

## **MARKERS AND CELLULAR ANTECEDENTS OF RHEUMATOID ARTHRITIS FLARES**

### **STATEMENT OF GOVERNMENT RIGHTS**

**[0001]** This invention was made with government support under numbers NS034389, NS081706, NS097404 and 1UM1HG008901 awarded by the National Institutes of Health. The government has certain rights in the invention.

### **FIELD OF THE INVENTION**

**[0002]** The present invention relates generally to the identification and characterization of biological markers which are molecular antecedents of rheumatoid arthritis (RA) flares. The invention further relates to RNA and protein markers that can predict an RA flare one or two weeks prior to the flare. The invention further relates to blood circulating cells, particularly pre-inflammatory mesenchymal cells, which are cellular precursors and indicators of an impending RA flare. The present invention relates to methods, kits and markers for the identification and monitoring of flares in RA patients and their application as markers and targets in and for treatment of rheumatoid arthritis and conditions induced or related to rheumatoid arthritis.

### **BACKGROUND OF THE INVENTION**

**[0003]** Rheumatoid arthritis (RA) is a chronic inflammatory disorder and is the most common form of autoimmune arthritis, affecting more than 1.3 million Americans. About 75% of RA patients are women and between 1 and 3% of women may get rheumatoid arthritis in their lifetime. RA is a chronic disease affecting the lining of joints that causes joint pain, stiffness, swelling and decreased movement of the joints and can eventually result in bone erosion and joint deformity.

**[0004]** Treatments for RA can stop joint pain and swelling and prevent joint damage. Early treatment will give better long term results and patients receiving early treatment are less likely to have the type of joint damage that leads to joint replacement. The main treatment goals with rheumatoid arthritis are to control inflammation, relieve pain, and reduce disability associated with RA. Treatment usually includes medications, occupational or physical therapy, and regular exercise, although some patients ultimately need surgery, including synovectomy, tendon repair, joint fusion or total joint replacement to correct joint damage. Nonsteroidal anti-inflammatory drugs (NSAIDs) provide 'first-line'

RA medicines to relieve pain and reduce inflammation. NSAIDs include non-prescription drugs acetylsalicylate (aspirin), ibuprofen (Advil, Motrin IB) and naproxen sodium (Aleve, Naprosyn) and prescription NSAIDs such as etodolac (Lodine) and diclofenac (Voltaren). Steroids are anti-inflammatory or immunosuppressant agents and are prescribed for more severe RA or when RA symptoms flare to ease joint pain and stiffness. Examples of recognized steroids include glucocorticosteroids or corticosteroids such as prednisone, cortisone and methylprednisolone. Disease-modifying antirheumatic drugs (DMARDs) are prescribed and utilized to slow the progression of RA and save joints and other tissues from permanent damage. Common DMARDs include methotrexate (Trexall, Otrexup), leflunomide (Arava), hydroxychloroquine (Plaquenil) and sulfasalazine (Azulfidine). DMARDs curb the overactive immune system in RA but aren't selective in their targets. Side effects vary but may include liver damage, bone marrow suppression and severe lung infections. Biologics - genetically engineered proteins which target a specific aspect or part of the immune system and act as immunosuppressants - are an increasingly important component in treatment of RA. Tumor necrosis factor (TNF) inhibitors and non-TNF inhibitors (such as cytokine inhibitors, T or B cell inhibitors) are included among the recognized biologics for RA. Biologics include abatacept (Orencia), adalimumab (Humira), anakinra (Kineret), baricitinib (Olmiant), certolizumab (Cimzia), etanercept (Enbrel), golimumab (Simponi), infliximab (Remicade), rituximab (Rituxan), sarilumab (Kevzara), tocilizumab (Actemra) and tofacitinib (Xeljanz). Adalimumab, etanercept, infliximab, golimumab and certolizumab target TNF (Lis K et al (2014) Arch Med Sci 10(6):1175-1185). Rituximab depletes B cells. Anakinra blocks the action of interleukin-1 (IL-1), a master cytokine. Abatacept targets T cells. These types of drugs also increase the risk of infections. Biologic DMARDs are usually most effective when paired with a nonbiologic DMARD, such as methotrexate. New drugs which are specific in their targets but are not biologics include oral small molecule Janus kinase (JAK) inhibitors such as tofacitinib (Xeljanz and Xeljanz XR), baricitinib (Olmiant), and upadacitinib (Rinvoq). The antimetabolite Methotrexate is also often used to treat RA, including in combination with other DMARD drugs including biologic DMARDs.

**[0005]** Results from recent patient surveys report that three-fourths of RA patients are not satisfied with treatments and patients continued to experience bothersome symptoms that impacted their daily activities and life (Radawski C et al (2019) Rheumatol Ther 6(3):461-471). RA, like many inflammatory diseases, is characterized by episodes of quiescence and exacerbation (flares). Flares are severe episodes of symptoms and reflect increased disease activity during which joint pain, swelling, and stiffness are more severe. The duration and intensity of flares vary, the flares are unpredictable, and the molecular events leading to flares are unknown. Such waxing/waning clinical courses are characteristic of many autoimmune diseases, including multiple sclerosis (MS) (Steinman L. (2014) Annu Rev Immunol 32:257-81), systemic lupus erythematosus (SLE) (Fava A, Petri M. (2019) J Autoimmun 96:1-13), and

inflammatory bowel disease (IBD) (Braun J, Wei B (2007) Annu Rev Pathol 2:401-29; Braun J et al (2007) Arthritis Rheum 57:639-47.).

**[0006]** Like with RA, each and all of these common autoimmune diseases would be more appropriately managed and effectively treated if the clinical course could be more effectively evaluated and flares and disease exacerbations could be predicted or identified and treatment or therapeutic intervention could be initiated sooner and with better short and long-term results. There is need to develop approaches to understand what triggers transitions from quiescence to flare in autoimmune disease. There remains a need for improved disease management among currently treated RA and other auto-immune disease patients. The present invention addresses such unmet needs in the field and particularly with regard to rheumatoid arthritis (RA).

**[0007]** The citation of references herein shall not be construed as an admission that such is prior art to the present invention.

#### SUMMARY OF THE INVENTION

**[0008]** In a general aspect, the present invention provides antecedents of an RA flare. RNA markers and protein markers have been identified which are differentially expressed or preferentially expressed prior to an RA flare in an RA patient(s). These RNA transcripts provide markers which can predict an impending flare and the determination and presence of which can be utilized to implement and prescribe treatment and therapy to a patient(s).

**[0009]** The invention provides a method for monitoring and predicting a rheumatoid arthritis (RA) flare or increased RA disease activity in a patient comprising:

- (a) isolating a blood sample from said patient;
- (b) evaluating the blood sample for expression or quantitatively increased amounts of one or more sets of antecedent RNA markers, protein markers or cell markers selected from:
  - (i) AC2 markers or proteins as provided in Table 7;
  - (ii) AC3 markers or proteins as provided in Table 8;
  - (iii) markers or proteins selected from COL1A2, COL5A1, COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1, ZFHX4, COL3A1, COMP, FNDC1, GALNT15, SULF1, GPX8 and IGFBP6 as set out in Table 5;
  - (iv) markers or proteins selected from COL1A2, COL5A1, COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1 and ZFHX4 as set out in Table 9;
  - (v) cell markers CD45- CD31-PDPN+;

(c) wherein the expression or quantitatively increased amounts of the RNA markers or proteins or the presence of the cell markers predicts an impending RA flare.

**[00010]** The invention provides a method for monitoring and predicting a rheumatoid arthritis (RA) flare or increased RA disease activity in a patient comprising:

- (a) isolating a blood sample from said patient;
- (b) evaluating the blood sample for expression or quantitatively increased amounts of one or more sets of antecedent RNA markers, protein markers or cell markers selected from:
  - (i) markers or proteins selected from COL1A2, COL5A1, COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1, ZFHX4, COL3A1, COMP, FNDC1, GALNT15, SULF1, GPX8 and IGFBP6 as set out in Table 5;
  - (ii) markers or proteins selected from COL1A2, COL5A1, COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1 and ZFHX4 as set out in Table 9;
  - (iii) AC2 markers or proteins as provided in Table 7;
  - (iv) AC3 markers or proteins as provided in Table 8; and
  - (v) cell markers CD45- CD31-PDPN+;

(c) wherein the expression or quantitatively increased amounts of the RNA markers or proteins or the presence of the cell markers predicts an impending RA flare.

**[00011]** In an embodiment of the method, the expression or quantitatively increased amounts of the AC2 RNA markers or proteins predicts an RA flare in about 2 weeks or about 12-14 days. In an embodiment of the method, the expression or quantitatively increased amounts of the AC2 RNA markers or proteins predicts an RA flare in about 2 weeks, with a margin of error of about a week or further 7 days, thus in 7-21 days, or in up or about three weeks, up to 21 days or so.

**[00012]** In an embodiment of the method, the expression or quantitatively increased amounts of the AC3 RNA markers or proteins predicts an RA flare in about 1 week or about 5-7 days. In an embodiment of the method, the expression or quantitatively increased amounts of the AC3 RNA markers or proteins predicts an RA flare in about 1 week, with a margin of error of about a week or further 7 days, thus in 0-14 days, or in up or about two weeks, up to 14 days or so.

**[00013]** In an embodiment of the method, a subset of at least 20 of the AC2 or AC3 markers are evaluated. In an embodiment, a subset of at least 10 of the AC2 or AC3 markers are evaluated. At least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, at least 25, at least 30, at least 35, at least 40, at least 45, at least 50 of the AC2 or AC3 markers may be evaluated.

**[00014]** In an embodiment of the method, a subset of at least 20 of the AC2 and at least 20 of the AC3 markers are evaluated. In an embodiment, a subset of at least 10 of the AC2 and the AC3 markers

are evaluated. At least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, least 15, at least 16, at least 17, at least 18, at least 19, at least 20, at least 25, at least 30, at least 35, at least 40, at least 45, at least 50 of the AC2 and the AC3 markers may evaluated.

**[00015]** In an embodiment, sublining fibroblast markers selected from the AC3 markers or proteins are evaluated. In an embodiment, AC3 markers or proteins expressed by CD34+, HLADR+ and DKK3+ cells are evaluated. In an embodiment, AC3 markers or proteins expressed by CD45-, CD34+, HLADR+ and DKK3+ cells are evaluated.

**[00016]** The method includes, wherein the cell marker IL17RD is also evaluated.

**[00017]** The invention further provides a method(s) wherein the antecedent RNA markers or protein markers or selected from:

(a) AC3 markers or proteins as provided in Table 8;  
 (b) markers or proteins selected from COL1A2, COL5A1, COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1, ZFHX4, COL3A1, COMP, FNDC1, GALNT15, SULF1, GPX8 and IGFBP6 as set out in Table 5; and

(c) markers or proteins selected from COL1A2, COL5A1, COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1 and ZFHX4 as set out in Table 9;

are reduced, significantly decreased, nearly absent, or absent in peripheral blood during an RA flare or once a patient exhibits symptoms of an RA flare.

**[00018]** The invention further provides a method(s) wherein the antecedent RNA markers or protein markers or selected from:

(a) markers or proteins selected from COL1A2, COL5A1, COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1, ZFHX4, COL3A1, COMP, FNDC1, GALNT15, SULF1, GPX8 and IGFBP6 as set out in Table 5;

(b) markers or proteins selected from COL1A2, COL5A1, COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1 and ZFHX4 as set out in Table 9; and

(c) AC3 markers or proteins as provided in Table 8;

are reduced, significantly decreased, nearly absent, or absent in peripheral blood during an RA flare or once a patient exhibits symptoms of an RA flare.

**[00019]** The invention provides a method for predicting an impending RA flare and treating a flare in a patient, the method comprising:

a) isolating a blood sample from the patient;

b) contacting the blood sample with reagents specific for markers selected from a panel of RNA or protein markers to assess expression of the RNA or protein markers, wherein the panel of RNA or protein markers is selected from:

- (i) AC2 markers or proteins as provided in Table 7;
- (ii) AC3 markers or proteins as provided in Table 8;
- (iii) markers or proteins selected from COL1A2, COL5A1, COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1, ZFHX4, COL3A1, COMP, FNDC1, GALNT15, SULF1, GPX8 and IGFBP6 as set out in Table 5; and
- (iv) markers or proteins selected from COL1A2, COL5A1, COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1 and ZFHX4 as set out in Table 9;

c) comparing expression of the markers selected from a panel of RNA or protein markers in the blood sample to expression of the markers in a control blood sample to determine if expression of the markers selected from a panel of RNA or protein markers in the blood sample is increased relative to expression in the control blood sample, wherein detection of increased expression serves to predict an impending RA flare in a patient; and treating the patient thereby diagnosed with an impending RA flare by administering a therapeutically effective amount of one or more disease modifying agent for treating RA.

**[00020]** The invention provides a method for predicting an impending RA flare and treating a flare in a patient, the method comprising:

- a) isolating a blood sample from the patient;
- b) contacting the blood sample with reagents specific for markers selected from a panel of RNA or protein markers to assess expression of the RNA or protein markers, wherein the panel of RNA or protein markers is selected from:
  - (i) markers or proteins selected from COL1A2, COL5A1, COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1, ZFHX4, COL3A1, COMP, FNDC1, GALNT15, SULF1, GPX8 and IGFBP6 as set out in Table 5;
  - (ii) markers or proteins selected from COL1A2, COL5A1, COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1 and ZFHX4 as set out in Table 9;
  - (iii) AC2 markers or proteins as provided in Table 7; and
  - (iv) AC3 markers or proteins as provided in Table 8;
- c) comparing expression of the markers selected from a panel of RNA or protein markers in the blood sample to expression of the markers in a control blood sample to determine if expression of the markers selected from a panel of RNA or protein markers in the blood sample is increased relative to

expression in the control blood sample, wherein detection of increased expression serves to predict an impending RA flare in a patient;

and treating the patient thereby diagnosed with an impending RA flare by administering a therapeutically effective amount of one or more disease modifying agent for treating RA.

**[00021]** In an embodiment of the method, the expression, differential expression, or quantitatively increased amounts of the AC2 RNA markers or proteins predicts an RA flare in about 2 weeks, about 14 days, or about 12-14 days.

**[00022]** In an embodiment of the method, the expression or quantitatively increased amounts of the AC3 RNA markers or proteins predicts an RA flare in about one week, about 7 days, or about 5-7 days. In an embodiment of the method, the expression, differential expression, or quantitatively increased amounts of the markers or proteins selected from COL1A2, COL5A1, COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1, ZFH4, COL3A1, COMP, FNDC1, GALNT15, SULF1, GPX8 and IGFBP6 or of the markers or proteins selected from COL1A2, COL5A1, COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1 and ZFH4 predicts an RA flare in about one week, about 7 days, or about 5-7 days.

**[00023]** In an embodiment of the method, the expression or quantitatively increased amounts of RNA or protein markers selected from:

- (a) the AC3 RNA markers or proteins;
  - (b) markers or proteins selected from COL1A2, COL5A1, COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1, ZFH4, COL3A1, COMP, FNDC1, GALNT15, SULF1, GPX8 and IGFBP6; and
  - (c) markers or proteins selected from COL1A2, COL5A1, COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1 and ZFH4;
- predicts an RA flare in about 1 week or about 5-7 days.

**[00024]** In an embodiment of the method, the expression or quantitatively increased amounts of RNA or protein markers selected from:

- (a) markers or proteins selected from COL1A2, COL5A1, COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1, ZFH4, COL3A1, COMP, FNDC1, GALNT15, SULF1, GPX8 and IGFBP6;
  - (b) markers or proteins selected from COL1A2, COL5A1, COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1 and ZFH4; and
  - (c) the AC3 RNA markers or proteins;
- predicts an RA flare in about 1 week or about 5-7 days.

**[00025]** Evaluation of RNA or protein expression may be evaluated or assessed using any method known in the art. Thus, in accordance with the methods of the invention, RNA expression may be assessed by RT PCR. In accordance with the method, protein expression may be assessed using specific antibodies.

**[00026]** Cell marker expression or presence on the surface of cells in the blood in accordance with the methods of the invention may be determined using standard and known methods. Cell markers may be evaluated using antibodies. Cell markers may be evaluated using Fluorescent Activated Cell Sorting (FACs) analysis. Cells or cell markers may be evaluated using cell sorting or single cell assessments.

**[00027]** In embodiments of the method of the invention, the disease modifying agent for treating RA may be selected from standard or clinically recognized agents or therapies for RA or arthritic conditions or inflammatory diseases and conditions. In embodiments of the method of the invention, the disease modifying agent for treating RA may be one or more agent selected from a nonsteroidal anti-inflammatory drug (NSAID), steroid, methotrexate, disease-modifying antirheumatic drug (DMARDs), biologic DMARD, and oral janus kinase (JAK) inhibitor. In an embodiment, the DMARD is selected from methotrexate (Trexall, Otrexup), leflunomide (Arava), hydroxychloroquine (Plaquenil) and sulfasalazine (Azulfidine). There are a variety of known biologic DMARD agents, including various agents being evaluated or with application to RA and/or other arthritic and/or inflammatory conditions. In an aspect, the biologic DMARD may be selected from abatacept (Orencia), adalimumab (Humira), anakinra (Kineret), baricitinib (Olmiant), certolizumab (Cimzia), etanercept (Enbrel), golimumab (Simponi), infliximab (Remicade), rituximab (Rituxan), sarilumab (Kevzara), tocilizumab (Actemra) and tofacitinib (Xeljanz). The biologic DMARD may be a tumor necrosis factor (TNF) inhibitor. In an aspect, the biologic DMARD may be an anti-inflammatory antibody or an antibody directed to an inflammation or immune modulatory molecule. In an aspect, the antibody may be an interleukin antibody. The antibody may be an IL-17 specific antibody or an IL-17RD specific or IL-17RD blocking or neutralizing antibody.

**[00028]** In an embodiment, the biologic DMARD is combined with an NSAID and/or with methotrexate. In an embodiment, the JAK inhibitor is selected from tofacitinib (Xeljanz and Xeljanz XR), baricitinib (Olmiant), and upadacitinib (Rinvoq).

**[00029]** The invention provides and relates to a circulating pre-inflammatory mesenchymal (PRIME) cell characterized as a CD45-CD31-PDPN+ cell, wherein the presence of the cell in peripheral blood is indicative or predictive of an impending RA flare. In an embodiment, the PRIME cell additionally expresses IL17RD and is IL17RD+. In an embodiment, a subset of PRIME cells additionally expresses IL17RD and is IL17RD+.

