herein, an extracellular domain of a PRO polypeptide, with or without the signal sequence, as disclosed herein or any other fragment of a full-length PRO polypeptide sequence as disclosed herein. Variants do not encompass the native nucleotide sequence.

Ordinarily, PRO variant polynucleotides are at least about 30 nucleotides in length, alternatively at least about 60 nucleotides in length, alternatively at least about 90 nucleotides in length, alternatively at least about 120 nucleotides in length, alternatively at least about 150 nucleotides in length, alternatively at least about 180 nucleotides in length, alternatively at least about 210 nucleotides in length, alternatively at least about 240 nucleotides in length, alternatively at least about 270 nucleotides in length, alternatively at least about 300 nucleotides in length, alternatively at least about 450 nucleotides in length, alternatively at least about 600 nucleotides in length, alternatively at least about 900 nucleotides in length, or more.

"Percent (%) nucleic acid sequence identity" with respect to PRO-encoding nucleic acid sequences identified herein is defined as the percentage of nucleotides in a candidate sequence that are identical with the nucleotides in the PRO nucleic acid sequence of interest, after aligning the sequences and introducing gaps, if necessary, to achieve the maximum percent sequence identity. Alignment for purposes of determining percent nucleic acid sequence identity can be achieved in various ways that are within the skill in the art, for instance, using publicly available computer software such as BLAST, BLAST-2, ALIGN or Megalign (DNASTAR) software. For purposes herein, however, % nucleic acid sequence identity values are generated using the sequence comparison computer program ALIGN-2, wherein the complete source code

for the ALIGN-2 program is provided in Table 1 below. The ALIGN-2 sequence comparison computer program was authored by Genentech, Inc. and the source code shown in Table 1 below has been filed with user documentation in the U.S. Copyright Office, Washington D.C., 20559, where it is registered under U.S. Copyright Registration No. TXU510087. The ALIGN-2 program is publicly available through Genentech, Inc., South San Francisco, California or may be compiled from the source code provided in Table 1 below. The ALIGN-2 program should be compiled for use on a UNIX operating system, preferably digital UNIX V4.0D. All sequence comparison parameters are set by the ALIGN-2 program and do not vary.

In situations where ALIGN-2 is employed for nucleic acid sequence comparisons, the % nucleic acid sequence identity of a given nucleic acid sequence C to, with, or against a given nucleic acid sequence D (which can alternatively be phrased as a given nucleic acid sequence C that has or comprises a certain % nucleic acid sequence identity to, with, or against a given nucleic acid sequence D) is calculated as follows:

$$100 \text{ times the fraction } W/Z$$

where W is the number of nucleotides scored as identical matches by the sequence alignment program ALIGN-2 in that program's alignment of C and D, and where Z is the total number of nucleotides in D. It will be appreciated that where the length of nucleic acid sequence C is not equal to the length of nucleic acid sequence D, the % nucleic acid sequence identity of C to D will not equal the % nucleic acid sequence identity of D to C. As examples of % nucleic acid sequence identity calculations, Tables 4 and 5, demonstrate how to calculate the % nucleic acid sequence identity of the nucleic acid sequence designated "Comparison DNA" to the nucleic acid sequence designated "PRO-DNA", wherein "PRO-DNA" represents a hypothetical PRO-encoding nucleic acid sequence of interest, "Comparison DNA" represents the nucleotide sequence of a nucleic acid molecule against which the "PRO-DNA" nucleic acid molecule of interest is being compared, and "N", "L" and "V" each represent different hypothetical nucleotides.

Unless specifically stated otherwise, all % nucleic acid sequence identity values used herein are obtained as described in the immediately preceding paragraph using the ALIGN-2 computer program. However, % nucleic acid sequence identity values may also be obtained as described below by using the WU-BLAST-2 computer program (Altschul et al., *Methods in Enzymology* 266:460-480 (1996)). Most of the WU-BLAST-2 search parameters are set to the default values. Those not set to default values, i.e., the adjustable parameters, are set with the following values: overlap span = 1, overlap fraction = 0.125, word threshold (T) = 11, and scoring matrix = BLOSUM62. When WU-BLAST-2 is employed, a % nucleic acid sequence identity value is determined by dividing (a) the number of matching identical nucleotides between the nucleic acid sequence of the PRO polypeptide-encoding nucleic acid molecule of interest having a sequence derived from the native sequence PRO polypeptide-encoding nucleic acid and the comparison nucleic acid molecule of interest (i.e., the sequence against which the PRO polypeptide-encoding nucleic acid molecule of interest is being compared which may be a variant PRO polynucleotide) as determined by WU-BLAST-2 by (b) the total number of nucleotides of the PRO polypeptide-encoding nucleic acid molecule of interest. For example, in the statement "an isolated nucleic acid molecule comprising a nucleic acid sequence A which has or having at least 80% nucleic acid sequence identity to the nucleic acid sequence B", the nucleic acid sequence A is the comparison nucleic acid molecule of interest and the nucleic

acid sequence B is the nucleic acid sequence of the PRO polypeptide-encoding nucleic acid molecule of interest.

Percent nucleic acid sequence identity may also be determined using the sequence comparison program NCBI-BLAST2 (Altschul et al., Nucleic Acids Res. 25:3389-3402 (1997)). The NCBI-BLAST2 sequence comparison program may be downloaded from <http://www.ncbi.nlm.nih.gov> or otherwise obtained from the National Institute of Health, Bethesda, MD. NCBI-BLAST2 uses several search parameters, wherein all of those search parameters are set to default values including, for example, unmask = yes, strand = all, expected occurrences = 10, minimum low complexity length = 15/5, multi-pass e-value = 0.01, constant for multi-pass = 25, dropoff for final gapped alignment = 25 and scoring matrix = BLOSUM62.

In situations where NCBI-BLAST2 is employed for sequence comparisons, the % nucleic acid sequence identity of a given nucleic acid sequence C to, with, or against a given nucleic acid sequence D (which can alternatively be phrased as a given nucleic acid sequence C that has or comprises a certain % nucleic acid sequence identity to, with, or against a given nucleic acid sequence D) is calculated as follows:

100 times the fraction W/Z

where W is the number of nucleotides scored as identical matches by the sequence alignment program NCBI-BLAST2 in that program's alignment of C and D, and where Z is the total number of nucleotides in D. It will be appreciated that where the length of nucleic acid sequence C is not equal to the length of nucleic acid sequence D, the % nucleic acid sequence identity of C to D will not equal the % nucleic acid sequence identity of D to C.

In other embodiments, PRO variant polynucleotides are nucleic acid molecules that encode an active PRO polypeptide and which are capable of hybridizing, preferably under stringent hybridization and wash conditions, to nucleotide sequences encoding a full-length PRO polypeptide as disclosed herein. PRO variant polypeptides may be those that are encoded by a PRO variant polynucleotide.

"Isolated," when used to describe the various polypeptides disclosed herein, means polypeptide that has been identified and separated and/or recovered from a component of its natural environment. Contaminant components of its natural environment are materials that would typically interfere with diagnostic or therapeutic uses for the polypeptide, and may include enzymes, hormones, and other proteinaceous or non-proteinaceous solutes. In preferred embodiments, the polypeptide will be purified (1) to a degree sufficient to obtain at least 15 residues of N-terminal or internal amino acid sequence by use of a spinning cup sequenator, or (2) to homogeneity by SDS-PAGE under non-reducing or reducing conditions using Coomassie blue or, preferably, silver stain. Isolated polypeptide includes polypeptide *in situ* within recombinant cells, since at least one component of the PRO polypeptide natural environment will not be present. Ordinarily, however, isolated polypeptide will be prepared by at least one purification step.

An "isolated" PRO polypeptide-encoding nucleic acid or other polypeptide-encoding nucleic acid is a nucleic acid molecule that is identified and separated from at least one contaminant nucleic acid molecule with which it is ordinarily associated in the natural source of the polypeptide-encoding nucleic acid. An isolated polypeptide-encoding nucleic acid molecule is other than in the form or setting in which it is found in nature. Isolated polypeptide-encoding nucleic acid molecules therefore are distinguished from the

specific polypeptide-encoding nucleic acid molecule as it exists in natural cells. However, an isolated polypeptide-encoding nucleic acid molecule includes polypeptide-encoding nucleic acid molecules contained in cells that ordinarily express the polypeptide where, for example, the nucleic acid molecule is in a chromosomal location different from that of natural cells.

5 The term "control sequences" refers to DNA sequences necessary for the expression of an operably linked coding sequence in a particular host organism. The control sequences that are suitable for prokaryotes, for example, include a promoter, optionally an operator sequence, and a ribosome binding site. Eukaryotic cells are known to utilize promoters, polyadenylation signals, and enhancers.

10 Nucleic acid is "operably linked" when it is placed into a functional relationship with another nucleic acid sequence. For example, DNA for a presequence or secretory leader is operably linked to DNA for a polypeptide if it is expressed as a preprotein that participates in the secretion of the polypeptide; a promoter or enhancer is operably linked to a coding sequence if it affects the transcription of the sequence; or a ribosome binding site is operably linked to a coding sequence if it is positioned so as to facilitate translation. Generally, "operably linked" means that the DNA sequences being linked are contiguous, and, 15 in the case of a secretory leader, contiguous and in reading phase. However, enhancers do not have to be contiguous. Linking is accomplished by ligation at convenient restriction sites. If such sites do not exist, the synthetic oligonucleotide adaptors or linkers are used in accordance with conventional practice.

The term "antibody" is used in the broadest sense and specifically covers, for example, single anti-PRO monoclonal antibodies (including agonist, antagonist, and neutralizing antibodies), anti-PRO antibody 20 compositions with polyepitopic specificity, single chain anti-PRO antibodies, and fragments of anti-PRO antibodies (see below). The term "monoclonal antibody" as used herein refers to an antibody obtained from a population of substantially homogeneous antibodies, i.e., the individual antibodies comprising the population are identical except for possible naturally-occurring mutations that may be present in minor amounts.

25 "Stringency" of hybridization reactions is readily determinable by one of ordinary skill in the art, and generally is an empirical calculation dependent upon probe length, washing temperature, and salt concentration. In general, longer probes require higher temperatures for proper annealing, while shorter probes need lower temperatures. Hybridization generally depends on the ability of denatured DNA to reanneal when complementary strands are present in an environment below their melting temperature. The 30 higher the degree of desired homology between the probe and hybridizable sequence, the higher the relative temperature which can be used. As a result, it follows that higher relative temperatures would tend to make the reaction conditions more stringent, while lower temperatures less so. For additional details and explanation of stringency of hybridization reactions, see Ausubel et al., Current Protocols in Molecular Biology, Wiley Interscience Publishers, (1995).

35 "Stringent conditions" or "high stringency conditions", as defined herein, may be identified by those that: (1) employ low ionic strength and high temperature for washing, for example 0.015 M sodium chloride/0.0015 M sodium citrate/0.1% sodium dodecyl sulfate at 50°C; (2) employ during hybridization a denaturing agent, such as formamide, for example, 50% (v/v) formamide with 0.1% bovine serum albumin/0.1% Ficoll/0.1% polyvinylpyrrolidone/50mM sodium phosphate buffer at pH 6.5 with 750 mM 40 sodium chloride, 75 mM sodium citrate at 42°C; or (3) employ 50% formamide, 5 x SSC (0.75 M NaCl,

0.075 M sodium citrate), 50 mM sodium phosphate (pH 6.8), 0.1% sodium pyrophosphate, 5 x Denhardt's solution, sonicated salmon sperm DNA (50 µg/ml), 0.1% SDS, and 10% dextran sulfate at 42°C, with washes at 42°C in 0.2 x SSC (sodium chloride/sodium citrate) and 50% formamide at 55°C, followed by a high-stringency wash consisting of 0.1 x SSC containing EDTA at 55°C.

5 "Moderately stringent conditions" may be identified as described by Sambrook et al., Molecular Cloning: A Laboratory Manual, New York: Cold Spring Harbor Press, 1989, and include the use of washing solution and hybridization conditions (e.g., temperature, ionic strength and %SDS) less stringent than those described above. An example of moderately stringent conditions is overnight incubation at 37°C in a solution comprising: 20% formamide, 5 x SSC (150 mM NaCl, 15 mM trisodium citrate), 50 mM sodium
10 phosphate (pH 7.6), 5 x Denhardt's solution, 10% dextran sulfate, and 20 mg/ml denatured sheared salmon sperm DNA, followed by washing the filters in 1 x SSC at about 37-50°C. The skilled artisan will recognize how to adjust the temperature, ionic strength, etc. as necessary to accommodate factors such as probe length and the like.

The term "epitope tagged" when used herein refers to a chimeric polypeptide comprising a PRO
15 polypeptide fused to a "tag polypeptide". The tag polypeptide has enough residues to provide an epitope against which an antibody can be made, yet is short enough such that it does not interfere with activity of the polypeptide to which it is fused. The tag polypeptide preferably also is fairly unique so that the antibody does not substantially cross-react with other epitopes. Suitable tag polypeptides generally have at least six amino acid residues and usually between about 8 and 50 amino acid residues (preferably, between about 10
20 and 20 amino acid residues).

As used herein, the term "immunoadhesin" designates antibody-like molecules which combine the binding specificity of a heterologous protein (an "adhesin") with the effector functions of immunoglobulin constant domains. Structurally, the immunoadhesins comprise a fusion of an amino acid sequence with the desired binding specificity which is other than the antigen recognition and binding site of an antibody (i.e., is
25 "heterologous"), and an immunoglobulin constant domain sequence. The adhesin part of an immunoadhesin molecule typically is a contiguous amino acid sequence comprising at least the binding site of a receptor or a ligand. The immunoglobulin constant domain sequence in the immunoadhesin may be obtained from any immunoglobulin, such as IgG-1, IgG-2, IgG-3, or IgG-4 subtypes, IgA (including IgA-1 and IgA-2), IgE, IgD or IgM.

30 "Active" or "activity" for the purposes herein refers to form(s) of a PRO polypeptide which retain a biological and/or an immunological activity of native or naturally-occurring PRO, wherein "biological" activity refers to a biological function (either inhibitory or stimulatory) caused by a native or naturally-occurring PRO other than the ability to induce the production of an antibody against an antigenic epitope possessed by a native or naturally-occurring PRO and an "immunological" activity refers to the ability to
35 induce the production of an antibody against an antigenic epitope possessed by a native or naturally-occurring PRO.

The term "antagonist" is used in the broadest sense, and includes any molecule that partially or fully blocks, inhibits, or neutralizes a biological activity of a native PRO polypeptide disclosed herein. In a similar manner, the term "agonist" is used in the broadest sense and includes any molecule that mimics a
40 biological activity of a native PRO polypeptide disclosed herein. Suitable agonist or antagonist molecules

specifically include agonist or antagonist antibodies or antibody fragments, fragments or amino acid sequence variants of native PRO polypeptides, peptides, antisense oligonucleotides, small organic molecules, etc. Methods for identifying agonists or antagonists of a PRO polypeptide may comprise contacting a PRO polypeptide with a candidate agonist or antagonist molecule and measuring a detectable change in one or more biological activities normally associated with the PRO polypeptide.

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

"Chronic" administration refers to administration of the agent(s) in a continuous mode as opposed to an acute mode, so as to maintain the initial therapeutic effect (activity) for an extended period of time. "Intermittent" administration is treatment that is not consecutively done without interruption, but rather is cyclic in nature.

"Mammal" for purposes of treatment refers to any animal classified as a mammal, including humans, domestic and farm animals, and zoo, sports, or pet animals, such as dogs, cats, cattle, horses, sheep, pigs, goats, rabbits, etc. Preferably, the mammal is human.

Administration "in combination with" one or more further therapeutic agents includes simultaneous (concurrent) and consecutive administration in any order.

"Carriers" as used herein include pharmaceutically acceptable carriers, excipients, or stabilizers which are nontoxic to the cell or mammal being exposed thereto at the dosages and concentrations employed. Often the physiologically acceptable carrier is an aqueous pH buffered solution. Examples of physiologically acceptable carriers include buffers such as phosphate, citrate, and other organic acids; antioxidants including ascorbic acid; low molecular weight (less than about 10 residues) polypeptide; proteins, such as serum albumin, gelatin, or immunoglobulins; hydrophilic polymers such as polyvinylpyrrolidone; amino acids such as glycine, glutamine, asparagine, arginine or lysine; monosaccharides, disaccharides, and other carbohydrates including glucose, mannose, or dextrans; chelating agents such as EDTA; sugar alcohols such as mannitol or sorbitol; salt-forming counterions such as sodium; and/or nonionic surfactants such as TWEENTM, polyethylene glycol (PEG), and PLURONICTM.

"Antibody fragments" comprise a portion of an intact antibody, preferably the antigen binding or variable region of the intact antibody. Examples of antibody fragments include Fab, Fab', F(ab')₂, and Fv fragments; diabodies; linear antibodies (Zapata et al., *Protein Eng.* 8(10): 1057-1062 [1995]); single-chain antibody molecules; and multispecific antibodies formed from antibody fragments.

Papain digestion of antibodies produces two identical antigen-binding fragments, called "Fab" fragments, each with a single antigen-binding site, and a residual "Fc" fragment, a designation reflecting the ability to crystallize readily. Pepsin treatment yields an F(ab')₂ fragment that has two antigen-combining sites and is still capable of cross-linking antigen.

"Fv" is the minimum antibody fragment which contains a complete antigen-recognition and -binding site. This region consists of a dimer of one heavy- and one light-chain variable domain in tight, non-covalent association. It is in this configuration that the three CDRs of each variable domain interact to define an antigen-binding site on the surface of the V_H-V_L dimer. Collectively, the six CDRs confer antigen-

binding specificity to the antibody. However, even a single variable domain (or half of an Fv comprising only three CDRs specific for an antigen) has the ability to recognize and bind antigen, although at a lower affinity than the entire binding site.

The Fab fragment also contains the constant domain of the light chain and the first constant domain (CH1) of the heavy chain. Fab fragments differ from Fab' fragments by the addition of a few residues at the carboxy terminus of the heavy chain CH1 domain including one or more cysteines from the antibody hinge region. Fab'-SH is the designation herein for Fab' in which the cysteine residue(s) of the constant domains bear a free thiol group. F(ab')₂ antibody fragments originally were produced as pairs of Fab' fragments which have hinge cysteines between them. Other chemical couplings of antibody fragments are also known.

The "light chains" of antibodies (immunoglobulins) from any vertebrate species can be assigned to one of two clearly distinct types, called kappa and lambda, based on the amino acid sequences of their constant domains.

Depending on the amino acid sequence of the constant domain of their heavy chains, immunoglobulins can be assigned to different classes. There are five major classes of immunoglobulins: IgA, IgD, IgE, IgG, and IgM, and several of these may be further divided into subclasses (isotypes), e.g., IgG1, IgG2, IgG3, IgG4, IgA, and IgA2.

"Single-chain Fv" or "sFv" antibody fragments comprise the V_H and V_L domains of antibody, wherein these domains are present in a single polypeptide chain. Preferably, the Fv polypeptide further comprises a polypeptide linker between the V_H and V_L domains which enables the sFv to form the desired structure for antigen binding. For a review of sFv, see Pluckthun in The Pharmacology of Monoclonal Antibodies, vol. 113, Rosenberg and Moore eds., Springer-Verlag, New York, pp. 269-315 (1994).

The term "diabodies" refers to small antibody fragments with two antigen-binding sites, which fragments comprise a heavy-chain variable domain (V_H) connected to a light-chain variable domain (V_L) in the same polypeptide chain (V_H-V_L). By using a linker that is too short to allow pairing between the two domains on the same chain, the domains are forced to pair with the complementary domains of another chain and create two antigen-binding sites. Diabodies are described more fully in, for example, EP 404,097; WO 93/11161; and Hollinger et al., Proc. Natl. Acad. Sci. USA, 90:6444-6448 (1993).

An "isolated" antibody is one which has been identified and separated and/or recovered from a component of its natural environment. Contaminant components of its natural environment are materials which would interfere with diagnostic or therapeutic uses for the antibody, and may include enzymes, hormones, and other proteinaceous or nonproteinaceous solutes. In preferred embodiments, the antibody will be purified (1) to greater than 95% by weight of antibody as determined by the Lowry method, and most preferably more than 99% by weight, (2) to a degree sufficient to obtain at least 15 residues of N-terminal or internal amino acid sequence by use of a spinning cup sequenator, or (3) to homogeneity by SDS-PAGE under reducing or nonreducing conditions using Coomassie blue or, preferably, silver stain. Isolated antibody includes the antibody in situ within recombinant cells since at least one component of the antibody's natural environment will not be present. Ordinarily, however, isolated antibody will be prepared by at least one purification step.

An antibody that "specifically binds to" or is "specific for" a particular polypeptide or an epitope on a particular polypeptide is one that binds to that particular polypeptide or epitope on a particular polypeptide without substantially binding to any other polypeptide or polypeptide epitope.

The word "label" when used herein refers to a detectable compound or composition which is conjugated directly or indirectly to the antibody so as to generate a "labeled" antibody. The label may be detectable by itself (e.g. radioisotope labels or fluorescent labels) or, in the case of an enzymatic label, may catalyze chemical alteration of a substrate compound or composition which is detectable.

By "solid phase" is meant a non-aqueous matrix to which the antibody of the present invention can adhere. Examples of solid phases encompassed herein include those formed partially or entirely of glass (e.g., controlled pore glass), polysaccharides (e.g., agarose), polyacrylamides, polystyrene, polyvinyl alcohol and silicones. In certain embodiments, depending on the context, the solid phase can comprise the well of an assay plate; in others it is a purification column (e.g., an affinity chromatography column). This term also includes a discontinuous solid phase of discrete particles, such as those described in U.S. Patent No. 4,275,149.

A "liposome" is a small vesicle composed of various types of lipids, phospholipids and/or surfactant which is useful for delivery of a drug (such as a PRO polypeptide or antibody thereto) to a mammal. The components of the liposome are commonly arranged in a bilayer formation, similar to the lipid arrangement of biological membranes.

A "small molecule" is defined herein to have a molecular weight below about 500 Daltons.

The term "immune related disease" means a disease in which a component of the immune system of a mammal causes, mediates or otherwise contributes to a morbidity in the mammal. Also included are diseases in which stimulation or intervention of the immune response has an ameliorative effect on progression of the disease. Included within this term are immune-mediated inflammatory diseases, non-immune-mediated inflammatory diseases, infectious diseases, immunodeficiency diseases, neoplasia, etc.

The term "T cell mediated disease" means a disease in which T cells directly or indirectly mediate or otherwise contribute to a morbidity in a mammal. The T cell mediated disease may be associated with cell mediated effects, lymphokine mediated effects, etc., and even effects associated with B cells if the B cells are stimulated, for example, by the lymphokines secreted by T cells.

Examples of immune-related and inflammatory diseases, some of which are immune or T cell mediated, which can be treated according to the invention include systemic lupus erythematosus, rheumatoid arthritis, juvenile chronic arthritis, spondyloarthropathies, systemic sclerosis (scleroderma), idiopathic inflammatory myopathies (dermatomyositis, polymyositis), Sjögren's syndrome, systemic vasculitis, sarcoidosis, autoimmune hemolytic anemia (immune pancytopenia, paroxysmal nocturnal hemoglobinuria), autoimmune thrombocytopenia (idiopathic thrombocytopenic purpura, immune-mediated thrombocytopenia), thyroiditis (Grave's disease, Hashimoto's thyroiditis, juvenile lymphocytic thyroiditis, atrophic thyroiditis), diabetes mellitus, immune-mediated renal disease (glomerulonephritis, tubulointerstitial nephritis), demyelinating diseases of the central and peripheral nervous systems such as multiple sclerosis, idiopathic demyelinating polyneuropathy or Guillain-Barré syndrome, and chronic inflammatory demyelinating polyneuropathy, hepatobiliary diseases such as infectious hepatitis (hepatitis A, B, C, D, E and other non-hepatotropic viruses), autoimmune chronic active hepatitis, primary biliary cirrhosis,

granulomatous hepatitis, and sclerosing cholangitis, inflammatory bowel disease (ulcerative colitis: Crohn's disease), gluten-sensitive enteropathy, and Whipple's disease, autoimmune or immune-mediated skin diseases including bullous skin diseases, erythema multiforme and contact dermatitis, psoriasis, allergic diseases such as asthma, allergic rhinitis, atopic dermatitis, food hypersensitivity and urticaria, immunologic diseases of the lung such as eosinophilic pneumonias, idiopathic pulmonary fibrosis and hypersensitivity pneumonitis, transplantation associated diseases including graft rejection and graft -versus-host-disease. Infectious diseases including viral diseases such as AIDS (HIV infection), hepatitis A, B, C, D, and E, herpes, etc., bacterial infections, fungal infections, protozoal infections and parasitic infections.

The term "effective amount" is a concentration or amount of a PRO polypeptide and/or agonist/antagonist which results in achieving a particular stated purpose. An "effective amount" of a PRO polypeptide or agonist or antagonist thereof may be determined empirically. Furthermore, a "therapeutically effective amount" is a concentration or amount of a PRO polypeptide and/or agonist/antagonist which is effective for achieving a stated therapeutic effect. This amount may also be determined empirically.

The term "cytotoxic agent" as used herein refers to a substance that inhibits or prevents the function of cells and/or causes destruction of cells. The term is intended to include radioactive isotopes (e.g., I^{131} , I^{125} , Y^{90} and Re^{186}), chemotherapeutic agents, and toxins such as enzymatically active toxins of bacterial, fungal, plant or animal origin, or fragments thereof.

A "chemotherapeutic agent" is a chemical compound useful in the treatment of cancer. Examples of chemotherapeutic agents include adriamycin, doxorubicin, epirubicin, 5-fluorouracil, cytosine arabinoside ("Ara-C"), cyclophosphamide, thiotepa, busulfan, cytosin, taxoids, e.g., paclitaxel (Taxol, Bristol-Myers Squibb Oncology, Princeton, NJ), and doxorubicin (Taxotere, Rhône-Poulenc Rorer, Antony, France), taxotere, methotrexate, cisplatin, melphalan, vinblastine, bleomycin, etoposide, ifosfamide, mitomycin C, mitoxantrone, vincristine, vinorelbine, carboplatin, teniposide, daunomycin, carminomycin, aminopterin, dactinomycin, mitomycins, esperamicins (see U.S. Pat. No. 4,675,187), melphalan and other related nitrogen mustards. Also included in this definition are hormonal agents that act to regulate or inhibit hormone action on tumors such as tamoxifen and onapristone.