**[00030]** The invention further provides a method of predicting an impending RA flare comprising evaluating a blood sample from a patient for the presence of a PRIME cell characterized as a CD45-CD31-PDPN+ cell, wherein the presence of detectable PRIME cells in peripheral blood in a patient predicts an impending RA flare in the patient. In an embodiment thereof, the method includes further evaluating for the presence of IL17RD on a CD45-CD31-PDPN+ cell.

**[00031]** Methods are provided for evaluating and treating an impending flare in an RA patient comprising evaluating the peripheral blood of a patient for the presence of a PRIME cell characterized as a CD45-CD31-PDPN+ cell and treating a patient that is positive for PRIME cells in their peripheral blood with a disease modifying agent for RA. Methods are provided for evaluating and treating an impending flare in an RA patient comprising evaluating the peripheral blood of a patient for the presence of a PRIME cell characterized as a CD45-CD31-PDPN+IL17RD+ cell and treating a patient that is positive for PRIME cells in their peripheral blood with a disease modifying agent for RA.

**[00032]** In an additional embodiment of the method, the patient is treated with an IL-17 or IL-17RD antibody. In another embodiment, the patient is further treated with an anti-inflammatory agent and/or an immune modulating agent.

**[00033]** Methods are provided for evaluating and treating an impending flare in an RA patient comprising evaluating the peripheral blood of a patient for the presence of RNA(s) or protein(s) expressed, specifically expressed or particularly expressed by a PRIME cell characterized as a CD45-CD31-PDPN+ cell and treating a patient that is positive for expressing, specifically expressing or particularly expressing RNA(s) or protein(s) of PRIME cells in their peripheral blood with a disease modifying agent for RA. Methods are provided for evaluating and treating an impending flare in an RA patient comprising evaluating the peripheral blood of a patient for the presence of RNA(s) or protein(s) expressed, specifically expressed or particularly expressed by a cell characterized as a CD45-CD31-PDPN+IL17RD+ cell and treating a patient that is positive for the presence of RNA(s) or protein(s) expressed, specifically expressed or particularly expressed by a cell characterized as a CD45-CD31-PDPN+IL17RD+ cell in their peripheral blood with a disease modifying agent for RA.

**[00034]** The invention includes a set of RNA or protein markers for evaluating and predicting an impending RA flare in a patient comprising the markers selected from:

- (i) a subset of at least 20 markers from the AC2 markers provided in Table 7;
- (ii) a subset of at least 20 markers from the AC3 markers provided in Table 8;
- (iii) markers selected from COL1A2, COL5A1, COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1, ZFH4, COL3A1, COMP, FNDC1, GALNT15, SULF1, GPX8 and IGFBP6 as set out in Table 5;

(iv) markers selected from COL1A2, COL5A1, COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1 and ZFH4 as set out in Table 9.

**[00035]** In an aspect of the method, a subset of at least 20 of the AC2 or AC3 markers are provided. In an aspect, a subset of at least 10 of the AC2 or AC3 markers are provided. At least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, at least 25, at least 30, at least 35, at least 40, at least 45, at least 50 of the AC2 or AC3 markers may be provided.

**[00036]** In an embodiment, the subset of AC2 markers comprises naïve B cell gene markers and markers of developmental pathways for naïve B cells and leukocytes. In an embodiment, wherein the subset of AC3 markers comprises markers of cartilage morphogenesis, endochondral bone growth, extracellular matrix organization and sublining fibroblasts.

**[00037]** In another embodiment of the invention a set of one or more markers selected from COL1A2, COL5A1, COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1, ZFH4, COL3A1, COMP, FNDC1, GALNT15, SULF1, GPX8 and IGFBP6 is provided and/or utilized in accordance with the methods hereof. In an aspect, a set of one or more markers selected from COL1A2, COL5A1, COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1 and ZFH4 is provided and/or utilized in accordance with the methods hereof. In an aspect, a set of two or more, three or more, four or more, five or more, six or more, seven or more, eight or more, nine or more, ten or more, a dozen, at least two, at least three, at least four, at least five, at least six, at least seven, at least eight, at least nine, at least ten, a set of 5-10, a set of 3-5, a set of 5-7, a set of 3-7, a set of 5-8 selected from COL1A2, COL5A1, COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1, ZFH4, COL3A1, COMP, FNDC1, GALNT15, SULF1, GPX8 and IGFBP6 is provided and/or utilized in accordance with the methods hereof. In an aspect, a set of two or more, three or more, four or more, five or more, six or more, seven or more, eight or more, nine or more, ten or more, a dozen, at least two, at least three, at least four, at least five, at least six, at least seven, at least eight, at least nine, at least ten, a set of 5-10, a set of 3-5, a set of 5-7, a set of 3-7, a set of 5-8 selected from COL1A2, COL5A1, COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1 and ZFH4 is provided and/or utilized in accordance with the methods hereof.

**[00038]** The invention also provides a system or kit for predicting an impending RA flare comprising a set of markers as described and provided herein or a set of probes and/or antibodies for evaluating a set of markers as described and provided herein. As an example, a kit or system may include a set of markers or a set of probes and/or antibodies for evaluating a set of markers selected from or for a or any combination of:

- (i) a subset of at least 20 markers from the AC2 markers provided in Table 7;

- (ii) a subset of at least 20 markers from the AC3 markers provided in Table 8;
- (iii) markers selected from COL1A2, COL5A1, COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1, ZFHX4, COL3A1, COMP, FNDC1, GALNT15, SULF1, GPX8 and IGFBP6 as set out in Table 5;
- (iv) markers selected from COL1A2, COL5A1, COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1 and ZFHX4 as set out in Table 9.

**[00039]** The system or kit may further comprise a means for collection of the patient's blood by fingerstick.

**[00040]** Other objects and advantages will become apparent to those skilled in the art from a review of the ensuing detailed description, which proceeds with reference to the following illustrative drawings, and the attendant claims.

#### BRIEF DESCRIPTION OF THE DRAWINGS

**[00041]** The patent or patent application contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawing(s) will be provided by the U.S. Patent and Trademark Office upon request and payment of the necessary fee.

**[00042]** **Figure 1** depicts the study overview and validation of in-home assessments of disease activity and gene expression. **A.** Clinical data collection and RNA analysis over time. Study overview of clinical data and sample collection over time. **B.** Clinical and patient reported assessments of disease activity. Correlation between disease activity scores measured in clinic (DAS28) and at home (RAPID3 questionnaire) from the index patient. Locally Weighted Smoothed Scatterplots Showing the Relationship between the Change in RAPID3 scores and DAS28 in the index patient. The solid line represents the point estimates and the gray area represents the 95 percent confidence intervals. **C.** Clinical blood counts and RNASeq-inferred blood counts. Neutrophil, lymphocyte, and monocyte counts measured from paired clinical complete blood counts from venipuncture blood draws and CIBERSORTx inferred blood counts from RNAseq data from finger stick blood draws (N=38 paired samples).

**[00043]** **Figure 2** provides clinical and transcriptional characteristics of RA flares in index patient. **A.** Index Patient disease activity over time. Disease activity (RAPID3 questionnaire, N=356), over the course of four years in index patient. Time points are colored according to disease activity category. **B.** Differential expression of genes in flare. Volcano plot of differential gene expression of flare (N=46) versus baseline (N=33), plotting statistical significance ( $-\log_{10}(\text{FDR})$ ) against fold change ( $\log_2(\text{FC})$ ) (gray points are non-significant genes, i.e.,  $\text{FDR} > 0.1$ , red indicates  $\text{FDR} < 0.1$  and  $\log_2$  fold change  $> 0$ ,

blue indicates  $FDR < 0.1$  and  $\log_2$  fold change  $< 0$ ). Pathways enriched in significantly increased (C.) (Pathways increased in flare) or decreased genes (D.) (Pathways decreased in flare) in flare relative to baseline.

**[00044] Figure 3** provides transcriptional characteristics of immune activation prior to symptom onset in RA flares. **A.** Disease activity scores over time to flare (measured in days). Box represents disease activity from day -56 to +28 over time to flare. Vertical arrows (in A-D) represent start of flare. **B.** Hierarchical clustering of z scores of 2791 significantly differentially expressed genes over time to flare. Statistically significant clusters are labeled by color. AC2 and AC3 refer to clusters that changed antecedent to flare. **C.** Detailed representation of cluster 1, antecedent cluster 2 (AC2), and antecedent cluster 3 (AC3) genes from Figure 3B over time to flare. **D.** Mean standardized cluster gene expression over time to flare. Light grey lines represent expression of individual genes in the cluster. Dashed horizontal line represents mean baseline gene expression (weeks -8 to -4). Dashed vertical line represents start of flare. **E.** Pathways enriched in clusters 1, AC2, and AC3.

**[00045] Figure 4.** PRIME cells express AC3 genes. **A.** Synovial cell subtype marker genes in clusters identified in blood (Figure 3A). Enrichment scores of 200 single cell RNAseq marker genes from 18 synovial subset cell types. Dashed line represents threshold for significance ( $FDR < 0.05$  or  $-\log_{10} FDR > 1.3$ ). **B.** Mean standardized gene expression and 95% confidence intervals of genes common to synovial sublining fibroblasts (CD34+, DKK+ and HLA-DRA+ fibroblasts) and AC3 in blood over time to flare (dashed vertical line represents start of flare). Error bars represent confidence intervals. **C.** Venn diagram of AC3 genes that decrease during flare in 4 patients. **D.** Flow cytometry of blood samples from 19 RA patients and 18 healthy volunteers (HV). Percent PDPN+/CD45- cells of TOPRO-(live)/CD31- cells is presented. P value represents result of two sided t-test. **E.**  $\log_2$  fold change of AC3 genes expressed in PRIME cells (flow sorted CD45-/CD31-/PDPN+ cells) versus hematopoietic cells (flow sorted CD45+) and  $\log_2$  fold change of input cells (stained PBMC but not flow sorted) versus hematopoietic cells (flow sorted CD45+) as technical control for stress of flow sorting.

**[00046] Figure 5** provides a model of blood and synovial gene expression changes antecedent to and during RA flares. Inflammatory signals activate naïve B cells (AC2; Figure 3C-E), which in turn activate PRIME cells (AC3; Figure 3C-E) which harbor the signature of synovial sublining fibroblast genes (Figure 4A). The model proposes that PRIME cells demarginate and are increased in blood prior to flare and then decrease (Figure 4B) just after symptom onset; these cells or their progeny are increased in inflammatory RA synovium where they contribute to and may be sufficient to cause joint inflammation.

**[00047] Figure 6** depicts RNA quality and quantity by volume of fixative. 3 drops of blood harvested with a 21 gauge lancet were added to a microtainer tube prefilled with either 250, 500 or 750ul of PAX gene fixative. Samples were stored at room temperature for 3 days and then RNA was extracted using the

PAX gene RNA kit and RIN scores and quantity of RNA was assessed using the Agilent 2100 Bioanalyzer picochip. Padj= ANOVA, followed by Dunnett's multiple comparisons test, using 250ul as the reference group.

**[00048]** Figure 7 depicts RNA quality and quantity by time at room temperature. 100ul of whole blood was added to a microtainer tube prefilled with 250ul PAX gene fixative and frozen after 2 hours, 3 days, or 7 days incubation at room temperature. RNA was extracted using the PAX gene RNA kit with scaled down washes and elutions and RIN scores and quantity of RNA was assessed using the Agilent 2100 BioAnalyzer RNA picochip. Padj= ANOVA, followed by Dunnett's multiple comparisons test, using Day 0 as the reference group.

**[00049]** Figure 8 depicts RNA quality and quantity of fresh and mailed samples. 100ul of whole blood was added to a microtainer tube prefilled with 250ul PAX gene fixative and frozen after 2-hour incubation at room temperature or mailed. RNA was extracted using the PAX gene RNA kit and RIN scores and quantity of RNA was assessed using the Agilent 2100 BioAnalyzer RNA picochip.

**[00050]** Figure 9 depicts RNA quality and quantity by volume of extraction and washes. 3 drops of blood harvested with a 21 guage lancet were added to a microtainer tube prefilled with 250ul of PAX gene fixative. Samples were stored at room temperature for 3 days and then RNA was extracted using the PAXgeneRNA kit according to manufacturer's directions or with a scaled down version of the PAX protocol, using 25% of the recommended volumes for all washes and elutions. RIN scores and quantity of RNA was assessed using the Agilent 2100 BioAnalyzerRNA picochip. P= unpaired two-sided t test.

**[00051]** Figure 10 depicts RNA quality and quantity with and without TriZol reagent extraction step. Mailed patient finger stick samples were stored in PAXgeneRNA buffer at -80°C. 142 samples had RNA extracted with PAXgeneRNA extraction with low volume washes, 13 samples were thawed and mixed with 700ul Trizol-LS, and 250ul chloroform. After centrifugation, the top layer was precipitated with isopropanol and glycogen and washed with 80% cold ethanol, centrifuged and the pellet was dried, resuspended in PBS and then purified using the Roche High Pure Isolation kit. P values represent significance of unpaired T tests.

**[00052]** Figure 11 depicts Cycle Times for HbgA2, 18S RNA, and TNF alpha after GlobinZero depletion. Since ribosomal and hemoglobin RNA represent approximately 98% and 70% of the RNA in whole blood, respectively, we tested standard commercial kits for removing these RNAs prior to RNAseq. 4ml heparinized blood, treated with 1ug/ml LPS for one hour at 37°C and placed 250ul into 250ul PAXgene fixative into replicate microtainer tubes. After RNA extraction samples were either left undepleted or treated with the globin zero depletion kit and then quantitative PCR was performed to test for hemoglobin A2, 18S RNA, or TNF alpha mRNA expression. GlobinZero kits depleted both hemoglobin A2 and 18S ribosomal RNA (increased mean cycle time from 11 to 28 and 10 to 30,

respectively) with relative preservation of TNFalpha mRNA. P values represent results of ordinary one-way ANOVA with Tukey's multiple comparisons test.

**[00053] Figure 12** provides RNASeq QC metrics of RNA with various quality scores prepared with Illumina TruSeq or Kapa Hyper Prep Kits. **A.** (Left Panel): Distribution of mapping, uniquely mapping, and duplicate reads. **B.** (Right Panel): Distribution of tags assigned to UTR (untranslated region), intergenic, intronic, and CDS (coding sequence) of whole blood RNA samples prepared with Illumina TruSeq or Kapa Hyper Prep Kits with various input RNA quality and quantity. The Illumina TruSeq library Prep demonstrated increased mapping to coding sequence and fewer intergenic reads and was ultimately used for downstream experiments.

**[00054] Figure 13** provides comparison of patient reported (RAPID3) and clinical (DAS28) disease activity scores of 4 patients. Paired RAPID3 scores and DAS28-CRP scores were collected from 91 clinic visits of 4 RA patients. The patient reported RAPID3 questionnaire was significantly correlated with clinician generated DAS28 score in all 4 patients.

**[00055] Figure 14** depicts clinical features of baseline, flare and on steroid treatment. RAPID3 questionnaire responses from 360 time points and DAS28 ESR, TJC, SJC, ESR, DAS28 CRP, platelet counts and absolute neutrophil counts from 43 clinic visits for one patient over four years. Time points are positioned and colored according to disease activity category: The first (left) set in each graph is baseline, the middle set in each graph is flare, and the third (right) set in each graph is steroid. Steroid treatment was defined as any time point when the patient took any dose of steroid that day, or if the calculated dose, using washout kinetics, was greater than 0.01mg/ml. Samples acquired between two time points that met criteria for flare that did not meet flare criteria were still categorized as flare up until treatment with steroid. TJC indicates tender joint count. SJC indicates swollen joint count. P values represent ANOVA across three disease categories. Flare was associated with significantly increased RAPID3, DAS28 ESR, TJC, SJC, ESR, DAS28CRP, platelets and neutrophils.

**[00056] Figure 15** depicts that differentially expressed flare genes are reproducibly altered in repeated flares. **A.** Index patient disease activity (RAPID3) over time. Top panel dots are colored by disease activity assignment. Bottom panel dots are colored according to clinical flare event number. **B.** Unsupervised hierarchical clustering of genes differentially expressed between baseline and flare. Top bar indicates samples colored according to disease activity assignment. Bottom bar indicates samples colored according to clinical flare event number. Data shows differentially expressed flare genes are represented by multiple clinical events.

**[00057] Figure 16** provides deconvolution of blood cell types over time to flare. Mean cell type trajectories of **A.** ABIS inferred cell types, and **B.** CIBERSORTx inferred cell types over time to flare are plotted (excluding those that were 0 all throughout) showing the mean score with standard error of the

mean as a ribbon. These data independently confirm data in main Figure 4A identifying activation of B cells in AC2.

**[00058] Figure 17** depicts that distinct analysis approaches identify activation of naïve B cells in blood 2 weeks prior to flare. **A.** CIBERSORTx inferred naïve B cells by week to flare. **B.** ABIS inferred naïve B cells by week to flare. **C.** Mean expression of 190 synovial single cell RNAseq naïve B cell marker genes by week to flare. **D.** IGHM (blue/top) and IGHD (red/bottom) gene expression by week to flare. Dashed line indicates first day of symptoms of RA flare, red arrows indicate peak in B cell signature 2 weeks prior to flare.

**[00059] Figure 18** provides mean standardized gene expression of genes common to synovial sublining fibroblasts (CD34+, DKK+, and HLA-DR+ fibroblasts) and AC3 in blood over time to flare. Light gray lines represent the expression of individual genes over time to flare in patient 1 over all flares.

**[00060] Figure 19** depicts gating strategy for quantification of PRIME cells in blood samples. Previously frozen peripheral blood mononuclear cells were thawed and stained with antibodies to CD31, PDPN, and CD45 as well as TOPRO. Live CD31- cells were gated and PDPN +, CD45- cells were enumerated.

**[00061] Figure 20** demonstrates PRIME cells are nucleated. PBMC of RA donor was stained with CD45/CD31/PDPN and either TOPRO (Not Permeabilized) or permeabilization and TOPRO (Permeabilized) and assessed by flow cytometry. PRIME cells were gated as CD45-/CD31-/PDPN+ cells and TOPRO staining of permeabilized and not permeabilized cells is presented. The increased fluorescence of TOPRO in the permeabilized PRIME cells indicates the presence of double stranded nucleic acid.

**[00062] Figure 21** depicts that sorted PRIME cells express synovial fibroblast genes. Log2 fold change of various synovial single cell RNAseq marker genes in PRIME cells (flow sorted CD45-/CD31-/PDPN+ cells) versus hematopoietic cells (flow sorted CD45+) and Log2 fold change of Input cells (stained PBMC but not flow sorted) versus hematopoietic cells (flow sorted CD45+) as technical control for stress of flow sorting. These data show that single cell marker genes of fibroblasts (SC-F1, SC-F2, SC-F3, SC-F4) but not B cells (SC-B1-4), macrophages (SC-M1-4), or T cells (SC-T1-6) are enriched in sorted PRIME cells. Fibroblast genes (as marked) were the only set of synovial cell marker genes enriched in PRIME cells.

**[00063] Figure 22** depicts that sorted PRIME cells express classic synovial fibroblast genes. Volcano plot of Log10(-padj) vs Log2 fold change of PRIME cells (flow sorted CD45-/CD31-/PDPN+ cells) versus hematopoietic cells (flow sorted CD45+). Classic fibroblast genes are significantly increased in PRIME cells relative to hematopoietic cells.

### DETAILED DESCRIPTION

**[00064]** In accordance with the present invention there may be employed conventional molecular biology, microbiology, and recombinant DNA techniques within the skill of the art. Such techniques are explained fully in the literature. See, e.g., Sambrook et al, "Molecular Cloning: A Laboratory Manual" (1989); "Current Protocols in Molecular Biology" Volumes I-III [Ausubel, R. M., ed. (1994)]; "Cell Biology: A Laboratory Handbook" Volumes I-III [J. E. Celis, ed. (1994)]; "Current Protocols in Immunology" Volumes I-III [Coligan, J. E., ed. (1994)]; "Oligonucleotide Synthesis" (M.J. Gait ed. 1984); "Nucleic Acid Hybridization" [B.D. Hames & S.J. Higgins eds. (1985)]; "Transcription And Translation" [B.D. Hames & S.J. Higgins, eds. (1984)]; "Animal Cell Culture" [R.I. Freshney, ed. (1986)]; "Immobilized Cells And Enzymes" [IRL Press, (1986)]; B. Perbal, "A Practical Guide To Molecular Cloning" (1984).

**[00065]** Therefore, if appearing herein, the following terms shall have the definitions set out below.

#### A. TERMINOLOGY

**[00066]** The term "rheumatoid arthritis" or "RA" refers to a chronic disease, which is immune-mediated and inflammatory and is an autoimmune disorder, affecting the lining of joints that causes joint pain, stiffness, swelling and decreased movement of the joints and can eventually result in bone erosion and joint deformity. RA is a systemic autoimmune disease characterized by the simultaneous inflammation of the synovium of multiple joints.

**[00067]** An "RA flare" or "flare" refers to a surge in immune-mediated and/or inflammatory activity that is periodically experienced by a patient(s) with RA. During a flare, the level of fatigue and joint symptoms such as pain, swelling, and stiffness temporarily increase. Flares are periods of increased disease activity during which people's arthritis symptoms, which typically include joint pain, swelling, and stiffness, are more severe. An RA flare can involve an exacerbation of any symptom of the disease, but most commonly includes intense stiffness in the joints. People with RA report these common symptoms of flares: increased stiffness in joints, pain throughout the entire body, increased difficulty doing everyday tasks, swelling, such as causing shoes not to fit, intense fatigue, flu-like symptoms.

**[00068]** The term "antibody" describes an immunoglobulin whether natural or partly or wholly synthetically produced. The term also covers any polypeptide or protein having a binding domain which is, or is homologous to, an antibody binding domain. CDR grafted antibodies are also contemplated by this term. An "antibody" is any immunoglobulin, including antibodies and fragments thereof, that binds a specific epitope. The term encompasses polyclonal, monoclonal, and chimeric antibodies. The term "antibody(ies)" includes a wild type immunoglobulin (Ig) molecule, generally comprising four full length polypeptide chains, two heavy (H) chains and two light (L) chains, or an equivalent Ig homologue thereof

(e.g., a camelid nanobody, which comprises only a heavy chain); including full length functional mutants, variants, or derivatives thereof, which retain the essential epitope binding features of an Ig molecule, and including dual specific, bispecific, multispecific, and dual variable domain antibodies; Immunoglobulin molecules can be of any class (e.g., IgG, IgE, IgM, IgD, IgA, and IgY), or subclass (e.g., IgG1, IgG2, IgG3, IgG4, IgA1, and IgA2). Also included within the meaning of the term “antibody” are any “antibody fragment”.

**[00069]** An “antibody fragment” means a molecule comprising at least one polypeptide chain that is not full length, including (i) a Fab fragment, which is a monovalent fragment consisting of the variable light (VL), variable heavy (VH), constant light (CL) and constant heavy 1 (CH1) domains; (ii) a F(ab')<sub>2</sub> fragment, which is a bivalent fragment comprising two Fab fragments linked by a disulfide bridge at the hinge region; (iii) a heavy chain portion of an Fab (Fd) fragment, which consists of the VH and CH1 domains; (iv) a variable fragment (Fv), which consists of the VL and VH domains of a single arm of an antibody, (v) a domain antibody (dAb) fragment, which comprises a single variable domain (Ward, E.S. et al., *Nature* 341, 544-546 (1989)); (vi) a camelid antibody; (vii) an isolated complementarity determining region (CDR); (viii) a Single Chain Fv Fragment wherein a VH domain and a VL domain are linked by a peptide linker which allows the two domains to associate to form an antigen binding site (Bird et al, *Science*, 242, 423-426, 1988; Huston et al, *PNAS USA*, 85, 5879-5883, 1988); (ix) a diabody, which is a bivalent, bispecific antibody in which VH and VL domains are expressed on a single polypeptide chain, but using a linker that is too short to allow for pairing between the two domains on the same chain, thereby forcing the domains to pair with the complementarity domains of another chain and creating two antigen binding sites (WO94/13804; P. Holliger et al *Proc. Natl. Acad. Sci. USA* 90 6444-6448, (1993)); and (x) a linear antibody, which comprises a pair of tandem Fv segments (VH-CH1-VH-CH1) which, together with complementarity light chain polypeptides, form a pair of antigen binding regions; (xi) multivalent antibody fragments (scFv dimers, trimers and/or tetramers (Power and Hudson, *J Immunol. Methods* 242: 193-204 9 (2000)); (xii) a minibody, which is a bivalent molecule comprised of scFv fused to constant immunoglobulin domains, CH3 or CH4, wherein the constant CH3 or CH4 domains serve as dimerization domains (Olafsen T et al (2004) *Prot Eng Des Sel* 17(4):315-323; Hollinger P and Hudson PJ (2005) *Nature Biotech* 23(9):1126-1136); and (xiii) other non-full length portions of heavy and/or light chains, or mutants, variants, or derivatives thereof, alone or in any combination.

**[00070]** As antibodies can be modified in a number of ways, the term “antibody” should be construed as covering any specific binding member or substance having a binding domain with the required specificity. Thus, this term covers antibody fragments, derivatives, functional equivalents and homologues of antibodies, including any polypeptide comprising an immunoglobulin binding domain,

whether natural or wholly or partially synthetic. Chimeric molecules comprising an immunoglobulin binding domain, or equivalent, fused to another polypeptide are therefore included.

**[00071]** The term “adjuvant(s)” describes a substance, compound, agent or material useful for improving an immune response or immune cell or component stimulation, and may in some instances be combined with any particular antigen in an immunological, pharmaceutical or vaccine composition. Adjuvants can be used to increase the amount of antibody and effector T cells produced and to reduce the quantity of antigen or immune stimulant or modulator and the frequency of injection. An adjuvant can serve as a tissue depot that slowly releases the antigen and also as a lymphoid system activator that non-specifically enhances the immune response. In a preferred aspect an adjuvant is physiologically and/or pharmaceutically acceptable in a mammal, particularly a human.

**[00072]** The term “specific” may be used to refer to the situation in which one member of a specific binding pair will not show any significant binding to molecules other than its specific binding partner(s). The term is also applicable where *e.g.* an antigen binding domain is specific for a particular epitope which is carried by a number of antigens, in which case the specific binding member carrying the antigen binding domain will be able to bind to the various antigens carrying the epitope.

**[00073]** The term “comprise” generally used in the sense of include, that is to say permitting the presence of one or more features or components. The term “consisting essentially of” refers to a product, such as a peptide sequence, of a defined number of residues which is not covalently attached to a larger product.

**[00074]** The term “oligonucleotide,” as used herein in referring to a probe of use the present invention, is defined as a molecule comprised of two or more ribonucleotides, preferably more than three. Its exact size will depend upon many factors which, in turn, depend upon the ultimate function and use of the oligonucleotide. The term “primer” as used herein refers to an oligonucleotide, which is capable of acting as a point of initiation of synthesis when placed under conditions in which synthesis of a primer extension product, which is complementary to a nucleic acid strand, is induced, *i.e.*, in the presence of nucleotides and an inducing agent such as a DNA polymerase and at a suitable temperature and pH. The primer may be either single-stranded or double-stranded and must be sufficiently long to prime the synthesis of the desired extension product in the presence of the inducing agent. The exact length of the primer will depend upon many factors, including temperature, source of primer and use of the method. For example, for diagnostic applications, depending on the complexity of the target sequence, the oligonucleotide primer typically contains 15-25 or more nucleotides, although it may contain fewer nucleotides.

**[00075]** The term “agent” means any molecule, including polypeptides, antibodies, polynucleotides, chemical compounds and small molecules. In particular the term agent includes compounds such as test compounds or drug candidate compounds.

**[00076]** The term "assay" means any process used to measure a specific property of a compound. A "screening assay" means a process used to characterize or select compounds based upon their activity from a collection of compounds.

**[00077]** The term "protein" is used herein to mean protein, polypeptide, oligopeptide or peptide. The terms "protein marker", "biomarker" or "protein marker of impending flare" are used herein to refer to proteins associated with or predictive or which precede specific diseases or conditions or symptoms, including proteins from or associated with aspects, cells or tissues affected by a disease or condition or symptom. In accordance with the present invention, the increase in marker expression relative to that detected or characteristic of a subject/s without overt organic RA disease or significant joint or pain symptoms or without an impending flare or a normal, healthy subject/s (control/controls) is positively correlated with, indicative of, or diagnostic for the impending presence or flare or flare-up of a disease or condition or symptoms thereof particularly an exacerbation of disease or symptoms, such as rheumatoid arthritis and particularly an RA flare, in a patient.

**[00078]** As used herein, the terms "increase" in marker expression or "differential expression" of a marker refer to a statistically significant increase or presence. The term statistically significant is used in the art to refer to the likelihood that a result or relationship is caused by something other than mere random chance. Statistical hypothesis testing is traditionally employed to determine if a result is statistically significant or not. Such testing provides a "p-value" representing the probability that random chance could explain the result. In general, a 5% or lower p-value is considered to be statistically significant.

**[00079]** A skilled practitioner would, moreover, appreciate that a relative increase or decrease in a particular protein (a protein marker) or a particular RNA (an RNA marker) in a sample alone may be weakly indicative or predictive of disease, but may not be diagnostic per se, if noted as a single determinant. If, however, a plurality of such single determinants are noted in a biological sample, the combined detection of several, even weakly indicative, determinants may serve to identify a strong combinatorial diagnostic indicator of impending disease or symptomatic disease aspects, such as impending RA flare. Furthermore, the single protein/determinant need not approach the threshold of weak diagnostic by itself but in combination with the detection of an increase of another protein or proteins or RNA or RNAs (other markers) may serve as a strong combinatorial diagnostic indication of an impending disease state. Accordingly, also encompassed herein are combinatorial diagnostic indicators or combinatorial markers that are associated with a particular disease or an impending disease and not observed in healthy subjects or patients with other diseases.

**[00080]** Accordingly, selected sets of one, two, three, several, at least 10, about 10, a dozen, 10-15, about 20, at least 20, 25, 30, about 30 and more, etc of the markers of this invention (up to the number

equivalent to all of the markers, or all in a set of markers, including any intervening number, in whole number increments, e.g., 1, 2, 3, 4, 5, 6 ... ) can be used as diagnostic indicators and predictors of an impending flare for methods and/or in kits described herein. In one embodiment, larger numbers of the markers identified herein are used in methods or kits of the invention, since the accuracy of the method or kit may improve as the number of markers screened increases. With respect to aspects of the invention pertaining to evaluating therapeutic efficacy, the methods and kits of the present invention include evaluating whether administration of a therapeutic composition causes a change, either a transient change or a long term change, in expression of one or more of the markers; in expression of two or more of the markers; in expression of three or more of the biomarkers; in expression of four or more of the biomarkers; in expression of five or more of the biomarkers, in expression of six or more of the biomarkers, etc.

**[00081]** As an example, a straightforward identification of a protein marker or an RNA marker is the presence of a protein or RNA associated with an impending disease or condition and not with other conditions that might be clinically confused with the disease under consideration. Variations to this scenario include the situation wherein a marker is present in an increased quantity compared to other conditions or controls. Although not a protein marker, an example is the presence of glucose in the blood in high quantities in diabetics compared to normal individuals who have glucose present but not in elevated quantities. A variation is where the functional marker is not just one protein but two or more in combination that can be quantitatively different, wherein the ensemble defines its marker potential.

**[00082]** In some embodiments, a marker of the invention is a member of a biological pathway. As used herein, the term "precursor" or "successor" refers to molecules that precede or follow the marker in the biological pathway. Thus, once a marker is identified as a member of one or more biological pathways, the present invention can include additional members of the biological pathway that come before (are upstream of or a precursor of) or follow (are downstream of) the marker. Such identification of biological pathways and their members is within the skill of one in the art.

**[00083]** Also encompassed herein is the analysis of markers identified and listed in the tables presented herein to identify metabolic pathways implicated in the pathogenesis, maintenance, and/or progression of a disease or an impending disease or system or flare. Such analyses may utilize a variety of software programs or approaches known and available to the skilled artisan. Multiple hits in a particular metabolic pathway underscore the potential importance of the pathway for the disease and direct therapeutic intervention toward appropriate modulation of same. Accordingly, the present methods encompass such analyses and the identification of metabolic pathways of potential significance in a particular disease or impending disease aspect or symptom. Knowing that, for example, activation of a metabolic pathway appears to be linked or associated with a particular disease or impending symptom presents the

opportunity to test pharmaceutical modulators of the pathway (i.e., inhibitors) to determine if such modulators could be used as therapeutics for treatment of patients with the disease or impending disease or symptoms. This and these aspects are illustrated and described herein including in the examples.

**[00084]** Polypeptide or protein markers and RNA(s) or RNA markers may be isolated or evaluated by any suitable method known in the art. Proteins or RNAs can be purified or assayed by standard methods known in the art such as via immunoassay, ELISA, nucleic acid probes, primers, oligonucleotides, antibody affinity methods, RNA sequencing etc. In one embodiment, polypeptide and metabolite markers may be isolated from a biological sample using standard techniques known in the art, for example, affinity purification using substrate-bound antibodies that specifically bind to the marker. As described herein, immunoaffinity depletion of abundant RNA(s) or proteins (with masking potential) enhances coverage and detection of low abundance proteins or RNA(s).

**[00085]** Antibodies immunospecific for any one of the markers provided herein may be known and available to the public and may be accessed via the scientific community or purchased from a commercial vendor. Readily searchable databases or web browsers may be utilized for example for identifying potential suppliers for such antibodies.

**[00086]** In accordance with the present disclosure, the tables present information with which an ordinarily skilled practitioner can access the amino acid sequences of the proteins and RNAs identified herein as markers, as well as nucleic acid sequences encoding same. A stepwise protocol or means for identification of the sequences listed in the tables presented herein may include the artisan accessing one of the publicly available databases and entering the ensembl number or gene name or symbol to identify the sequence and relevant marker information. Such information may be used to design probes for detection of any of the proteins, genes, RNAs listed therein or to identify commercially available probes or antibodies therefore or thereof. Primers for detection of nucleic acid sequences encoding any of the proteins listed in the tables presented herein are also envisioned as are primers for PCR including RT PCR. Such primers may be used to detect RNA expression levels (including relative increases or decreases as compared to controls) of a marker relevant to the invention. The design of primers for detecting expression levels of RNA (e.g., mRNA) of a marker or markers listed herein is a matter of routine practice with the nucleic acid sequence in hand as provided by publicly available websites such as those mentioned above. Such probes and primers are useful for the kits described herein.

**[00087]** The term "preventing" or "prevention" refers to a reduction in risk of acquiring or developing a disease or disorder (i.e., causing at least one of the clinical symptoms of the disease not to develop) in a subject that may be exposed to a disease-causing agent, or predisposed to the disease in advance of disease onset. The term "prophylaxis" is related to and encompassed in the term 'prevention', and refers to a measure or procedure the purpose of which is to prevent, rather than to treat or cure a disease. Non-

limiting examples of prophylactic measures may include the administration of vaccines; the administration of low molecular weight heparin to hospital patients at risk for thrombosis due, for example, to immobilization; and the administration of an anti-malarial agent such as chloroquine, in advance of a visit to a geographical region where malaria is endemic or the risk of contracting malaria is high.

**[00088]** "Therapeutically effective amount" means that amount of a drug, compound, antibody, or pharmaceutical agent that will elicit the biological or medical response of a subject that is being sought by a medical doctor or other clinician. In particular, with regard to gram-positive bacterial infections and growth of gram-positive bacteria, the term "effective amount" is intended to include an effective amount of a compound or agent that will bring about a biologically meaningful decrease in the amount of or extent of disease or flare free time period and or increase in length of a subject's survival or period disease-free or in remission or free of flare(s). The phrase "therapeutically effective amount" is used herein to mean an amount sufficient to prevent, and preferably reduce by at least about 30 percent, more preferably by at least 50 percent, most preferably by at least 90 percent, a clinically significant change, or enhanced survival or disease-free period by at least about 30 percent, more preferably by at least 50 percent, most preferably by at least 90 percent.

**[00089]** The term "treating" or "treatment" of any disease, condition, or infection refers, in one embodiment, to ameliorating the disease or infection (i.e., arresting the disease or growth of the infectious agent or bacteria or reducing the manifestation, extent or severity of at least one of the clinical symptoms thereof). In another embodiment "treating" or "treatment" refers to ameliorating at least one physical parameter, which may not be discernible by the subject. In another embodiment, "treating" or "treatment" refers to modulating the disease or infection, either physically, (e.g., stabilization of a discernible symptom), physiologically, (e.g., stabilization of a physical parameter), or both. In a further embodiment, "treating" or "treatment" relates to slowing the progression of a disease or reducing an infection.