A "growth inhibitory agent" when used herein refers to a compound or composition which inhibits growth of a cell, especially cancer cell overexpressing any of the genes identified herein, either *in vitro* or *in vivo*. Thus, the growth inhibitory agent is one which significantly reduces the percentage of cells overexpressing such genes in S phase. Examples of growth inhibitory agents include agents that block cell cycle progression (at a place other than S phase), such as agents that induce G1 arrest and M-phase arrest. Classical M-phase blockers include the vincas (vincristine and vinblastine), taxol, and topo II inhibitors such as doxorubicin, epirubicin, daunorubicin, etoposide, and bleomycin. Those agents that arrest G1 also spill over into S-phase arrest, for example, DNA alkylating agents such as tamoxifen, prednisone, dacarbazine, mechlorethamine, cisplatin, methotrexate, 5-fluorouracil, and ara-C. Further information can be found in *The Molecular Basis of Cancer*, Mendelsohn and Israel, eds., Chapter 1, entitled "Cell cycle regulation, oncogens, and antineoplastic drugs" by Murakami *et al.* (WB Saunders: Philadelphia, 1995), especially p. 13.

The term "cytokine" is a generic term for proteins released by one cell population which act on another cell as intercellular mediators. Examples of such cytokines are lymphokines, monokines, and

traditional polypeptide hormones. Included among the cytokines are growth hormone such as human growth hormone, N-methionyl human growth hormone, and bovine growth hormone; parathyroid hormone; thyroxine; insulin; proinsulin; relaxin; prolaxin; glycoprotein hormones such as follicle stimulating hormone (FSH), thyroid stimulating hormone (TSH), and luteinizing hormone (LH); hepatic growth factor; 5 fibroblast growth factor; prolactin; placental lactogen; tumor necrosis factor- α and - β ; mullerian-inhibiting substance; mouse gonadotropin-associated peptide; inhibin; activin; vascular endothelial growth factor; integrin; thrombopoietin (TPO); nerve growth factors such as NGF- β ; platelet-growth factor; transforming growth factors (TGFs) such as TGF- α and TGF- β ; insulin-like growth factor-I and -II; erythropoietin (EPO); osteoinductive factors; interferons such as interferon- α , - β , and - γ ; colony stimulating factors (CSFs) such as 10 macrophage-CSF (M-CSF); granulocyte-macrophage-CSF (GM-CSF); and granulocyte-CSF (G-CSF); interleukins (ILs) such as IL-1, IL-1 α , IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-11, IL-12; a tumor necrosis factor such as TNF- α or TNF- β ; and other polypeptide factors including LIF and kit ligand (KL). As used herein, the term cytokine includes proteins from natural sources or from recombinant cell culture and biologically active equivalents of the native sequence cytokines.

15 As used herein, the term "immunoadhesin" designates antibody-like molecules which combine the binding specificity of a heterologous protein (an "adhesin") with the effector functions of immunoglobulin constant domains. Structurally, the immunoadhesins comprise a fusion of an amino acid sequence with the desired binding specificity which is other than the antigen recognition and binding site of an antibody (*i.e.*, is "heterologous"), and an immunoglobulin constant domain sequence. The adhesin part of an immunoadhesin 20 molecule typically is a contiguous amino acid sequence comprising at least the binding site of a receptor or a ligand. The immunoglobulin constant domain sequence in the immunoadhesin may be obtained from any immunoglobulin, such as IgG-1, IgG-2, IgG-3, or IgG-4 subtypes, IgA (including IgA-1 and IgA-2), IgE, IgD or IgM.

25 As used herein, the term "inflammatory cells" designates cells that enhance the inflammatory response such as mononuclear cells, eosinophils, macrophages, and polymorphonuclear neutrophils (PMN).

Table 1

```

/*
5  *
  * C-C increased from 12 to 15
  * Z is average of EQ
  * B is average of ND
  * match with stop is _M; stop-stop = 0; J (joker) match = 0
10 */
#define _M      -8      /* value of a match with a stop */

int
/* A B C D E F G H I J K L M N O P Q R S T U V W X Y Z */
15 /* A */ { 2, 0, -2, 0, 0, -4, 1, -1, -1, 0, -1, -2, -1, 0, _M, 1, 0, -2, 1, 1, 0, 0, -6, 0, -3, 0},
/* B */ { 0, 3, -4, 3, 2, -5, 0, 1, -2, 0, 0, -3, -2, 2, _M, -1, 1, 0, 0, 0, 0, -2, -5, 0, -3, 1},
/* C */ {-2, -4, 15, -5, -5, -4, -3, -3, -2, 0, -5, -6, -5, -4, _M, -3, -5, -4, 0, -2, 0, -2, -8, 0, 0, -5},
/* D */ { 0, 3, -5, 4, 3, -6, 1, 1, -2, 0, 0, -4, -3, 2, _M, -1, 2, -1, 0, 0, 0, -2, -7, 0, -4, 2},
/* E */ { 0, 2, -5, 3, 4, -5, 0, 1, -2, 0, 0, -3, -2, 1, _M, -1, 2, -1, 0, 0, 0, -2, -7, 0, -4, 3},
20 /* F */ {-4, -5, -4, -6, -5, 9, -5, -2, 1, 0, -5, 2, 0, -4, _M, -5, -5, -4, -3, -3, 0, -1, 0, 0, 7, -5},
/* G */ { 1, 0, -3, 1, 0, -5, 5, -2, -3, 0, -2, -4, -3, 0, _M, -1, -1, -3, 1, 0, 0, -1, -7, 0, -5, 0},
/* H */ {-1, 1, -3, 1, 1, -2, -2, 6, -2, 0, 0, -2, -2, 2, _M, 0, 3, 2, -1, -1, 0, -2, -3, 0, 0, 2},
/* I */ {-1, -2, -2, -2, 1, -3, -2, 5, 0, -2, 2, 2, -2, _M, -2, -2, -2, -1, 0, 0, 4, -5, 0, -1, -2},
/* J */ { 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, _M, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0},
25 /* K */ {-1, 0, -5, 0, 0, -5, -2, 0, -2, 0, 5, -3, 0, 1, _M, -1, 1, 3, 0, 0, 0, -2, -3, 0, -4, 0},
/* L */ {-2, -3, -6, -4, -3, 2, -4, -2, 2, 0, -3, 6, 4, -3, _M, -3, -2, -3, -3, -1, 0, 2, -2, 0, -1, -2},
/* M */ {-1, -2, -5, -3, -2, 0, -3, -2, 2, 0, 0, 4, 6, -2, _M, -2, -1, 0, -2, -1, 0, 2, -4, 0, -2, -1},
/* N */ { 0, 2, -4, 2, 1, -4, 0, 2, -2, 0, 1, -3, -2, 2, _M, -1, 1, 0, 1, 0, 0, -2, -4, 0, -2, 1},
/* O */ { _M, _M, _M, _M, _M, _M, _M, _M, _M, _M, _M, _M, _M, _M, _M, _M, _M, _M, _M, _M, _M, _M, _M, _M, _M},
30 /* P */ { 1, -1, -3, -1, -1, -5, -1, 0, -2, 0, -1, -3, -2, -1, _M, 6, 0, 0, 1, 0, 0, -1, -6, 0, -5, 0},
/* Q */ { 0, 1, -5, 2, 2, -5, -1, 3, -2, 0, 1, -2, -1, 1, _M, 0, 4, 1, -1, -1, 0, -2, -5, 0, -4, 3},
/* R */ {-2, 0, -4, -1, -1, -4, -3, 2, -2, 0, 3, -3, 0, 0, _M, 0, 1, 6, 0, -1, 0, -2, 2, 0, -4, 0},
/* S */ { 1, 0, 0, 0, 0, -3, 1, -1, -1, 0, 0, -3, -2, 1, _M, 1, -1, 0, 2, 1, 0, -1, -2, 0, -3, 0},
/* T */ { 1, 0, -2, 0, 0, -3, 0, -1, 0, 0, 0, -1, -1, 0, _M, 0, -1, -1, 1, 3, 0, 0, -5, 0, -3, 0},
35 /* U */ { 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, _M, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0},
/* V */ { 0, -2, -2, -2, -2, -1, -1, -2, 4, 0, -2, 2, 2, -2, _M, -1, -2, -2, -1, 0, 0, 4, -6, 0, -2, -2},
/* W */ {-6, -5, -8, -7, -7, 0, -7, -3, -5, 0, -3, -2, -4, -4, _M, -6, -5, 2, -2, -5, 0, -6, 17, 0, 0, -6},
/* X */ { 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, _M, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0},
/* Y */ {-3, -3, 0, -4, -4, 7, -5, 0, -1, 0, -4, -1, -2, -2, _M, -5, -4, -4, -3, -3, 0, -2, 0, 0, 10, -4},
40 /* Z */ { 0, 1, -5, 2, 3, -5, 0, 2, -2, 0, 0, -2, -1, 1, _M, 0, 3, 0, 0, 0, 0, -2, -6, 0, -4, 4}
};

```

Table 1 (cont')

```

/*
*/
#include <stdio.h>
#include <ctype.h>

#define MAXJMP 16 /* max jumps in a diag */
#define MAXGAP 24 /* don't continue to penalize gaps larger than this */
#define JMPS 1024 /* max jumps in an path */
10 #define MX 4 /* save if there's at least MX-1 bases since last jmp */

#define DMAT 3 /* value of matching bases */
#define DMIS 0 /* penalty for mismatched bases */
#define DINS0 8 /* penalty for a gap */
15 #define DINS1 1 /* penalty per base */
#define PINS0 8 /* penalty for a gap */
#define PINS1 4 /* penalty per residue */

struct jmp {
20     short      n[MAXJMP]; /* size of jmp (neg for dely) */
     unsigned short x[MAXJMP]; /* base no. of jmp in seq x */
}; /* limits seq to 2^16 -1 */

struct diag {
25     int      score; /* score at last jmp */
     long     offset; /* offset of prev block */
     short    jmp; /* current jmp index */
     struct jmp list; /* list of jmps */
};

30 struct path {
     int      spc; /* number of leading spaces */
     short    n[JMPMS]; /* size of jmp (gap) */
     int      x[JMPMS]; /* loc of jmp (last elem before gap) */
35 };

char      *ofile; /* output file name */
char      *namex[2]; /* seq names: getseqs() */
char      *prog; /* prog name for crr msgs */
40 char      *seqx[2]; /* seqs: getseqs() */
int      dmax; /* best diag: nw() */
int      dmax0; /* final diag */
int      dna; /* set if dna: main() */
int      endgaps; /* set if penalizing end gaps */
45 int      gapx, gapy; /* total gaps in seqs */
int      len0, len1; /* seq lens */
int      ngapx, ngapy; /* total size of gaps */
int      smax; /* max score: nw() */
int      *xbm; /* bitmap for matching */
50 long     offset; /* current offset in jmp file */
struct    diag *dx; /* holds diagonals */
struct    path pp[2]; /* holds path for seqs */

char      *calloc(), *malloc(), *index(), *strcpy();
55 char      *getseq(), *g_calloc();

```

60

Table 1 (cont')

```

/* Needleman-Wunsch alignment program
*
* usage: prog file1 file2
* where file1 and file2 are two dna or two protein sequences.
* The sequences can be in upper- or lower-case and may contain ambiguity
* Any lines beginning with '!', '>' or '<' are ignored
* Max file length is 65535 (limited by unsigned short x in the jmp struct)
* A sequence with 1/3 or more of its elements ACGTU is assumed to be DNA
* Output is in the file "align.out"
*
* The program may create a tmp file in /tmp to hold info about traceback.
* Original version developed under BSD 4.3 on a vax 8650
*/
15 #include "nw.h"
#include "day.h"

static _dbval[26] = {
20 1,14,2,13,0,0,4,11,0,0,12,0,3,15,0,0,0,5,6,8,8,7,9,0,10,0
};

static _pbval[26] = {
25 1, 2[(1<<('D'-'A'))|(1<<('N'-'A'))], 4, 8, 16, 32, 64,
128, 256, 0xFFFFFFF, 1<<10, 1<<11, 1<<12, 1<<13, 1<<14,
1<<15, 1<<16, 1<<17, 1<<18, 1<<19, 1<<20, 1<<21, 1<<22,
1<<23, 1<<24, 1<<25[(1<<('E'-'A'))|(1<<('Q'-'A'))]
};

main(ac, av)
30 main
int ac;
char *av[ ];
{
35 prog = av[0];
if (ac != 3) {
fprintf(stderr, "usage: %s file1 file2\n", prog);
fprintf(stderr, "where file1 and file2 are two dna or two protein sequences.\n");
fprintf(stderr, "The sequences can be in upper- or lower-case\n");
40 fprintf(stderr, "Any lines beginning with '!' or '<' are ignored\n");
fprintf(stderr, "Output is in the file \"align.out\"\n");
exit(1);
}
namex[0] = av[1];
namex[1] = av[2];
45 seqx[0] = getseq(namex[0], &len0);
seqx[1] = getseq(namex[1], &len1);
xbm = (dna)? _dbval : _pbval;

endgaps = 0; /* 1 to penalize endgaps */
50 ofile = "align.out"; /* output file */

nw(); /* fill in the matrix, get the possible jmps */
readjmps(); /* get the actual jmps */
print(); /* print stats, alignment */
55 cleanup(); /* unlink any tmp files */
}
60

```

Table 1 (cont')

```

/* do the alignment, return best score: main()
 * dna: values in Fitch and Smith, PNAS, 80, 1382-1386, 1983
 * pro: PAM 250 values
5  * When scores are equal, we prefer mismatches to any gap, prefer
   * a new gap to extending an ongoing gap, and prefer a gap in seqx
   * to a gap in seq y.
   */
nw()
10 {
    char      *px, *py;          /* seqs and pirs */
    int        *ndely, *dely;    /* keep track of dely */
    int        ndelx, delx;      /* keep track of delx */
    int        *tmp;             /* for swapping row0, row1 */
    int        mis;              /* score for each type */
    int        ins0, ins1;       /* insertion penalties */
    register   id;               /* diagonal index */
    register   ij;               /* jmp index */
    register   *col0, *col1;      /* score for curr, last row */
    register   xx, yy;           /* index into seqs */

    dx = (struct diag *)g_calloc("to get diag", len0+len1+1, sizeof(struct diag));

25  ndely = (int *)g_calloc("to get ndely", len1+1, sizeof(int));
    dely = (int *)g_calloc("to get dely", len1+1, sizeof(int));
    col0 = (int *)g_calloc("to get col0", len1+1, sizeof(int));
    col1 = (int *)g_calloc("to get col1", len1+1, sizeof(int));
    ins0 = (dna)? DINS0 : PINS0;
    ins1 = (dna)? DINS1 : PINS1;

    smax = -10000;
    if (endgaps) {
35      for (col0[0] = dely[0] = -ins0, yy = 1; yy <= len1; yy++) {
          col0[yy] = dely[yy] = col0[yy-1] - ins1;
          ndely[yy] = yy;
      }
      col0[0] = 0;          /* Waterman Bull Math Biol 84 */
    }
    else
40      for (yy = 1; yy <= len1; yy++)
          dely[yy] = -ins0;

    /* fill in match matrix
    */
45  for (px = seqx[0], xx = 1; xx <= len0; px++, xx++) {
        /* initialize first entry in col
        */
50      if (endgaps) {
          if (xx == 1)
              col1[0] = delx = -(ins0+ins1);
          else
              col1[0] = delx = col0[0] - ins1;
          ndelx = xx;
55      }
      else {
          col1[0] = 0;
          delx = -ins0;
          ndelx = 0;
60      }
    }

```

Table 1 (cont²)

```

...nw
for (py = seqx[1], yy = 1; yy <= len1; py++, yy++) {
5      mis = col0[yy-1];
      if (dna)
          mis += (xbm[*px-'A']&xbm[*py-'A'])? DMAT : DMIS;
      else
          mis += _day[*px-'A'][*py-'A'];

10      /* update penalty for del in x seq;
       * favor new del over ongoing del
       * ignore MAXGAP if weighting endgaps
       */
      if (endgaps || ndely[yy] < MAXGAP) {
15          if (col0[yy] - ins0 >= dely[yy]) {
              dely[yy] = col0[yy] - (ins0+ins1);
              ndely[yy] = 1;
          } else {
              dely[yy] -= ins1;
              ndely[yy]++;
20          }
      } else {
          if (col0[yy] - (ins0+ins1) >= dely[yy]) {
              dely[yy] = col0[yy] - (ins0+ins1);
              ndely[yy] = 1;
25          } else
              ndely[yy]++;
      }

30      /* update penalty for del in y seq;
       * favor new del over ongoing del
       */
      if (endgaps || ndelx < MAXGAP) {
          if (col1[yy-1] - ins0 >= delx) {
35              delx = col1[yy-1] - (ins0+ins1);
              ndelx = 1;
          } else {
              delx -= ins1;
              ndelx++;
40          }
      } else {
          if (col1[yy-1] - (ins0+ins1) >= delx) {
              delx = col1[yy-1] - (ins0+ins1);
              ndelx = 1;
45          } else
              ndelx++;
      }

50      /* pick the maximum score; we're favoring
       * mis over any del and delx over dely
       */
55
60

```

Table 1 (cont²)

...nw

```

5      id = xx - yy + len1 - 1;
      if (mis >= delx && mis >= dely[yy])
          col1[yy] = mis;
      else if (delx >= dely[yy]) {
10         col1[yy] = delx;
          ij = dx[id].ijmp;
          if (dx[id].jp.n[0] && (ldna || (ndelx >= MAXJMP
15         && xx > dx[id].jp.x[ij]+MX) || mis > dx[id].score+DINS0)) {
              dx[id].ijmp++;
              if (++ij >= MAXJMP) {
                  writejumps(id);
                  ij = dx[id].ijmp = 0;
                  dx[id].offset = offset;
                  offset += sizeof(struct jmp) + sizeof(offset);
              }
              dx[id].jp.n[ij] = ndelx;
20             dx[id].jp.x[ij] = xx;
              dx[id].score = delx;
          }
      }
      else {
25         col1[yy] = dely[yy];
          ij = dx[id].ijmp;
          if (dx[id].jp.n[0] && (ldna || (ndely[yy] >= MAXJMP
              && xx > dx[id].jp.x[ij]+MX) || mis > dx[id].score+DINS0)) {
30             dx[id].ijmp++;
              if (++ij >= MAXJMP) {
                  writejumps(id);
                  ij = dx[id].ijmp = 0;
                  dx[id].offset = offset;
                  offset += sizeof(struct jmp) + sizeof(offset);
              }
35             dx[id].jp.n[ij] = -ndely[yy];
              dx[id].jp.x[ij] = xx;
              dx[id].score = dely[yy];
          }
40         if (xx == len0 && yy < len1) {
            /* last col
            */
            if (endgaps)
45                 col1[yy] -= ins0+ins1*(len1-yy);
            if (col1[yy] > smax) {
                smax = col1[yy];
                dmax = id;
            }
50         }
      }
      if (endgaps && xx < len0)
          col1[yy-1] -= ins0+ins1*(len0-xx);
      if (col1[yy-1] > smax) {
55         smax = col1[yy-1];
          dmax = id;
      }
      tmp = col0; col0 = col1; col1 = tmp;
60  }
      (void) free((char *)ndely);
      (void) free((char *)dely);
      (void) free((char *)col0);
      (void) free((char *)col1);
    }

```

Table 1 (cont²)

```

/*
 *
 * print() -- only routine visible outside this module
 *
5  * static:
 * getmat() -- trace back best path, count matches: print()
 * pr_align() -- print alignment of described in array p[ ]; print()
 * dumpblock() -- dump a block of lines with numbers, stars: pr_align()
10 * nums() -- put out a number line: dumpblock()
 * putline() -- put out a line (name, [num], seq, [num]): dumpblock()
 * stars() -- put a line of stars: dumpblock()
 * stripname() -- strip any path and prefix from a sequence
 */
15 #include "nw.h"

#define SPC      3
#define P_LINE   256 /* maximum output line */
20 #define P_SPC   3 /* space between name or num and seq */

extern _day[26][26];
int olen; /* set output line length */
FILE *fx; /* output file */
25 print()

{
    print
    {
        int lx, ly, firstgap, lastgap; /* overlap */
30         if ((fx = fopen(ofile, "w")) == 0) {
            fprintf(stderr, "%s: can't write %s\n", prog, ofile);
            cleanup(1);
        }
35         fprintf(fx, "<first sequence: %s (length = %d)\n", namex[0], len0);
        fprintf(fx, "<second sequence: %s (length = %d)\n", namex[1], len1);
        olen = 60;
        lx = len0;
        ly = len1;
40         firstgap = lastgap = 0;
        if (dmax < len1 - 1) { /* leading gap in x */
            pp[0].spc = firstgap = len1 - dmax - 1;
            ly -= pp[0].spc;
        }
45         else if (dmax > len1 - 1) { /* leading gap in y */
            pp[1].spc = firstgap = dmax - (len1 - 1);
            lx -= pp[1].spc;
        }
        if (dmax0 < len0 - 1) { /* trailing gap in x */
50             lastgap = len0 - dmax0 - 1;
            lx -= lastgap;
        }
        else if (dmax0 > len0 - 1) { /* trailing gap in y */
55             lastgap = dmax0 - (len0 - 1);
            ly -= lastgap;
        }
        getmat(lx, ly, firstgap, lastgap);
        pr_align();
60     }
}

```

Table 1 (cont')

```

/*
 * trace back the best path, count matches
 */
5 static
getmat(lx, ly, firstgap, lastgap)                                getmat
    int      lx, ly;
    int      firstgap, lastgap;
                                /* "core" (minus endgaps) */
                                /* leading trailing overlap */
{
10     int      nm, i0, i1, siz0, siz1;
    char      outx[32];
    double     pct;
    register   n0, n1;
    register char *p0, *p1;

15     /* get total matches, score
    */
    i0 = i1 = siz0 = siz1 = 0;
    p0 = seqx[0] + pp[1].spc;
    p1 = seqx[1] + pp[0].spc;
20     n0 = pp[1].spc + 1;
    n1 = pp[0].spc + 1;

    nm = 0;
25     while ( *p0 && *p1 ) {
        if (siz0) {
            p1++;
            n1++;
            siz0--;
30         }
        else if (siz1) {
            p0++;
            n0++;
            siz1--;
35         }
        else {
            if (xbm[ *p0-'A' ] & xbm[ *p1-'A' ])
                nm++;
            if (n0++ == pp[0].n[i0])
                siz0 = pp[0].n[i0++];
40             if (n1++ == pp[1].n[i1])
                siz1 = pp[1].n[i1++];
            p0++;
            p1++;
45         }
    }

    /* pct homology:
    * if penalizing endgaps, base is the shorter seq
    * else, knock off overhangs and take shorter core
    */
50     if (endgaps)
        lx = (len0 < len1)? len0 : len1;
    else
        lx = (lx < ly)? lx : ly;
55     pct = 100.*((double)nm)/((double)lx);
    fprintf(fx, "%n");
    fprintf(fx, "< %d match%s in an overlap of %d: %.2f percent similarity\n",
60         nm, (nm == 1)? "" : "es", lx, pct);

```

Table 1 (cont')

```

5      fprintf(fx, "<gaps in first sequence: %d", gapx);
      if (gapx) {
          (void) sprintf(outx, " (%d %s%s)",
              gapx, (dna)? "base": "residue", (ngapx == 1)? "" : "s");
          fprintf(fx, "%s", outx);

10      fprintf(fx, ", gaps in second sequence: %d", gapy);
      if (gapy) {
          (void) sprintf(outx, " (%d %s%s)",
              gapy, (dna)? "base": "residue", (ngapy == 1)? "" : "s");
          fprintf(fx, "%s", outx);
      }
15      if (dna)
          fprintf(fx,
              "\n<score: %d (match = %d, mismatch = %d, gap penalty = %d + %d per base)\n",
              smax, DMAT, DMIS, DINSO, DINS1);
      else
20      fprintf(fx,
              "\n<score: %d (Dayhoff PAM 250 matrix, gap penalty = %d + %d per residue)\n",
              smax, PINSO, PINS1);
      if (endgaps)
          fprintf(fx,
25      "<endgaps penalized. left endgap: %d %s%s, right endgap: %d %s%s\n",
              firstgap, (dna)? "base": "residue", (firstgap == 1)? "" : "s",
              lastgap, (dna)? "base": "residue", (lastgap == 1)? "" : "s");
      else
          fprintf(fx, "<endgaps not penalized\n");
30  }
      static      nm;          /* matches in core -- for checking */
      static      lmax;        /* lengths of stripped file names */
      static      ij[2];       /* jmp index for a path */
      static      nc[2];       /* number at start of current line */
35      static      ni[2];       /* current elem number -- for gapping */
      static      siz[2];
      static char  *ps[2];      /* ptr to current element */
      static char  *po[2];      /* ptr to next output char slot */
      static char  out[2][P_LINE]; /* output line */
40      static char star[P_LINE]; /* set by stars() */

      /*
      * print alignment of described in struct path pp[ ]
      */
45      static
      pr_align()
      {
          int      nn;          /* char count */
          int      more;
          register  i;

50      for (i = 0, lmax = 0; i < 2; i++) {
          nn = strlen(name[i]);
          if (nn > lmax)
75      lmax = nn;

          nc[i] = 1;
          ni[i] = 1;
          siz[i] = ij[i] = 0;
          ps[i] = seqx[i];
          po[i] = out[i];
60      }