**[00090]** The phrase "pharmaceutically acceptable" refers to molecular entities and compositions that are physiologically tolerable and do not typically produce an allergic or similar untoward reaction, such as gastric upset, dizziness and the like, when administered to a human.

**[00091]** As used herein, "pg" means picogram, "ng" means nanogram, "ug" or "μg" mean microgram, "mg" means milligram, "ul" or "μl" mean microliter, "ml" means milliliter, "l" means liter.

#### B. DETAILED DISCLOSURE.

**[00092]** The invention relates to and provides previously unidentified and unrecognized markers, particularly RNA markers and protein markers, which are indicators and antecedents of an impending rheumatoid arthritis (RA) flare. The markers are differentially expressed or preferentially expressed prior to an RA flare in an RA patient and provide markers which can predict an impending flare and can be utilized to implement and prescribe treatment and therapy to a patient.

**[00093]** Arthritis is a disease that may cause damage to the healthy cartilage of joints, leading to degenerative changes, loss of function and joint instability. Inflammatory arthritis describes conditions characterized by pain, swelling, tenderness and warmth in the joints, as well as morning stiffness that lasts for more than an hour. An increase of cytokines leads to degradation of articular cartilage and a decrease of growth factors which induce chondrogenesis in inflammatory arthritis. The most common inflammatory arthritis associated disorders rheumatoid arthritis (RA), psoriatic arthritis (PsA), systemic lupus erythematosus (SLE, lupus), ankylosing spondylitis (AS), and gouty arthritis (gout). Arthritis damages the cartilage within joints, resulting in degenerative changes, including loss of function and joint instability. Ankylosing spondylitis (AS) is a chronic inflammatory condition affecting the spine and bone-to-tendon attachment area within the sacroiliac joint leading to back pain and progressive spinal stiffness. Rheumatoid arthritis is a chronic, systemic autoimmune disease characterized by the simultaneous inflammation of the synovium of multiple joints, leading to joint damage (e.g., destruction, deformation and disability). Gout is a chronic inflammatory disease that causes an alteration of joints resulting in severe pain and is associated with an accumulation of uric acid within the body resulting from dysregulated purine metabolism, causing recurrent paroxysmal inflammation in the joints. Allopurinol and febuxostat are the primary treatment options for individuals with gout.

**[00094]** Various disease modifying agents for treating or modifying RA, including for management and alleviation of RA flares, are known and in use clinically. Nonsteroidal anti-inflammatory drugs (NSAIDs) or conventional disease-modifying antirheumatic drug (DMARDs) have been used for the treatment of these inflammatory diseases, particularly RA. More recently, biologic DMARDs have been introduced with excellent results. NSAIDs include non-prescription drugs acetylsalicylate (aspirin), ibuprofen (Advil, Motrin IB) and naproxen sodium (Aleve, Naprosyn) and prescription NSAIDs such as etodolac (Lodine) and diclofenac (Voltaren). Steroids are anti-inflammatory or immunosuppressants agents and are prescribed for more severe RA or when RA symptoms flare to ease joint pain and stiffness. Examples include glucocorticosteroids or corticosteroids such as prednisone, cortisone and methylprednisolone. DMARDs are prescribed and utilized to slow the progression of RA and save joints and other tissues from permanent damage. Common conventional DMARDs include methotrexate (Trexall, Otrexup), leflunomide (Arava), hydroxychloroquine (Plaquenil) and sulfasalazine (Azulfidine). DMARDs curb the overactive immune system in RA but aren't selective in their targets. Biologics - genetically engineered proteins which target a specific aspect or part of the immune system and act as immunosuppressants - are an increasingly important component in treatment of RA and are commonly denoted biologic DMARDs or bDMARDs. Biologics include abatacept (Orencia), adalimumab (Humira), anakinra (Kineret), baricitinib (Olumiant), certolizumab (Cimzia), etanercept (Enbrel), golimumab (Simponi), infliximab (Remicade), rituximab (Rituxan), sarilumab (Kevzara), tocilizumab (Actemra) and

tofacitinib (Xeljanz). Adalimumab, etanercept, infliximab, golimumab and certolizumab target tumor necrosis factor (TNF). Rituximab is effective against B cells. Anakinra blocks the action of interleukin-1 (IL-1), a master cytokine. Abatacept targets T cells. Biologic DMARDs are usually most effective when paired with a nonbiologic DMARD, such as methotrexate. New DMARD drugs which are specific in their targets but are not biologics include oral small molecule Janus kinase (JAK) inhibitors such as tofacitinib (Xeljanz and Xeljanz XR), baricitinib (Olumiant), and upadacitinib (Rinvoq).

**[00095]** The American College of Rheumatology (ACR) has recommendations for RA patient treatment given various disease parameters (e.g., Singh J et al (2016) *Arthritis Rheumatol* 68:1-26). Disease activity scales are utilized in managing RA patients and choosing appropriate treatment modalities, including the routine assessment of patient index data 3 (RAPID3) and the disease activity score 28 (DAS28) (Fransen, J et al (2003) *Arthritis Rheum* 49 Suppl:S214-24), which incorporates tenderness and swelling from 28 joints, erythrocyte sedimentation rate (ESR) and patient global assessment of disease activity, both of which have been utilized in studies described herein. Additional assessment instruments include Patient Activity Scale (PAS) or PASII (Wolfe, F et al (2005) *J Rheumatol* 32:2410-5), Clinical Disease Activity Index (CDAI) (Aletaha, D et al (2005) *Arthritis Res Ther* 7:R796-806) and Simplified Disease Activity Index (SDAI) (Smolen, JS et al (2003) *Rheumatology* 42:244-57). Each of these scales and assessments are applicable in treatment once a patient has symptomatic aspects or indicators of a flare or of disease. These scales cannot predict a flare, they are indicators of a flare or of exacerbation of disease.

**[00096]** RA patients are not able to predict a flare and are therefore subject to unpredictable exacerbations of disease and disease-associated symptoms and continual, progressive joint damage. The availability of dependable markers of impending flare(s), which can be readily and reliably assessed, particularly without significant clinical intervention, would significantly impact the treatment and management of RA patients and reduce the impact and long-term effects of the disease.

**[00097]** Toward that end, the invention provides a first set of markers that are expressed two weeks or about two weeks prior to an RA flare. The timing before flare can have a margin of error of about a week or 7 days. Referring to the studies provided herein, patients' symptoms were assessed using a questionnaire that asked about how they were doing over the past week, therefore there is a possible 7 day margin of error in timing. For instance, given the questionnaire, the researchers could not necessarily discriminate between symptoms that started that day (or on day 1) vs 6 days earlier, or about a week or up to 7 days earlier. Therefore, the timing of the first set of markers is about two weeks, with a margin of error up to an additional 7 days, therefore up to 3 weeks or a week up to three weeks or 7-21 days. A first set of markers can be identified and characterized in a patient sample, particularly a blood sample, including a finger stick sample of blood, two weeks or about two weeks, about 14 days, approximately 14 days, more than one week, more than 12 days, more than 10 days, about 10-14 days, about 12-14 days prior to an RA

flare, with a margin of error in each instance of up to about a week or 7 days, therefore, with a margin of error up to three weeks, at least a week, about two or three weeks, two or three weeks, about 7-21 days, up to 21 days, at least 7-10 days, about two to three weeks prior to an RA flare. These antecedent markers, particularly denoted AC2 markers, are provided in Table 7.

**[00098]** Another and second set of markers are provided that are expressed one week or about one week, or about 7 days, approximately 7 days, prior to an RA flare. The timing before flare can have a margin of error of about a week or 7 days. Referring to the studies provided herein, patients symptoms were assessed using a questionnaire that asked about how they were doing over the past week, therefore there is a possible 7 day margin of error in timing. For instance, given the questionnaire, the researchers could not necessarily discriminate between symptoms that started that day (or on day 1) vs 6 days earlier, or about a week or up to 7 days earlier. The second set of markers can be identified and characterized in a patient sample, particularly a blood sample, including a finger stick sample of blood, about one week, or about 7 days, approximately 7 days, about 5-7 days prior to an RA flare, with a margin of error in each instance of up to about a week or 7 days, therefore, with a margin of error up to two weeks, up to 14 days, 0-14 days, about one to two weeks, at least a week, about a week to 10 days, 7-14 days, 5-14 days prior to a flare. These antecedent markers, particularly denoted AC3 markers, are provided in Table 8. The set of AC2 markers or the first set of markers are expressed further out from a flare and more than a week before flare, up to three weeks prior to an RA flare, while the set of AC3 markers or the second set of markers are expressed thereafter or closer to a flare and about a week or up to two weeks prior to a flare.

**[00099]** In an aspect, the AC3 markers, or one or more AC3 marker, or AC3 markers which are sublining fibroblast genes, are decreased during flare or after the commencement of a flare or once a patient experiences physical indicators or symptoms of a flare. Physical indicators or symptoms of a flare may be selected from stiffness in joints, pain throughout the body, increased difficulty doing everyday tasks, swelling, fatigue and flu-like symptoms. In an aspect, synovial cell marker genes or proteins among the AC3 markers and Table 8 are selected. A flare(s) may be evaluated by recognition of the symptoms in a patient and/or utilizing any recognized disease activity scales, including as described and provided herein.

**[000100]** RNA markers and protein markers of impending flare which are particularly selected for determining and predicting impending RA flares are provided in Table 9. The markers COL1A2, COL5A1, COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1 and ZFHX4. RNAs or their encoded proteins selected from COL1A2, COL5A1, COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1 and ZFHX4 are expressed one week or about one week, or about 7 days, approximately 7 days, about 5-7 days, at least 5 days prior to an RA flare. Markers selected from COL1A2, COL5A1, COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1 and ZFHX4. RNAs or their encoded proteins selected from COL1A2, COL5A1,

COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1 and ZFHX4 are expressed one week or about one week, or about 7 days, approximately 7 days, about 5-7 days, at least 5 days prior to an RA flare. In particular, the markers are differentially expressed in a patient prior to a flare. Markers selected from COL1A2, COL5A1, COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1 and ZFHX4. RNAs or their encoded proteins selected from COL1A2, COL5A1, COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1 and ZFHX4 are differentially expressed, their expression is increased or higher relative to other markers or proteins, or their expression is significantly increased relative to expression in a normal sample or a sample from an individual that does not have RA or any other recognized inflammatory or autoimmune disease, one week or about one week, or about 7 days, approximately 7 days, about 5-7 days, at least 5 days prior to an RA flare. As noted above, the margin of error in timing may be up to a week or 7 days. Therefore expression of these markers selected from COL1A2, COL5A1, COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1 and ZFHX4. RNAs or their encoded proteins selected from COL1A2, COL5A1, COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1 and ZFHX4 maybe increased one top two weeks or 0-14 days, or about a week or two prior to a flare. Expression of RNAs or their encoded proteins selected from COL1A2, COL5A1, COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1 and ZFHX4 are reduced, significantly decreased, nearly absent, or absent in peripheral blood during an RA flare. Expression of RNAs or their encoded proteins selected from COL1A2, COL5A1, COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1 and ZFHX4 are reduced, significantly decreased, or nearly absent peripheral blood during an RA flare in comparison to their expression prior to a flare, particularly their expression about a week, or up to two weeks, prior to a flare.

**[000101]** RNA markers and transcripts or protein markers common to synovial sublining fibroblasts which are markers of impending flare and are capable of predicting or determining an impending flare as set out in Table 5. The markers comprise COL1A2, COL5A1, COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1, ZFHX4, COL3A1, COMP, FNDC1, GALNT15, SULF1, GPX8 and IGFBP6. The markers are COL1A2, COL5A1, COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1, ZFHX4, COL3A1, COMP, FNDC1, GALNT15, SULF1, GPX8 and IGFBP6. The markers are selected from COL1A2, COL5A1, COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1, ZFHX4, COL3A1, COMP, FNDC1, GALNT15, SULF1, GPX8 and IGFBP6. RNAs or their encoded proteins selected from COL1A2, COL5A1, COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1, ZFHX4, COL3A1, COMP, FNDC1, GALNT15, SULF1, GPX8 and IGFBP6 are expressed one week or about one week, or about 7 days, approximately 7 days, about 5-7 days, at least 5 days, prior to an RA flare. As noted above, the margin of

error in timing may be up to a week or 7 days. Therefore, expression of these markers of impending flare may be found or evident a week or up to two weeks, at least about a week, about 0- 14 days, up to two weeks, 5-14 days prior to a flare. Expression of RNAs or their encoded proteins selected from COL1A2, COL5A1, COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1, ZFX4, COL3A1, COMP, FNDC1, GALNT15, SULF1, GPX8 and IGFBP6 are reduced, significantly decreased, nearly absent, or absent in peripheral blood during an RA flare.

**[000102]** In accordance with the invention herein, the recognition of unique markers in peripheral blood has led to the identification and characterization of a distinctive and specific cell or cell type circulating in the blood of a patient or individual prior to a flare. This unique and specific blood circulating cell is an novel indicator of an impending RA flare. The invention includes a unique blood circulating cell, denoted a Pre-Inflammatory mesenchymal (PRIME) cell, which has been identified and characterized as circulating in peripheral blood in a patient, particularly an RA patient, particularly a human, prior to an RA flare. The presence of this cell in peripheral blood indicates that an RA flare will occur or become evident by way of one or more patient symptom(s). The cell can be identified in patient peripheral blood about one week, one week, about 7 days, about 5-8 days, about 5-7 days, 5-8 days, 5-7 days, about 4-7 days, 4-7 days, about 3-7 days, 3-7 days prior to an RA flare. The cell can be identified in patient peripheral blood about one week, one week, about 7 days, about 5-8 days, about 5-7 days, 5-8 days, 5-7 days, about 4-7 days, 4-7 days, about 3-7 days, 3-7 days prior to inflammation of one or more joints or pain in one or more joints in a patient. As noted above, the margin of error in timing may be up to a week or about 7 days. Therefore, the cell can be identified in patient peripheral blood about one week to about 2 weeks, about 7-14 days, up to 14 days, 0-14 days, about 3-14 days, about 5-14 days prior to an RA flare. In an embodiment, PRIME cell(s) can be identified and characterized as a CD45-CD31-PDPN+ cell, particularly as a CD45-CD31-PDPN+ cell in peripheral blood. In another embodiment, PRIME cell(s) can be identified and characterized as a CD45-CD31-PDPN+IL-17RD+ cell, particularly as a CD45-CD31-PDPN+IL-17RD+ cell in peripheral blood.

**[000103]** In an embodiment, identifying and characterizing the presence of CD45-CD31-PDPN+ cells or CD45-CD31-PDPN+IL-17RD+ cells in peripheral blood provides a diagnostic which is predictive of an impending flare in an RA patient. In an embodiment, identifying and characterizing the presence of CD45-CD31-PDPN+ cells or CD45-CD31-PDPN+IL-17RD+ cells in peripheral blood provides a diagnostic which is predictive of an impending flare, or of stiffness in joints, pain throughout the body, increased difficulty doing everyday tasks, swelling, fatigue and/or flu-like symptoms in a patient, including an RA patient, or a patient which is suspected of having RA or an arthritic or inflammatory disease.

**[000104]** The invention thus provides a method for monitoring and predicting a rheumatoid arthritis (RA) flare or increased RA disease activity in a patient comprising:

- (a) isolating a blood sample from said patient;
- (b) evaluating the blood sample for expression or quantitatively increased amounts of one or more sets of antecedent RNA markers, protein markers or cell markers selected from:

- (i) AC2 markers or proteins as provided in Table 7;
- (ii) AC3 markers or proteins as provided in Table 8;
- (iii) markers or proteins selected from COL1A2, COL5A1, COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1, ZFHX4, COL3A1, COMP, FNDC1, GALNT15, SULF1, GPX8 and IGFBP6 as set out in Table 5;
- (iv) markers or proteins selected from COL1A2, COL5A1, COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1 and ZFHX4 as set out in Table 9;
- (v) cell markers CD45- CD31-PDPN+;

- (c) wherein the expression or quantitatively increased amounts of the RNA markers or proteins or the presence of the cell markers predicts an impending RA flare.

**[000105]** The expression or quantitatively increased amounts of the AC2 RNA markers or proteins predicts an RA flare in about 2 weeks or about 12-14 days, with a margin of error of up to about a week or 7 days, thus in about 7-21 days. Differential expression of AC2 markers has been identified and characterized in RA patients approximately two weeks prior to the presence of symptoms indicative of an RA flare in the patients. The expression or quantitatively increased amounts of the AC3 RNA markers or proteins predicts an RA flare in about 1 week or about 5-7 days, with a margin of error of about a week or 7 days, thus in about a week or up to 2 weeks, or up to 14 days. Differential expression of AC3 markers has been identified and characterized in RA patients approximately one week or about 5-7 days prior to the presence of symptoms indicative of an RA flare in the patients. The period of time prior to recognition of flare symptoms may vary by a day, a few days or several days from either a week before or two weeks before. The variation may be as a result of the timing of blood collection or sample collection for evaluation of the marker(s). The variation may be as a result of the sensitivity of the patient to symptoms of an RA flare or the ability of a patient to identify or recognize the symptoms or any clinical parameter of a flare. In as much as physical indicators or symptoms of a flare may be selected from stiffness in joints, pain throughout the body, increased difficulty doing everyday tasks, swelling, fatigue and flu-like symptoms, these may be recognized immediately or in the short term or may be recognized after a day or two or several days of symptoms in and by a patient.

**[000106]** Any applicable and sufficient number of markers may be evaluated in a patient to determine or predict an impending flare. Thus, the markers should be sufficient to reliably predict an impending

flare. One skilled in the art will be able to utilize the data herein and available to provide a set of markers necessary or sufficient to predict a flare. In particular and for example, markers which are associated with certain pathways or responses may be selected. Pathways involved in myeloid, neutrophil, Fc receptor signaling and platelet activation may be selected. Genes or markers associated with developmental pathways for naïve B cells and leukocytes may be selected from among the AC2 genes. Naïve B cell genes may be selected from among AC2 genes. Pathways related to extracellular matrix, collagen and connective tissue development may be selected, and may be particularly selected from among the AC3 genes. The invention describes that AC3 was enriched for pathways not typical of blood samples, including cartilage morphogenesis, endochondral bone growth, and extracellular matrix organization. Genes for these pathways or associated with these may be selected from the AC3 genes as markers for predicting RA flares. AC3 is described as enriched with sublining fibroblast genes, in a particular aspect the sublining fibroblast genes CD34+, HLA-DR+, and DKK3+. AC3 is described as enriched with sublining fibroblast genes, in a particular aspect the sublining fibroblast genes CD45-CD34+, CD45-HLA-DR+, and CD45-DKK3+. In an aspect, these may be particularly selected from or included in the markers selected from the AC3 genes. In an embodiment, sublining fibroblast markers selected from the AC3 markers or proteins are selected and evaluated. In an embodiment, AC3 markers or proteins expressed by CD34+, HLADR+ and DKK3+ cells are evaluated. In an embodiment, AC3 markers or proteins expressed by CD45-CD34+, CD45-HLADR+ and CD45-DKK3+ cells are evaluated. The method includes wherein the cell marker IL17RD is also evaluated. In an embodiment, AC3 markers or proteins expressed by PRIME cells, CD45-CD31-PDPN+ cells, or CD45-CD31-PDPN+IL17RD+ cells are evaluated.