```

...getmat

pr_align

Table 1 (cont²)

```

5      for (nn = nm = 0, more = 1; more; ) {
        for (i = more = 0; i < 2; i++) {
            /*
            * do we have more of this sequence?
            */
            if (!*ps[i])
10                continue;

            more++;

            if (pp[i].spc) { /* leading space */
                *po[i]++ = ' ';
                pp[i].spc--;
15            }
            else if (siz[i]) { /* in a gap */
                *po[i]++ = '-';
                siz[i]--;
20            }
            else { /* we're putting a seq element
            */
                *po[i] = *ps[i];
                if (islower(*ps[i]))
25                    *ps[i] = toupper(*ps[i]);
                po[i]++;
                ps[i]++;

                /*
                * are we at next gap for this seq?
                */
                if (ni[i] == pp[i].x[ij[i]]) {
                    /*
                    * we need to merge all gaps
                    * at this location
                    */
35                    siz[i] = pp[i].n[ij[i]++];
                    while (ni[i] == pp[i].x[ij[i]])
                        siz[i] += pp[i].n[ij[i]++];
40                }
                ni[i]++;
            }
        }
        if (++nn == olen || !more && nr) {
45            dumpblock();
            for (i = 0; i < 2; i++)
                po[i] = out[i];
            nn = 0;
        }
50    }

    /*
    * dump a block of lines, including numbers, stars: pr_align()
    */
55    static
    dumpblock()
    {
        register i;
        for (i = 0; i < 2; i++)
60            *po[i]-- = '\0';
    }

```

...pr_align

Table 1 (cont')

```

5      (void) puts("\n", fx);
      for (i = 0; i < 2; i++) {
          if (*out[i] && (*out[i] != ' ' || *(po[i]) != ' ')) {
              if (i == 0)
                  nums(i);
              if (i == 0 && *out[1])
10                  stars();
                  putline(i);
                  if (i == 0 && *out[1])
                      fprintf(fx, star);
15                  if (i == 1)
                      nums(i);
              }
          }
      }

20  /*
    * put out a number line: dumpblock()
    */
    static
    nums(ix)
25      int      ix;      /* index in out[ ] holding seq line */
    {
        char      nline[P_LINE];
        register  i, j;
        register  char *pn, *px, *py;
30
        for (pn = nline, i = 0; i < lmax+P_SPC; i++, pn++)
            *pn = ' ';
        for (i = nc[ix], py = out[ix]; *py; py++, pn++) {
            if (*py == ' ' || *py == '\n')
35                *pn = ' ';
            else {
                if (i%10 == 0 || (i == 1 && nc[ix] != 1)) {
                    j = (i < 0)? -i : i;
                    for (px = pn; j; j /= 10, px--)
40                        *px = j%10 + '0';
                    if (i < 0)
                        *px = '-';
                }
                else
45                    *pn = ' ';
                i++;
            }
        }
        *pn = '\0';
        nc[ix] = i;
        for (pn = nline; *pn; pn++)
            (void) puts(*pn, fx);
        (void) puts("\n", fx);
55    }

    /*
    * put out a line (name, [num], seq, [num]): dumpblock()
    */
    static
60    putline(ix)
        int      ix;
        {

```

...dumpblock

nums

putline

Table 1 (cont')

...putline

```

5      int          i;
      register char *px;

      for (px = namex[ix], i = 0; *px && *px != ':'; px++, i++)
          (void) putc(*px, fx);
10     for (; i < lmax+P_SPC; i++)
          (void) putc(' ', fx);

      /* these count from 1:
       * nif[] is current element (from 1)
       * ncl[] is number at start of current line
       */
15     for (px = out[ix]; *px; px++)
          (void) putc(*px&0x7F, fx);
      (void) putc('\n', fx);
20 }

/*
 * put a line of stars (seqs always in out[0], out[1]): dumpblock()
 */
25 static
stars()
{
    int          i;
30    register char *p0, *p1, cx, *px;

    if (!*out[0] || (*out[0] == '' && *(p0[0]) == ' ') ||
        !*out[1] || (*out[1] == '' && *(p0[1]) == ' '))
        return;
35    px = star;
    for (i = lmax+P_SPC; i; i--)
        *px++ = ' ';

    for (p0 = out[0], p1 = out[1]; *p0 && *p1; p0++, p1++) {
40        if (isalpha(*p0) && isalpha(*p1)) {
            if (xbmn[*p0-'A']&xbmn[*p1-'A']) {
                cx = '*';
                nm++;
            }
45            else if (!dna && _day[*p0-'A'][*p1-'A'] > 0)
                cx = '!';
            else
                cx = ' ';
50        }
        else
            cx = ' ';
        *px++ = cx;
55    }
    *px++ = '\n';
    *px = '\0';
}
60

```

Table 1 (cont')

```

/*
 * strip path or prefix from pn, return len: pr_align()
 */
5 static
  stripname(pn)
    stripname
      char *pn; /* file name (may be path) */
10 {
    register char *px, *py;

    py = 0;
    for (px = pn; *px; px++)
      if (*px == '/')
15         py = px + 1;
    if (py)
      (void) strcpy(pa, py);
    return(strlen(pn));
20 }

25

30

35

40

45

50

55

60

```

Table 1 (cont')

```

/*
 * cleanup() -- cleanup any tmp file
 * getseq() -- read in seq, set dna, len, maxlen
5  * g_alloc() -- alloc() with error checkin
 * readjumps() -- get the good jumps, from tmp file if necessary
 * writejumps() -- write a filled array of jumps to a tmp file: nw()
 */
#include "nw.h"
10 #include <sys/file.h>

char *jname = "/tmp/homgXXXXXX"; /* tmp file for jumps */
FILE *fj;

15 int cleanup(); /* cleanup tmp file */
long lseek();

/*
 * remove any tmp file if we blow
20 */
cleanup(i)
    int i;
{
    if (fj)
25         (void) unlink(jname);
    exit(i);
}

/*
 * read, return ptr to seq, set dna, len, maxlen
 * skip lines starting with ';', '<', or '>'
 * seq in upper or lower case
30 */
char *
35 getseq(file, len)
    char *file; /* file name */
    int *len; /* seq len */
{
    char line[1024], *pseq;
40     register char *px, *py;
    int natgc, tlen;
    FILE *fp;

    if ((fp = fopen(file, "r")) == 0) {
45         fprintf(stderr, "%s: can't read %s\n", prog, file);
        exit(1);
    }
    tlen = natgc = 0;
    while (fgets(line, 1024, fp)) {
50         if (*line == ';' || *line == '<' || *line == '>')
            continue;
        for (px = line; *px != '\n'; px++)
            if (isupper(*px) || islower(*px))
                tlen++;
55     }
    if ((pseq = malloc((unsigned)(tlen+6))) == 0) {
        fprintf(stderr, "%s: malloc() failed to get %d bytes for %s\n", prog, tlen+6, file);
        exit(1);
    }
60     pseq[0] = pseq[1] = pseq[2] = pseq[3] = '\0';

```

cleanup

getseq

Table 1 (cont')

```

5      py = pseq + 4;
      *len = tlen;
      rewind(fp);

      while (fgets(line, 1024, fp)) {
          if (*line == ';' || *line == '<' || *line == '>')
              continue;
10         for (px = line; *px != '\n'; px++) {
              if (isupper(*px))
                  *py++ = *px;
              else if (islower(*px))
                  *py++ = toupper(*px);
15             if (index("ATGCU", *(py-1)))
                 natgc++;
          }
      }
      *py++ = '\0';
      *py = '\0';
      (void) fclose(fp);
      dna = natgc > (tlen/3);
      return(pseq+4);
25 }

char *
g_alloc(msg, nx, sz)
char *msg; /* program, calling routine */
int nx, sz; /* number and size of elements */
30 {
    char *px, *calloc();

    if ((px = calloc((unsigned)nx, (unsigned)sz)) == 0) {
        if (*msg) {
35             fprintf(stderr, "%s: g_alloc() failed %s (n=%d, sz=%d)\n", prog, msg, nx, sz);
            exit(1);
        }
    }
    return(px);
40 }

/*
 * get final jmps from dx[ ] or tmp file, set pp[ ], reset dmax: main()
 */
45 readjmps()
    readjmps
{
    int fd = -1;
    int siz, i0, i1;
50 register i, j, xx;

    if (!f) {
        (void) fclose(f);
        if ((fd = open(jname, O_RDONLY, 0)) < 0) {
55             fprintf(stderr, "%s: can't open() %s\n", prog, jname);
            cleanup(1);
        }
    }
    for (i = i0 = i1 = 0, dmax0 = dmax, xx = len0; i++) {
60         while (1) {
            for (j = dx[dmax].ijmp; j >= 0 && dx[dmax].jp.x[j] >= xx; j--)
                ;

```

Table 1 (cont²)

...readjumps

```

5         if (j < 0 && dx[dmax].offset && fj) {
            (void) lseek(fd, dx[dmax].offset, 0);
            (void) read(fd, (char *)dx[dmax].jp, sizeof(struct jmp));
            (void) read(fd, (char *)dx[dmax].offset, sizeof(dx[dmax].offset));
            dx[dmax].jmp = MAXJMP-1;
        }
10        else
            break;
    }
    if (i >= JMPS) {
        fprintf(stderr, "%s: too many gaps in alignment\n", prog);
        cleanup(1);
15    }
    if (j >= 0) {
        siz = dx[dmax].jp.n[j];
        xx = dx[dmax].jp.x[j];
        dmax += siz;
20        if (siz < 0) { /* gap in second seq */
            pp[1].n[i1] = -siz;
            xx += siz;
            /* id = xx - yy + len1 - 1
            */
            pp[1].x[i1] = xx - dmax + len1 - 1;
            gapy++;
            ngapy -= siz;
        /* ignore MAXGAP when doing endgaps */
        siz = (-siz < MAXGAP || endgaps)? -siz : MAXGAP;
30        i1++;
        }
        else if (siz > 0) { /* gap in first seq */
            pp[0].n[i0] = siz;
            pp[0].x[i0] = xx;
35            gapx++;
            ngapx += siz;
        /* ignore MAXGAP when doing endgaps */
        siz = (siz < MAXGAP || endgaps)? siz : MAXGAP;
40        i0++;
        }
    }
    else
        break;
}

45    /* reverse the order of jumps
    */
    for (j = 0, i0--; j < i0; j++, i0--) {
        i = pp[0].n[j]; pp[0].n[j] = pp[0].n[i0]; pp[0].n[i0] = i;
        i = pp[0].x[j]; pp[0].x[j] = pp[0].x[i0]; pp[0].x[i0] = i;
50    }
    for (j = 0, i1--; j < i1; j++, i1--) {
        i = pp[1].n[j]; pp[1].n[j] = pp[1].n[i1]; pp[1].n[i1] = i;
        i = pp[1].x[j]; pp[1].x[j] = pp[1].x[i1]; pp[1].x[i1] = i;
55    }
    if (fd >= 0)
        (void) close(fd);
    if (fj) {
        (void) unlink(jname);
60        fj = 0;
        offset = 0;
    }
}

```

Table 1 (cont')

```

/*
* write a filled jmp struct offset of the prev one (if any): nw()
*/
5 writejumps(ix)
    writejumps
    int    ix;
10 {
    char    *mktemp();

    if (!fj) {
        if (mktemp(jname) < 0) {
            fprintf(stderr, "%s: can't mktemp() %s\n", prog, jname);
            cleanup(1);
15         }
        if ((fj = fopen(jname, "w")) == 0) {
            fprintf(stderr, "%s: can't write %s\n", prog, jname);
            exit(1);
20         }
    }
    (void) fwrite((char *)&dx[ix].jp, sizeof(struct jmp), 1, fj);
    (void) fwrite((char *)&dx[ix].offset, sizeof(dx[ix].offset), 1, fj);
25 }

```

Table 2

5	PRO	XXXXXXXXXXXXXXXXX	(Length = 15 amino acids)
	Comparison Protein	XXXXXXXXYYYYYY	(Length = 12 amino acids)
	% amino acid sequence identity =		

(the number of identically matching amino acid residues between the two polypeptide sequences as determined by ALIGN-2) divided by (the total number of amino acid residues of the PRO polypeptide) = 5 divided by 15 = 33.3%

Table 3

15	PRO	XXXXXXXXXX	(Length = 10 amino acids)
	Comparison Protein	XXXXXXXXYYYZZYZ	(Length = 15 amino acids)
	% amino acid sequence identity =		

(the number of identically matching amino acid residues between the two polypeptide sequences as determined by ALIGN-2) divided by (the total number of amino acid residues of the PRO polypeptide) = 5 divided by 10 = 50%

Table 4

25	PRO-DNA	NNNNNNNNNNNNNN	(Length = 14 nucleotides)
	Comparison DNA	NNNNNNLLLLLLLL	(Length = 16 nucleotides)

% nucleic acid sequence identity =

(the number of identically matching nucleotides between the two nucleic acid sequences as determined by ALIGN-2) divided by (the total number of nucleotides of the PRO-DNA nucleic acid sequence) = 6 divided by 14 = 42.9%

Table 5

35	PRO-DNA	NNNNNNNNNNNN	(Length = 12 nucleotides)
	Comparison DNA	NNNNLLLVV	(Length = 9 nucleotides)

% nucleic acid sequence identity =

40

(the number of identically matching nucleotides between the two nucleic acid sequences as determined by ALIGN-2) divided by (the total number of nucleotides of the PRO-DNA nucleic acid sequence) = 4 divided by 12 = 33.3%

5 II. Compositions and Methods of the Invention

A. Full-Length PRO Polypeptides

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO polypeptides. In particular, cDNAs encoding various PRO polypeptides have been identified and isolated, as disclosed in further detail in the Examples
10 below. However, for sake of simplicity, in the present specification the protein encoded by the full length native nucleic acid molecules disclosed herein as well as all further native homologues and variants included in the foregoing definition of PRO, will be referred to as "PRO/number", regardless of their origin or mode of preparation.

As disclosed in the Examples below, various cDNA clones have been disclosed. The predicted
15 amino acid sequence can be determined from the nucleotide sequence using routine skill. For the PRO polypeptides and encoding nucleic acids described herein, Applicants have identified what is believed to be the reading frame best identifiable with the sequence information available at the time.

B. PRO Polypeptide Variants

In addition to the full-length native sequence PRO polypeptides described herein, it is contemplated
20 that PRO variants can be prepared. PRO variants can be prepared by introducing appropriate nucleotide changes into the PRO DNA, and/or by synthesis of the desired PRO polypeptide. Those skilled in the art will appreciate that amino acid changes may alter post-translational processes of the PRO, such as changing the number or position of glycosylation sites or altering the membrane anchoring characteristics.

Variations in the native full-length sequence PRO or in various domains of the PRO described
25 herein, can be made, for example, using any of the techniques and guidelines for conservative and non-conservative mutations set forth, for instance, in U.S. Patent No. 5,364,934. Variations may be a substitution, deletion or insertion of one or more codons encoding the PRO that results in a change in the amino acid sequence of the PRO as compared with the native sequence PRO. Optionally, the variation is by substitution of at least one amino acid with any other amino acid in one or more of the domains of the PRO.
30 Guidance in determining which amino acid residue may be inserted, substituted or deleted without adversely affecting the desired activity may be found by comparing the sequence of the PRO with that of homologous known protein molecules and minimizing the number of amino acid sequence changes made in regions of high homology. Amino acid substitutions can be the result of replacing one amino acid with another amino acid having similar structural and/or chemical properties, such as the replacement of a leucine with a serine,
35 i.e., conservative amino acid replacements. Insertions or deletions may optionally be in the range of about 1 to 5 amino acids. The variation allowed may be determined by systematically making insertions, deletions or substitutions of amino acids in the sequence and testing the resulting variants for activity exhibited by the full-length or mature native sequence.

PRO polypeptide fragments are provided herein. Such fragments may be truncated at the N-
40 terminus or C-terminus, or may lack internal residues, for example, when compared with a full length native

protein. Certain fragments lack amino acid residues that are not essential for a desired biological activity of the PRO polypeptide.

PRO fragments may be prepared by any of a number of conventional techniques. Desired peptide fragments may be chemically synthesized. An alternative approach involves generating PRO fragments by enzymatic digestion, e.g., by treating the protein with an enzyme known to cleave proteins at sites defined by particular amino acid residues, or by digesting the DNA with suitable restriction enzymes and isolating the desired fragment. Yet another suitable technique involves isolating and amplifying a DNA fragment encoding a desired polypeptide fragment, by polymerase chain reaction (PCR). Oligonucleotides that define the desired termini of the DNA fragment are employed at the 5' and 3' primers in the PCR. Preferably, PRO polypeptide fragments share at least one biological and/or immunological activity with the native PRO polypeptide disclosed herein.

In particular embodiments, conservative substitutions of interest are shown in Table 6 under the heading of preferred substitutions. If such substitutions result in a change in biological activity, then more substantial changes, denominated exemplary substitutions in Table 6, or as further described below in reference to amino acid classes, are introduced and the products screened.

Table 6

	Original Residue	Exemplary Substitutions	Preferred Substitutions
20	Ala (A)	val; leu; ile	val
	Arg (R)	lys; gln; asn	lys
	Asn (N)	gln; his; lys; arg	gln
	Asp (D)	glu	glu
	Cys (C)	ser	ser
25	Gln (Q)	asn	asn
	Glu (E)	asp	asp
	Gly (G)	pro; ala	ala
	His (H)	asn; gln; lys; arg	arg
	Ile (I)	leu; val; met; ala; phe; norleucine	leu
30	Leu (L)	norleucine; ile; val; met; ala; phe	ile
	Lys (K)	arg; gln; asn	arg
	Met (M)	leu; phe; ile	leu
35	Phe (F)	leu; val; ile; ala; tyr	leu
	Pro (P)	ala	ala
	Ser (S)	thr	thr
	Thr (T)	ser	ser
	Trp (W)	tyr; phe	tyr
40	Tyr (Y)	trp; phe; thr; ser	phe
	Val (V)	ile; leu; met; phe; ala; norleucine	leu

Substantial modifications in function or immunological identity of the PRO polypeptide are accomplished by selecting substitutions that differ significantly in their effect on maintaining (a) the structure of the polypeptide backbone in the area of the substitution, for example, as a sheet or helical conformation, (b) the charge or hydrophobicity of the molecule at the target site, or (c) the bulk of the side chain. Naturally occurring residues are divided into groups based on common side-chain properties:

(1) hydrophobic: norleucine, met, ala, val, leu, ile;

- (2) neutral hydrophilic: cys, ser, thr;
- (3) acidic: asp, glu;
- (4) basic: asn, gln, his, lys, arg;
- (5) residues that influence chain orientation: gly, pro; and
- (6) aromatic: trp, tyr, phe.

Non-conservative substitutions will entail exchanging a member of one of these classes for another class. Such substituted residues also may be introduced into the conservative substitution sites or, more preferably, into the remaining (non-conserved) sites.

The variations can be made using methods known in the art such as oligonucleotide-mediated (site-directed) mutagenesis, alanine scanning, and PCR mutagenesis. Site-directed mutagenesis [Carter et al., *Nucl. Acids Res.*, **13**:4331 (1986); Zoller et al., *Nucl. Acids Res.*, **10**:6487 (1987)], cassette mutagenesis [Wells et al., *Gene*, **34**:315 (1985)], restriction selection mutagenesis [Wells et al., *Philos. Trans. R. Soc. London SerA*, **317**:415 (1986)] or other known techniques can be performed on the cloned DNA to produce the PRO variant DNA.

Scanning amino acid analysis can also be employed to identify one or more amino acids along a contiguous sequence. Among the preferred scanning amino acids are relatively small, neutral amino acids. Such amino acids include alanine, glycine, serine, and cysteine. Alanine is typically a preferred scanning amino acid among this group because it eliminates the side-chain beyond the beta-carbon and is less likely to alter the main-chain conformation of the variant [Cunningham and Wells, *Science*, **244**: 1081-1085 (1989)]. Alanine is also typically preferred because it is the most common amino acid. Further, it is frequently found in both buried and exposed positions [Creighton, *The Proteins*, (W.H. Freeman & Co., N.Y.); Chothia, *J. Mol. Biol.*, **150**:1 (1976)]. If alanine substitution does not yield adequate amounts of variant, an isoteric amino acid can be used.

C. Modifications of PRO

Covalent modifications of PRO are included within the scope of this invention. One type of covalent modification includes reacting targeted amino acid residues of a PRO polypeptide with an organic derivatizing agent that is capable of reacting with selected side chains or the N- or C- terminal residues of the PRO. Derivatization with bifunctional agents is useful, for instance, for crosslinking PRO to a water-insoluble support matrix or surface for use in the method for purifying anti-PRO antibodies, and vice-versa. Commonly used crosslinking agents include, e.g., 1,1-bis(diazoacetyl)-2-phenylethane, glutaraldehyde, N-hydroxysuccinimide esters, for example, esters with 4-azidosalicylic acid, homobifunctional imidoesters, including disuccinimidyl esters such as 3,3'-dithiobis(succinimidylpropionate), bifunctional maleimides such as bis-N-maleimido-1,8-octane and agents such as methyl-3-[(p-azidophenyl)dithio]propioimidate.

Other modifications include dcamidation of glutamyl and asparagyl residues to the corresponding glutamyl and aspartyl residues, respectively, hydroxylation of proline and lysine, phosphorylation of hydroxyl groups of seryl or threonyl residues, methylation of the α -amino groups of lysine, arginine, and histidine side chains [T.E. Creighton, *Proteins: Structure and Molecular Properties*, W.H. Freeman & Co., San Francisco, pp. 79-86 (1983)], acetylation of the N-terminal amine, and amidation of any C-terminal carboxyl group.

Another type of covalent modification of the PRO polypeptide included within the scope of this invention comprises altering the native glycosylation pattern of the polypeptide. "Altering the native glycosylation pattern" is intended for purposes herein to mean deleting one or more carbohydrate moieties found in native sequence PRO (either by removing the underlying glycosylation site or by deleting the glycosylation by chemical and/or enzymatic means), and/or adding one or more glycosylation sites that are not present in the native sequence PRO. In addition, the phrase includes qualitative changes in the glycosylation of the native proteins, involving a change in the nature and proportions of the various carbohydrate moieties present.

Addition of glycosylation sites to the PRO polypeptide may be accomplished by altering the amino acid sequence. The alteration may be made, for example, by the addition of, or substitution by, one or more serine or threonine residues to the native sequence PRO (for O-linked glycosylation sites). The PRO amino acid sequence may optionally be altered through changes at the DNA level, particularly by mutating the DNA encoding the PRO polypeptide at preselected bases such that codons are generated that will translate into the desired amino acids.

Another means of increasing the number of carbohydrate moieties on the PRO polypeptide is by chemical or enzymatic coupling of glycosides to the polypeptide. Such methods are described in the art, e.g., in WO 87/05330 published 11 September 1987, and in Aplin and Wriston, CRC Crit. Rev. Biochem., pp. 259-306 (1981).

Removal of carbohydrate moieties present on the PRO polypeptide may be accomplished chemically or enzymatically or by mutational substitution of codons encoding for amino acid residues that serve as targets for glycosylation. Chemical deglycosylation techniques are known in the art and described, for instance, by Hakimuddin, et al., Arch. Biochem. Biophys., 259:52 (1987) and by Edge et al., Anal. Biochem., 118:131 (1981). Enzymatic cleavage of carbohydrate moieties on polypeptides can be achieved by the use of a variety of endo- and exo-glycosidases as described by Thotakura et al., Meth. Enzymol., 138:350 (1987).

Another type of covalent modification of PRO comprises linking the PRO polypeptide to one of a variety of nonproteinaceous polymers, e.g., polyethylene glycol (PEG), polypropylene glycol, or polyoxyalkylenes, in the manner set forth in U.S. Patent Nos. 4,640,835; 4,496,689; 4,301,144; 4,670,417; 4,791,192 or 4,179,337.

The PRO of the present invention may also be modified in a way to form a chimeric molecule comprising PRO fused to another, heterologous polypeptide or amino acid sequence.

In one embodiment, such a chimeric molecule comprises a fusion of the PRO with a tag polypeptide which provides an epitope to which an anti-tag antibody can selectively bind. The epitope tag is generally placed at the amino- or carboxyl- terminus of the PRO. The presence of such epitope-tagged forms of the PRO can be detected using an antibody against the tag polypeptide. Also, provision of the epitope tag enables the PRO to be readily purified by affinity purification using an anti-tag antibody or another type of affinity matrix that binds to the epitope tag. Various tag polypeptides and their respective antibodies are well known in the art. Examples include poly-histidine (poly-his) or poly-histidine-glycine (poly-his-gly) tags; the flu HA tag polypeptide and its antibody 12CA5 [Field et al., Mol. Cell. Biol., 8:2159-2165 (1988)]; the c-myc tag and the 8F9, 3C7, 6E10, G4, B7 and 9E10 antibodies thereto [Evan et al.,

Molecular and Cellular Biology, 5:3610-3616 (1985)]; and the Herpes Simplex virus glycoprotein D (gD) tag and its antibody [Paborsky et al., Protein Engineering, 3(6):547-553 (1990)]. Other tag polypeptides include the Flag-peptide [Hopp et al., BioTechnology, 6:1204-1210 (1988)]; the KT3 epitope peptide [Martin et al., Science, 255:192-194 (1992)]; an alpha-tubulin epitope peptide [Skinner et al., J. Biol. Chem., 266:15163-15166 (1991)]; and the T7 gene 10 protein peptide tag [Lutz-Freyermuth et al., Proc. Natl. Acad. Sci. USA, 87:6393-6397 (1990)].

In an alternative embodiment, the chimeric molecule may comprise a fusion of the PRO with an immunoglobulin or a particular region of an immunoglobulin. For a bivalent form of the chimeric molecule (also referred to as an "immunoadhesin"), such a fusion could be to the Fc region of an IgG molecule. The Ig fusions preferably include the substitution of a soluble (transmembrane domain deleted or inactivated) form of a PRO polypeptide in place of at least one variable region within an Ig molecule. In a particularly preferred embodiment, the immunoglobulin fusion includes the hinge, CH2 and CH3, or the hinge, CH1, CH2 and CH3 regions of an IgG1 molecule. For the production of immunoglobulin fusions see also US Patent No. 5,428,130 issued June 27, 1995.

15 D. Preparation of PRO

The description below relates primarily to production of PRO by culturing cells transformed or transfected with a vector containing PRO nucleic acid. It is, of course, contemplated that alternative methods, which are well known in the art, may be employed to prepare PRO. For instance, the PRO sequence, or portions thereof, may be produced by direct peptide synthesis using solid-phase techniques [see, e.g., Stewart et al., Solid-Phase Peptide Synthesis, W.H. Freeman Co., San Francisco, CA (1969); 20 Merrifield, J. Am. Chem. Soc., 85:2149-2154 (1963)]. *In vitro* protein synthesis may be performed using manual techniques or by automation. Automated synthesis may be accomplished, for instance, using an Applied Biosystems Peptide Synthesizer (Foster City, CA) using manufacturer's instructions. Various portions of the PRO may be chemically synthesized separately and combined using chemical or enzymatic 25 methods to produce the full-length PRO.