**[000107]** Notably, many of the relevant and most particular markers provided herein are unusual in peripheral blood and/or are not necessarily or particularly associated with inflammation or an inflammatory condition per se. This facilitates their specificity, relevance and significance in particularly or specifically predicting or implying an impending RA flare, and/or exacerbation of joint symptoms. Some prior marker studies have identified inflammatory genes, such as inflammation gene expression panels, wherein the genes are associated with RA or inflammatory type conditions of RA, such as described in US Patent 7,935,482. These inflammatory genes provide a distinct profile and profiling from those provided herein, are particularly skewed and relevant for inflammation, and are not predictive of an impending flare.

**[000108]** A subset of at least 20 of the AC2 or AC3 markers may be evaluated. In an aspect, a subset of at least 10 of the AC2 or AC3 markers are evaluated. At least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, at least 25, at least 30, at least 35, at least 40, at least 45, at least 50 of the

AC2 or AC3 markers may be evaluated. A subset of at least 20 of the AC2 and at least 20 of the AC3 markers may be evaluated. In an aspect, a subset of at least 10 of the AC2 and the AC3 markers are evaluated. At least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, at least 25, at least 30, at least 35, at least 40, at least 45, at least 50 of the AC2 and the AC3 markers may be evaluated.

**[000109]** The invention particularly relates to predicting an impending RA flare in a patient and treating for the impending flare so that the patient experiences a reduced flare, fewer pathologies and/or symptoms associated with a flare, or such that a flare and its associated disease exacerbations are reduced, limited in duration, or avoided. This method is provided herein for predicting an impending flare and treating a flare, including thereby preventing a flare, so that prophylaxis may be achieved. This serves to significantly reduce the disease and the associated difficulties for an RA patient and provides a clinically more stable RA scenario.

**[000110]** Methods are provided for predicting an impending RA flare and treating a flare in a patient, including comprising:

- a) isolating a blood sample from the patient;
  - b) contacting the blood sample with reagents specific for markers selected from a panel of RNA or protein markers to assess expression of the RNA or protein markers, wherein the panel of RNA or protein markers is selected from:
    - (i) AC2 markers or proteins as provided in Table 7;
    - (ii) AC3 markers or proteins as provided in Table 8;
    - (iii) markers or proteins selected from COL1A2, COL5A1, COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1, ZFHX4, COL3A1, COMP, FNDC1, GALNT15, SULF1, GPX8 and IGFBP6 as set out in Table 5;
    - (iv) markers or proteins selected from COL1A2, COL5A1, COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1 and ZFHX4 as set out in Table 9; and
  - c) comparing expression of the markers selected from a panel of RNA or protein markers in the blood sample to expression of the markers in a control blood sample to determine if expression of the markers selected from a panel of RNA or protein markers in the blood sample is increased relative to expression in the control blood sample, wherein detection of increased expression serves to predict an impending RA flare in a patient;
- and treating the patient thereby diagnosed with an impending RA flare by administering a therapeutically effective amount of one or more disease modifying agent for treating RA.

**[000111]** The expression, differential expression, or quantitatively increased amounts of the AC2 RNA markers or proteins may predict or may be utilized to predict an RA flare in about 2 weeks, about 14 days,

or about 12-14 days, up to in about 3 weeks or about 21 days, given margin of error. The expression or quantitatively increased amounts of the AC3 RNA markers or proteins may predict or may be utilized to predict an RA flare in about one week, about 7 days, or about 5-7 days, up to or about up to two weeks or about 14 days, given margin of error. In an aspect of the method, the expression, differential expression, or quantitatively increased amounts of the markers or proteins selected from COL1A2, COL5A1, COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1, ZFHX4, COL3A1, COMP, FNDC1, GALNT15, SULF1, GPX8 and IGFBP6 or of the markers or proteins selected from COL1A2, COL5A1, COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1 and ZFHX4 predicts an RA flare in about one week, about 7 days, or about 5-7 days, up to about two weeks or 14 days given margin of error.

**[000112]** Evaluation of RNA or protein expression may be conducted using any method known in the art. Thus, in accordance with the methods of the invention, RNA expression may be assessed by RT PCR. RNA expression may be determined by RNA sequencing. In accordance with the method, protein expression may be assessed using specific antibodies, assessing for protein activity, utilizing protein ligands.

**[000113]** Cell marker expression or presence on the surface of cells in the blood in accordance with the methods of the invention may be determined using standard and known methods. Cell markers may be evaluated using antibodies. Cell markers may be evaluated using FACs analysis. Cells or cell markers may be evaluated using cell sorting or single cell assessments. Cells, including the PRIME cells of the invention may be isolated using cell surface marker antibodies. Methods of isolating PRIME cells, characterized as CD45-CD31-PDPN+ cells, using or via cell surface markers are thus provided in an embodiment of the invention.

**[000114]** The disease modifying agent for treating RA may be selected from standard or clinically recognized agents or therapies for RA or arthritic conditions or inflammatory diseases and conditions. In aspects, the disease modifying agent for treating RA may be one or more agent selected from a nonsteroidal anti-inflammatory drug (NSAID), steroid, methotrexate, disease-modifying antirheumatic drug (DMARDs), biologic DMARD, and oral janus kinase (JAK) inhibitor. DMARD may be one or more of methotrexate (Trexall, Otrexup), leflunomide (Arava), hydroxychloroquine (Plaquenil) and sulfasalazine (Azulfidine). Biologic DMARD may be one or more or any of abatacept (Orencia), adalimumab (Humira), anakinra (Kineret), baricitinib (Olmiant), certolizumab (Cimzia), etanercept (Enbrel), golimumab (Simponi), infliximab (Remicade), rituximab (Rituxan), sarilumab (Kevzara), tocilizumab (Actemra) and tofacitinib (Xeljanz). Exemplary JAK inhibitor include tofacitinib (Xeljanz and Xeljanz XR), baricitinib (Olmiant), and upadacitinib (Rinvoq). The biologic DMARD may be a tumor necrosis factor (TNF) inhibitor. In an aspect, the biologic DMARD may be an anti-inflammatory

antibody or an antibody directed to an inflammation or immune modulatory molecule. In an aspect, the antibody may be an interleukin antibody. The antibody may be an IL-17 specific antibody or an IL-17RD specific or IL-17RD blocking or neutralizing antibody. The antibody may be a podoplanin (PDPN) antibody. The antibody may be a bispecific podoplanin (PDPN) antibody, such as a bispecific PDPN IL17RD antibody.

**[000115]** A novel and unique circulating cell has been identified as a cellular indicator of an impending flare and which specifically contributes to the impending flare. Thus, a circulating pre-inflammatory mesenchymal (PRIME) cell, characterized as a CD45-CD31-PDPN+ cell, has been identified and is provided herein wherein the presence of the cell in peripheral blood is indicative or predictive of an impending RA flare. In an aspect, the PRIME cell additionally expresses IL17RD and is IL17RD+. In an aspect, a subset of PRIME cells additionally expresses IL17RD and is IL17RD+. Methods for isolating PRIME cells, CD45-CD31-PDPN+ cells, and additionally IL17RD+ cells, including for analysis and/or evaluation with potential therapeutics or cell modulators, are provided as an embodiment of the invention. The cells may be selected or isolated via their cell surface markers, including as CD45-CD31-PDPN+, additionally including IL17RD+. Methods for evaluating agents that modulate or inhibit CD45-CD31-PDPN+ cells, and additionally IL17RD+ cells, are provided.

**[000116]** A method is herein now provided for predicting an impending RA flare comprising evaluating a blood sample from a patient for the presence of a PRIME cell characterized as a CD45-CD31-PDPN+ cell, wherein the presence of detectable PRIME cells in peripheral blood in a patient predicts an impending RA flare in the patient. In an aspect thereof, the method includes further evaluating for the presence of IL17RD on a CD45-CD31-PDPN+ cell. Methods are provided for evaluating and treating an impending flare in an RA patient comprising evaluating the peripheral blood of a patient for the presence of a PRIME cell characterized as a CD45-CD31-PDPN+ cell and treating a patient that is positive for PRIME cells in their peripheral blood with a disease modifying agent for RA. Methods are provided for evaluating and treating an impending flare in an RA patient comprising evaluating the peripheral blood of a patient for the presence of a PRIME cell characterized as a CD45-CD31-PDPN+IL17RD+ cell and treating a patient that is positive for PRIME cells in their peripheral blood with a disease modifying agent for RA.

**[000117]** Methods are provided for evaluating and treating an impending flare in an RA patient comprising evaluating the peripheral blood of a patient for the presence of RNA(s) or protein(s) expressed, specifically expressed or particularly expressed by a PRIME cell characterized as a CD45-CD31-PDPN+ cell and treating a patient that is positive for expressing, specifically expressing or particularly expressing RNA(s) or protein(s) of PRIME cells in their peripheral blood with a disease modifying agent for RA. Methods are provided for evaluating and treating an impending flare in an RA

patient comprising evaluating the peripheral blood of a patient for the presence of RNA(s) or protein(s) expressed, specifically expressed or particularly expressed by a cell characterized as a CD45-CD31-PDPN+IL17RD+ cell and treating a patient that is positive for the presence of RNA(s) or protein(s) expressed, specifically expressed or particularly expressed by a cell characterized as a CD45-CD31-PDPN+IL17RD+ cell in their peripheral blood with a disease modifying agent for RA. The specification details the overlapping expression of various and numerous specific AC3 marker genes with gene expression (for example as detected by RNA presence) in PRIME cells characterized as a CD45-CD31-PDPN+ cells.

**[000118]** The disease modifying agent may be selected from those as described and provided herein or as known and recognized to a clinician or physician. Antibodies directed to immune modulators or inflammatory modulators may be selected. In an aspect, the patient is treated with an IL-17 or IL-17RD antibody. In another aspect, the patient is further treated with an anti-inflammatory agent and/or an immune modulating agent. In an aspect the patient is treated with a podaplanin (PDPN) antibody. In an aspect the patient is treated with one or more antibody directed to a surface marker on the PRIME cell, for example a marker from among the AC3 gene markers which is expressed on the cell surface. In an aspect the patient is treated with one or more antibody directed to a surface marker selected from the markers or proteins COL1A2, COL5A1, COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1, ZFHX4, COL3A1, COMP, FNDC1, GALNT15, SULF1, GPX8 and IGFBP6.

**[000119]** Two monoclonal antibodies targeting IL-17A (Secukinumab (AIN457, Novartis), Ixekizumab (LY2439821, EliLilly) and one against the IL-17 receptor (Brodalumab (KHK4827, AMG827, Kyowa/Amgen) are approved for the treatment of moderate-to-severe plaque psoriasis (Silfvast-Kaiser A et al (2019) Expert Opin Biol Ther 19(1):45-54;doi: 10.1080/14712598.2019.1555235). Other IL-17A antibodies include Remtolumab (ABT-122, Abbvie), ALX-0761 (MSB0010841, Ablynx/Merck), BCD-085 (Biocad), COVA322 (Covagen), LY3114062 (EliLilly), Perakizumab (RG4934, RO5310074, Hoffman-LaRoche), Vunakizumab (SHR-1314, Jiangsu Hengrui), CNTO 6785 (Morphosys/Janssen), CJM112 (Novartis) and Bimekizumab (UCB4940, UCB) (Ibrahim S et al (2017) Clin Colorectal Cancer 17(1):e109-13). The IL-17A specific antibody secukinumab and other anti-IL-17 agents have also been reported effective in ankylosing spondylitis (Wendling D et al (2019) Expert Opin Biol Ther 19(1):55-64. doi: 10.1080/14712598.2019.1554053). These antibodies are of use and application in accordance with the invention.

**[000120]** Podaplanin (PDPN) antibodies have also been described. These include the anti-podaplanin antibody clone 8.1.1 (Lax S et al (2017) BMJ Open Respiratory Res 4:e000257;doi:10.1136/bmjresp-2017-000257), a chimeric mouse-human podaplanin antibody chLpMab-7 (Kato Y (2015) Oncotarget

6(34):36003-36018) and anti-human podoplanin rat antibody NZ-1 and chimeric rat-human antibody derived therefrom (NZ-8) Abe S et al (2013) J Immunol 190(12):6239-6249).

**[000121]** Immune modulators may be included in a composition with or administered with antibodies or agents, including those targeting the markers or proteins of the invention, and/or administered at a different time to enhance immune modulation and/or RA therapy, including immune therapies directed against RA or RA flares. An immune modulator may be an adjuvant. Applicable immune modulators include IDO, TDO (Platten M (2012) Cancer Research 72(21):5435-40),  $\alpha$ -galactosyl ceramide and analogs thereof such as threitolceramide (ThrCer) and ThrCer 6, TLR ligands such as poly I:C (TLR3), MPL (TLR4), imiquimod (TLR7), R848 (TLR8) or CpG (TLR9), iCOS, CTLA-4, PD1, PD1 ligand, OX40 and OX40 ligand, Lag3, GITR, GITR ligand interleukins, tumor necrosis factor (TNF) or other growth factors, colony stimulating factors, T cell modulators including modulators of CD8<sup>+</sup> T cells, cytokines or hormones which stimulate the immune response or reduction or elimination of cancer cells or tumors (Mellman I (2011) Nature (480):480 - 489). Additional immunomodulators are small molecules, antagonist antibodies or agonist antibodies targeting the applicable immune modulators including IDO, TDO, Toll like receptor family or iCOS, CTLA-4, PD1, PD1 ligand, OX40 and OX40 ligand, interleukins, tumor necrosis factor (TNF) or other growth factors, colony stimulating factors, T cell modulators including modulators of CD8<sup>+</sup> T cells, cytokines which stimulate the immune response or reduction or elimination of cancer cells or tumors. Additional immune modulators, including TLR ligands such as poly I:C (TLR3), MPL (TLR4), imiquimod (TLR7), R848 (TLR8) or CpG (TLR9) can be used, including in combination with other modulators, agents or antibodies.

**[000122]** The unique specificity of the markers of the invention provides diagnostic and therapeutic uses to identify, characterize and target RA flares or conditions and symptoms associated with an arthritis and/or inflammatory condition, particularly prior to the appearance of clinical symptoms. In particular, markers of the invention are useful in modulating arthritic or inflammatory disease, particularly RA. Markers of the invention are useful in inflammatory arthritis associated disorders, particularly rheumatoid arthritis (RA). Markers may further be useful in other conditions of inflammatory arthritis, particularly psoriatic arthritis (PsA), systemic lupus erythematosus (SLE, lupus), ankylosing spondylitis (AS), and gouty arthritis (gout). In an aspect thereof, antibodies or agents targeting the RNA markers or protein marks are useful in modulating an RA flare or joint inflammation or other physical indicators and symptoms of an RA flare. The antibodies or agents have applicability in therapeutic treatment or management of RA. The antibodies or agents may further have applicability in other common inflammatory arthritis associated disorders, particularly and such as psoriatic arthritis (PsA), systemic lupus erythematosus (SLE, lupus), ankylosing spondylitis (AS), and gouty arthritis (gout). The antibodies or agents targeting the RNA markers or proteins have applicability in enhancing the

therapeutic effect including the anti-rheumatic effect of traditional RA disease modifying agents or therapy(ies).

**[000123]** The invention includes a set of RNA or protein markers for evaluating and predicting an impending RA flare in a patient comprising the markers selected from:

- (i) a subset of at least 20 markers from the AC2 markers provided in Table 7;
- (ii) a subset of at least 20 markers from the AC3 markers provided in Table 8;
- (iii) markers selected from COL1A2, COL5A1, COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1, ZFH4, COL3A1, COMP, FNDC1, GALNT15, SULF1, GPX8 and IGFBP6 as set out in Table 5;
- (iv) markers selected from COL1A2, COL5A1, COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1 and ZFH4 as set out in Table 9.

**[000124]** The markers may be a subset of at least 20 of the AC2 or AC3 markers, a subset of at least 10 of the AC2 or AC3 markers. At least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, at least 25, at least 30, at least 35, at least 40, at least 45, at least 50 of the AC2 or AC3 markers may be included. Particular markers may be selected and utilized. An AC2 marker subset may comprise naïve B cell gene markers and markers of developmental pathways for naïve B cells and leukocytes. A subset of AC3 markers may comprise markers of cartilage morphogenesis, endochondral bone growth, extracellular matrix organization and sublining fibroblasts. A subset of AC3 markers may comprise markers which are expressed or differentially expressed by PRIME cells, CD45-CD31-PDPN+ or are CD45-CD31-PDPN+IL17RD+ cells, cells precursors to sublining fibroblasts, particularly RA sublining fibroblasts.

**[000125]** The set of markers provided and/or utilized in accordance with the methods hereof may be one or more markers selected from COL1A2, COL5A1, COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1, ZFH4, COL3A1, COMP, FNDC1, GALNT15, SULF1, GPX8 and IGFBP6. In an aspect, a set of one or more markers selected from COL1A2, COL5A1, COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1 and ZFH4 is provided and/or utilized in accordance with the methods hereof. A set of, or one or more sets of, two or more, three or more, four or more, five or more, six or more, seven or more, eight or more, nine or more, ten or more, a dozen, at least two, at least three, at least four, at least five, at least six, at least seven, at least eight, at least nine, at least ten, a set of 5-10, a set of 3-5, a set of 5-7, a set of 3-7, a set of 5-8 selected from COL1A2, COL5A1, COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1, ZFH4, COL3A1, COMP, FNDC1, GALNT15, SULF1, GPX8 and IGFBP6 is provided and/or utilized in accordance with the methods hereof. A set of, or one or more sets of, two or more, three or more, four or more, five or more, six or more, seven or more, eight or more, nine or more, ten or more, a dozen, at least

two, at least three, at least four, at least five, at least six, at least seven, at least eight, at least nine, at least ten, a set of 5-10, a set of 3-5, a set of 5-7, a set of 3-7, a set of 5-8 selected from COL1A2, COL5A1, COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1 and ZFHX4 is provided and/or utilized in accordance with the methods hereof. Multiple sets may be utilized, for example a set of markers of one type or metabolic pathway, combined with a distinct set of another type or metabolic or cellular pathway or cell.