1. Isolation of DNA Encoding PRO

DNA encoding PRO may be obtained from a cDNA library prepared from tissue believed to possess the PRO mRNA and to express it at a detectable level. Accordingly, human PRO DNA can be conveniently obtained from a cDNA library prepared from human tissue, such as described in the Examples. 30 The PRO-encoding gene may also be obtained from a genomic library or by known synthetic procedures (e.g., automated nucleic acid synthesis).

Libraries can be screened with probes (such as antibodies to the PRO or oligonucleotides of at least about 20-80 bases) designed to identify the gene of interest or the protein encoded by it. Screening the cDNA or genomic library with the selected probe may be conducted using standard procedures, such as 35 described in Sambrook et al., Molecular Cloning: A Laboratory Manual (New York: Cold Spring Harbor Laboratory Press, 1989). An alternative means to isolate the gene encoding PRO is to use PCR methodology [Sambrook et al., supra; Dieffenbach et al., PCR Primer: A Laboratory Manual (Cold Spring Harbor Laboratory Press, 1995)].

The Examples below describe techniques for screening a cDNA library. The oligonucleotide 40 sequences selected as probes should be of sufficient length and sufficiently unambiguous that false positives

are minimized. The oligonucleotide is preferably labeled such that it can be detected upon hybridization to DNA in the library being screened. Methods of labeling are well known in the art, and include the use of radiolabels like ^{32}P -labeled ATP, biotinylation or enzyme labeling. Hybridization conditions, including moderate stringency and high stringency, are provided in Sambrook et al., *supra*.

Sequences identified in such library screening methods can be compared and aligned to other known sequences deposited and available in public databases such as GenBank or other private sequence databases. Sequence identity (at either the amino acid or nucleotide level) within defined regions of the molecule or across the full-length sequence can be determined using methods known in the art and as described herein.

Nucleic acid having protein coding sequence may be obtained by screening selected cDNA or genomic libraries using the deduced amino acid sequence disclosed herein for the first time, and, if necessary, using conventional primer extension procedures as described in Sambrook et al., *supra*, to detect precursors and processing intermediates of mRNA that may not have been reverse-transcribed into cDNA.

2. Selection and Transformation of Host Cells

Host cells are transfected or transformed with expression or cloning vectors described herein for PRO production and cultured in conventional nutrient media modified as appropriate for inducing promoters, selecting transformants, or amplifying the genes encoding the desired sequences. The culture conditions, such as media, temperature, pH and the like, can be selected by the skilled artisan without undue experimentation. In general, principles, protocols, and practical techniques for maximizing the productivity of cell cultures can be found in *Mammalian Cell Biotechnology: a Practical Approach*, M. Butler, ed. (IRL Press, 1991) and Sambrook et al., *supra*.

Methods of eukaryotic cell transfection and prokaryotic cell transformation are known to the ordinarily skilled artisan, for example, CaCl_2 , CaPO_4 , liposome-mediated and electroporation. Depending on the host cell used, transformation is performed using standard techniques appropriate to such cells. The calcium treatment employing calcium chloride, as described in Sambrook et al., *supra*, or electroporation is generally used for prokaryotes. Infection with *Agrobacterium tumefaciens* is used for transformation of certain plant cells, as described by Shaw et al., *Gene*, 23:315 (1983) and WO 89/05859 published 29 June 1989. For mammalian cells without such cell walls, the calcium phosphate precipitation method of Graham and van der Eb, *Virology*, 52:456-457 (1978) can be employed. General aspects of mammalian cell host system transfections have been described in U.S. Patent No. 4,399,216. Transformations into yeast are typically carried out according to the method of Van Solingen et al., *J. Bact.*, 130:946 (1977) and Hsiao et al., *Proc. Natl. Acad. Sci. (USA)*, 76:3829 (1979). However, other methods for introducing DNA into cells, such as by nuclear microinjection, electroporation, bacterial protoplast fusion with intact cells, or polycations, e.g., polybrene, polyornithine, may also be used. For various techniques for transforming mammalian cells, see Keown et al., *Methods in Enzymology*, 185:527-537 (1990) and Mansour et al., *Nature*, 336:348-352 (1988).

Suitable host cells for cloning or expressing the DNA in the vectors herein include prokaryote, yeast, or higher eukaryote cells. Suitable prokaryotes include but are not limited to eubacteria, such as Gram-negative or Gram-positive organisms, for example, Enterobacteriaceae such as *E. coli*. Various *E. coli*

strains are publicly available, such as *E. coli* K12 strain MM294 (ATCC 31,446); *E. coli* X1776 (ATCC 31,537); *E. coli* strain W3110 (ATCC 27,325) and K5 772 (ATCC 53,635). Other suitable prokaryotic host cells include Enterobacteriaceae such as *Escherichia*, e.g., *E. coli*, *Enterobacter*, *Erwinia*, *Klebsiella*, *Proteus*, *Salmonella*, e.g., *Salmonella typhimurium*, *Serratia*, e.g., *Serratia marcescens*, and *Shigella*, as well as *Bacilli* such as *B. subtilis* and *B. licheniformis* (e.g., *B. licheniformis* 41P disclosed in DD 266,710 published 12 April 1989), *Pseudomonas* such as *P. aeruginosa*, and *Streptomyces*. These examples are illustrative rather than limiting. Strain W3110 is one particularly preferred host or parent host because it is a common host strain for recombinant DNA product fermentations. Preferably, the host cell secretes minimal amounts of proteolytic enzymes. For example, strain W3110 may be modified to effect a genetic mutation in the genes encoding proteins endogenous to the host, with examples of such hosts including *E. coli* W3110 strain 1A2, which has the complete genotype *tonA*; *E. coli* W3110 strain 9E4, which has the complete genotype *tonA ptr3*; *E. coli* W3110 strain 27C7 (ATCC 55,244), which has the complete genotype *tonA ptr3 phoA E15 (argF-lac)169 degP ompT kan'*; *E. coli* W3110 strain 37D6, which has the complete genotype *tonA ptr3 phoA E15 (argF-lac)169 degP ompT rbs7 ilvG kan'*; *E. coli* W3110 strain 40B4, which is strain 37D6 with a non-kanamycin resistant *degP* deletion mutation; and an *E. coli* strain having mutant periplasmic protease disclosed in U.S. Patent No. 4,946,783 issued 7 August 1990. Alternatively, *in vitro* methods of cloning, e.g., PCR or other nucleic acid polymerase reactions, are suitable.

In addition to prokaryotes, eukaryotic microbes such as filamentous fungi or yeast are suitable cloning or expression hosts for PRO-encoding vectors. *Saccharomyces cerevisiae* is a commonly used lower eukaryotic host microorganism. Others include *Schizosaccharomyces pombe* (Beach and Nurse, *Nature*, 290: 140 [1981]; EP 139,383 published 2 May 1985); *Kluyveromyces* hosts (U.S. Patent No. 4,943,529; Fleer et al., *Bio/Technology*, 9:968-975 (1991)) such as, e.g., *K. lactis* (MW98-8C, CBS683, CBS4574; Louvencourt et al., *J. Bacteriol.*, 154(2):737-742 [1983]), *K. fragilis* (ATCC 12,424), *K. bulgaricus* (ATCC 16,045), *K. wickerhamii* (ATCC 24,178), *K. waltii* (ATCC 56,500), *K. drosophilae* (ATCC 36,906; Van den Berg et al., *Bio/Technology*, 8:135 (1990)), *K. thermotolerans*, and *K. marxianus*; *Yarrowia* (EP 402,226); *Pichia pastoris* (EP 183,070; Sreekrishna et al., *J. Basic Microbiol.*, 28:265-278 [1988]); *Candida*; *Trichoderma reesia* (EP 244,234); *Neurospora crassa* (Case et al., *Proc. Natl. Acad. Sci. USA*, 76:5259-5263 [1979]); *Schwanniomyces* such as *Schwanniomyces occidentalis* (EP 394,538 published 31 October 1990); and filamentous fungi such as, e.g., *Neurospora*, *Penicillium*, *Tolypocladium* (WO 91/00357 published 10 January 1991), and *Aspergillus* hosts such as *A. nidulans* (Ballance et al., *Biochem. Biophys. Res. Commun.*, 112:284-289 [1983]; Tilburn et al., *Gene*, 26:205-221 [1983]; Yelton et al., *Proc. Natl. Acad. Sci. USA*, 81: 1470-1474 [1984]) and *A. niger* (Kelly and Hynes, *EMBO J.*, 4:475-479 [1985]). Methylophilic yeasts are suitable herein and include, but are not limited to, yeast capable of growth on methanol selected from the genera consisting of *Hansenula*, *Candida*, *Kloeckera*, *Pichia*, *Saccharomyces*, *Torulopsis*, and *Rhodotorula*. A list of specific species that are exemplary of this class of yeasts may be found in C. Anthony, *The Biochemistry of Methylophilic*, 269 (1982).

Suitable host cells for the expression of glycosylated PRO are derived from multicellular organisms. Examples of invertebrate cells include insect cells such as *Drosophila* S2 and *Spodoptera* Sf9, as well as plant cells. Examples of useful mammalian host cell lines include Chinese hamster ovary (CHO) and COS cells. More specific examples include monkey kidney CV1 line transformed by SV40 (COS-7, ATCC

CRL 1651); human embryonic kidney line (293 or 293 cells subcloned for growth in suspension culture, Graham et al., *J. Gen. Virol.*, 36:59 (1977)); Chinese hamster ovary cells/-DHFR (CHO, Urlaub and Chasin, *Proc. Natl. Acad. Sci. USA*, 77:4216 (1980)); mouse sertoli cells (TM4, Mather, *Biol. Reprod.*, 23:243-251 (1980)); human lung cells (W138, ATCC CCL 75); human liver cells (Hep G2, HB 8065); and mouse mammary tumor (MMT 060562, ATCC CCL51). The selection of the appropriate host cell is deemed to be within the skill in the art.

3. Selection and Use of a Replicable Vector

The nucleic acid (e.g., cDNA or genomic DNA) encoding PRO may be inserted into a replicable vector for cloning (amplification of the DNA) or for expression. Various vectors are publicly available. The vector may, for example, be in the form of a plasmid, cosmid, viral particle, or phage. The appropriate nucleic acid sequence may be inserted into the vector by a variety of procedures. In general, DNA is inserted into an appropriate restriction endonuclease site(s) using techniques known in the art. Vector components generally include, but are not limited to, one or more of a signal sequence, an origin of replication, one or more marker genes, an enhancer element, a promoter, and a transcription termination sequence. Construction of suitable vectors containing one or more of these components employs standard ligation techniques which are known to the skilled artisan.

The PRO may be produced recombinantly not only directly, but also as a fusion polypeptide with a heterologous polypeptide, which may be a signal sequence or other polypeptide having a specific cleavage site at the N-terminus of the mature protein or polypeptide. In general, the signal sequence may be a component of the vector, or it may be a part of the PRO-encoding DNA that is inserted into the vector. The signal sequence may be a prokaryotic signal sequence selected, for example, from the group of the alkaline phosphatase, penicillinase, lpp, or heat-stable enterotoxin II leaders. For yeast secretion the signal sequence may be, e.g., the yeast invertase leader, alpha factor leader (including *Saccharomyces* and *Kluyveromyces* α -factor leaders, the latter described in U.S. Patent No. 5,010,182), or acid phosphatase leader, the *C. albicans* glucoamylase leader (EP 362,179 published 4 April 1990), or the signal described in WO 90/13646 published 15 November 1990. In mammalian cell expression, mammalian signal sequences may be used to direct secretion of the protein, such as signal sequences from secreted polypeptides of the same or related species, as well as viral secretory leaders.

Both expression and cloning vectors contain a nucleic acid sequence that enables the vector to replicate in one or more selected host cells. Such sequences are well known for a variety of bacteria, yeast, and viruses. The origin of replication from the plasmid pBR322 is suitable for most Gram-negative bacteria, the 2 μ plasmid origin is suitable for yeast, and various viral origins (SV40, polyoma, adenovirus, VSV or BPV) are useful for cloning vectors in mammalian cells.

Expression and cloning vectors will typically contain a selection gene, also termed a selectable marker. Typical selection genes encode proteins that (a) confer resistance to antibiotics or other toxins, e.g., ampicillin, neomycin, methotrexate, or tetracycline, (b) complement auxotrophic deficiencies, or (c) supply critical nutrients not available from complex media, e.g., the gene encoding D-alanine racemase for *Bacilli*.

An example of suitable selectable markers for mammalian cells are those that enable the identification of cells competent to take up the PRO-encoding nucleic acid, such as DHFR or thymidine kinase. An appropriate host cell when wild-type DHFR is employed is the CHO cell line deficient in DHFR

activity, prepared and propagated as described by Urlaub et al., *Proc. Natl. Acad. Sci. USA*, 77:4216 (1980). A suitable selection gene for use in yeast is the *trp1* gene present in the yeast plasmid YRp7 [Stinchcomb et al., *Nature*, 282:39 (1979); Kingsman et al., *Gene*, 7:141 (1979); Tschemper et al., *Gene*, 10:157 (1980)]. The *trp1* gene provides a selection marker for a mutant strain of yeast lacking the ability to grow in tryptophan, for example, ATCC No. 44076 or PEP4-1 [Jones, *Genetics*, 85:12 (1977)].

Expression and cloning vectors usually contain a promoter operably linked to the PRO-encoding nucleic acid sequence to direct mRNA synthesis. Promoters recognized by a variety of potential host cells are well known. Promoters suitable for use with prokaryotic hosts include the β -lactamase and lactose promoter systems [Chang et al., *Nature*, 275:615 (1978); Goeddel et al., *Nature*, 281:544 (1979)], alkaline phosphatase, a tryptophan (*trp*) promoter system [Goeddel, *Nucleic Acids Res.*, 8:4057 (1980); EP 36,776], and hybrid promoters such as the *tac* promoter [deBoer et al., *Proc. Natl. Acad. Sci. USA*, 80:21-25 (1983)]. Promoters for use in bacterial systems also will contain a Shine-Dalgarno (S.D.) sequence operably linked to the DNA encoding PRO.

Examples of suitable promoting sequences for use with yeast hosts include the promoters for 3-phosphoglycerate kinase [Hitzeman et al., *J. Biol. Chem.*, 255:2073 (1980)] or other glycolytic enzymes [Hess et al., *J. Adv. Enzyme Reg.*, 7:149 (1968); Holland, *Biochemistry*, 17:4900 (1978)], such as enolase, glyceraldehyde-3-phosphate dehydrogenase, hexokinase, pyruvate decarboxylase, phosphofructokinase, glucose-6-phosphate isomerase, 3-phosphoglycerate mutase, pyruvate kinase, triosephosphate isomerase, phosphoglucose isomerase, and glucokinase.

Other yeast promoters, which are inducible promoters having the additional advantage of transcription controlled by growth conditions, are the promoter regions for alcohol dehydrogenase 2, isocytocrome C, acid phosphatase, degradative enzymes associated with nitrogen metabolism, metallothionein, glyceraldehyde-3-phosphate dehydrogenase, and enzymes responsible for maltose and galactose utilization. Suitable vectors and promoters for use in yeast expression are further described in EP 73,657.

PRO transcription from vectors in mammalian host cells is controlled, for example, by promoters obtained from the genomes of viruses such as polyoma virus, fowlpox virus (UK 2,211,504 published 5 July 1989), adenovirus (such as Adenovirus 2), bovine papilloma virus, avian sarcoma virus, cytomegalovirus, a retrovirus, hepatitis-B virus and Simian Virus 40 (SV40), from heterologous mammalian promoters, e.g., the actin promoter or an immunoglobulin promoter, and from heat-shock promoters, provided such promoters are compatible with the host cell systems.

Transcription of a DNA encoding the PRO by higher eukaryotes may be increased by inserting an enhancer sequence into the vector. Enhancers are cis-acting elements of DNA, usually about from 10 to 300 bp, that act on a promoter to increase its transcription. Many enhancer sequences are now known from mammalian genes (globin, elastase, albumin, α -fetoprotein, and insulin). Typically, however, one will use an enhancer from a eukaryotic cell virus. Examples include the SV40 enhancer on the late side of the replication origin (bp 100-270), the cytomegalovirus early promoter enhancer, the polyoma enhancer on the late side of the replication origin, and adenovirus enhancers. The enhancer may be spliced into the vector at a position 5' or 3' to the PRO coding sequence, but is preferably located at a site 5' from the promoter.

Expression vectors used in eukaryotic host cells (yeast, fungi, insect, plant, animal, human, or nucleated cells from other multicellular organisms) will also contain sequences necessary for the termination of transcription and for stabilizing the mRNA. Such sequences are commonly available from the 5' and, occasionally 3', untranslated regions of eukaryotic or viral DNAs or cDNAs. These regions contain nucleotide segments transcribed as polyadenylated fragments in the untranslated portion of the mRNA encoding PRO.

Still other methods, vectors, and host cells suitable for adaptation to the synthesis of PRO in recombinant vertebrate cell culture are described in Gething et al., *Nature*, 293:620-625 (1981); Mantei et al., *Nature*, 281:40-46 (1979); EP 117,060; and EP 117,058.

4. Detecting Gene Amplification/Expression

Gene amplification and/or expression may be measured in a sample directly, for example, by conventional Southern blotting, Northern blotting to quantitate the transcription of mRNA [Thomas, *Proc. Natl. Acad. Sci. USA*, 77:5201-5205 (1980)], dot blotting (DNA analysis), or *in situ* hybridization, using an appropriately labeled probe, based on the sequences provided herein. Alternatively, antibodies may be employed that can recognize specific duplexes, including DNA duplexes, RNA duplexes, and DNA-RNA hybrid duplexes or DNA-protein duplexes. The antibodies in turn may be labeled and the assay may be carried out where the duplex is bound to a surface, so that upon the formation of duplex on the surface, the presence of antibody bound to the duplex can be detected.

Gene expression, alternatively, may be measured by immunological methods, such as immunohistochemical staining of cells or tissue sections and assay of cell culture or body fluids, to quantitate directly the expression of gene product. Antibodies useful for immunohistochemical staining and/or assay of sample fluids may be either monoclonal or polyclonal, and may be prepared in any mammal. Conveniently, the antibodies may be prepared against a native sequence PRO polypeptide or against a synthetic peptide based on the DNA sequences provided herein or against exogenous sequence fused to PRO DNA and encoding a specific antibody epitope.

5. Purification of Polypeptide

Forms of PRO may be recovered from culture medium or from host cell lysates. If membrane-bound, it can be released from the membrane using a suitable detergent solution (e.g. Triton-X 100) or by enzymatic cleavage. Cells employed in expression of PRO can be disrupted by various physical or chemical means, such as freeze-thaw cycling, sonication, mechanical disruption, or cell lysing agents.

It may be desired to purify PRO from recombinant cell proteins or polypeptides. The following procedures are exemplary of suitable purification procedures: by fractionation on an ion-exchange column; ethanol precipitation; reverse phase HPLC; chromatography on silica or on a cation-exchange resin such as DEAF; chromatofocusing; SDS-PAGE; ammonium sulfate precipitation; gel filtration using, for example, Sephadex G-75; protein A Sepharose columns to remove contaminants such as IgG; and metal chelating columns to bind epitope-tagged forms of the PRO. Various methods of protein purification may be employed and such methods are known in the art and described for example in Deutscher, *Methods in Enzymology*, 182 (1990); Scopes, *Protein Purification: Principles and Practice*, Springer-Verlag, New York (1982). The purification step(s) selected will depend, for example, on the nature of the production process used and the particular PRO produced.

E. Tissue Distribution

The location of tissues expressing the PRO can be identified by determining mRNA expression in various human tissues. The location of such genes provides information about which tissues are most likely to be affected by the stimulating and inhibiting activities of the PRO polypeptides. The location of a gene in a specific tissue also provides sample tissue for the activity blocking assays discussed below.

As noted before, gene expression in various tissues may be measured by conventional Southern blotting, Northern blotting to quantitate the transcription of mRNA (Thomas, *Proc. Natl. Acad. Sci. USA*, 77:5201-5205 [1980]), dot blotting (DNA analysis), or *in situ* hybridization, using an appropriately labeled probe, based on the sequences provided herein. Alternatively, antibodies may be employed that can recognize specific duplexes, including DNA duplexes, RNA duplexes, and DNA-RNA hybrid duplexes or DNA-protein duplexes.

Gene expression in various tissues, alternatively, may be measured by immunological methods, such as immunohistochemical staining of tissue sections and assay of cell culture or body fluids, to quantitate directly the expression of gene product. Antibodies useful for immunohistochemical staining and/or assay of sample fluids may be either monoclonal or polyclonal, and may be prepared in any mammal. Conveniently, the antibodies may be prepared against a native sequence of a PRO polypeptide or against a synthetic peptide based on the DNA sequences encoding the PRO polypeptide or against an exogenous sequence fused to a DNA encoding a PRO polypeptide and encoding a specific antibody epitope. General techniques for generating antibodies, and special protocols for Northern blotting and *in situ* hybridization are provided below.

F. Antibody Binding Studies

The activity of the PRO polypeptides can be further verified by antibody binding studies, in which the ability of anti-PRO antibodies to inhibit the effect of the PRO polypeptides, respectively, on tissue cells is tested. Exemplary antibodies include polyclonal, monoclonal, humanized, bispecific, and heteroconjugate antibodies, the preparation of which will be described hereinbelow.

Antibody binding studies may be carried out in any known assay method, such as competitive binding assays, direct and indirect sandwich assays, and immunoprecipitation assays. Zola, *Monoclonal Antibodies: A Manual of Techniques*, pp.147-158 (CRC Press, Inc., 1987).

Competitive binding assays rely on the ability of a labeled standard to compete with the test sample analyte for binding with a limited amount of antibody. The amount of target protein in the test sample is inversely proportional to the amount of standard that becomes bound to the antibodies. To facilitate determining the amount of standard that becomes bound, the antibodies preferably are insolubilized before or after the competition, so that the standard and analyte that are bound to the antibodies may conveniently be separated from the standard and analyte which remain unbound.

Sandwich assays involve the use of two antibodies, each capable of binding to a different immunogenic portion, or epitope, of the protein to be detected. In a sandwich assay, the test sample analyte is bound by a first antibody which is immobilized on a solid support, and thereafter a second antibody binds to the analyte, thus forming an insoluble three-part complex. See, e.g., US Pat No. 4,376,110. The second antibody may itself be labeled with a detectable moiety (direct sandwich assays) or may be measured using

an anti-immunoglobulin antibody that is labeled with a detectable moiety (indirect sandwich assay). For example, one type of sandwich assay is an ELISA assay, in which case the detectable moiety is an enzyme.

For immunohistochemistry, the tissue sample may be fresh or frozen or may be embedded in paraffin and fixed with a preservative such as formalin, for example.

5 G. Cell-Based Assays

Cell-based assays and animal models for immune related diseases can be used to further understand the relationship between the genes and polypeptides identified herein and the development and pathogenesis of immune related disease.

10 In a different approach, cells of a cell type known to be involved in a particular immune related disease are transfected with the cDNAs described herein, and the ability of these cDNAs to stimulate or inhibit immune function is analyzed. Suitable cells can be transfected with the desired gene, and monitored for immune function activity. Such transfected cell lines can then be used to test the ability of poly- or monoclonal antibodies or antibody compositions to inhibit or stimulate immune function, for example to modulate T-cell proliferation or inflammatory cell infiltration. Cells transfected with the coding sequences
15 of the genes identified herein can further be used to identify drug candidates for the treatment of immune related diseases.

In addition, primary cultures derived from transgenic animals (as described below) can be used in the cell-based assays herein, although stable cell lines are preferred. Techniques to derive continuous cell lines from transgenic animals are well known in the art (see, e.g., Small *et al.*, *Mol. Cell. Biol.* 5: 642-648
20 [1985]).

One suitable cell based assay is the mixed lymphocyte reaction (MLR). *Current Protocols in Immunology*, unit 3.12; edited by J E Coligan, A M Kruisbeek, D H Marglies, E M Shevach, W Strober, National Institutes of Health, Published by John Wiley & Sons, Inc. In this assay, the ability of a test compound to stimulate or inhibit the proliferation of activated T cells is assayed. A suspension of responder
25 T cells is cultured with allogeneic stimulator cells and the proliferation of T cells is measured by uptake of tritiated thymidine. This assay is a general measure of T cell reactivity. Since the majority of T cells respond to and produce IL-2 upon activation, differences in responsiveness in this assay in part reflect differences in IL-2 production by the responding cells. The MLR results can be verified by a standard lymphokine (IL-2) detection assay. *Current Protocols in Immunology*, above, 3.15, 6.3.

30 A proliferative T cell response in an MLR assay may be due to direct mitogenic properties of an assayed molecule or to external antigen induced activation. Additional verification of the T cell stimulatory activity of the PRO polypeptides can be obtained by a costimulation assay. T cell activation requires an antigen specific signal mediated through the T-cell receptor (TCR) and a costimulatory signal mediated through a second ligand binding interaction, for example, the B7 (CD80, CD86)/CD28 binding interaction.
35 CD28 crosslinking increases lymphokine secretion by activated T cells. T cell activation has both negative and positive controls through the binding of ligands which have a negative or positive effect. CD28 and CTLA-4 are related glycoproteins in the Ig superfamily which bind to B7. CD28 binding to B7 has a positive costimulation effect of T cell activation; conversely, CTLA-4 binding to B7 has a T cell deactivating effect. Chambers, C. A. and Allison, J. P., *Curr. Opin. Immunol.* (1997) 9:396. Schwartz, R.
40 H., *Cell* (1992) 71:1065; Linsey, P. S. and Ledbetter, J. A., *Annu. Rev. Immunol.* (1993) 11:191; June, C. H.

et al, Immunol. Today (1994) 15:321; Jenkins, M. K., *Immunity* (1994) 1:405. In a costimulation assay, the PRO polypeptides are assayed for T cell costimulatory or inhibitory activity.

Direct use of a stimulating compound as in the invention has been validated in experiments with 4-1BB glycoprotein, a member of the tumor necrosis factor receptor family, which binds to a ligand (4-1BBL) expressed on primed T cells and signals T cell activation and growth. Alderson, M. E. *et al, J. Immunol.* (1994) 24:2219.

The use of an agonist stimulating compound has also been validated experimentally. Activation of 4-1BB by treatment with an agonist anti-4-1BB antibody enhances eradication of tumors. Hellstrom, I. and Hellstrom, K. E., *Crit. Rev. Immunol.* (1998) 18:1. Immunoadjuvant therapy for treatment of tumors, described in more detail below, is another example of the use of the stimulating compounds of the invention.

Alternatively, an immune stimulating or enhancing effect can also be achieved by administration of a PRO which has vascular permeability enhancing properties. Enhanced vascular permeability would be beneficial to disorders which can be attenuated by local infiltration of immune cells (*e.g.*, monocytes, eosinophils, PMNs) and inflammation.

On the other hand, PRO polypeptides, as well as other compounds of the invention, which are direct inhibitors of T cell proliferation/activation, lymphokine secretion, and/or vascular permeability can be directly used to suppress the immune response. These compounds are useful to reduce the degree of the immune response and to treat immune related diseases characterized by a hyperactive, superoptimal, or autoimmune response. This use of the compounds of the invention has been validated by the experiments described above in which CTLA-4 binding to receptor B7 deactivates T cells. The direct inhibitory compounds of the invention function in an analogous manner. The use of compound which suppress vascular permeability would be expected to reduce inflammation. Such uses would be beneficial in treating conditions associated with excessive inflammation.

Alternatively, compounds, *e.g.*, antibodies, which bind to stimulating PRO polypeptides and block the stimulating effect of these molecules produce a net inhibitory effect and can be used to suppress the T cell mediated immune response by inhibiting T cell proliferation/activation and/or lymphokine secretion. Blocking the stimulating effect of the polypeptides suppresses the immune response of the mammal. This use has been validated in experiments using an anti-IL2 antibody. In these experiments, the antibody binds to IL2 and blocks binding of IL2 to its receptor thereby achieving a T cell inhibitory effect.

H. Animal Models

The results of the cell based *in vitro* assays can be further verified using *in vivo* animal models and assays for T-cell function. A variety of well known animal models can be used to further understand the role of the genes identified herein in the development and pathogenesis of immune related disease, and to test the efficacy of candidate therapeutic agents, including antibodies, and other antagonists of the native polypeptides, including small molecule antagonists. The *in vivo* nature of such models makes them predictive of responses in human patients. Animal models of immune related diseases include both non-recombinant and recombinant (transgenic) animals. Non-recombinant animal models include, for example, rodent, *e.g.*, murine models. Such models can be generated by introducing cells into syngeneic mice using

standard techniques, e.g., subcutaneous injection, tail vein injection, spleen implantation, intraperitoneal implantation, implantation under the renal capsule, etc.

Graft-versus-host disease occurs when immunocompetent cells are transplanted into immunosuppressed or tolerant patients. The donor cells recognize and respond to host antigens. The response can vary from life threatening severe inflammation to mild cases of diarrhea and weight loss. Graft-versus-host disease models provide a means of assessing T cell reactivity against MHC antigens and minor transplant antigens. A suitable procedure is described in detail in *Current Protocols in Immunology*, above, unit 4.3.

An animal model for skin allograft rejection is a means of testing the ability of T cells to mediate *in vivo* tissue destruction and a measure of their role in transplant rejection. The most common and accepted models use murine tail-skin grafts. Repeated experiments have shown that skin allograft rejection is mediated by T cells, helper T cells and killer-effector T cells, and not antibodies. Auchincloss, H. Jr. and Sachs, D. H., *Fundamental Immunology*, 2nd ed., W. E. Paul ed., Raven Press, NY, 1989, 889-992. A suitable procedure is described in detail in *Current Protocols in Immunology*, above, unit 4.4. Other transplant rejection models which can be used to test the compounds of the invention are the allogeneic heart transplant models described by Tanabe, M. *et al*, *Transplantation* (1994) 58:23 and Tinubu, S. A. *et al*, *J. Immunol.* (1994) 4330-4338.

Animal models for delayed type hypersensitivity provides an assay of cell mediated immune function as well. Delayed type hypersensitivity reactions are a T cell mediated *in vivo* immune response characterized by inflammation which does not reach a peak until after a period of time has elapsed after challenge with an antigen. These reactions also occur in tissue specific autoimmune diseases such as multiple sclerosis (MS) and experimental autoimmune encephalomyelitis (EAE, a model for MS). A suitable procedure is described in detail in *Current Protocols in Immunology*, above, unit 4.5.

EAE is a T cell mediated autoimmune disease characterized by T cell and mononuclear cell inflammation and subsequent demyelination of axons in the central nervous system. EAE is generally considered to be a relevant animal model for MS in humans. Bolton, C., *Multiple Sclerosis* (1995) 1:143. Both acute and relapsing-remitting models have been developed. The compounds of the invention can be tested for T cell stimulatory or inhibitory activity against immune mediated demyelinating disease using the protocol described in *Current Protocols in Immunology*, above, units 15.1 and 15.2. See also the models for myelin disease in which oligodendrocytes or Schwann cells are grafted into the central nervous system as described in Duncan, I. D. *et al*, *Molec. Med. Today* (1997) 554-561.

Contact hypersensitivity is a simple delayed type hypersensitivity *in vivo* assay of cell mediated immune function. In this procedure, cutaneous exposure to exogenous haptens which gives rise to a delayed type hypersensitivity reaction which is measured and quantitated. Contact sensitivity involves an initial sensitizing phase followed by an elicitation phase. The elicitation phase occurs when the T lymphocytes encounter an antigen to which they have had previous contact. Swelling and inflammation occur, making this an excellent model of human allergic contact dermatitis. A suitable procedure is described in detail in *Current Protocols in Immunology*, Eds. J. E. Coligan, A. M. Kruisbeek, D. H. Margulies, E. M. Shevach and W. Strober, John Wiley & Sons, Inc., 1994, unit 4.2. See also Grabbe, S. and Schwarz, T., *Immun. Today* 19 (1): 37-44 (1998).

An animal model for arthritis is collagen-induced arthritis. This model shares clinical, histological and immunological characteristics of human autoimmune rheumatoid arthritis and is an acceptable model for human autoimmune arthritis. Mouse and rat models are characterized by synovitis, erosion of cartilage and subchondral bone. The compounds of the invention can be tested for activity against autoimmune arthritis using the protocols described in *Current Protocols in Immunology*, above, units 15.5. See also the model using a monoclonal antibody to CD18 and VLA-4 integrins described in Issekutz, A.C. *et al.*, *Immunology* (1996) 88:569.

A model of asthma has been described in which antigen-induced airway hyper-reactivity, pulmonary eosinophilia and inflammation are induced by sensitizing an animal with ovalbumin and then challenging the animal with the same protein delivered by aerosol. Several animal models (guinea pig, rat, non-human primate) show symptoms similar to atopic asthma in humans upon challenge with aerosol antigens. Murine models have many of the features of human asthma. Suitable procedures to test the compounds of the invention for activity and effectiveness in the treatment of asthma are described by Wolyniec, W. W. *et al.*, *Am. J. Respir. Cell Mol. Biol.* (1998) 18:777 and the references cited therein.

Additionally, the compounds of the invention can be tested on animal models for psoriasis like diseases. Evidence suggests a T cell pathogenesis for psoriasis. The compounds of the invention can be tested in the scid/scid mouse model described by Schon, M. P. *et al.*, *Nat. Med.* (1997) 3:183, in which the mice demonstrate histopathologic skin lesions resembling psoriasis. Another suitable model is the human skin/scid mouse chimera prepared as described by Nickoloff, B. J. *et al.*, *Am. J. Path.* (1995) 146:580.

Recombinant (transgenic) animal models can be engineered by introducing the coding portion of the genes identified herein into the genome of animals of interest, using standard techniques for producing transgenic animals. Animals that can serve as a target for transgenic manipulation include, without limitation, mice, rats, rabbits, guinea pigs, sheep, goats, pigs, and non-human primates, *e.g.*, baboons, chimpanzees and monkeys. Techniques known in the art to introduce a transgene into such animals include pronucleic microinjection (Hoppe and Wang, U.S. Patent No. 4,873,191); retrovirus-mediated gene transfer into germ lines (*e.g.*, Van der Putten *et al.*, *Proc. Natl. Acad. Sci. USA* 82, 6148-615 [1985]); gene targeting in embryonic stem cells (Thompson *et al.*, *Cell* 56, 313-321 [1989]); electroporation of embryos (Lo, *Mol. Cell Biol.* 3, 1803-1814 [1983]); sperm-mediated gene transfer (Lavitrano *et al.*, *Cell* 57, 717-73 [1989]). For review, see, for example, U.S. Patent No. 4,736,866.

For the purpose of the present invention, transgenic animals include those that carry the transgene only in part of their cells ("mosaic animals"). The transgene can be integrated either as a single transgene, or in concatamers, *e.g.*, head-to-head or head-to-tail tandems. Selective introduction of a transgene into a particular cell type is also possible by following, for example, the technique of Lasko *et al.*, *Proc. Natl. Acad. Sci. USA* 89, 6232-636 (1992).

The expression of the transgene in transgenic animals can be monitored by standard techniques. For example, Southern blot analysis or PCR amplification can be used to verify the integration of the transgene. The level of mRNA expression can then be analyzed using techniques such as *in situ* hybridization, Northern blot analysis, PCR, or immunocytochemistry.

The animals may be further examined for signs of immune disease pathology, for example by histological examination to determine infiltration of immune cells into specific tissues. Blocking

experiments can also be performed in which the transgenic animals are treated with the compounds of the invention to determine the extent of the T cell proliferation stimulation or inhibition of the compounds. In these experiments, blocking antibodies which bind to the PRO polypeptide, prepared as described above, are administered to the animal and the effect on immune function is determined.

Alternatively, "knock out" animals can be constructed which have a defective or altered gene encoding a polypeptide identified herein, as a result of homologous recombination between the endogenous gene encoding the polypeptide and altered genomic DNA encoding the same polypeptide introduced into an embryonic cell of the animal. For example, cDNA encoding a particular polypeptide can be used to clone genomic DNA encoding that polypeptide in accordance with established techniques. A portion of the genomic DNA encoding a particular polypeptide can be deleted or replaced with another gene, such as a gene encoding a selectable marker which can be used to monitor integration. Typically, several kilobases of unaltered flanking DNA (both at the 5' and 3' ends) are included in the vector [see *e.g.*, Thomas and Capecchi, *Cell*, 51:503 (1987) for a description of homologous recombination vectors]. The vector is introduced into an embryonic stem cell line (*e.g.*, by electroporation) and cells in which the introduced DNA has homologously recombined with the endogenous DNA are selected [see *e.g.*, Li *et al.*, *Cell*, 69:915 (1992)]. The selected cells are then injected into a blastocyst of an animal (*e.g.*, a mouse or rat) to form aggregation chimeras [see *e.g.*, Bradley, in *Teratocarcinomas and Embryonic Stem Cells: A Practical Approach*, E. J. Robertson, ed. (IRL, Oxford, 1987), pp. 113-152]. A chimeric embryo can then be implanted into a suitable pseudopregnant female foster animal and the embryo brought to term to create a "knock out" animal. Progeny harboring the homologously recombined DNA in their germ cells can be identified by standard techniques and used to breed animals in which all cells of the animal contain the homologously recombined DNA. Knockout animals can be characterized for instance, for their ability to defend against certain pathological conditions and for their development of pathological conditions due to absence of the polypeptide.

I. ImmunoAdjuvant Therapy

In one embodiment, the immunostimulating compounds of the invention can be used in immunoadjuvant therapy for the treatment of tumors (cancer). It is now well established that T cells recognize human tumor specific antigens. One group of tumor antigens, encoded by the MAGE, BAGE and GAGE families of genes, are silent in all adult normal tissues, but are expressed in significant amounts in tumors, such as melanomas, lung tumors, head and neck tumors, and bladder carcinomas. DeSmet, C. *et al.*, (1996) *Proc. Natl. Acad. Sci. USA*, 93:7149. It has been shown that costimulation of T cells induces tumor regression and an antitumor response both *in vitro* and *in vivo*. Melero, I. *et al.*, *Nature Medicine* (1997) 3:682; Kwon, E. D. *et al.*, *Proc. Natl. Acad. Sci. USA* (1997) 94: 8099; Lynch, D. H. *et al.*, *Nature Medicine* (1997) 3:625; Finn, O. J. and Lotze, M. T., *J. Immunol.* (1998) 21:114. The stimulatory compounds of the invention can be administered as adjuvants, alone or together with a growth regulating agent, cytotoxic agent or chemotherapeutic agent, to stimulate T cell proliferation/activation and an antitumor response to tumor antigens. The growth regulating, cytotoxic, or chemotherapeutic agent may be administered in conventional amounts using known administration regimes. Immunostimulating activity by the compounds of the invention allows reduced amounts of the growth regulating, cytotoxic, or chemotherapeutic agents thereby potentially lowering the toxicity to the patient.

J. Screening Assays for Drug Candidates

Screening assays for drug candidates are designed to identify compounds that bind to or complex with the polypeptides encoded by the genes identified herein or a biologically active fragment thereof, or otherwise interfere with the interaction of the encoded polypeptides with other cellular proteins. Such screening assays will include assays amenable to high-throughput screening of chemical libraries, making them particularly suitable for identifying small molecule drug candidates. Small molecules contemplated include synthetic organic or inorganic compounds, including peptides, preferably soluble peptides, (poly)peptide-immunoglobulin fusions, and, in particular, antibodies including, without limitation, poly- and monoclonal antibodies and antibody fragments, single-chain antibodies, anti-idiotypic antibodies, and chimeric or humanized versions of such antibodies or fragments, as well as human antibodies and antibody fragments. The assays can be performed in a variety of formats, including protein-protein binding assays, biochemical screening assays, immunoassays and cell based assays, which are well characterized in the art. All assays are common in that they call for contacting the drug candidate with a polypeptide encoded by a nucleic acid identified herein under conditions and for a time sufficient to allow these two components to interact.

In binding assays, the interaction is binding and the complex formed can be isolated or detected in the reaction mixture. In a particular embodiment, the polypeptide encoded by the gene identified herein or the drug candidate is immobilized on a solid phase, *e.g.*, on a microtiter plate, by covalent or non-covalent attachments. Non-covalent attachment generally is accomplished by coating the solid surface with a solution of the polypeptide and drying. Alternatively, an immobilized antibody, *e.g.*, a monoclonal antibody, specific for the polypeptide to be immobilized can be used to anchor it to a solid surface. The assay is performed by adding the non-immobilized component, which may be labeled by a detectable label, to the immobilized component, *e.g.*, the coated surface containing the anchored component. When the reaction is complete, the non-reacted components are removed, *e.g.*, by washing, and complexes anchored on the solid surface are detected. When the originally non-immobilized component carries a detectable label, the detection of label immobilized on the surface indicates that complexing occurred. Where the originally non-immobilized component does not carry a label, complexing can be detected, for example, by using a labelled antibody specifically binding the immobilized complex.

If the candidate compound interacts with but does not bind to a particular protein encoded by a gene identified herein, its interaction with that protein can be assayed by methods well known for detecting protein-protein interactions. Such assays include traditional approaches, such as, cross-linking, co-immunoprecipitation, and co-purification through gradients or chromatographic columns. In addition, protein-protein interactions can be monitored by using a yeast-based genetic system described by Fields and co-workers [Fields and Song, *Nature (London)* 340, 245-246 (1989); Chien *et al.*, *Proc. Natl. Acad. Sci. USA* 88, 9578-9582 (1991)] as disclosed by Chevray and Nathans, *Proc. Natl. Acad. Sci. USA* 89, 5789-5793 (1991). Many transcriptional activators, such as yeast GAL4, consist of two physically discrete modular domains, one acting as the DNA-binding domain, while the other one functioning as the transcription activation domain. The yeast expression system described in the foregoing publications (generally referred to as the "two-hybrid system") takes advantage of this property, and employs two hybrid proteins, one in which the target protein is fused to the DNA-binding domain of GAL4, and another, in which candidate

activating proteins are fused to the activation domain. The expression of a GAL1-*lacZ* reporter gene under control of a GAL4-activated promoter depends on reconstitution of GAL4 activity via protein-protein interaction. Colonies containing interacting polypeptides are detected with a chromogenic substrate for β -galactosidase. A complete kit (MATCHMAKER™) for identifying protein-protein interactions between two
 5 specific proteins using the two-hybrid technique is commercially available from Clontech. This system can also be extended to map protein domains involved in specific protein interactions as well as to pinpoint amino acid residues that are crucial for these interactions.

In order to find compounds that interfere with the interaction of a gene identified herein and other intra- or extracellular components can be tested, a reaction mixture is usually prepared containing the
 10 product of the gene and the intra- or extracellular component under conditions and for a time allowing for the interaction and binding of the two products. To test the ability of a test compound to inhibit binding, the reaction is run in the absence and in the presence of the test compound. In addition, a placebo may be added to a third reaction mixture, to serve as positive control. The binding (complex formation) between the test compound and the intra- or extracellular component present in the mixture is monitored as described above.
 15 The formation of a complex in the control reaction(s) but not in the reaction mixture containing the test compound indicates that the test compound interferes with the interaction of the test compound and its reaction partner.

K. Compositions and Methods for the Treatment of Immune Related Diseases

The compositions useful in the treatment of immune related diseases include, without limitation,
 20 proteins, antibodies, small organic molecules, peptides, phosphopeptides, antisense and ribozyme molecules, triple helix molecules, *etc.* that inhibit or stimulate immune function, for example, T cell proliferation/activation, lymphokine release, or immune cell infiltration.

For example, antisense RNA and RNA molecules act to directly block the translation of mRNA by hybridizing to targeted mRNA and preventing protein translation. When antisense DNA is used,
 25 oligodeoxynucleotides derived from the translation initiation site, *e.g.*, between about -10 and +10 positions of the target gene nucleotide sequence, are preferred.

Ribozymes are enzymatic RNA molecules capable of catalyzing the specific cleavage of RNA. Ribozymes act by sequence-specific hybridization to the complementary target RNA, followed by endonucleolytic cleavage. Specific ribozyme cleavage sites within a potential RNA target can be identified
 30 by known techniques. For further details see, *e.g.*, Rossi, *Current Biology* 4, 469-471 (1994), and PCT publication No. WO 97/33551 (published September 18, 1997).

Nucleic acid molecules in triple helix formation used to inhibit transcription should be single-stranded and composed of deoxynucleotides. The base composition of these oligonucleotides is designed such that it promotes triple helix formation via Hoogsteen base pairing rules, which generally require
 35 sizeable stretches of purines or pyrimidines on one strand of a duplex. For further details see, *e.g.*, PCT publication No. WO 97/33551, *supra*.

These molecules can be identified by any or any combination of the screening assays discussed above and/or by any other screening techniques well known for those skilled in the art.

L. Anti-PRO Antibodies

The present invention further provides anti-PRO antibodies. Exemplary antibodies include polyclonal, monoclonal, humanized, bispecific, and heteroconjugate antibodies.

1. Polyclonal Antibodies

The anti-PRO antibodies may comprise polyclonal antibodies. Methods of preparing polyclonal antibodies are known to the skilled artisan. Polyclonal antibodies can be raised in a mammal, for example, by one or more injections of an immunizing agent and, if desired, an adjuvant. Typically, the immunizing agent and/or adjuvant will be injected in the mammal by multiple subcutaneous or intraperitoneal injections.

The immunizing agent may include the PRO polypeptide or a fusion protein thereof. It may be useful to conjugate the immunizing agent to a protein known to be immunogenic in the mammal being immunized. Examples of such immunogenic proteins include but are not limited to keyhole limpet hemocyanin, serum albumin, bovine thyroglobulin, and soybean trypsin inhibitor. Examples of adjuvants which may be employed include Freund's complete adjuvant and MPL-TDM adjuvant (monophosphoryl Lipid A, synthetic trehalose dicorynomycolate). The immunization protocol may be selected by one skilled in the art without undue experimentation.

2. Monoclonal Antibodies

The anti-PRO antibodies may, alternatively, be monoclonal antibodies. Monoclonal antibodies may be prepared using hybridoma methods, such as those described by Kohler and Milstein, *Nature*, 256:495 (1975). In a hybridoma method, a mouse, hamster, or other appropriate host animal, is typically immunized with an immunizing agent to elicit lymphocytes that produce or are capable of producing antibodies that will specifically bind to the immunizing agent. Alternatively, the lymphocytes may be immunized *in vitro*.

The immunizing agent will typically include the PRO polypeptide or a fusion protein thereof. Generally, either peripheral blood lymphocytes ("PBLs") are used if cells of human origin are desired, or spleen cells or lymph node cells are used if non-human mammalian sources are desired. The lymphocytes are then fused with an immortalized cell line using a suitable fusing agent, such as polyethylene glycol, to form a hybridoma cell [Goding, *Monoclonal Antibodies: Principles and Practice*, Academic Press, (1986) pp. 59-103]. Immortalized cell lines are usually transformed mammalian cells, particularly myeloma cells of rodent, bovine and human origin. Usually, rat or mouse myeloma cell lines are employed. The hybridoma cells may be cultured in a suitable culture medium that preferably contains one or more substances that inhibit the growth or survival of the unfused, immortalized cells. For example, if the parental cells lack the enzyme hypoxanthine guanine phosphoribosyl transferase (HGPRT or HPRT), the culture medium for the hybridomas typically will include hypoxanthine, aminopterin, and thymidine ("HAT medium"), which substances prevent the growth of HGPRT-deficient cells.

Preferred immortalized cell lines are those that fuse efficiently, support stable high level expression of antibody by the selected antibody-producing cells, and are sensitive to a medium such as HAT medium. More preferred immortalized cell lines are murine myeloma lines, which can be obtained, for instance, from the Salk Institute Cell Distribution Center, San Diego, California and the American Type Culture Collection, Manassas, Virginia. Human myeloma and mouse-human heteromyeloma cell lines also have been described for the production of human monoclonal antibodies [Kozbor, *J. Immunol.*, 133:3001 (1984); Brodeur et al.,

Monoclonal Antibody Production Techniques and Applications, Marcel Dekker, Inc., New York, (1987) pp. 51-63].

5 The culture medium in which the hybridoma cells are cultured can then be assayed for the presence of monoclonal antibodies directed against PRO. Preferably, the binding specificity of monoclonal antibodies produced by the hybridoma cells is determined by immunoprecipitation or by an *in vitro* binding assay, such as radioimmunoassay (RIA) or enzyme-linked immunoabsorbent assay (ELISA). Such techniques and assays are known in the art. The binding affinity of the monoclonal antibody can, for example, be determined by the Scatchard analysis of Munson and Pollard, Anal. Biochem., 107:220 (1980).

10 After the desired hybridoma cells are identified, the clones may be subcloned by limiting dilution procedures and grown by standard methods [Goding, *supra*]. Suitable culture media for this purpose include, for example, Dulbecco's Modified Eagle's Medium and RPMI-1640 medium. Alternatively, the hybridoma cells may be grown *in vivo* as ascites in a mammal.

15 The monoclonal antibodies secreted by the subclones may be isolated or purified from the culture medium or ascites fluid by conventional immunoglobulin purification procedures such as, for example, protein A-Sepharose, hydroxylapatite chromatography, gel electrophoresis, dialysis, or affinity chromatography.

The monoclonal antibodies may also be made by recombinant DNA methods, such as those described in U.S. Patent No. 4,816,567. DNA encoding the monoclonal antibodies of the invention can be readily isolated and sequenced using conventional procedures (e.g., by using oligonucleotide probes that are capable of binding specifically to genes encoding the heavy and light chains of murine antibodies). The hybridoma cells of the invention serve as a preferred source of such DNA. Once isolated, the DNA may be placed into expression vectors, which are then transfected into host cells such as simian COS cells, Chinese hamster ovary (CHO) cells, or myeloma cells that do not otherwise produce immunoglobulin protein, to obtain the synthesis of monoclonal antibodies in the recombinant host cells. The DNA also may be modified, for example, by substituting the coding sequence for human heavy and light chain constant domains in place of the homologous murine sequences [U.S. Patent No. 4,816,567; Morrison et al., *supra*] or by covalently joining to the immunoglobulin coding sequence all or part of the coding sequence for a non-immunoglobulin polypeptide. Such a non-immunoglobulin polypeptide can be substituted for the constant domains of an antibody of the invention, or can be substituted for the variable domains of one antigen-combining site of an antibody of the invention to create a chimeric bivalent antibody.

30 The antibodies may be monovalent antibodies. Methods for preparing monovalent antibodies are well known in the art. For example, one method involves recombinant expression of immunoglobulin light chain and modified heavy chain. The heavy chain is truncated generally at any point in the Fc region so as to prevent heavy chain crosslinking. Alternatively, the relevant cysteine residues are substituted with another amino acid residue or are deleted so as to prevent crosslinking.

In vitro methods are also suitable for preparing monovalent antibodies. Digestion of antibodies to produce fragments thereof, particularly, Fab fragments, can be accomplished using routine techniques known in the art.

3. Human and Humanized Antibodies

The anti-PRO antibodies of the invention may further comprise humanized antibodies or human antibodies. Humanized forms of non-human (e.g., murine) antibodies are chimeric immunoglobulins, immunoglobulin chains or fragments thereof (such as Fv, Fab, Fab', F(ab')₂ or other antigen-binding subsequences of antibodies) which contain minimal sequence derived from non-human immunoglobulin. Humanized antibodies include human immunoglobulins (recipient antibody) in which residues from a complementary determining region (CDR) of the recipient are replaced by residues from a CDR of a non-human species (donor antibody) such as mouse, rat or rabbit having the desired specificity, affinity and capacity. In some instances, Fv framework residues of the human immunoglobulin are replaced by corresponding non-human residues. Humanized antibodies may also comprise residues which are found neither in the recipient antibody nor in the imported CDR or framework sequences. In general, the humanized antibody will comprise substantially all of at least one, and typically two, variable domains, in which all or substantially all of the CDR regions correspond to those of a non-human immunoglobulin and all or substantially all of the FR regions are those of a human immunoglobulin consensus sequence. The humanized antibody optimally also will comprise at least a portion of an immunoglobulin constant region (Fc), typically that of a human immunoglobulin [Jones et al., *Nature*, 321:522-525 (1986); Riechmann et al., *Nature*, 332:323-329 (1988); and Presta, *Curr. Op. Struct. Biol.*, 2:593-596 (1992)].