**[000126]** The present invention also relates to a variety of diagnostic applications, including methods for detecting the expression of or elevated presence of any of the makers of the invention, particularly the RNA markers or protein markers described and provided herein. Thus, the presence or amount of RNA or protein is evaluated. Protein may be evaluated by reference to their ability to be recognized by a specific antibody directed thereto. Peptide complexes can be identified, targeted, labeled, and/or quantitated on cells, including cell(s) in peripheral blood. Diagnostic applications include *in vitro* and *in vivo* applications well known and standard to the skilled artisan and based on the present description. Diagnostic assays and kits for *in vitro* assessment and evaluation of marker status or marker amounts may be utilized to diagnose, evaluate and monitor patient samples including those known to have or suspected of having arthritis, inflammatory arthritis, or RA. The assessment and evaluation of RA disease status is useful in determining the suitability of a patient for a clinical trial of a drug or for the administration of a particular therapy or disease modifying agent, including a DMARD or an antibody, including as described herein, including combinations thereof, versus a different agent or therapy. This type of diagnostic monitoring and assessment is already in practice utilizing antibodies against the HER2 protein in breast cancer (Hercep Test, Dako Corporation), where the assay is also used to evaluate patients for antibody therapy using Herceptin. *In vivo* applications may include imaging of joints, including radioimaging.

**[000127]** In a further embodiment, commercial test kits suitable for use by a medical specialist may be prepared to determine the presence or absence of aberrant, differential or increased expression of one or more or of a subset of markers described herein. One class of kits will contain at least the labeled marker or its binding partner, for instance an antibody specific thereto, and directions, of course, depending upon the method selected. The kits may also contain peripheral reagents such as buffers, stabilizers, etc.

**[000128]** Accordingly, a test kit may be prepared for the demonstration of the presence of or elevated levels of one or more marker or protein marker of an impending RA flare, comprising:

- (a) a predetermined amount of at least one labeled immunochemically reactive component obtained by the direct or indirect attachment of the protein marker or a specific binding partner or antibody thereto, to a detectable label;
- (b) other reagents; and
- (c) directions for use of said kit.

In accordance with the above, an assay system for screening potential drugs effective to modulate an RA flare or prevent an RA flare and/or the activity of a marker or protein marker of the present invention may be prepared. The marker peptide or antibody thereto may be introduced into a test system, and the prospective drug may also be introduced into the resulting system cell culture, and the culture thereafter examined to observe any changes in the activity of the cells, binding of the antibody, or amount and extent of the marker due either to the addition of the prospective drug alone, or due to the effect of added quantities of a known agent(s).

**[000129]** The invention provides a system or kit for predicting an impending RA flare comprising a set of markers as described and provided herein or a set of probes and/or antibodies for evaluating a set of markers as described and provided herein.

**[000130]** As an example, a kit or system may include a set of markers or a set of probes and/or antibodies for evaluating a set of markers selected from or for a or any combination of:

- (i) a subset of at least 20 markers from the AC2 markers provided in Table 7;
- (ii) a subset of at least 20 markers from the AC3 markers provided in Table 8;
- (iii) markers selected from COL1A2, COL5A1, COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1, ZFH4, COL3A1, COMP, FNDC1, GALNT15, SULF1, GPX8 and IGFBP6 as set out in Table 5;
- (iv) markers selected from COL1A2, COL5A1, COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1 and ZFH4 as set out in Table 9.

**[000131]** The system or kit may further comprise a means for collection of the patient's blood by fingerstick.

**[000132]** The invention may be better understood by reference to the following non-limiting Examples, which are provided as exemplary of the invention. The following examples are presented in order to more fully illustrate the preferred embodiments of the invention and should in no way be construed, however, as limiting the broad scope of the invention.

#### EXAMPLE 1

##### Longitudinal Genomics Identifies PRIME cells as Antecedents of Rheumatoid Arthritis Flares

**[000133]** Rheumatoid arthritis (RA), like many inflammatory diseases, is characterized by episodes of quiescence and exacerbation (flares). The molecular events leading to flares are unknown. We established a clinical and technical protocol for repeated home blood collection in RA patients to allow for longitudinal RNA sequencing (RNAseq). Samples were obtained from 364 time points from eight flares over four years in our index patient, and 235 time points from flares in three additional patients. We identified transcripts that were differentially expressed antecedent to flares and compared these to

synovial single cell RNAseq (scRNAseq). Flow cytometry and sorted blood cell RNAseq in additional RA patients were used to validate the findings.

**[000134]** Consistent changes were observed in blood transcriptional profiles one to two weeks antecedent to RA flare. B cell activation was followed by expansion of a previously unexplored circulating CD45-/CD31-/PDPN+, PRe-Inflammatory MEsenchymal ("PRIME") cell in RA patient blood, which shared features of inflammatory synovial fibroblasts. Circulating PRIME cells decreased during flares from all four patients, and flow cytometry and sorted cell RNAseq confirmed the presence of PRIME cells in 19 additional RA patients.

**[000135]** Longitudinal genomic analysis of RA flares reveals PRIME cells in RA blood, and suggests a model in which they become activated by B cells in the weeks prior to RA flare, and then migrate out of the blood to the synovium. Longitudinal RNAseq analysis can be used to reveal dynamic changes leading to flares of chronic inflammatory disease.

**[000136]** Rheumatoid arthritis (RA) symptoms are highly dynamic, with stable periods interrupted by unpredictable flares of disease activity. Such waxing/waning clinical courses are characteristic of many autoimmune diseases, including multiple sclerosis (1), systemic lupus erythematosus (2), and inflammatory bowel disease (3,4), underscoring a need to develop approaches to understand what triggers transitions from quiescence to flare in autoimmune disease.

**[000137]** This study explores disease pathophysiology with a longitudinal, prospective analysis of blood transcriptional profiles in individual RA patients over time. Previous microarray studies of RA blood samples from relatively sparse time series data have identified few significant gene changes associated with disease activity (5-8). Here we provide the first RA study to look for molecular changes in blood that anticipate clinical flares. To do so we optimized methods by which RA patients themselves could collect high quality finger stick blood samples for RNA sequencing (RNAseq), facilitating weekly blood sampling for months to years.

**[000138]** We analyzed patient reports of clinical disease activity and RNAseq data from four patients across multiple clinical flares. In our most deeply studied index case, we assessed 364 time points by RAPID3 from eight flares over four years, and analyzed 84 time points assessed by RNAseq. Collecting samples longitudinally enabled a search for transcriptional signatures that preceded clinical symptoms. Comparing these blood RNA profiles to synovial single cell RNAseq (scRNAseq) data (9) provided evidence that a biologically coherent set of transcripts are significantly increased in the blood prior to symptom onset, and a subset of these decrease as the patients begin to experience symptoms. These latter transcripts overlap with and likely demarcate cellular precursors to a novel subset of synovial sublining fibroblast cell types detected in inflamed RA synovium using scRNAseq. Analysis in 19 additional RA patients corroborated our findings. Our data suggests a model in which a previously unexplored

circulating mesenchymal cell type, detectable in the weeks prior to RA flare, becomes activated by B cells and subsequently leaves the blood, traffics to synovium, and contributes to disease activity.

## METHODS

### [000139] Patient data

[000140] All patients met American College of Rheumatology/European League Against Rheumatism 2010 (10,11) criteria for RA and were seropositive for cyclized citrullinated protein antibody (CCP). Disease activity was assessed from home each week, or up to 4 times daily during escalation of flares, using the routine assessment of patient index data 3 (RAPID3) questionnaire (12). Disease activity was also assessed at clinic visits, each month, and during flares, using both the RAPID3 and the disease activity score 28 (DAS28), which incorporates tenderness and swelling from 28 joints, erythrocyte sedimentation rate (ESR) and patient global assessment of disease activity. Complete blood counts (CBC) including white blood cells (WBC), neutrophils, monocytes, lymphocytes, and platelets were performed by the clinical lab at Memorial Sloan Kettering Cancer Center. We collected 43 clinic visits from the index patient, and 25, 14 and 12 clinic visits for the other three patients studied longitudinally. Nineteen additional seropositive RA patients and 18 age and sex matched non-RA patients, for whom peripheral blood mononuclear cells (PBMC) were available, were also studied for the presence of PRIME cells by FACS and RNAseq analysis.

### [000141] RNA preparation from Finger Stick blood

[000142] Patients self-performed finger sticks at home to collect three drops of blood into a microtainer tube prefilled with fixative, and samples were mailed overnight each week. RNA was extracted using the PAXgene RNA kit and purified per manufacturer's protocols, except the volume of all washes and elutions was decreased to 25% of the recommended volume by the manufacturer. RNA was assessed using the Agilent BioAnalyzer for quantity and quality. For library preparation, we used the GlobinZero kit (EpiCentre #GZG1224) and Illumina's Truseq mRNA Stranded Library kit, with 11-12 PCR cycles for 5-8nM input and sequenced on HiSeq2500 with 150 base paired-end reads. Reads were aligned to Gencodev18 using STAR and quantified using featureCounts (v1.5.0-p2). Samples with at least four million paired-end reads were retained for analysis.

### [000143] Data analysis:

### [000144] Comparison of disease activity measures

[000145] To describe the bivariate relationship of disease activity with RAPID3, we used the locally weighted scatterplot smoothing (LOWESS) technique.  $R^2$  were calculated to assess correlations of CBC counts inferred from CIBERSORTx and counts measured by clinical labs. Inferred CIBERSORTx lymphocyte counts were the sum of B cells naive + B cells memory + T cells CD8 + T cells CD4 naive + T cells CD4 memory resting + T cells CD4 memory activated. Monocytes, Macrophages M0,

Macrophages M1, and Macrophages M2 were summed to infer CIBERSORTx monocyte counts. One-way ANOVA was used to test for significant differences among various clinical features according to disease activity state.

**[000146]** Differential expression analyses across patients

**[000147]** Samples were labeled "baseline" (stable RAPID3), "flare" (RAPID3 scores rose over two standard deviations above the baseline mean), or "steroid". EdgeR (v3.24.3) (13) was used to analyze flare vs baseline differential gene expression. Permutation test ( $n=1 \times 10^6$ ) was used to test for the significance of overlap between genes decreased in flares in the index patient and patients 2, 3, and 4. GO enrichment (goana, from limma v3.38.3) (14) was used to identify enriched pathways in significantly differentially expressed genes in the index patient ( $FDR < 0.1$ ) and consistent in the direction of expression in both the index and replication patients (i.e., log fold change either both positive or both negative).

**[000148]** Time series analysis of index patient

**[000149]** We performed longitudinal data analysis on the index patient using ImpulseDE2 (v1.8.0) (15). Flare onset was defined clinically (as above) and samples from 8 weeks prior to flare up to 4 weeks after flare were analyzed (excluding any samples during which the patient was taking steroids,  $n=65$  samples). The date of library preparation was included in the model for batch correction, and the genefilter (v1.64.0) package (16) was used to filter out lowly expressed genes.

**[000150]** Identification and characterization of coexpressed gene modules

**[000151]** We hierarchically clustered mean expression of significantly differentially expressed genes identified in the ImpulseDE2 analysis by week to flare initiation (batch corrected logrpkm expression values were calculated using edgeR) and identified five coexpressed gene modules (Clusters 1-5). We analyzed these five modules for GO term enrichment (goana).

**[000152]** To compare differentially expressed gene modules and to further characterize expression patterns in gene modules over time, for each module, the mean expression level for each gene was calculated across flares per week, then normalized across weeks. ABIS (17) and CIBERSORTx (18) were used to deconvolute gene expression data. To aggregate a given cluster of genes or cell type with gene markers, the mean of standardized gene expression scores or deconvolved cell type scores, respectively, within each week were plotted. To identify synovial scRNAseq cluster specific marker gene signatures, we used a previously published dataset (18) to compare the cells from one scRNAseq cluster with cells from all the other scRNAseq clusters using the single-cell RNA-seq  $\log_2(\text{CPM} + 1)$  matrix. We generated lists of the top 200 marker genes for each cluster using the criteria of 1)  $\log_2\text{FC}$  greater than 1, 2) auc greater than 0.6, and 3) percent of expressing cells greater than 0.4. We used Fisher's exact test to evaluate enrichment of synovial cell subtype marker genes in the 5 coexpressed gene modules. P-values were corrected for multiple hypothesis test correction using the Benjamini-Hochberg procedure.

**[000153]** Flow cytometry and sorting

**[000154]** To assess percentages of PRIME cells in peripheral blood mononuclear cells, samples from PBMC were stained with antibodies to: CD31-APC, (WM59), Mouse IgG1-APC (MOPC-21), PDPN-PerCP (NZ1.3), Rat IgG2a (eBR2a)-PerCP, CD45-PE (HI30), Mouse IgG1-PE (MOPC-21) and TO-PRO®-3 and analyzed on BD-FACSCalibur using FlowJo 10.6.1. To flow sort and sequence PRIME cells, 20-100 Million cells from CD14-depleted leukapheresates were stained with CD31-APC(WM59), Mouse IgG1-APC(MOPC-21), PDPN-PerCP(NZ1.3), Rat IgG2a-PerCP(eBR2a), CD45-FITC(HI30), Mouse IgG1-FITC(MOPC-21), and DAPI (4',6-Diamidino-2-Phenylindole, Dihydrochloride) and sorted on a BD FACSaria II. Illumina Stranded TruSeq library kit was used to generate cDNA libraries that were sequenced on MiSeq. DESeq2 (v1.24.0) (19) was used for differential expression analysis.

**[000155]** Statistics

**[000156]** R2 and Pearson correlation coefficients were calculated to assess the bivariate linear fit of disease activity measured by RAPID3 and DAS28 as well as CBC counts inferred from CIBERSORT cell counts and counts measured by clinical labs. Inferred CIBERSORTx lymphocyte counts were the sum of B cells naive + B cells memory + T cells CD8 + T cells CD4 naive + T cells CD4 memory resting + T cells CD4 memory activated. One way ANOVA was used to test for significant differences among various clinical features according to disease activity state. Monocytes, Macrophages M0, Macrophages M1, and Macrophages M2 were summed to infer CIBERSORTx monocytes.

**RESULTS****[000157]** Clinical Protocol Development

**[000158]** We developed strategies for home blood collection that would allow high quality and quantity RNA for sequencing (Figures 6-12; 15-50 ng RNA; RNA integrity (RIN) scores (mean 6.9 +/- standard deviation 1.7). Study patients also documented disease activity (RAPID3 questionnaires). Four RA patients were followed for one to four years with weekly home collection of finger stick blood samples coupled with completion of RAPID3 and monthly clinic visits, where DAS28 were collected (Figure 1A). RNA was sequenced from a total of 189 finger stick blood samples from 4 patients, of which 162 (87%) passed quality control filtering.

**[000159]** To assess the validity of patient reported disease activity, we compared their RAPID3 scores with clinician collected DAS28. Significant correlations were evident between RAPID3 and DAS28 for each of the four patients (Figure 1B and Figure 13). To assess the validity of fingerstick blood data, we compared RNAseq inferred white blood cell counts with clinical laboratory measurements of complete blood counts and again observed significant correlations (Figure 1C), suggesting RNAseq of finger stick blood was of sufficient quality to provide information that correlated with gold standard clinical

measurements of blood counts. Taken together, these data indicate that patient reports of disease activity paired with fingerstick blood samples provide a high quality and robust means by which individuals can participate in longitudinal clinical research studies.

**[000160]** Clinical and Molecular Features of RA Flare Compared to Baseline

**[000161]** Flares were associated with increases in objective clinical and laboratory measures of RA related disease activity in the index patient (Figure 2A and Figure 14). Fingerstick RNAseq identified 2613 genes differentially expressed at flare versus baseline ( $FDR < 0.1$ ), with 1437 increased during flare ( $\log FC > 0$ ; Figure 2B and Table 1).

TABLE 1

|                                                     |               |            |
|-----------------------------------------------------|---------------|------------|
| Genes differentially expressed at flare vs baseline | $FDR < 0.1$   | 2613 genes |
| Genes increased during flare                        | $\log FC > 0$ | 1437 genes |

**[000162]** Pathway analysis identified enrichment in myeloid, neutrophil, Fc receptor signaling and platelet activation (Figure 2C and Table 2), consistent with clinical blood count measurements during flares (Figure 14). Interestingly, 1176 genes were significantly decreased during flare, and pathway analysis of these genes were enriched for extracellular matrix, collagen and connective tissue development (Figure 2D and Table 2).

**[000163]** Time Series Analysis of Molecular Events Leading to RA Flares

**[000164]** To analyze the trajectories of gene expression over time and identify potential antecedents to flare, we performed time series analysis of the RNAseq data (Figure 3A). Notably, disease activity scores in the weeks just prior to flare were the same as baseline scores two months prior to flare, underscoring the challenges of identifying both a time frame and gene expression signature that is antecedent to flare. We focused the analysis on 65 samples acquired 8 weeks prior to flare and 4 weeks after flare initiation, binning samples according to the week they were drawn. This identified 2791 genes with significant differential expression over time to flare ( $FDR < 0.05$ ), and hierarchical clustering of gene expression identified five clusters (Figure 3B and Table 3).

TABLE 3

Differentially Expressed Genes

|                       |                                                                                         |
|-----------------------|-----------------------------------------------------------------------------------------|
| 27,775 genes analyzed | 2,791 genes with significant differential expression over time to flare ( $FDR < 0.5$ ) |
|-----------------------|-----------------------------------------------------------------------------------------|

**[000165]** Cluster 1 represented a group of genes which increased after symptom onset (Figure 3C and D) and was highly overlapping (Figure 3E) with genes increased in the flare versus baseline analysis (Figure 2B). These gene expression clusters were reproducibly altered in 5 separate clinical flare events (Figure 15).

**[000166]** We further focused on two clusters that were differentially expressed antecedent to flare (Figure 3C-D). Antecedent cluster 2 (AC2) transcripts increased two weeks prior to flare and were enriched with developmental pathways for naive B cells and leukocytes. Two additional means of deconvoluting the RNAseq data, CIBERSORTx and ABIS, independently confirmed evidence of B cell and T cell populations antecedent to flare, and all analyses showed evidence of innate inflammatory signatures (neutrophils and monocytes) during flare (Figures 16-17).