Methods for humanizing non-human antibodies are well known in the art. Generally, a humanized antibody has one or more amino acid residues introduced into it from a source which is non-human. These non-human amino acid residues are often referred to as "import" residues, which are typically taken from an "import" variable domain. Humanization can be essentially performed following the method of Winter and co-workers [Jones et al., *Nature*, 321:522-525 (1986); Riechmann et al., *Nature*, 332:323-327 (1988); Verhoeven et al., *Science*, 239:1534-1536 (1988)], by substituting rodent CDRs or CDR sequences for the corresponding sequences of a human antibody. Accordingly, such "humanized" antibodies are chimeric antibodies (U.S. Patent No. 4,816,567), wherein substantially less than an intact human variable domain has been substituted by the corresponding sequence from a non-human species. In practice, humanized antibodies are typically human antibodies in which some CDR residues and possibly some FR residues are substituted by residues from analogous sites in rodent antibodies.

Human antibodies can also be produced using various techniques known in the art, including phage display libraries [Hoogenboom and Winter, *J. Mol. Biol.*, 227:381 (1991); Marks et al., *J. Mol. Biol.*, 222:581 (1991)]. The techniques of Cole et al. and Boerner et al. are also available for the preparation of human monoclonal antibodies (Cole et al., *Monoclonal Antibodies and Cancer Therapy*, Alan R. Liss, p. 77 (1985) and Boerner et al., *J. Immunol.*, 147(1):86-95 (1991)]. Similarly, human antibodies can be made by introducing of human immunoglobulin loci into transgenic animals, e.g., mice in which the endogenous immunoglobulin genes have been partially or completely inactivated. Upon challenge, human antibody production is observed, which closely resembles that seen in humans in all respects, including gene rearrangement, assembly, and antibody repertoire. This approach is described, for example, in U.S. Patent Nos. 5,545,807; 5,545,806; 5,569,825; 5,625,126; 5,633,425; 5,661,016, and in the following scientific publications: Marks et al., *BioTechnology* 10, 779-783 (1992); Lonberg et al., *Nature* 368 856-859 (1994);

Morrison, *Nature* 368, 812-13 (1994); Fishwild *et al.*, *Nature Biotechnology* 14, 845-51 (1996); Neuberger, *Nature Biotechnology* 14, 826 (1996); Lonberg and Huszar, *Intern. Rev. Immunol.* 13 65-93 (1995).

The antibodies may also be affinity matured using known selection and/or mutagenesis methods as described above. Preferred affinity matured antibodies have an affinity which is five times, more preferably 10 times, even more preferably 20 or 30 times greater than the starting antibody (generally murine, humanized or human) from which the matured antibody is prepared.

4. Bispecific Antibodies

Bispecific antibodies are monoclonal, preferably human or humanized, antibodies that have binding specificities for at least two different antigens. In the present case, one of the binding specificities is for the PRO, the other one is for any other antigen, and preferably for a cell-surface protein or receptor or receptor subunit.

Methods for making bispecific antibodies are known in the art. Traditionally, the recombinant production of bispecific antibodies is based on the co-expression of two immunoglobulin heavy-chain/light-chain pairs, where the two heavy chains have different specificities [Milstein and Cuello, *Nature*, 305:537-539 (1983)]. Because of the random assortment of immunoglobulin heavy and light chains, these hybridomas (quadromas) produce a potential mixture of ten different antibody molecules, of which only one has the correct bispecific structure. The purification of the correct molecule is usually accomplished by affinity chromatography steps. Similar procedures are disclosed in WO 93/08829, published 13 May 1993, and in Trautnecker *et al.*, *EMBO J.*, 10:3655-3659 (1991).

Antibody variable domains with the desired binding specificities (antibody-antigen combining sites) can be fused to immunoglobulin constant domain sequences. The fusion preferably is with an immunoglobulin heavy-chain constant domain, comprising at least part of the hinge, CH2, and CH3 regions. It is preferred to have the first heavy-chain constant region (CH1) containing the site necessary for light-chain binding present in at least one of the fusions. DNAs encoding the immunoglobulin heavy-chain fusions and, if desired, the immunoglobulin light chain, are inserted into separate expression vectors, and are co-transfected into a suitable host organism. For further details of generating bispecific antibodies see, for example, Suresh *et al.*, *Methods in Enzymology*, 121:210 (1986).

According to another approach described in WO 96/27011, the interface between a pair of antibody molecules can be engineered to maximize the percentage of heterodimers which are recovered from recombinant cell culture. The preferred interface comprises at least a part of the CH3 region of an antibody constant domain. In this method, one or more small amino acid side chains from the interface of the first antibody molecule are replaced with larger side chains (e.g. tyrosine or tryptophan). Compensatory "cavities" of identical or similar size to the large side chain(s) are created on the interface of the second antibody molecule by replacing large amino acid side chains with smaller ones (e.g. alanine or threonine). This provides a mechanism for increasing the yield of the heterodimer over other unwanted end-products such as homodimers.

Bispecific antibodies can be prepared as full length antibodies or antibody fragments (e.g. F(ab')₂ bispecific antibodies). Techniques for generating bispecific antibodies from antibody fragments have been described in the literature. For example, bispecific antibodies can be prepared can be prepared using

chemical linkage. Brennan *et al.*, *Science* 229:81 (1985) describe a procedure wherein intact antibodies are proteolytically cleaved to generate F(ab')₂ fragments. These fragments are reduced in the presence of the dithiol complexing agent sodium arsenite to stabilize vicinal dithiols and prevent intermolecular disulfide formation. The Fab' fragments generated are then converted to thionitrobenzoate (TNB) derivatives. One of the Fab'-TNB derivatives is then reconverted to the Fab'-thiol by reduction with mercaptoethylamine and is mixed with an equimolar amount of the other Fab'-TNB derivative to form the bispecific antibody. The bispecific antibodies produced can be used as agents for the selective immobilization of enzymes.

Fab' fragments may be directly recovered from *E. coli* and chemically coupled to form bispecific antibodies. Shalaby *et al.*, *J. Exp. Med.*, 175:217-225 (1992) describe the production of a fully humanized bispecific antibody F(ab')₂ molecule. Each Fab' fragment was separately secreted from *E. coli* and subjected to directed chemical coupling *in vitro* to form the bispecific antibody. The bispecific antibody thus formed was able to bind to cells overexpressing the ErbB2 receptor and normal human T cells, as well as trigger the lytic activity of human cytotoxic lymphocytes against human breast tumor targets.

Various technique for making and isolating bispecific antibody fragments directly from recombinant cell culture have also been described. For example, bispecific antibodies have been produced using leucine zippers. Kostelny *et al.*, *J. Immunol.*, 148(5):1547-1553 (1992). The leucine zipper peptides from the Fos and Jun proteins were linked to the Fab' portions of two different antibodies by gene fusion. The antibody homodimers were reduced at the hinge region to form monomers and then re-oxidized to form the antibody heterodimers. This method can also be utilized for the production of antibody homodimers. The "diabody" technology described by Hollinger *et al.*, *Proc. Natl. Acad. Sci. USA* 90:6444-6448 (1993) has provided an alternative mechanism for making bispecific antibody fragments. The fragments comprise a heavy-chain variable domain (V_H) connected to a light-chain variable domain (V_L) by a linker which is too short to allow pairing between the two domains on the same chain. Accordingly, the V_H and V_L domains of one fragment are forced to pair with the complementary V_L and V_H domains of another fragment, thereby forming two antigen-binding sites. Another strategy for making bispecific antibody fragments by the use of single-chain Fv (sFv) dimers has also been reported. See, Gruber *et al.*, *J. Immunol.*, 152:5368 (1994). Antibodies with more than two valencies are contemplated. For example, trispecific antibodies can be prepared. Tutt *et al.*, *J. Immunol.*, 147:60 (1991).

Exemplary bispecific antibodies may bind to two different epitopes on a given PRO polypeptide herein. Alternatively, an anti-PRO polypeptide arm may be combined with an arm which binds to a triggering molecule on a leukocyte such as a T-cell receptor molecule (e.g. CD2, CD3, CD28, or B7), or Fc receptors for IgG (FcγR), such as FcγRI (CD64), FcγRII (CD32) and FcγRIII (CD16) so as to focus cellular defense mechanisms to the cell expressing the particular PRO polypeptide. Bispecific antibodies may also be used to localize cytotoxic agents to cells which express a particular PRO polypeptide. These antibodies possess a PRO-binding arm and an arm which binds a cytotoxic agent or a radionuclide chelator, such as EOTUBE, DPTA, DOTA, or TETA. Another bispecific antibody of interest binds the PRO polypeptide and further binds tissue factor (TF).

5. Heteroconjugate Antibodies

Heteroconjugate antibodies are also within the scope of the present invention. Heteroconjugate antibodies are composed of two covalently joined antibodies. Such antibodies have, for example, been

proposed to target immune system cells to unwanted cells [U.S. Patent No. 4,676,980], and for treatment of HIV infection [WO 91/00360; WO 92/200373; EP 03089]. It is contemplated that the antibodies may be prepared *in vitro* using known methods in synthetic protein chemistry, including those involving crosslinking agents. For example, immunotoxins may be constructed using a disulfide exchange reaction or by forming a thioether bond. Examples of suitable reagents for this purpose include iminothiolate and methyl-4-mercaptobutyrimidate and those disclosed, for example, in U.S. Patent No. 4,676,980.

6. Effector Function Engineering

It may be desirable to modify the antibody of the invention with respect to effector function, so as to enhance, *e.g.*, the effectiveness of the antibody in treating cancer. For example, cysteine residue(s) may be introduced into the Fc region, thereby allowing interchain disulfide bond formation in this region. The homodimeric antibody thus generated may have improved internalization capability and/or increased complement-mediated cell killing and antibody-dependent cellular cytotoxicity (ADCC). See Caron *et al.*, *J. Exp. Med.*, 176: 1191-1195 (1992) and Shopes, *J. Immunol.*, 148: 2918-2922 (1992). Homodimeric antibodies with enhanced anti-tumor activity may also be prepared using heterobifunctional cross-linkers as described in Wolff *et al.*, *Cancer Research*, 53: 2560-2565 (1993). Alternatively, an antibody can be engineered that has dual Fc regions and may thereby have enhanced complement lysis and ADCC capabilities. See Stevenson *et al.*, *Anti-Cancer Drug Design*, 3: 219-230 (1989).

7. Immunoconjugates

The invention also pertains to immunoconjugates comprising an antibody conjugated to a cytotoxic agent such as a chemotherapeutic agent, toxin (*e.g.*, an enzymatically active toxin of bacterial, fungal, plant, or animal origin, or fragments thereof), or a radioactive isotope (*i.e.*, a radioconjugate).

Chemotherapeutic agents useful in the generation of such immunoconjugates have been described above. Enzymatically active toxins and fragments thereof that can be used include diphtheria A chain, nonbinding active fragments of diphtheria toxin, exotoxin A chain (from *Pseudomonas aeruginosa*), ricin A chain, abrin A chain, modeccin A chain, alpha-sarcin, *Aleurites fordii* proteins, dianthin proteins, *Phytolacca americana* proteins (PAPI, PAPII, and PAP-S), momordica charantia inhibitor, curcin, crotin, sapaonaria officinalis inhibitor, gelonin, mitogellin, restrictocin, phenomycin, enomycin, and the tricothecenes. A variety of radionuclides are available for the production of radioconjugated antibodies. Examples include ^{212}Bi , ^{131}I , ^{131}In , ^{90}Y , and ^{186}Re .

Conjugates of the antibody and cytotoxic agent are made using a variety of bifunctional protein-coupling agents such as N-succinimidyl-3-(2-pyridyldithiol) propionate (SPDP), iminothiolane (IT), bifunctional derivatives of imidoesters (such as dimethyl adipimidate HCL), active esters (such as disuccinimidyl suberate), aldehydes (such as glutaraldehyde), bis-azido compounds (such as bis-(p-azidobenzoyl) hexanediamine), bis-diazonium derivatives (such as bis-(p-diazoniumbenzoyl)-ethylenediamine), diisocyanates (such as tolyene 2,6-diisocyanate), and bis-active fluorine compounds (such as 1,5-difluoro-2,4-dinitrobenzene). For example, a ricin immunotoxin can be prepared as described in Vitetta *et al.*, *Science*, 238: 1098 (1987). Carbon-14-labeled 1-isothiocyanatobenzyl-3-methyldiethylene triaminopentaacetic acid (MX-DTPA) is an exemplary chelating agent for conjugation of radionuclide to the antibody. See WO94/11026.

In another embodiment, the antibody may be conjugated to a "receptor" (such streptavidin) for utilization in tumor pretargeting wherein the antibody-receptor conjugate is administered to the patient, followed by removal of unbound conjugate from the circulation using a clearing agent and then administration of a "ligand" (e.g., avidin) that is conjugated to a cytotoxic agent (e.g., a radionucleotide).

8. Immunoliposomes

The antibodies disclosed herein may also be formulated as immunoliposomes. Liposomes containing the antibody are prepared by methods known in the art, such as described in Epstein *et al.*, Proc. Natl. Acad. Sci. USA, **82**: 3688 (1985); Hwang *et al.*, Proc. Natl. Acad. Sci. USA, **77**: 4030 (1980); and U.S. Pat. Nos. 4,485,045 and 4,544,545. Liposomes with enhanced circulation time are disclosed in U.S. Patent

No. 5,013,556. Particularly useful liposomes can be generated by the reverse-phase evaporation method with a lipid composition comprising phosphatidylcholine, cholesterol, and PEG-derivatized phosphatidylethanolamine (PEG-PE). Liposomes are extruded through filters of defined pore size to yield liposomes with the desired diameter. Fab' fragments of the antibody of the present invention can be conjugated to the liposomes as described in Martin *et al.*, J. Biol. Chem., **257**: 286-288 (1982) via a disulfide-interchange reaction. A chemotherapeutic agent (such as Doxorubicin) is optionally contained within the liposome. See Gabizon *et al.*, J. National Cancer Inst., **81**(19): 1484 (1989).

M. Pharmaceutical Compositions

The active PRO molecules of the invention (e.g., PRO polypeptides, anti-PRO antibodies, and/or variants of each) as well as other molecules identified by the screening assays disclosed above, can be administered for the treatment of immune related diseases, in the form of pharmaceutical compositions.

Therapeutic formulations of the active PRO molecule, preferably a polypeptide or antibody of the invention, are prepared for storage by mixing the active molecule having the desired degree of purity with optional pharmaceutically acceptable carriers, excipients or stabilizers (*Remington's Pharmaceutical Sciences* 16th edition, Osol, A. Ed. [1980]), in the form of lyophilized formulations or aqueous solutions. Acceptable carriers, excipients, or stabilizers are nontoxic to recipients at the dosages and concentrations employed, and include buffers such as phosphate, citrate, and other organic acids; antioxidants including ascorbic acid and methionine; preservatives (such as octadecyldimethylbenzyl ammonium chloride; hexamethonium chloride; benzalkonium chloride, benzethonium chloride; phenol, butyl or benzyl alcohol; alkyl parabens such as methyl or propyl paraben; catechol; resorcinol; cyclohexanol; 3-pentanol; and m-cresol); low molecular weight (less than about 10 residues) polypeptides; proteins, such as serum albumin, gelatin, or immunoglobulins; hydrophilic polymers such as polyvinylpyrrolidone; amino acids such as glycine, glutamine, asparagine, histidine, arginine, or lysine; monosaccharides, disaccharides, and other carbohydrates including glucose, mannose, or dextrans; chelating agents such as EDTA; sugars such as sucrose, mannitol, trehalose or sorbitol; salt-forming counter-ions such as sodium; metal complexes (e.g., Zn-protein complexes); and/or non-ionic surfactants such as TWEENTM, PLURONICSTM or polyethylene glycol (PEG).

Compounds identified by the screening assays disclosed herein can be formulated in an analogous manner, using standard techniques well known in the art.

Lipofections or liposomes can also be used to deliver the PRO molecule into cells. Where antibody fragments are used, the smallest inhibitory fragment which specifically binds to the binding domain of the target protein is preferred. For example, based upon the variable region sequences of an antibody, peptide molecules can be designed which retain the ability to bind the target protein sequence. Such peptides can be synthesized chemically and/or produced by recombinant DNA technology (see, e.g., Marasco *et al.*, *Proc. Natl. Acad. Sci. USA* **90**, 7889-7893 [1993]).

The formulation herein may also contain more than one active compound as necessary for the particular indication being treated, preferably those with complementary activities that do not adversely affect each other. Alternatively, or in addition, the composition may comprise a cytotoxic agent, cytokine or growth inhibitory agent. Such molecules are suitably present in combination in amounts that are effective for the purpose intended.

The active PRO molecules may also be entrapped in microcapsules prepared, for example, by coacervation techniques or by interfacial polymerization, for example, hydroxymethylcellulose or gelatin-microcapsules and poly-(methylmethacrylate) microcapsules, respectively, in colloidal drug delivery systems (for example, liposomes, albumin microspheres, microemulsions, nano-particles and nanocapsules) or in macroemulsions. Such techniques are disclosed in *Remington's Pharmaceutical Sciences* 16th edition, Osol, A. Ed. (1980).

The formulations to be used for *in vivo* administration must be sterile. This is readily accomplished by filtration through sterile filtration membranes.

Sustained-release preparations of the PRO molecules may be prepared. Suitable examples of sustained-release preparations include semipermeable matrices of solid hydrophobic polymers containing the antibody, which matrices are in the form of shaped articles, e.g., films, or microcapsules. Examples of sustained-release matrices include polyesters, hydrogels (for example, poly(2-hydroxyethyl-methacrylate), or poly(vinylalcohol)), polylactides (U.S. Pat. No. 3,773,919), copolymers of L-glutamic acid and γ -ethyl-L-glutamate, non-degradable ethylene-vinyl acetate, degradable lactic acid-glycolic acid copolymers such as the LUPRON DEPOTTM (injectable microspheres composed of lactic acid-glycolic acid copolymer and leuprolide acetate), and poly-D-(-)-3-hydroxybutyric acid. While polymers such as ethylene-vinyl acetate and lactic acid-glycolic acid enable release of molecules for over 100 days, certain hydrogels release proteins for shorter time periods. When encapsulated antibodies remain in the body for a long time, they may denature or aggregate as a result of exposure to moisture at 37°C, resulting in a loss of biological activity and possible changes in immunogenicity. Rational strategies can be devised for stabilization depending on the mechanism involved. For example, if the aggregation mechanism is discovered to be intermolecular S-S bond formation through thio-disulfide interchange, stabilization may be achieved by modifying sulfhydryl residues, lyophilizing from acidic solutions, controlling moisture content, using appropriate additives, and developing specific polymer matrix compositions.

N. Methods of Treatment

It is contemplated that the polypeptides, antibodies and other active compounds of the present invention may be used to treat various immune related diseases and conditions, such as T cell mediated diseases, including those characterized by infiltration of inflammatory cells into a tissue, stimulation of T-

cell proliferation, inhibition of T-cell proliferation, increased or decreased vascular permeability or the inhibition thereof.

Exemplary conditions or disorders to be treated with the polypeptides, antibodies and other compounds of the invention, include, but are not limited to systemic lupus erythematosus, rheumatoid arthritis, juvenile chronic arthritis, osteoarthritis, spondyloarthropathies, systemic sclerosis (scleroderma), idiopathic inflammatory myopathies (dermatomyositis, polymyositis), Sjögren's syndrome, systemic vasculitis, sarcoidosis, autoimmune hemolytic anemia (immune pancytopenia, paroxysmal nocturnal hemoglobinuria), autoimmune thrombocytopenia (idiopathic thrombocytopenic purpura, immune-mediated thrombocytopenia), thyroiditis (Grave's disease, Hashimoto's thyroiditis, juvenile lymphocytic thyroiditis, atrophic thyroiditis), diabetes mellitus, immune-mediated renal disease (glomerulonephritis, tubulointerstitial nephritis), demyelinating diseases of the central and peripheral nervous systems such as multiple sclerosis, idiopathic demyelinating polyneuropathy or Guillain-Barré syndrome, and chronic inflammatory demyelinating polyneuropathy, hepatobiliary diseases such as infectious hepatitis (hepatitis A, B, C, D, E and other non-hepatotropic viruses), autoimmune chronic active hepatitis, primary biliary cirrhosis, granulomatous hepatitis, and sclerosing cholangitis, inflammatory bowel disease (ulcerative colitis: Crohn's disease), gluten-sensitive enteropathy, and Whipple's disease, autoimmune or immune-mediated skin diseases including bullous skin diseases, erythema multiforme and contact dermatitis, psoriasis, allergic diseases such as asthma, allergic rhinitis, atopic dermatitis, food hypersensitivity and urticaria, immunologic diseases of the lung such as eosinophilic pneumonias, idiopathic pulmonary fibrosis and hypersensitivity pneumonitis, transplantation associated diseases including graft rejection and graft-versus-host-disease.

In systemic lupus erythematosus, the central mediator of disease is the production of auto-reactive antibodies to self proteins/tissues and the subsequent generation of immune-mediated inflammation. Antibodies either directly or indirectly mediate tissue injury. Though T lymphocytes have not been shown to be directly involved in tissue damage, T lymphocytes are required for the development of auto-reactive antibodies. The genesis of the disease is thus T lymphocyte dependent. Multiple organs and systems are affected clinically including kidney, lung, musculoskeletal system, mucocutaneous, eye, central nervous system, cardiovascular system, gastrointestinal tract, bone marrow and blood.

Rheumatoid arthritis (RA) is a chronic systemic autoimmune inflammatory disease that mainly involves the synovial membrane of multiple joints with resultant injury to the articular cartilage. The pathogenesis is T lymphocyte dependent and is associated with the production of rheumatoid factors, auto-antibodies directed against self IgG, with the resultant formation of immune complexes that attain high levels in joint fluid and blood. These complexes in the joint may induce the marked infiltrate of lymphocytes and monocytes into the synovium and subsequent marked synovial changes; the joint space/fluid is infiltrated by similar cells with the addition of numerous neutrophils. Tissues affected are primarily the joints, often in symmetrical pattern. However, extra-articular disease also occurs in two major forms. One form is the development of extra-articular lesions with ongoing progressive joint disease and typical lesions of pulmonary fibrosis, vasculitis, and cutaneous ulcers. The second form of extra-articular disease is the so called Felty's syndrome which occurs late in the RA disease course, sometimes after joint disease has become quiescent, and involves the presence of neutropenia, thrombocytopenia and splenomegaly. This can be accompanied by vasculitis in multiple organs with formations of infarcts, skin

ulcers and gangrene. Patients often also develop rheumatoid nodules in the subcutis tissue overlying affected joints; the nodules late stage have necrotic centers surrounded by a mixed inflammatory cell infiltrate. Other manifestations which can occur in RA include: pericarditis, pleuritis, coronary arteritis, interstitial pneumonitis with pulmonary fibrosis, keratoconjunctivitis sicca, and rheumatoid nodules.

5 Juvenile chronic arthritis is a chronic idiopathic inflammatory disease which begins often at less than 16 years of age. Its phenotype has some similarities to RA; some patients which are rheumatoid factor positive are classified as juvenile rheumatoid arthritis. The disease is sub-classified into three major categories: pauciarticular, polyarticular, and systemic. The arthritis can be severe and is typically destructive and leads to joint ankylosis and retarded growth. Other manifestations can include chronic
10 anterior uveitis and systemic amyloidosis.

Spondyloarthropathies are a group of disorders with some common clinical features and the common association with the expression of HLA-B27 gene product. The disorders include: ankylosing spondylitis, Reiter's syndrome (reactive arthritis), arthritis associated with inflammatory bowel disease, spondylitis associated with psoriasis, juvenile onset spondyloarthropathy and undifferentiated
15 spondyloarthropathy. Distinguishing features include sacroileitis with or without spondylitis; inflammatory asymmetric arthritis; association with HLA-B27 (a serologically defined allele of the HLA-B locus of class I MHC); ocular inflammation, and absence of autoantibodies associated with other rheumatoid disease. The cell most implicated as key to induction of the disease is the CD8+ T lymphocyte, a cell which targets antigen presented by class I MHC molecules. CD8+ T cells may react against the class I MHC allele HLA-
20 B27 as if it were a foreign peptide expressed by MHC class I molecules. It has been hypothesized that an epitope of HLA-B27 may mimic a bacterial or other microbial antigenic epitope and thus induce a CD8+ T cells response.

Systemic sclerosis (scleroderma) has an unknown etiology. A hallmark of the disease is induration of the skin; likely this is induced by an active inflammatory process. Scleroderma can be localized or
25 systemic; vascular lesions are common and endothelial cell injury in the microvasculature is an early and important event in the development of systemic sclerosis; the vascular injury may be immune mediated. An immunologic basis is implied by the presence of mononuclear cell infiltrates in the cutaneous lesions and the presence of anti-nuclear antibodies in many patients. ICAM-1 is often upregulated on the cell surface of fibroblasts in skin lesions suggesting that T cell interaction with these cells may have a role in the
30 pathogenesis of the disease. Other organs involved include: the gastrointestinal tract: smooth muscle atrophy and fibrosis resulting in abnormal peristalsis/motility; kidney: concentric subendothelial intimal proliferation affecting small arcuate and interlobular arteries with resultant reduced renal cortical blood flow, results in proteinuria, azotemia and hypertension; skeletal muscle: atrophy, interstitial fibrosis; inflammation; lung: interstitial pneumonitis and interstitial fibrosis; and heart: contraction band necrosis,
35 scarring/fibrosis.

Idiopathic inflammatory myopathies including dermatomyositis, polymyositis and others are disorders of chronic muscle inflammation of unknown etiology resulting in muscle weakness. Muscle injury/inflammation is often symmetric and progressive. Autoantibodies are associated with most forms. These myositis-specific autoantibodies are directed against and inhibit the function of components, proteins
40 and RNA's, involved in protein synthesis.

Sjögren's syndrome is due to immune-mediated inflammation and subsequent functional destruction of the tear glands and salivary glands. The disease can be associated with or accompanied by inflammatory connective tissue diseases. The disease is associated with autoantibody production against Ro and La antigens, both of which are small RNA-protein complexes. Lesions result in keratoconjunctivitis sicca, xerostomia, with other manifestations or associations including biliary cirrhosis, peripheral or sensory neuropathy, and palpable purpura.

Systemic vasculitis are diseases in which the primary lesion is inflammation and subsequent damage to blood vessels which results in ischemia/necrosis/degeneration to tissues supplied by the affected vessels and eventual end-organ dysfunction in some cases. Vasculitides can also occur as a secondary lesion or sequelae to other immune-inflammatory mediated diseases such as rheumatoid arthritis, systemic sclerosis, etc., particularly in diseases also associated with the formation of immune complexes. Diseases in the primary systemic vasculitis group include: systemic necrotizing vasculitis; polyarteritis nodosa, allergic angiitis and granulomatosis, polyangiitis; Wegener's granulomatosis; lymphomatoid granulomatosis; and giant cell arteritis. Miscellaneous vasculitides include: mucocutaneous lymph node syndrome (MLNS or Kawasaki's disease), isolated CNS vasculitis, Behet's disease, thromboangiitis obliterans (Buerger's disease) and cutaneous necrotizing vasculitis. The pathogenic mechanism of most of the types of vasculitis listed is believed to be primarily due to the deposition of immunoglobulin complexes in the vessel wall and subsequent induction of an inflammatory response either via ADCC, complement activation, or both.

Sarcoidosis is a condition of unknown etiology which is characterized by the presence of epithelioid granulomas in nearly any tissue in the body; involvement of the lung is most common. The pathogenesis involves the persistence of activated macrophages and lymphoid cells at sites of the disease with subsequent chronic sequelae resultant from the release of locally and systemically active products released by these cell types.

Autoimmune hemolytic anemia including autoimmune hemolytic anemia, immune pancytopenia, and paroxysmal nocturnal hemoglobinuria is a result of production of antibodies that react with antigens expressed on the surface of red blood cells (and in some cases other blood cells including platelets as well) and is a reflection of the removal of those antibody coated cells via complement mediated lysis and/or ADCC/Fc-receptor-mediated mechanisms.

In autoimmune thrombocytopenia including thrombocytopenic purpura, and immune-mediated thrombocytopenia in other clinical settings, platelet destruction/removal occurs as a result of either antibody or complement attaching to platelets and subsequent removal by complement lysis, ADCC or FC-receptor mediated mechanisms.

Thyroiditis including Grave's disease, Hashimoto's thyroiditis, juvenile lymphocytic thyroiditis, and atrophic thyroiditis, are the result of an autoimmune response against thyroid antigens with production of antibodies that react with proteins present in and often specific for the thyroid gland. Experimental models exist including spontaneous models: rats (BUF and BB rats) and chickens (obese chicken strain); inducible models: immunization of animals with either thyroglobulin, thyroid microsomal antigen (thyroid peroxidase).

Type I diabetes mellitus or insulin-dependent diabetes is the autoimmune destruction of pancreatic islet β cells; this destruction is mediated by auto-antibodies and auto-reactive T cells. Antibodies to insulin or the insulin receptor can also produce the phenotype of insulin-non-responsiveness.

Immune mediated renal diseases, including glomerulonephritis and tubulointerstitial nephritis, are the result of antibody or T lymphocyte mediated injury to renal tissue either directly as a result of the production of autoreactive antibodies or T cells against renal antigens or indirectly as a result of the deposition of antibodies and/or immune complexes in the kidney that are reactive against other, non-renal antigens. Thus other immune-mediated diseases that result in the formation of immune-complexes can also induce immune mediated renal disease as an indirect sequelae. Both direct and indirect immune mechanisms result in inflammatory response that produces/induces lesion development in renal tissues with resultant organ function impairment and in some cases progression to renal failure. Both humoral and cellular immune mechanisms can be involved in the pathogenesis of lesions.

Demyelinating diseases of the central and peripheral nervous systems, including Multiple Sclerosis; idiopathic demyelinating polyneuropathy or Guillain-Barré syndrome; and Chronic Inflammatory Demyelinating Polyneuropathy, are believed to have an autoimmune basis and result in nerve demyelination as a result of damage caused to oligodendrocytes or to myelin directly. In MS there is evidence to suggest that disease induction and progression is dependent on T lymphocytes. Multiple Sclerosis is a demyelinating disease that is T lymphocyte-dependent and has either a relapsing-remitting course or a chronic progressive course. The etiology is unknown; however, viral infections, genetic predisposition, environment, and autoimmunity all contribute. Lesions contain infiltrates of predominantly T lymphocyte mediated, microglial cells and infiltrating macrophages; CD4+ T lymphocytes are the predominant cell type at lesions. The mechanism of oligodendrocyte cell death and subsequent demyelination is not known but is likely T lymphocyte driven.

Inflammatory and Fibrotic Lung Disease, including Eosinophilic Pneumonias; Idiopathic Pulmonary Fibrosis, and Hypersensitivity Pneumonitis may involve a dysregulated immune-inflammatory response. Inhibition of that response would be of therapeutic benefit.

Autoimmune or Immune-mediated Skin Disease including Bullous Skin Diseases, Erythema Multiforme, and Contact Dermatitis are mediated by auto-antibodies, the genesis of which is T lymphocyte-dependent.

Psoriasis is a T lymphocyte-mediated inflammatory disease. Lesions contain infiltrates of T lymphocytes, macrophages and antigen processing cells, and some neutrophils.

Allergic diseases, including asthma; allergic rhinitis; atopic dermatitis; food hypersensitivity; and urticaria are T lymphocyte dependent. These diseases are predominantly mediated by T lymphocyte induced inflammation, IgE mediated-inflammation or a combination of both.

Transplantation associated diseases, including Graft rejection and Graft-Versus-Host-Disease (GVHD) are T lymphocyte-dependent; inhibition of T lymphocyte function is ameliorative.

Other diseases in which intervention of the immune and/or inflammatory response have benefit are infectious disease including but not limited to viral infection (including but not limited to AIDS, hepatitis A, B, C, D, E and herpes) bacterial infection, fungal infections, and protozoal and parasitic infections (molecules (or derivatives/agonists) which stimulate the MLR can be utilized therapeutically to enhance the

immune response to infectious agents), diseases of immunodeficiency (molecules/derivatives/agonists) which stimulate the MLR can be utilized therapeutically to enhance the immune response for conditions of inherited, acquired, infectious induced (as in HIV infection), or iatrogenic (*i.e.*, as from chemotherapy) immunodeficiency, and neoplasia.

5 It has been demonstrated that some human cancer patients develop an antibody and/or T lymphocyte response to antigens on neoplastic cells. It has also been shown in animal models of neoplasia that enhancement of the immune response can result in rejection or regression of that particular neoplasm. Molecules that enhance the T lymphocyte response in the MLR have utility *in vivo* in enhancing the immune response against neoplasia. Molecules which enhance the T lymphocyte proliferative response in the MLR
10 (or small molecule agonists or antibodies that affected the same receptor in an agonistic fashion) can be used therapeutically to treat cancer. Molecules that inhibit the lymphocyte response in the MLR also function *in vivo* during neoplasia to suppress the immune response to a neoplasm; such molecules can either be expressed by the neoplastic cells themselves or their expression can be induced by the neoplasm in other cells. Antagonism of such inhibitory molecules (either with antibody, small molecule antagonists or other
15 means) enhances immune-mediated tumor rejection.

Additionally, inhibition of molecules with proinflammatory properties may have therapeutic benefit in reperfusion injury; stroke; myocardial infarction; atherosclerosis; acute lung injury; hemorrhagic shock; burn; sepsis/septic shock; acute tubular necrosis; endometriosis; degenerative joint disease and pancreatitis.

The compounds of the present invention, *e.g.*, polypeptides or antibodies, are administered to a
20 mammal, preferably a human, in accord with known methods, such as intravenous administration as a bolus or by continuous infusion over a period of time, by intramuscular, intraperitoneal, intracerebrospinal, subcutaneous, intra-articular, intrasynovial, intrathecal, oral, topical, or inhalation (intranasal, intrapulmonary) routes. Intravenous or inhaled administration of polypeptides and antibodies is preferred.

In immunoadjuvant therapy, other therapeutic regimens, such administration of an anti-cancer
25 agent, may be combined with the administration of the proteins, antibodies or compounds of the instant invention. For example, the patient to be treated with a the immunoadjuvant of the invention may also receive an anti-cancer agent (chemotherapeutic agent) or radiation therapy. Preparation and dosing schedules for such chemotherapeutic agents may be used according to manufacturers' instructions or as determined empirically by the skilled practitioner. Preparation and dosing schedules for such chemotherapy
30 are also described in *Chemotherapy Service* Ed., M.C. Perry, Williams & Wilkins, Baltimore, MD (1992). The chemotherapeutic agent may precede, or follow administration of the immunoadjuvant or may be given simultaneously therewith. Additionally, an anti-estrogen compound such as tamoxifen or an anti-progesterone such as onapristone (see, EP 616812) may be given in dosages known for such molecules.

It may be desirable to also administer antibodies against other immune disease associated or tumor
35 associated antigens, such as antibodies which bind to CD20, CD11a, CD18, ErbB2, EGFR, ErbB3, ErbB4, or vascular endothelial factor (VEGF). Alternatively, or in addition, two or more antibodies binding the same or two or more different antigens disclosed herein may be coadministered to the patient. Sometimes, it may be beneficial to also administer one or more cytokines to the patient. In one embodiment, the PRO polypeptides are coadministered with a growth inhibitory agent. For example, the growth inhibitory agent
40 may be administered first, followed by a PRO polypeptide. However, simultaneous administration or

administration first is also contemplated. Suitable dosages for the growth inhibitory agent are those presently used and may be lowered due to the combined action (synergy) of the growth inhibitory agent and the PRO polypeptide.

5 For the treatment or reduction in the severity of immune related disease, the appropriate dosage of an a compound of the invention will depend on the type of disease to be treated, as defined above, the severity and course of the disease, whether the agent is administered for preventive or therapeutic purposes, previous therapy, the patient's clinical history and response to the compound, and the discretion of the attending physician. The compound is suitably administered to the patient at one time or over a series of treatments.

10 For example, depending on the type and severity of the disease, about 1 µg/kg to 15 mg/kg (*e.g.*, 0.1-20 mg/kg) of polypeptide or antibody is an initial candidate dosage for administration to the patient, whether, for example, by one or more separate administrations, or by continuous infusion. A typical daily dosage might range from about 1 µg/kg to 100 mg/kg or more, depending on the factors mentioned above. For repeated administrations over several days or longer, depending on the condition, the treatment is
15 sustained until a desired suppression of disease symptoms occurs. However, other dosage regimens may be useful. The progress of this therapy is easily monitored by conventional techniques and assays.

O. Articles of Manufacture

In another embodiment of the invention, an article of manufacture containing materials (*e.g.*, comprising a PRO molecule) useful for the diagnosis or treatment of the disorders described above is
20 provided. The article of manufacture comprises a container and an instruction. Suitable containers include, for example, bottles, vials, syringes, and test tubes. The containers may be formed from a variety of materials such as glass or plastic. The container holds a composition which is effective for diagnosing or treating the condition and may have a sterile access port (for example the container may be an intravenous solution bag or a vial having a stopper pierceable by a hypodermic injection needle). The active agent in the
25 composition is usually a polypeptide or an antibody of the invention. An instruction or label on, or associated with, the container indicates that the composition is used for diagnosing or treating the condition of choice. The article of manufacture may further comprise a second container comprising a pharmaceutically-acceptable buffer, such as phosphate-buffered saline, Ringer's solution and dextrose solution. It may further include other materials desirable from a commercial and user standpoint, including
30 other buffers, diluents, filters, needles, syringes, and package inserts with instructions for use.

P. Diagnosis and Prognosis of Immune Related Disease

Cell surface proteins, such as proteins which are overexpressed in certain immune related diseases, are excellent targets for drug candidates or disease treatment. The same proteins along with secreted proteins encoded by the genes amplified in immune related disease states find additional use in the diagnosis
35 and prognosis of these diseases. For example, antibodies directed against the protein products of genes amplified in multiple sclerosis, rheumatoid arthritis, or another immune related disease, can be used as diagnostics or prognostics.

For example, antibodies, including antibody fragments, can be used to qualitatively or quantitatively detect the expression of proteins encoded by amplified or overexpressed genes ("marker gene
40 products"). The antibody preferably is equipped with a detectable, *e.g.*, fluorescent label, and binding can be

monitored by light microscopy, flow cytometry, fluorimetry, or other techniques known in the art. These techniques are particularly suitable, if the overexpressed gene encodes a cell surface protein. Such binding assays are performed essentially as described above.

In situ detection of antibody binding to the marker gene products can be performed, for example, by immunofluorescence or immunoelectron microscopy. For this purpose, a histological specimen is removed from the patient, and a labeled antibody is applied to it, preferably by overlaying the antibody on a biological sample. This procedure also allows for determining the distribution of the marker gene product in the tissue examined. It will be apparent for those skilled in the art that a wide variety of histological methods are readily available for *in situ* detection.

The following examples are offered for illustrative purposes only, and are not intended to limit the scope of the present invention in any way.

All patent and literature references cited in the present specification are hereby incorporated by reference in their entirety.

EXAMPLES

Commercially available reagents referred to in the examples were used according to manufacturer's instructions unless otherwise indicated. The source of those cells identified in the following examples, and throughout the specification, by ATCC accession numbers is the American Type Culture Collection, Manassas, VA.

EXAMPLE 1: Microarray analysis of stimulated T-cells

Nucleic acid microarrays, often containing thousands of gene sequences, are useful for identifying differentially expressed genes in diseased tissues as compared to their normal counterparts. Using nucleic acid microarrays, test and control mRNA samples from test and control tissue samples are reverse transcribed and labeled to generate cDNA probes. The cDNA probes are then hybridized to an array of nucleic acids immobilized on a solid support. The array is configured such that the sequence and position of each member of the array is known. For example, a selection of genes known to be expressed in certain disease states may be arrayed on a solid support. Hybridization of a labeled probe with a particular array member indicates that the sample from which the probe was derived expresses that gene. If the hybridization signal of a probe from a test (in this instance, activated CD4+ T cells) sample is greater than hybridization signal of a probe from a control (in this instance, non-stimulated CD4+ T cells) sample, the gene or genes overexpressed in the test tissue are identified. The implication of this result is that an overexpressed protein in a test tissue is useful not only as a diagnostic marker for the presence of the disease condition, but also as a therapeutic target for treatment of the disease condition.

The methodology of hybridization of nucleic acids and microarray technology is well known in the art. In one example, the specific preparation of nucleic acids for hybridization and probes, slides, and hybridization conditions are all detailed in PCT Patent Application Serial No. PCT/US01/10482, filed on March 30, 2001 and which is herein incorporated by reference.

In this experiment, CD4+ T cells were purified from a single donor using the RosetteSep™ protocol from (Stem Cell Technologies, Vancouver BC) which contains anti-CD8, anti-CD16, anti-CD19, anti-CD36 and anti-CD56 antibodies used to produce a population of isolated CD4+ T cells. Isolated CD4+

T cells were activated with an anti-CD3 antibody (used at a concentration that does not stimulate proliferation) together with either ICAM-1 or anti-CD28 antibody. At 24 or 72 hours cells were harvested, RNA extracted and analysis run on Affimax (Affymetrix Inc. Santa Clara, CA) microarray chips. Non-stimulated (resting) cells were harvested immediately after purification, and subjected to the same analysis.

- 5 Genes were compared whose expression was upregulated at either of the two timepoints in activated vs. resting cells.

Below are the results of these experiments, demonstrating that various PRO polypeptides of the present invention are differentially expressed in isolated CD4 + T cells activated by anti-CD3/ICAM-1 or anti-CD3/anti-CD28 as compared to isolated resting CD4+ T cells. As described above, these data
10 demonstrate that the PRO polypeptides of the present invention are useful not only as diagnostic markers for the presence of one or more immune disorders, but also serve as therapeutic targets for the treatment of those immune disorders.

The results of this experiment are Figures 1-7589 show increase or decrease in expression upon stimulation with anti-CD3/ICAM1 and also show increase or decrease in expression upon stimulation with anti-CD3/anti-CD28. The nucleic acids and encoded proteins of Figure 946, Figure 1520, Figure 1574,
15 Figure 1622, Figure 1816, Figure 2433, Figure 2986, Figure 3220, Figure 4120 and Figure 5421 are significantly overexpressed in isolated CD4 + T cells activated by anti-CD3/ICAM-1 or anti-CD3/anti-CD28 as compared to isolated resting CD4+ T cells.

20 EXAMPLE 2: Use of PRO as a hybridization probe

The following method describes use of a nucleotide sequence encoding PRO as a hybridization probe.

DNA comprising the coding sequence of full-length or mature PRO as disclosed herein is employed as a probe to screen for homologous DNAs (such as those encoding naturally-occurring variants of PRO) in
25 human tissue cDNA libraries or human tissue genomic libraries.

Hybridization and washing of filters containing either library DNAs is performed under the following high stringency conditions. Hybridization of radiolabeled PRO-derived probe to the filters is performed in a solution of 50% formamide, 5x SSC, 0.1% SDS, 0.1% sodium pyrophosphate, 50 mM sodium phosphate, pH 6.8, 2x Denhardt's solution, and 10% dextran sulfate at 42°C for 20 hours. Washing
30 of the filters is performed in an aqueous solution of 0.1x SSC and 0.1% SDS at 42°C.

DNAs having a desired sequence identity with the DNA encoding full-length native sequence PRO can then be identified using standard techniques known in the art.

EXAMPLE 3: Expression of PRO in *E. coli*

35 This example illustrates preparation of an unglycosylated form of PRO by recombinant expression in *E. coli*.

The DNA sequence encoding PRO is initially amplified using selected PCR primers. The primers should contain restriction enzyme sites which correspond to the restriction enzyme sites on the selected expression vector. A variety of expression vectors may be employed. An example of a suitable vector is
40 pBR322 (derived from *E. coli*; see Bolivar et al., *Gene*, 2:95 (1977)) which contains genes for ampicillin and

tetracycline resistance. The vector is digested with restriction enzyme and dephosphorylated. The PCR amplified sequences are then ligated into the vector. The vector will preferably include sequences which encode for an antibiotic resistance gene, a trp promoter, a polyhis leader (including the first six STII codons, polyhis sequence, and enterokinase cleavage site), the PRO coding region, lambda transcriptional terminator, and an argU gene.

The ligation mixture is then used to transform a selected *E. coli* strain using the methods described in Sambrook et al., supra. Transformants are identified by their ability to grow on LB plates and antibiotic resistant colonies are then selected. Plasmid DNA can be isolated and confirmed by restriction analysis and DNA sequencing.

Selected clones can be grown overnight in liquid culture medium such as LB broth supplemented with antibiotics. The overnight culture may subsequently be used to inoculate a larger scale culture. The cells are then grown to a desired optical density, during which the expression promoter is turned on.

After culturing the cells for several more hours, the cells can be harvested by centrifugation. The cell pellet obtained by the centrifugation can be solubilized using various agents known in the art, and the solubilized PRO protein can then be purified using a metal chelating column under conditions that allow tight binding of the protein.

PRO may be expressed in *E. coli* in a poly-His tagged form, using the following procedure. The DNA encoding PRO is initially amplified using selected PCR primers. The primers will contain restriction enzyme sites which correspond to the restriction enzyme sites on the selected expression vector, and other useful sequences providing for efficient and reliable translation initiation, rapid purification on a metal chelation column, and proteolytic removal with enterokinase. The PCR-amplified, poly-His tagged sequences are then ligated into an expression vector, which is used to transform an *E. coli* host based on strain 52 (W3110 fuhA(tonA) lon galE rpoHts(htpRts) clpP(lacIq). Transformants are first grown in LB containing 50 mg/ml carbenicillin at 30°C with shaking until an O.D.600 of 3-5 is reached. Cultures are then diluted 50-100 fold into CRAP media (prepared by mixing 3.57 g (NH₄)₂SO₄, 0.71 g sodium citrate•2H₂O, 1.07 g KCl, 5.36 g Difco yeast extract, 5.36 g Sheffield hycase SF in 500 mL water, as well as 110 mM MPOS, pH 7.3, 0.55% (w/v) glucose and 7 mM MgSO₄) and grown for approximately 20-30 hours at 30°C with shaking. Samples are removed to verify expression by SDS-PAGE analysis, and the bulk culture is centrifuged to pellet the cells. Cell pellets are frozen until purification and refolding.

E. coli paste from 0.5 to 1 L fermentations (6-10 g pellets) is resuspended in 10 volumes (w/v) in 7 M guanidine, 20 mM Tris, pH 8 buffer. Solid sodium sulfite and sodium tetrathionate is added to make final concentrations of 0.1M and 0.02 M, respectively, and the solution is stirred overnight at 4°C. This step results in a denatured protein with all cysteine residues blocked by sulfitolization. The solution is centrifuged at 40,000 rpm in a Beckman Ultracentrifuge for 30 min. The supernatant is diluted with 3-5 volumes of metal chelate column buffer (6 M guanidine, 20 mM Tris, pH 7.4) and filtered through 0.22 micron filters to clarify. The clarified extract is loaded onto a 5 ml Qiagen Ni-NTA metal chelate column equilibrated in the metal chelate column buffer. The column is washed with additional buffer containing 50 mM imidazole (Calbiochem, Utrol grade), pH 7.4. The protein is eluted with buffer containing 250 mM imidazole. Fractions containing the desired protein are pooled and stored at 4°C. Protein concentration is estimated by its absorbance at 280 nm using the calculated extinction coefficient based on its amino acid sequence.

The proteins are refolded by diluting the sample slowly into freshly prepared refolding buffer consisting of: 20 mM Tris, pH 8.6, 0.3 M NaCl, 2.5 M urea, 5 mM cysteine, 20 mM glycine and 1 mM EDTA. Refolding volumes are chosen so that the final protein concentration is between 50 to 100 micrograms/ml. The refolding solution is stirred gently at 4°C for 12-36 hours. The refolding reaction is quenched by the addition of TFA to a final concentration of 0.4% (pH of approximately 3). Before further purification of the protein, the solution is filtered through a 0.22 micron filter and acetonitrile is added to 2-10% final concentration. The refolded protein is chromatographed on a Poros R1/H reversed phase column using a mobile buffer of 0.1% TFA with elution with a gradient of acetonitrile from 10 to 80%. Aliquots of fractions with A280 absorbance are analyzed on SDS polyacrylamide gels and fractions containing homogeneous refolded protein are pooled. Generally, the properly refolded species of most proteins are eluted at the lowest concentrations of acetonitrile since those species are the most compact with their hydrophobic interiors shielded from interaction with the reversed phase resin. Aggregated species are usually eluted at higher acetonitrile concentrations. In addition to resolving misfolded forms of proteins from the desired form, the reversed phase step also removes endotoxin from the samples.

Fractions containing the desired folded PRO polypeptide are pooled and the acetonitrile removed using a gentle stream of nitrogen directed at the solution. Proteins are formulated into 20 mM Hepes, pH 6.8 with 0.14 M sodium chloride and 4% mannitol by dialysis or by gel filtration using G25 Superfine (Pharmacia) resins equilibrated in the formulation buffer and sterile filtered.

Many of the PRO polypeptides disclosed herein were successfully expressed as described above.

EXAMPLE 4: Expression of PRO in mammalian cells

This example illustrates preparation of a potentially glycosylated form of PRO by recombinant expression in mammalian cells.

The vector, pRK5 (see EP 307,247, published March 15, 1989), is employed as the expression vector. Optionally, the PRO DNA is ligated into pRK5 with selected restriction enzymes to allow insertion of the PRO DNA using ligation methods such as described in Sambrook et al., *supra*. The resulting vector is called pRK5-PRO.

In one embodiment, the selected host cells may be 293 cells. Human 293 cells (ATCC CCL 1573) are grown to confluence in tissue culture plates in medium such as DMEM supplemented with fetal calf serum and optionally, nutrient components and/or antibiotics. About 10 µg pRK5-PRO DNA is mixed with about 1 µg DNA encoding the VA RNA gene [Thimmappaya et al., *Cell*, 31:543 (1982)] and dissolved in 500 µl of 1 mM Tris-HCl, 0.1 mM EDTA, 0.227 M CaCl₂. To this mixture is added, dropwise, 500 µl of 50 mM HEPES (pH 7.35), 280 mM NaCl, 1.5 mM NaPO₄, and a precipitate is allowed to form for 10 minutes at 25°C. The precipitate is suspended and added to the 293 cells and allowed to settle for about four hours at 37°C. The culture medium is aspirated off and 2 ml of 20% glycerol in PBS is added for 30 seconds. The 293 cells are then washed with serum free medium, fresh medium is added and the cells are incubated for about 5 days.

Approximately 24 hours after the transfections, the culture medium is removed and replaced with culture medium (alone) or culture medium containing 200 µCi/ml ³⁵S-cysteine and 200 µCi/ml ³⁵S-methionine. After a 12 hour incubation, the conditioned medium is collected, concentrated on a spin filter,

and loaded onto a 15% SDS gel. The processed gel may be dried and exposed to film for a selected period of time to reveal the presence of PRO polypeptide. The cultures containing transfected cells may undergo further incubation (in serum free medium) and the medium is tested in selected bioassays.

In an alternative technique, PRO may be introduced into 293 cells transiently using the dextran sulfate method described by Sompayrac et al., *Proc. Natl. Acad. Sci.*, 12:7575 (1981). 293 cells are grown to maximal density in a spinner flask and 700 µg pRK5-PRO DNA is added. The cells are first concentrated from the spinner flask by centrifugation and washed with PBS. The DNA-dextran precipitate is incubated on the cell pellet for four hours. The cells are treated with 20% glycerol for 90 seconds, washed with tissue culture medium, and re-introduced into the spinner flask containing tissue culture medium, 5 µg/ml bovine insulin and 0.1 µg/ml bovine transferrin. After about four days, the conditioned media is centrifuged and filtered to remove cells and debris. The sample containing expressed PRO can then be concentrated and purified by any selected method, such as dialysis and/or column chromatography.