**[000167]** Antecedent cluster 3 (AC3) transcripts increased the week prior to flare and then decreased for the duration of flare (Figure 3C and D). AC3 was enriched for pathways not typical of blood samples, including cartilage morphogenesis, endochondral bone growth, and extracellular matrix organization (Figure 3E and Table 4), suggesting the presence of an uncharacterized cell type, a mesenchymal cell.

TABLE 4

| go.id      | Term                                      | N    | fdr.DE1     | fdr.DE2     | fdr.DE3  | fdr.DE4     | fdr.DE5     |
|------------|-------------------------------------------|------|-------------|-------------|----------|-------------|-------------|
| GO:0032501 | multicellular organismal process          | 7510 | 0.33779658  | 0.996446813 | 1.90E-13 | 0.18155513  | 0.996446813 |
| GO:0009887 | animal organ morphogenesis                | 982  | 1           | 1           | 2.60E-09 | 0.426866243 | 1           |
| GO:0009653 | anatomical structure morphogenesis        | 2604 | 0.017009962 | 0.739725387 | 3.66E-08 | 0.089707123 | 0.890858017 |
| GO:0048468 | cell development                          | 2093 | 0.325922506 | 0.824909599 | 4.99E-08 | 0.826157616 | 1           |
| GO:0007275 | multicellular organism development        | 5330 | 0.646941518 | 0.106039186 | 4.42E-07 | 0.016979265 | 0.129190893 |
| GO:0048856 | anatomical structure development          | 5810 | 0.111685048 | 0.184216961 | 5.65E-07 | 0.026184522 | 0.332210519 |
| GO:0030154 | cell differentiation                      | 4100 | 0.314553949 | 0.088217999 | 6.95E-07 | 0.437802459 | 0.771708045 |
| GO:0032502 | developmental process                     | 6212 | 0.143287026 | 0.135556704 | 7.02E-07 | 0.017411509 | 0.228640051 |
| GO:0007399 | nervous system development                | 2296 | 0.818972317 | 0.660623511 | 1.57E-06 | 0.179563884 | 1           |
| GO:0043269 | regulation of ion transport               | 660  | 1           | 1           | 1.82E-06 | 1           | 1           |
| GO:0048869 | cellular developmental process            | 4282 | 0.131591479 | 0.07488625  | 3.00E-06 | 0.474081007 | 0.996446813 |
| GO:0060536 | cartilage morphogenesis                   | 29   | 1           | 1           | 3.34E-06 | 1           | 1           |
| GO:0048731 | system development                        | 4783 | 0.739725387 | 0.088328136 | 3.53E-06 | 0.025908171 | 0.266607283 |
| GO:0034220 | ion transmembrane transport               | 1122 | 1           | 1           | 3.55E-06 | 1           | 1           |
| GO:0048729 | tissue morphogenesis                      | 612  | 0.996446813 | 1           | 6.32E-06 | 1           | 1           |
| GO:0006811 | ion transport                             | 1638 | 1           | 1           | 6.53E-06 | 1           | 1           |
| GO:0006812 | cation transport                          | 1128 | 1           | 1           | 9.04E-06 | 1           | 1           |
| GO:0098660 | inorganic ion transmembrane transport     | 824  | 1           | 1           | 9.45E-06 | 1           | 1           |
| GO:0003008 | system process                            | 2148 | 1           | 1           | 9.57E-06 | 1           | 1           |
| GO:0034765 | regulation of ion transmembrane transport | 454  | 1           | 1           | 1.87E-05 | 1           | 1           |
| GO:0003414 | chondrocyte morphogenesis involved in     | 18   | 1           | 1           | 1.93E-05 | 1           | 1           |

|            |                                                                         |      |             |             |             |             |             |
|------------|-------------------------------------------------------------------------|------|-------------|-------------|-------------|-------------|-------------|
|            | endochondral bone morphogenesis                                         |      |             |             |             |             |             |
| GO:0003429 | growth plate cartilage chondrocyte morphogenesis                        | 18   | 1           | 1           | 1.93E-05    | 1           | 1           |
| GO:0090171 | chondrocyte morphogenesis                                               | 18   | 1           | 1           | 1.93E-05    | 1           | 1           |
| GO:0030001 | metal ion transport                                                     | 858  | 0.616825534 | 1           | 2.52E-05    | 1           | 1           |
| GO:0003422 | growth plate cartilage morphogenesis                                    | 19   | 1           | 1           | 2.83E-05    | 1           | 1           |
| GO:0022008 | neurogenesis                                                            | 1555 | 0.665596251 | 1           | 3.83E-05    | 0.139859641 | 1           |
| GO:0007155 | cell adhesion                                                           | 1390 | 0.001076518 | 1           | 4.21E-05    | 0.598967854 | 1           |
| GO:0048699 | generation of neurons                                                   | 1459 | 0.650883021 | 1           | 4.35E-05    | 0.280105182 | 1           |
| GO:0022610 | biological adhesion                                                     | 1398 | 0.001270754 | 1           | 5.07E-05    | 0.445725934 | 1           |
| GO:0034762 | regulation of transmembrane transport                                   | 535  | 1           | 1           | 5.53E-05    | 1           | 1           |
| GO:0055085 | transmembrane transport                                                 | 1514 | 1           | 1           | 6.85E-05    | 1           | 1           |
| GO:0030182 | neuron differentiation                                                  | 1317 | 0.768500111 | 1           | 7.84E-05    | 0.415235372 | 1           |
| GO:0003416 | endochondral bone growth                                                | 43   | 1           | 1           | 8.11E-05    | 1           | 1           |
| GO:0003433 | chondrocyte development involved in endochondral bone morphogenesis     | 23   | 1           | 1           | 0.000111249 | 1           | 1           |
| GO:0098868 | bone growth                                                             | 45   | 1           | 1           | 0.000118729 | 1           | 1           |
| GO:0032989 | cellular component morphogenesis                                        | 1079 | 0.019925787 | 0.99915203  | 0.000144687 | 0.890858017 | 0.757703978 |
| GO:0003418 | growth plate cartilage chondrocyte differentiation                      | 24   | 1           | 1           | 0.000151713 | 1           | 1           |
| GO:0003417 | growth plate cartilage development                                      | 36   | 1           | 1           | 0.000217688 | 1           | 1           |
| GO:0007268 | chemical synaptic transmission                                          | 690  | 0.480223653 | 1           | 0.000225474 | 0.324979313 | 1           |
| GO:0098916 | anterograde trans-synaptic signaling                                    | 690  | 0.480223653 | 1           | 0.000225474 | 0.324979313 | 1           |
| GO:0006814 | sodium ion transport                                                    | 215  | 1           | 1           | 0.00025748  | 1           | 1           |
| GO:0099537 | trans-synaptic signaling                                                | 698  | 0.517697406 | 1           | 0.000288644 | 0.347784599 | 1           |
| GO:0099536 | synaptic signaling                                                      | 703  | 0.275739603 | 1           | 0.000337001 | 0.357514166 | 1           |
| GO:0009888 | tissue development                                                      | 1961 | 1           | 1           | 0.000413598 | 1           | 1           |
| GO:0050954 | sensory perception of mechanical stimulus                               | 161  | 1           | 1           | 0.000527109 | 1           | 1           |
| GO:0003413 | chondrocyte differentiation involved in endochondral bone morphogenesis | 29   | 1           | 1           | 0.000545066 | 1           | 1           |
| GO:0007605 | sensory perception of sound                                             | 142  | 1           | 1           | 0.000581084 | 1           | 1           |
| GO:0032879 | regulation of localization                                              | 2746 | 4.21E-05    | 1           | 0.000674069 | 1           | 1           |
| GO:0060350 | endochondral bone morphogenesis                                         | 71   | 1           | 0.901231612 | 0.000675474 | 1           | 1           |
| GO:0098655 | cation transmembrane transport                                          | 827  | 1           | 1           | 0.00080515  | 1           | 1           |
| GO:2001223 | negative regulation of neuron migration                                 | 12   | 1           | 1           | 0.00080515  | 1           | 1           |

|            |                                                                   |      |             |             |             |             |             |
|------------|-------------------------------------------------------------------|------|-------------|-------------|-------------|-------------|-------------|
| GO:0000904 | cell morphogenesis involved in differentiation                    | 712  | 0.890858017 | 0.965146807 | 0.001032945 | 0.616825534 | 0.410213141 |
| GO:0002063 | chondrocyte development                                           | 45   | 1           | 1           | 0.001076518 | 1           | 1           |
| GO:0048513 | animal organ development                                          | 3455 | 1           | 0.063098951 | 0.00108333  | 0.745168516 | 0.665596251 |
| GO:0060349 | bone morphogenesis                                                | 111  | 1           | 0.469843251 | 0.00108657  | 1           | 1           |
| GO:0060351 | cartilage development involved in endochondral bone morphogenesis | 46   | 1           | 1           | 0.001251135 | 1           | 1           |
| GO:0000902 | cell morphogenesis                                                | 980  | 0.022949891 | 1           | 0.001401799 | 0.797071186 | 0.796314167 |
| GO:0007267 | cell-cell signaling                                               | 1584 | 0.543286651 | 1           | 0.001964875 | 0.171334526 | 1           |
| GO:0015672 | monovalent inorganic cation transport                             | 526  | 1           | 1           | 0.002079582 | 1           | 1           |
| GO:0098662 | inorganic cation transmembrane transport                          | 739  | 1           | 1           | 0.002079582 | 1           | 1           |
| GO:0044703 | multi-organism reproductive process                               | 1004 | 1           | 1           | 0.002354643 | 1           | 1           |
| GO:0048666 | neuron development                                                | 1071 | 0.745168516 | 1           | 0.002354643 | 0.489378401 | 1           |
| GO:0042391 | regulation of membrane potential                                  | 424  | 1           | 1           | 0.003216776 | 0.716801532 | 1           |
| GO:0006936 | muscle contraction                                                | 351  | 0.357514166 | 1           | 0.004649326 | 1           | 1           |
| GO:0048589 | developmental growth                                              | 646  | 1           | 1           | 0.004771785 | 1           | 1           |
| GO:0051049 | regulation of transport                                           | 1806 | 0.0059057   | 1           | 0.006500421 | 1           | 1           |
| GO:1904062 | regulation of cation transmembrane transport                      | 314  | 1           | 1           | 0.008881305 | 1           | 1           |
| GO:0048705 | skeletal system morphogenesis                                     | 236  | 1           | 1           | 0.009182742 | 0.996446813 | 1           |
| GO:0032412 | regulation of ion transmembrane transporter activity              | 238  | 1           | 1           | 0.009921143 | 1           | 1           |
| GO:0031175 | neuron projection development                                     | 941  | 0.594734994 | 1           | 0.010301477 | 0.317513419 | 1           |
| GO:0007389 | pattern specification process                                     | 434  | 1           | 1           | 0.011108198 | 1           | 1           |
| GO:0030198 | extracellular matrix organization                                 | 348  | 1           | 1           | 0.011108198 | 1           | 1           |
| GO:0098656 | anion transmembrane transport                                     | 268  | 1           | 1           | 0.011788736 | 1           | 1           |
| GO:0048812 | neuron projection morphogenesis                                   | 621  | 1           | 1           | 0.012239952 | 0.507490051 | 0.717048855 |
| GO:0032990 | cell part morphogenesis                                           | 655  | 1           | 1           | 0.01290706  | 0.646941518 | 0.802166171 |
| GO:0022898 | regulation of transmembrane transporter activity                  | 245  | 1           | 1           | 0.013282485 | 1           | 1           |
| GO:0007160 | cell-matrix adhesion                                              | 222  | 0.005606843 | 1           | 0.014820961 | 1           | 1           |
| GO:0022414 | reproductive process                                              | 1423 | 1           | 1           | 0.015397049 | 1           | 1           |
| GO:0072025 | distal convoluted tubule development                              | 5    | 1           | 1           | 0.015849029 | 1           | 1           |
| GO:0072221 | metanephric distal convoluted tubule development                  | 5    | 1           | 1           | 0.015849029 | 1           | 1           |
| GO:0000003 | reproduction                                                      | 1426 | 1           | 1           | 0.015996351 | 1           | 1           |
| GO:0002009 | morphogenesis of an epithelium                                    | 479  | 1           | 1           | 0.016789679 | 1           | 1           |

|            |                                                                                  |      |             |             |             |             |             |
|------------|----------------------------------------------------------------------------------|------|-------------|-------------|-------------|-------------|-------------|
| GO:0120039 | plasma membrane<br>bounded cell<br>projection<br>morphogenesis                   | 635  | 1           | 1           | 0.016801155 | 0.56362124  | 0.745168516 |
| GO:0048858 | cell projection<br>morphogenesis                                                 | 636  | 1           | 1           | 0.017059196 | 0.568448591 | 0.745168516 |
| GO:0017156 | calcium ion regulated<br>exocytosis                                              | 153  | 1           | 0.996446813 | 0.017665674 | 1           | 1           |
| GO:0098661 | inorganic anion<br>transmembrane<br>transport                                    | 110  | 1           | 1           | 0.019146167 | 1           | 1           |
| GO:0007215 | glutamate receptor<br>signaling pathway                                          | 90   | 1           | 1           | 0.019925787 | 0.665596251 | 1           |
| GO:0035249 | synaptic transmission,<br>glutamatergic                                          | 90   | 1           | 1           | 0.019925787 | 1           | 1           |
| GO:0050877 | nervous system<br>process                                                        | 1406 | 1           | 1           | 0.019979972 | 1           | 1           |
| GO:0003012 | muscle system process                                                            | 456  | 0.371617002 | 1           | 0.020005602 | 1           | 1           |
| GO:1901018 | positive regulation of<br>potassium ion<br>transmembrane<br>transporter activity | 24   | 1           | 1           | 0.020370955 | 1           | 1           |
| GO:0060429 | epithelium<br>development                                                        | 1227 | 1           | 1           | 0.020590857 | 1           | 1           |
| GO:0007417 | central nervous system<br>development                                            | 948  | 1           | 0.996446813 | 0.021561593 | 0.922242032 | 1           |
| GO:0051216 | cartilage development                                                            | 206  | 1           | 1           | 0.021561593 | 0.78080559  | 1           |
| GO:0019226 | transmission of nerve<br>impulse                                                 | 72   | 1           | 1           | 0.022053268 | 1           | 1           |
| GO:0051179 | localization                                                                     | 6555 | 4.55E-10    | 1           | 0.022789146 | 0.56362124  | 1           |
| GO:0032409 | regulation of<br>transporter activity                                            | 260  | 1           | 1           | 0.022963874 | 1           | 1           |
| GO:0060348 | bone development                                                                 | 208  | 1           | 0.489378401 | 0.023314211 | 1           | 1           |
| GO:0030048 | actin filament-based<br>movement                                                 | 136  | 1           | 1           | 0.023984508 | 1           | 1           |
| GO:0030049 | muscle filament<br>sliding                                                       | 39   | 1           | 1           | 0.024126389 | 1           | 1           |
| GO:0033275 | actin-myosin filament<br>sliding                                                 | 39   | 1           | 1           | 0.024126389 | 1           | 1           |
| GO:0070252 | actin-mediated cell<br>contraction                                               | 114  | 1           | 1           | 0.024126389 | 1           | 1           |
| GO:2001222 | regulation of neuron<br>migration                                                | 39   | 1           | 1           | 0.024126389 | 1           | 1           |
| GO:0061448 | connective tissue<br>development                                                 | 263  | 1           | 1           | 0.02536056  | 0.219616377 | 1           |
| GO:2001257 | regulation of cation<br>channel activity                                         | 162  | 1           | 1           | 0.026700112 | 1           | 1           |
| GO:0007423 | sensory organ<br>development                                                     | 532  | 1           | 1           | 0.027749721 | 1           | 1           |
| GO:0002062 | chondrocyte<br>differentiation                                                   | 117  | 1           | 1           | 0.0280421   | 1           | 1           |
| GO:0044057 | regulation of system<br>process                                                  | 569  | 0.278182469 | 1           | 0.031028127 | 1           | 1           |
| GO:0001501 | skeletal system<br>development                                                   | 506  | 1           | 0.823129385 | 0.031162918 | 1           | 0.996446813 |
| GO:1903818 | positive regulation of<br>voltage-gated<br>potassium channel<br>activity         | 15   | 1           | 1           | 0.031196003 | 1           | 1           |
| GO:0098742 | cell-cell adhesion via<br>plasma-membrane<br>adhesion molecules                  | 270  | 1           | 1           | 0.03127218  | 1           | 1           |
| GO:0007269 | neurotransmitter<br>secretion                                                    | 167  | 1           | 1           | 0.032811717 | 1           | 1           |
| GO:0099643 | signal release from                                                              | 167  | 1           | 1           | 0.032811717 | 1           | 1           |