In another embodiment, PRO can be expressed in CHO cells. The pRK5-PRO can be transfected into CHO cells using known reagents such as CaPO_4 or DEAE-dextran. As described above, the cell cultures can be incubated, and the medium replaced with culture medium (alone) or medium containing a radiolabel such as ^{35}S -methionine. After determining the presence of PRO polypeptide, the culture medium may be replaced with serum free medium. Preferably, the cultures are incubated for about 6 days, and then the conditioned medium is harvested. The medium containing the expressed PRO can then be concentrated and purified by any selected method.

Epitope-tagged PRO may also be expressed in host CHO cells. The PRO may be subcloned out of the pRK5 vector. The subclone insert can undergo PCR to fuse in frame with a selected epitope tag such as a poly-his tag into a Baculovirus expression vector. The poly-his tagged PRO insert can then be subcloned into a SV40 promoter/enhancer containing vector containing a selection marker such as DHFR for selection of stable clones. Finally, the CHO cells can be transfected (as described above) with the SV40 promoter/enhancer containing vector. Labeling may be performed, as described above, to verify expression. The culture medium containing the expressed poly-His tagged PRO can then be concentrated and purified by any selected method, such as by Ni^{2+} -chelate affinity chromatography.

PRO may also be expressed in CHO and/or COS cells by a transient expression procedure or in CHO cells by another stable expression procedure.

Stable expression in CHO cells is performed using the following procedure. The proteins are expressed as an IgG construct (immunoadhesin), in which the coding sequences for the soluble forms (e.g. extracellular domains) of the respective proteins are fused to an IgG1 constant region sequence containing the hinge, CH2 and CH2 domains and/or is a poly-His tagged form.

Following PCR amplification, the respective DNAs are subcloned in a CHO expression vector using standard techniques as described in Ausubel et al., *Current Protocols of Molecular Biology*, Unit 3.16, John Wiley and Sons (1997). CHO expression vectors are constructed to have compatible restriction sites 5' and 3' of the DNA of interest to allow the convenient shuttling of cDNA's. The vector used expression in CHO cells is as described in Lucas et al., *Nucl. Acids Res.*, 24:9 (1774-1779 (1996), and uses the SV40 early promoter/enhancer to drive expression of the cDNA of interest and dihydrofolate reductase (DHFR). DHFR expression permits selection for stable maintenance of the plasmid following transfection.

Twelve micrograms of the desired plasmid DNA is introduced into approximately 10 million CHO cells using commercially available transfection reagents Superfect® (Qiagen), Dospers® or Fugene® (Boehringer Mannheim). The cells are grown as described in Lucas et al., *supra*. Approximately 3×10^7 cells are frozen in an ampule for further growth and production as described below.

- 5 The ampules containing the plasmid DNA are thawed by placement into water bath and mixed by vortexing. The contents are pipetted into a centrifuge tube containing 10 mL of media and centrifuged at 1000 rpm for 5 minutes. The supernatant is aspirated and the cells are resuspended in 10 mL of selective media (0.2 μ m filtered PS20 with 5% 0.2 μ m diafiltered fetal bovine serum). The cells are then aliquoted into a 100 mL spinner containing 90 mL of selective media. After 1-2 days, the cells are transferred into a 10 250 mL spinner filled with 150 mL selective growth medium and incubated at 37°C. After another 2-3 days, 250 mL, 500 mL and 2000 mL spinners are seeded with 3×10^5 cells/mL. The cell media is exchanged with fresh media by centrifugation and resuspension in production medium. Although any suitable CHO media may be employed, a production medium described in U.S. Patent No. 5,122,469, issued June 16, 1992 may actually be used. A 3L production spinner is seeded at 1.2×10^6 cells/mL. On day 0, pH is determined. On 15 day 1, the spinner is sampled and sparging with filtered air is commenced. On day 2, the spinner is sampled, the temperature shifted to 33°C, and 30 mL of 500 g/L glucose and 0.6 mL of 10% antifoam (e.g., 35% polydimethylsiloxane emulsion, Dow Corning 365 Medical Grade Emulsion) taken. Throughout the production, the pH is adjusted as necessary to keep it at around 7.2. After 10 days, or until the viability dropped below 70%, the cell culture is harvested by centrifugation and filtering through a 0.22 μ m filter. 20 The filtrate was either stored at 4°C or immediately loaded onto columns for purification.

- For the poly-His tagged constructs, the proteins are purified using a Ni-NTA column (Qiagen). Before purification, imidazole is added to the conditioned media to a concentration of 5 mM. The conditioned media is pumped onto a 6 mL Ni-NTA column equilibrated in 20 mM Hepes, pH 7.4, buffer containing 0.3 M NaCl and 5 mM imidazole at a flow rate of 4-5 mL/min. at 4°C. After loading, the column 25 is washed with additional equilibration buffer and the protein eluted with equilibration buffer containing 0.25 M imidazole. The highly purified protein is subsequently desalted into a storage buffer containing 10 mM Hepes, 0.14 M NaCl and 4% mannitol, pH 6.8, with a 25 mL G25 Superfine (Pharmacia) column and stored at -80°C.

- Immunoadhesin (Fc-containing) constructs are purified from the conditioned media as follows. The 30 conditioned medium is pumped onto a 5 mL Protein A column (Pharmacia) which had been equilibrated in 20 mM Na phosphate buffer, pH 6.8. After loading, the column is washed extensively with equilibration buffer before elution with 100 mM citric acid, pH 3.5. The eluted protein is immediately neutralized by collecting 1 mL fractions into tubes containing 275 μ L of 1 M Tris buffer, pH 9. The highly purified protein is subsequently desalted into storage buffer as described above for the poly-His tagged proteins. The 35 homogeneity is assessed by SDS polyacrylamide gels and by N-terminal amino acid sequencing by Edman degradation.

Many of the PRO polypeptides disclosed herein were successfully expressed as described above.

EXAMPLE 5: Expression of PRO in Yeast

- 40 The following method describes recombinant expression of PRO in yeast.

First, yeast expression vectors are constructed for intracellular production or secretion of PRO from the ADH2/GAPDH promoter. DNA encoding PRO and the promoter is inserted into suitable restriction enzyme sites in the selected plasmid to direct intracellular expression of PRO. For secretion, DNA encoding PRO can be cloned into the selected plasmid, together with DNA encoding the ADH2/GAPDH promoter, a native PRO signal peptide or other mammalian signal peptide, or, for example, a yeast alpha-factor or invertase secretory signal/leader sequence, and linker sequences (if needed) for expression of PRO.

Yeast cells, such as yeast strain AB110, can then be transformed with the expression plasmids described above and cultured in selected fermentation media. The transformed yeast supernatants can be analyzed by precipitation with 10% trichloroacetic acid and separation by SDS-PAGE, followed by staining of the gels with Coomassie Blue stain.

Recombinant PRO can subsequently be isolated and purified by removing the yeast cells from the fermentation medium by centrifugation and then concentrating the medium using selected cartridge filters. The concentrate containing PRO may further be purified using selected column chromatography resins.

Many of the PRO polypeptides disclosed herein were successfully expressed as described above.

EXAMPLE 6: Expression of PRO in Baculovirus-Infected Insect Cells

The following method describes recombinant expression of PRO in Baculovirus-infected insect cells.

The sequence coding for PRO is fused upstream of an epitope tag contained within a baculovirus expression vector. Such epitope tags include poly-his tags and immunoglobulin tags (like Fc regions of IgG). A variety of plasmids may be employed, including plasmids derived from commercially available plasmids such as pVL1393 (Novagen). Briefly, the sequence encoding PRO or the desired portion of the coding sequence of PRO such as the sequence encoding the extracellular domain of a transmembrane protein or the sequence encoding the mature protein if the protein is extracellular is amplified by PCR with primers complementary to the 5' and 3' regions. The 5' primer may incorporate flanking (selected) restriction enzyme sites. The product is then digested with those selected restriction enzymes and subcloned into the expression vector.

Recombinant baculovirus is generated by co-transfecting the above plasmid and BaculoGold™ virus DNA (Pharmingen) into *Spodoptera frugiperda* ("Sf9") cells (ATCC CRL 1711) using lipofectin (commercially available from GIBCO-BRL). After 4 - 5 days of incubation at 28°C, the released viruses are harvested and used for further amplifications. Viral infection and protein expression are performed as described by O'Reilly et al., Baculovirus expression vectors: A Laboratory Manual, Oxford: Oxford University Press (1994).

Expressed poly-his tagged PRO can then be purified, for example, by Ni²⁺-chelate affinity chromatography as follows. Extracts are prepared from recombinant virus-infected Sf9 cells as described by Rupert et al., Nature, 362:175-179 (1993). Briefly, Sf9 cells are washed, resuspended in sonication buffer (25 mL Hepes, pH 7.9; 12.5 mM MgCl₂; 0.1 mM EDTA; 10% glycerol; 0.1% NP-40; 0.4 M KCl), and sonicated twice for 20 seconds on ice. The sonicates are cleared by centrifugation, and the supernatant is diluted 50-fold in loading buffer (50 mM phosphate, 300 mM NaCl, 10% glycerol, pH 7.8) and filtered through a 0.45 µm filter. A Ni²⁺-NTA agarose column (commercially available from Qiagen) is prepared

with a bed volume of 5 mL, washed with 25 mL of water and equilibrated with 25 mL of loading buffer. The filtered cell extract is loaded onto the column at 0.5 mL per minute. The column is washed to baseline A_{280} with loading buffer, at which point fraction collection is started. Next, the column is washed with a secondary wash buffer (50 mM phosphate; 300 mM NaCl, 10% glycerol, pH 6.0), which elutes

5 nonspecifically bound protein. After reaching A_{280} baseline again, the column is developed with a 0 to 500 mM Imidazole gradient in the secondary wash buffer. One mL fractions are collected and analyzed by SDS-PAGE and silver staining or Western blot with Ni^{2+} -NTA-conjugated to alkaline phosphatase (Qiagen). Fractions containing the eluted His₁₀-tagged PRO are pooled and dialyzed against loading buffer.

Alternatively, purification of the IgG tagged (or Fc tagged) PRO can be performed using known

10 chromatography techniques, including for instance, Protein A or protein G column chromatography.

Many of the PRO polypeptides disclosed herein were successfully expressed as described above.

EXAMPLE 7: Preparation of Antibodies that Bind PRO

This example illustrates preparation of monoclonal antibodies which can specifically bind PRO.

15 Techniques for producing the monoclonal antibodies are known in the art and are described, for instance, in Goding, *supra*. Immunogens that may be employed include purified PRO, fusion proteins containing PRO, and cells expressing recombinant PRO on the cell surface. Selection of the immunogen can be made by the skilled artisan without undue experimentation.

Mice, such as Balb/c, are immunized with the PRO immunogen emulsified in complete Freund's

20 adjuvant and injected subcutaneously or intraperitoneally in an amount from 1-100 micrograms. Alternatively, the immunogen is emulsified in MPL-TDM adjuvant (Ribi Immunochemical Research, Hamilton, MT) and injected into the animal's hind foot pads. The immunized mice are then boosted 10 to 12 days later with additional immunogen emulsified in the selected adjuvant. Thereafter, for several weeks, the mice may also be boosted with additional immunization injections. Serum samples may be periodically

25 obtained from the mice by retro-orbital bleeding for testing in ELISA assays to detect anti-PRO antibodies.

After a suitable antibody titer has been detected, the animals "positive" for antibodies can be injected with a final intravenous injection of PRO. Three to four days later, the mice are sacrificed and the spleen cells are harvested. The spleen cells are then fused (using 35% polyethylene glycol) to a selected murine myeloma cell line such as P3X63AgU.1, available from ATCC, No. CRL 1597. The fusions

30 generate hybridoma cells which can then be plated in 96 well tissue culture plates containing HAT (hypoxanthine, aminopterin, and thymidine) medium to inhibit proliferation of non-fused cells, myeloma hybrids, and spleen cell hybrids.

The hybridoma cells will be screened in an ELISA for reactivity against PRO. Determination of "positive" hybridoma cells secreting the desired monoclonal antibodies against PRO is within the skill in the

35 art.

The positive hybridoma cells can be injected intraperitoneally into syngeneic Balb/c mice to produce ascites containing the anti-PRO monoclonal antibodies. Alternatively, the hybridoma cells can be grown in tissue culture flasks or roller bottles. Purification of the monoclonal antibodies produced in the ascites can be accomplished using ammonium sulfate precipitation, followed by gel exclusion

chromatography. Alternatively, affinity chromatography based upon binding of antibody to protein A or protein G can be employed.

EXAMPLE 8: Purification of PRO Polypeptides Using Specific Antibodies

5 Native or recombinant PRO polypeptides may be purified by a variety of standard techniques in the art of protein purification. For example, pro-PRO polypeptide, mature PRO polypeptide, or pre-PRO polypeptide is purified by immunoaffinity chromatography using antibodies specific for the PRO polypeptide of interest. In general, an immunoaffinity column is constructed by covalently coupling the anti-PRO polypeptide antibody to an activated chromatographic resin.

10 Polyclonal immunoglobulins are prepared from immune sera either by precipitation with ammonium sulfate or by purification on immobilized Protein A (Pharmacia LKB Biotechnology, Piscataway, N.J.). Likewise, monoclonal antibodies are prepared from mouse ascites fluid by ammonium sulfate precipitation or chromatography on immobilized Protein A. Partially purified immunoglobulin is covalently attached to a chromatographic resin such as CNBr-activated SEPHAROSE™ (Pharmacia LKB
15 Biotechnology). The antibody is coupled to the resin, the resin is blocked, and the derivative resin is washed according to the manufacturer's instructions.

Such an immunoaffinity column is utilized in the purification of PRO polypeptide by preparing a fraction from cells containing PRO polypeptide in a soluble form. This preparation is derived by solubilization of the whole cell or of a subcellular fraction obtained via differential centrifugation by the
20 addition of detergent or by other methods well known in the art. Alternatively, soluble PRO polypeptide containing a signal sequence may be secreted in useful quantity into the medium in which the cells are grown.

A soluble PRO polypeptide-containing preparation is passed over the immunoaffinity column, and the column is washed under conditions that allow the preferential absorbance of PRO polypeptide (*e.g.*, high
25 ionic strength buffers in the presence of detergent). Then, the column is eluted under conditions that disrupt antibody/PRO polypeptide binding (*e.g.*, a low pH buffer such as approximately pH 2-3, or a high concentration of a chaotrope such as urea or thiocyanate ion), and PRO polypeptide is collected.

EXAMPLE 9: Drug Screening

30 This invention is particularly useful for screening compounds by using PRO polypeptides or binding fragment thereof in any of a variety of drug screening techniques. The PRO polypeptide or fragment employed in such a test may either be free in solution, affixed to a solid support, borne on a cell surface, or located intracellularly. One method of drug screening utilizes eukaryotic or prokaryotic host cells which are stably transformed with recombinant nucleic acids expressing the PRO polypeptide or fragment.
35 Drugs are screened against such transformed cells in competitive binding assays. Such cells, either in viable or fixed form, can be used for standard binding assays. One may measure, for example, the formation of complexes between PRO polypeptide or a fragment and the agent being tested. Alternatively, one can examine the diminution in complex formation between the PRO polypeptide and its target cell or target receptors caused by the agent being tested.

Thus, the present invention provides methods of screening for drugs or any other agents which can affect a PRO polypeptide-associated disease or disorder. These methods comprise contacting such an agent with an PRO polypeptide or fragment thereof and assaying (i) for the presence of a complex between the agent and the PRO polypeptide or fragment, or (ii) for the presence of a complex between the PRO

polypeptide or fragment and the cell, by methods well known in the art. In such competitive binding assays, the PRO polypeptide or fragment is typically labeled. After suitable incubation, free PRO polypeptide or fragment is separated from that present in bound form, and the amount of free or uncomplexed label is a measure of the ability of the particular agent to bind to PRO polypeptide or to interfere with the PRO polypeptide/cell complex.

Another technique for drug screening provides high throughput screening for compounds having suitable binding affinity to a polypeptide and is described in detail in WO 84/03564, published on September 13, 1984. Briefly stated, large numbers of different small peptide test compounds are synthesized on a solid substrate, such as plastic pins or some other surface. As applied to a PRO polypeptide, the peptide test compounds are reacted with PRO polypeptide and washed. Bound PRO polypeptide is detected by methods well known in the art. Purified PRO polypeptide can also be coated directly onto plates for use in the aforementioned drug screening techniques. In addition, non-neutralizing antibodies can be used to capture the peptide and immobilize it on the solid support.

This invention also contemplates the use of competitive drug screening assays in which neutralizing antibodies capable of binding PRO polypeptide specifically compete with a test compound for binding to PRO polypeptide or fragments thereof. In this manner, the antibodies can be used to detect the presence of any peptide which shares one or more antigenic determinants with PRO polypeptide.

EXAMPLE 10: Rational Drug Design

The goal of rational drug design is to produce structural analogs of biologically active polypeptide of interest (*i.e.*, a PRO polypeptide) or of small molecules with which they interact, *e.g.*, agonists, antagonists, or inhibitors. Any of these examples can be used to fashion drugs which are more active or stable forms of the PRO polypeptide or which enhance or interfere with the function of the PRO polypeptide *in vivo* (*c.f.*, Hodgson, BioTechnology, 9: 19-21 (1991)).

In one approach, the three-dimensional structure of the PRO polypeptide, or of a PRO polypeptide-inhibitor complex, is determined by x-ray crystallography, by computer modeling or, most typically, by a combination of the two approaches. Both the shape and charges of the PRO polypeptide must be ascertained to elucidate the structure and to determine active site(s) of the molecule. Less often, useful information regarding the structure of the PRO polypeptide may be gained by modeling based on the structure of homologous proteins. In both cases, relevant structural information is used to design analogous PRO polypeptide-like molecules or to identify efficient inhibitors. Useful examples of rational drug design may include molecules which have improved activity or stability as shown by Braxton and Wells, Biochemistry, 31:7796-7801 (1992) or which act as inhibitors, agonists, or antagonists of native peptides as shown by Athauda *et al.*, J. Biochem., 113:742-746 (1993).

It is also possible to isolate a target-specific antibody, selected by functional assay, as described above, and then to solve its crystal structure. This approach, in principle, yields a pharmacore upon which

subsequent drug design can be based. It is possible to bypass protein crystallography altogether by generating anti-idiotypic antibodies (anti-ids) to a functional, pharmacologically active antibody. As a mirror image of a mirror image, the binding site of the anti-ids would be expected to be an analog of the original receptor. The anti-id could then be used to identify and isolate peptides from banks of chemically or
5 biologically produced peptides. The isolated peptides would then act as the pharmacore.

By virtue of the present invention, sufficient amounts of the PRO polypeptide may be made available to perform such analytical studies as X-ray crystallography. In addition, knowledge of the PRO polypeptide amino acid sequence provided herein will provide guidance to those employing computer modeling techniques in place of or in addition to x-ray crystallography.

10 The foregoing written specification is considered to be sufficient to enable one skilled in the art to practice the invention. The present invention is not to be limited in scope by the construct deposited, since the deposited embodiment is intended as a single illustration of certain aspects of the invention and any constructs that are functionally equivalent are within the scope of this invention. The deposit of material herein does not constitute an admission that the written description herein contained is inadequate to enable
15 the practice of any aspect of the invention, including the best mode thereof, nor is it to be construed as limiting the scope of the claims to the specific illustrations that it represents. Indeed, various modifications of the invention in addition to those shown and described herein will become apparent to those skilled in the art from the foregoing description and fall within the scope of the appended claims.

The claims defining the invention are as follows:

1. An isolated nucleic acid having at least 80% nucleic acid sequence identity to a nucleotide sequence identity to:
 - (a) the nucleotide sequence shown in Figure 4569 (SEQ ID NO: 4569); or
 - (b) the nucleotide sequence encoding the polypeptide shown in Figure 4570 (SEQ ID NO: 4570).
2. A vector comprising a nucleic acid according to claim 1.
3. A vector according to claim 2, wherein the nucleic acid is operably linked to control sequences.
4. A host cell comprising a vector according to claim 2 or 3.
5. A host cell according to claim 4, wherein said cell is a CHO cell, an *E.coli* cell or a yeast cell.
6. A process for producing a polypeptide comprising culturing a host cell according to claim 4 or 5 under conditions suitable for expression of said polypeptide and recovering said polypeptide from the cell culture.
7. An isolated polypeptide having at least 95% amino acid sequence identity to: (a) a polypeptide shown in Figure 4570 (SEQ ID NO: 4570); or (b) a polypeptide encoded by the full length coding region of the nucleotide sequence shown in Figure 4569 (SEQ ID NO: 4569).
8. A chimeric molecule comprising a polypeptide according to claim 7 fused to a heterologous amino acid sequence.

9. A chimeric molecule according to claim 8, wherein said heterologous amino acid sequence is an epitope tag sequence or an Fc region of an immunoglobulin.
- 5 10. An antibody which specifically binds to a polypeptide according to claim 7.
11. An antibody according to claim 10, wherein said
10 antibody is a monoclonal antibody, a humanized antibody or a single-chain antibody.
12. A composition of matter comprising (a) a polypeptide according to claim 7, or (b) an antibody that specifically
15 binds to said polypeptide, in combination with a carrier.
13. A composition of matter according to claim 12, wherein said carrier is a pharmaceutically acceptable carrier.
- 20 14. A composition of matter according to claim 13 comprising a therapeutically effective amount of (a) or b).
- 25 15. An article of manufacture, comprising: a container; a label on said container; and a composition of matter comprising (a) a polypeptide according to claim 7, or (b) an antibody that binds specifically to said polypeptide, contained within said container, wherein label on said
30 container indicates that said composition of matter can be used for treating an immune related disease.
16. A method of treating an immune related disorder in a mammal in need thereof comprising administering to said
35 mammal a therapeutically effective amount of (a) a polypeptide according to claim 7, or (b) an antibody that binds specifically to said polypeptide.

19 Aug 2009

2003302386

- 163 -

17. Use of a therapeutically effective amount of (a) a polypeptide according to claim 7, or (b) an antibody that binds specifically to said polypeptide for the treatment
5 of an immune related disorder in a mammal.

18. A method according to claim 16 or use according to claim 17, wherein the immune related disorder is systemic lupus erythematosus, rheumatoid arthritis, osteoarthritis,
10 juvenile chronic arthritis, a spondyloarthropathy, systemic sclerosis, an idiopathic inflammatory myopathy, Sjögren's syndrome, systemic vasculitis, sarcoidosis, autoimmune hemolytic anemia, autoimmune thrombocytopenia, thyroiditis, diabetes mellitus, immune-mediated renal
15 disease, a demyelinating disease of the central or peripheral nervous system, idiopathic demyelinating polyneuropathy, Guillain-Barré syndrome, a chronic inflammatory demyelinating polyneuropathy, a hepatobiliary disease, infectious or autoimmune chronic active
20 hepatitis, primary biliary cirrhosis, granulomatous hepatitis, sclerosing cholangitis, inflammatory bowel disease, gluten-sensitive enteropathy, Whipple's disease, an autoimmune or immune-mediated skin disease, a bullous skin disease, erythema multiforme, contact dermatitis,
25 psoriasis, an allergic disease, asthma, allergic rhinitis, atopic dermatitis, food hypersensitivity, urticaria, an immunologic disease of the lung, eosinophilic pneumonias, idiopathic pulmonary fibrosis, hypersensitivity pneumonitis, a transplantation associated disease, graft
30 rejection or graft-versus-host-disease.

19. A method for determining the presence of a polypeptide as described in Figure 4570 (SEQ ID NO: 4570), in a sample suspected of containing said polypeptide, said
35 method comprising exposing said sample to an antibody that specifically binds to a polypeptide described in Figure 4570 (SEQ ID NO: 4570), where the and determining binding

451601_1 (GHMatters) 19/08/09

of said antibody to a component of said sample.

20. A method of diagnosing an immune related disease in a mammal, said method comprising detecting the level of expression of a gene encoding a polypeptide as described in Figure 4570 (SEQ ID NO: 4570), (a) in a test sample of tissue cells obtained from the mammal, and (b) in a control sample of known normal tissue cells of the same cell type, wherein a higher or lower level of expression of said gene in the test sample as compared to the control sample is indicative of the presence of an immune related disease in the mammal from which the test tissue cells were obtained.

21. A method of diagnosing an immune related disease in a mammal, said method comprising (a) contacting an antibody that specifically binds to a polypeptide as described in Figure 4570 (SEQ ID NO: 4570), with a test sample of tissue cells obtained from said mammal and (b) detecting the formation of a complex between the antibody and the polypeptide in the test sample, wherein formation of said complex is indicative of the presence of an immune related disease in the mammal from which the test tissue cells were obtained.

22. A method of identifying a compound that inhibits the activity of a polypeptide as described in Figure 4570 (SEQ ID NO: 4570), said method comprising contacting cells which normally respond to said polypeptide with (a) said polypeptide and (b) a candidate compound, and determining the lack responsiveness by said cell to (a).

23. A method of identifying a compound that inhibits the expression of a gene encoding a polypeptide as described in Figure 4570 (SEQ ID NO: 4570), said method comprising contacting cells which normally express said polypeptide with a candidate compound, and determining the lack of

expression of said gene.

24. A method according to claim 23, wherein said candidate compound is an antisense nucleic acid.

5

25. A method of identifying a compound that mimics the activity of a polypeptide as described in Figure 4570 (SEQ ID NO: 4570), said method comprising contacting cells which normally respond to said polypeptide with a candidate compound, and determining the responsiveness by said cell to said candidate compound.

10

26. A method of stimulating the immune response in a mammal, said method comprising administering to said mammal an effective amount of a polypeptide as described in Figure 4570 (SEQ ID NO: 4570), wherein said immune response is stimulated.

15

27. A method of diagnosing an inflammatory immune response in a mammal, said method comprising detecting the level of expression of a gene encoding a polypeptide as described in Figure 4570 (SEQ ID NO: 4570), (a) in a test sample of tissue cells obtained from the mammal, and (b) in a control sample of known normal tissue cells of the same cell type, wherein a higher or lower level of expression of said gene in the test sample as compared to the control sample is indicative of the presence of an inflammatory immune response in the mammal from which the test tissue cells were obtained.

20

25

30

28. An isolated nucleic acid according to claim 1, an isolated polypeptide according to claim 7, or a method according to any one of claims 19 to 23 or 25 to 27, substantially as hereinbefore described with reference to any one of the examples.

35

EDITORIAL NOTE

2003302386

Drawings totalling 8433 pages are on CD and can be obtained by contacting IP Australia.