|            |                                                           |      |             |             |             |             |   |
|------------|-----------------------------------------------------------|------|-------------|-------------|-------------|-------------|---|
|            | synapse                                                   |      |             |             |             |             |   |
| GO:0050804 | modulation of chemical synaptic transmission              | 418  | 0.844000933 | 1           | 0.034515558 | 0.102842968 | 1 |
| GO:0099177 | regulation of trans-synaptic signaling                    | 419  | 0.857332482 | 1           | 0.035278512 | 0.10434846  | 1 |
| GO:0035265 | organ growth                                              | 195  | 1           | 1           | 0.037148224 | 1           | 1 |
| GO:0044706 | multi-multicellular organism process                      | 221  | 1           | 1           | 0.037148224 | 1           | 1 |
| GO:0021537 | telencephalon development                                 | 248  | 1           | 1           | 0.037418398 | 1           | 1 |
| GO:0016079 | synaptic vesicle exocytosis                               | 123  | 1           | 1           | 0.038417362 | 1           | 1 |
| GO:0051960 | regulation of nervous system development                  | 883  | 0.107843848 | 1           | 0.039675644 | 0.335240873 | 1 |
| GO:0072235 | metanephric distal tubule development                     | 7    | 1           | 1           | 0.039896554 | 1           | 1 |
| GO:0120036 | plasma membrane bounded cell projection organization      | 1462 | 0.430289651 | 1           | 0.040423722 | 0.184216961 | 1 |
| GO:0060537 | muscle tissue development                                 | 395  | 1           | 1           | 0.041122974 | 1           | 1 |
| GO:0043062 | extracellular structure organization                      | 402  | 1           | 1           | 0.04968339  | 1           | 1 |
| GO:0006928 | movement of cell or subcellular component                 | 2138 | 8.70E-05    | 1           | 0.052850381 | 0.108871927 | 1 |
| GO:0030029 | actin filament-based process                              | 732  | 0.028430549 | 1           | 0.055807618 | 1           | 1 |
| GO:0065008 | regulation of biological quality                          | 3891 | 1.72E-06    | 1           | 0.092517809 | 0.598967854 | 1 |
| GO:0031589 | cell-substrate adhesion                                   | 338  | 0.004206765 | 1           | 0.093681736 | 0.890858017 | 1 |
| GO:0051239 | regulation of multicellular organismal process            | 3093 | 2.64E-05    | 0.748743161 | 0.123095655 | 0.575098872 | 1 |
| GO:2000026 | regulation of multicellular organismal development        | 2064 | 0.030521352 | 0.966211545 | 0.211865167 | 0.24144412  | 1 |
| GO:0007154 | cell communication                                        | 6522 | 1.26E-09    | 1           | 0.2315925   | 0.035576453 | 1 |
| GO:0048167 | regulation of synaptic plasticity                         | 173  | 0.756136312 | 1           | 0.247322371 | 0.025766984 | 1 |
| GO:0009612 | response to mechanical stimulus                           | 204  | 0.016589491 | 1           | 0.264413515 | 1           | 1 |
| GO:0048646 | anatomical structure formation involved in morphogenesis  | 1151 | 0.017059196 | 0.665596251 | 0.278694883 | 0.131591479 | 1 |
| GO:0007166 | cell surface receptor signaling pathway                   | 2974 | 2.22E-07    | 0.664638292 | 0.280083899 | 0.024       | 1 |
| GO:0050793 | regulation of developmental process                       | 2607 | 0.00358275  | 0.489378401 | 0.299390486 | 0.136920059 | 1 |
| GO:0045944 | positive regulation of transcription by RNA polymerase II | 1181 | 1           | 0.028430549 | 0.358787418 | 1           | 1 |
| GO:0006937 | regulation of muscle contraction                          | 164  | 0.004919038 | 1           | 0.405813243 | 1           | 1 |
| GO:0006810 | transport                                                 | 5065 | 6.95E-11    | 1           | 0.455598256 | 1           | 1 |
| GO:0022603 | regulation of anatomical structure morphogenesis          | 1098 | 0.027537974 | 0.80941255  | 0.48419276  | 0.376392302 | 1 |
| GO:0023052 | signaling                                                 | 6475 | 5.74E-10    | 1           | 0.489378401 | 0.028424743 | 1 |
| GO:0060284 | regulation of cell development                            | 910  | 0.043655125 | 1           | 0.490789374 | 0.61494051  | 1 |

|            |                                                                           |      |             |             |             |             |             |
|------------|---------------------------------------------------------------------------|------|-------------|-------------|-------------|-------------|-------------|
| GO:0051234 | establishment of localization                                             | 5179 | 1.10E-10    | 1           | 0.491060511 | 1           | 1           |
| GO:0051270 | regulation of cellular component movement                                 | 1052 | 0.001076518 | 1           | 0.604011244 | 1           | 1           |
| GO:0031644 | regulation of neurological system process                                 | 127  | 1           | 1           | 0.649678872 | 0.017681195 | 1           |
| GO:0051240 | positive regulation of multicellular organismal process                   | 1753 | 0.000807618 | 1           | 0.664849722 | 1           | 1           |
| GO:0001568 | blood vessel development                                                  | 756  | 0.027692049 | 1           | 0.665596251 | 0.190308867 | 1           |
| GO:0072358 | cardiovascular system development                                         | 799  | 0.039048021 | 1           | 0.670434263 | 0.08846971  | 1           |
| GO:0048518 | positive regulation of biological process                                 | 6054 | 2.12E-09    | 0.078665529 | 0.745168516 | 0.670434263 | 1           |
| GO:0010574 | regulation of vascular endothelial growth factor production               | 32   | 0.006085233 | 1           | 0.762819911 | 1           | 1           |
| GO:0050896 | response to stimulus                                                      | 9106 | 1.30E-09    | 0.767683656 | 0.762982012 | 0.125702334 | 1           |
| GO:0001944 | vasculature development                                                   | 790  | 0.032663645 | 1           | 0.778782489 | 0.263544992 | 1           |
| GO:0043410 | positive regulation of MAPK cascade                                       | 562  | 0.000386618 | 1           | 0.794945764 | 1           | 1           |
| GO:0010573 | vascular endothelial growth factor production                             | 34   | 0.008756837 | 1           | 0.823129385 | 1           | 1           |
| GO:0045595 | regulation of cell differentiation                                        | 1788 | 0.004325196 | 1           | 0.877494832 | 0.996446813 | 1           |
| GO:1903523 | negative regulation of blood circulation                                  | 36   | 0.012075239 | 1           | 0.890858017 | 1           | 1           |
| GO:0045893 | positive regulation of transcription, DNA-templated                       | 1511 | 1           | 0.00087738  | 0.918797783 | 1           | 1           |
| GO:1902680 | positive regulation of RNA biosynthetic process                           | 1597 | 1           | 0.00087738  | 0.922242032 | 1           | 1           |
| GO:1903508 | positive regulation of nucleic acid-templated transcription               | 1596 | 1           | 0.00086646  | 0.922242032 | 1           | 1           |
| GO:0002223 | stimulatory C-type lectin receptor signaling pathway                      | 65   | 0.017009962 | 1           | 0.972458544 | 1           | 1           |
| GO:0010628 | positive regulation of gene expression                                    | 1957 | 1           | 0.004755649 | 0.995169577 | 1           | 1           |
| GO:0040011 | locomotion                                                                | 1909 | 2.16E-05    | 1           | 0.995169577 | 0.474177846 | 1           |
| GO:0002220 | innate immune response activating cell surface receptor signaling pathway | 68   | 0.022623601 | 1           | 0.996446813 | 1           | 1           |
| GO:0010646 | regulation of cell communication                                          | 3532 | 3.18E-07    | 0.996446813 | 0.996446813 | 0.007264557 | 1           |
| GO:0048514 | blood vessel morphogenesis                                                | 677  | 0.026184522 | 1           | 0.996446813 | 0.161086801 | 1           |
| GO:0071495 | cellular response to endogenous stimulus                                  | 1373 | 0.011622623 | 0.308597466 | 0.996446813 | 1           | 0.161929325 |
| GO:0000122 | negative regulation of transcription by RNA polymerase II                 | 835  | 1           | 4.26E-10    | 1           | 1           | 1           |
| GO:0000165 | MAPK cascade                                                              | 926  | 0.000542536 | 1           | 1           | 1           | 1           |
| GO:0000186 | activation of MAPKK activity                                              | 52   | 0.000574544 | 1           | 1           | 1           | 1           |
| GO:0000271 | polysaccharide biosynthetic process                                       | 74   | 0.009838404 | 1           | 1           | 1           | 1           |
| GO:0000272 | polysaccharide catabolic process                                          | 23   | 0.007542869 | 1           | 1           | 1           | 1           |

|            |                                                                    |      |             |             |   |             |             |
|------------|--------------------------------------------------------------------|------|-------------|-------------|---|-------------|-------------|
| GO:0001525 | angiogenesis                                                       | 587  | 0.009359443 | 1           | 1 | 0.211865167 | 1           |
| GO:0001702 | gastrulation with mouth forming second                             | 28   | 1           | 1           | 1 | 1           | 0.007070407 |
| GO:0001774 | microglial cell activation                                         | 33   | 0.007271618 | 1           | 1 | 1           | 1           |
| GO:0001775 | cell activation                                                    | 1407 | 9.24E-23    | 0.890858017 | 1 | 1           | 1           |
| GO:0001776 | leukocyte homeostasis                                              | 88   | 0.03127218  | 1           | 1 | 1           | 1           |
| GO:0001780 | neutrophil homeostasis                                             | 16   | 0.012199993 | 1           | 1 | 1           | 1           |
| GO:0001816 | cytokine production                                                | 716  | 8.54E-07    | 0.243930235 | 1 | 1           | 1           |
| GO:0001817 | regulation of cytokine production                                  | 647  | 9.86E-06    | 0.457630758 | 1 | 1           | 1           |
| GO:0001819 | positive regulation of cytokine production                         | 422  | 0.000246192 | 1           | 1 | 1           | 1           |
| GO:0001932 | regulation of protein phosphorylation                              | 1427 | 3.03E-07    | 1           | 1 | 1           | 1           |
| GO:0001934 | positive regulation of protein phosphorylation                     | 1008 | 1.75E-07    | 1           | 1 | 1           | 1           |
| GO:0002218 | activation of innate immune response                               | 252  | 3.46E-05    | 1           | 1 | 1           | 1           |
| GO:0002221 | pattern recognition receptor signaling pathway                     | 179  | 0.004057705 | 1           | 1 | 1           | 1           |
| GO:0002224 | toll-like receptor signaling pathway                               | 131  | 0.01844494  | 1           | 1 | 1           | 1           |
| GO:0002237 | response to molecule of bacterial origin                           | 337  | 0.000205114 | 1           | 1 | 1           | 1           |
| GO:0002244 | hematopoietic progenitor cell differentiation                      | 111  | 1           | 0.002200796 | 1 | 1           | 1           |
| GO:0002252 | immune effector process                                            | 1246 | 7.83E-19    | 1           | 1 | 1           | 1           |
| GO:0002253 | activation of immune response                                      | 645  | 4.02E-06    | 1           | 1 | 1           | 1           |
| GO:0002262 | myeloid cell homeostasis                                           | 146  | 0.041941486 | 0.025357726 | 1 | 1           | 1           |
| GO:0002263 | cell activation involved in immune response                        | 701  | 2.15E-17    | 1           | 1 | 1           | 1           |
| GO:0002269 | leukocyte activation involved in inflammatory response             | 33   | 0.007271618 | 1           | 1 | 1           | 1           |
| GO:0002274 | myeloid leukocyte activation                                       | 638  | 9.90E-23    | 1           | 1 | 1           | 1           |
| GO:0002275 | myeloid cell activation involved in immune response                | 540  | 3.02E-20    | 1           | 1 | 1           | 1           |
| GO:0002283 | neutrophil activation involved in immune response                  | 488  | 6.49E-20    | 1           | 1 | 1           | 1           |
| GO:0002366 | leukocyte activation involved in immune response                   | 697  | 1.62E-17    | 1           | 1 | 1           | 1           |
| GO:0002367 | cytokine production involved in immune response                    | 95   | 0.016140011 | 1           | 1 | 1           | 1           |
| GO:0002376 | immune system process                                              | 3074 | 1.22E-20    | 0.892839413 | 1 | 1           | 1           |
| GO:0002429 | immune response-activating cell surface receptor signaling pathway | 414  | 0.006508093 | 1           | 1 | 1           | 1           |
| GO:0002443 | leukocyte mediated immunity                                        | 868  | 9.50E-17    | 1           | 1 | 1           | 1           |

|            |                                                                    |      |             |             |   |             |             |
|------------|--------------------------------------------------------------------|------|-------------|-------------|---|-------------|-------------|
| GO:0002444 | myeloid leukocyte mediated immunity                                | 548  | 5.49E-20    | 1           | 1 | 1           | 1           |
| GO:0002446 | neutrophil mediated immunity                                       | 499  | 5.03E-20    | 1           | 1 | 1           | 1           |
| GO:0002520 | immune system development                                          | 912  | 0.009644361 | 0.000500171 | 1 | 1           | 0.405813243 |
| GO:0002521 | leukocyte differentiation                                          | 501  | 0.212378102 | 0.017749668 | 1 | 1           | 1           |
| GO:0002576 | platelet degranulation                                             | 128  | 1.37E-05    | 1           | 1 | 1           | 1           |
| GO:0002682 | regulation of immune system process                                | 1545 | 1.30E-09    | 1           | 1 | 1           | 1           |
| GO:0002684 | positive regulation of immune system process                       | 1098 | 1.33E-08    | 1           | 1 | 1           | 1           |
| GO:0002685 | regulation of leukocyte migration                                  | 180  | 0.013038389 | 1           | 1 | 1           | 1           |
| GO:0002687 | positive regulation of leukocyte migration                         | 121  | 0.009448392 | 0.931021722 | 1 | 1           | 1           |
| GO:0002688 | regulation of leukocyte chemotaxis                                 | 109  | 0.013452901 | 1           | 1 | 1           | 1           |
| GO:0002697 | regulation of immune effector process                              | 439  | 0.029881063 | 1           | 1 | 1           | 1           |
| GO:0002704 | negative regulation of leukocyte mediated immunity                 | 45   | 0.037418398 | 1           | 1 | 1           | 1           |
| GO:0002718 | regulation of cytokine production involved in immune response      | 77   | 0.046629493 | 0.997059037 | 1 | 1           | 1           |
| GO:0002755 | MyD88-dependent toll-like receptor signaling pathway               | 36   | 0.001691861 | 1           | 1 | 1           | 1           |
| GO:0002757 | immune response-activating signal transduction                     | 568  | 1.34E-05    | 1           | 1 | 1           | 1           |
| GO:0002758 | innate immune response-activating signal transduction              | 233  | 0.000110092 | 1           | 1 | 1           | 1           |
| GO:0002764 | immune response-regulating signaling pathway                       | 599  | 8.40E-06    | 1           | 1 | 1           | 1           |
| GO:0002768 | immune response-regulating cell surface receptor signaling pathway | 445  | 0.003916178 | 1           | 1 | 1           | 1           |
| GO:0002790 | peptide secretion                                                  | 582  | 0.028669624 | 1           | 1 | 1           | 1           |
| GO:0005976 | polysaccharide metabolic process                                   | 109  | 0.003588731 | 1           | 1 | 1           | 1           |
| GO:0006022 | aminoglycan metabolic process                                      | 167  | 0.01778747  | 0.870337648 | 1 | 1           | 1           |
| GO:0006139 | nucleobase-containing compound metabolic process                   | 6264 | 1           | 0.002380221 | 1 | 1           | 1           |
| GO:0006351 | transcription, DNA-templated                                       | 3600 | 1           | 5.47E-06    | 1 | 1           | 1           |
| GO:0006355 | regulation of transcription, DNA-templated                         | 3445 | 1           | 3.35E-06    | 1 | 1           | 1           |
| GO:0006357 | regulation of transcription by RNA polymerase II                   | 2632 | 1           | 6.40E-06    | 1 | 1           | 1           |
| GO:0006366 | transcription by RNA polymerase II                                 | 2768 | 1           | 8.50E-06    | 1 | 1           | 1           |
| GO:0006464 | cellular protein modification process                              | 4066 | 1.66E-05    | 0.93115264  | 1 | 1           | 1           |
| GO:0006468 | protein phosphorylation                                            | 1910 | 1.14E-06    | 1           | 1 | 0.635655637 | 1           |

|            |                                                                  |       |             |             |   |             |             |
|------------|------------------------------------------------------------------|-------|-------------|-------------|---|-------------|-------------|
| GO:0006629 | lipid metabolic process                                          | 1415  | 0.034515558 | 1           | 1 | 1           | 1           |
| GO:0006725 | cellular aromatic compound metabolic process                     | 6467  | 1           | 0.008831261 | 1 | 1           | 1           |
| GO:0006793 | phosphorus metabolic process                                     | 3236  | 1.32E-06    | 1           | 1 | 1           | 1           |
| GO:0006796 | phosphate-containing compound metabolic process                  | 3209  | 7.74E-07    | 1           | 1 | 1           | 1           |
| GO:0006826 | iron ion transport                                               | 61    | 0.044765835 | 1           | 1 | 1           | 1           |
| GO:0006886 | intracellular protein transport                                  | 1126  | 0.006155434 | 1           | 1 | 1           | 1           |
| GO:0006887 | exocytosis                                                       | 897   | 1.08E-23    | 1           | 1 | 1           | 1           |
| GO:0006897 | endocytosis                                                      | 783   | 2.44E-05    | 1           | 1 | 1           | 1           |
| GO:0006909 | phagocytosis                                                     | 342   | 0.011958563 | 1           | 1 | 1           | 1           |
| GO:0006914 | autophagy                                                        | 466   | 0.003701303 | 1           | 1 | 1           | 1           |
| GO:0006915 | apoptotic process                                                | 1966  | 0.001910279 | 1           | 1 | 1           | 1           |
| GO:0006935 | chemotaxis                                                       | 619   | 0.01174754  | 1           | 1 | 1           | 1           |
| GO:0006940 | regulation of smooth muscle contraction                          | 62    | 0.049426883 | 1           | 1 | 1           | 1           |
| GO:0006950 | response to stress                                               | 3908  | 5.50E-12    | 1           | 1 | 1           | 1           |
| GO:0006952 | defense response                                                 | 1658  | 5.06E-10    | 1           | 1 | 1           | 1           |
| GO:0006954 | inflammatory response                                            | 780   | 4.60E-06    | 1           | 1 | 1           | 1           |
| GO:0006955 | immune response                                                  | 2183  | 1.32E-19    | 1           | 1 | 1           | 1           |
| GO:0007159 | leukocyte cell-cell adhesion                                     | 327   | 0.002534667 | 1           | 1 | 1           | 1           |
| GO:0007165 | signal transduction                                              | 6031  | 1.51E-09    | 1           | 1 | 0.0521109   | 1           |
| GO:0007169 | transmembrane receptor protein tyrosine kinase signaling pathway | 694   | 0.006256544 | 1           | 1 | 0.996446813 | 1           |
| GO:0007249 | I-kappaB kinase/NF-kappaB signaling                              | 258   | 0.00466681  | 1           | 1 | 1           | 1           |
| GO:0007264 | small GTPase mediated signal transduction                        | 547   | 0.00566515  | 1           | 1 | 1           | 1           |
| GO:0007369 | gastrulation                                                     | 181   | 1           | 1           | 1 | 1           | 0.031028127 |
| GO:0007568 | aging                                                            | 311   | 1           | 0.019378819 | 1 | 1           | 1           |
| GO:0007596 | blood coagulation                                                | 334   | 1.70E-08    | 1           | 1 | 1           | 1           |
| GO:0007599 | hemostasis                                                       | 339   | 6.82E-09    | 0.901976979 | 1 | 1           | 1           |
| GO:0008104 | protein localization                                             | 2693  | 2.67E-05    | 1           | 1 | 1           | 1           |
| GO:0008152 | metabolic process                                                | 12421 | 1           | 0.031337146 | 1 | 1           | 1           |
| GO:0008154 | actin polymerization or depolymerization                         | 206   | 0.043279439 | 1           | 1 | 1           | 1           |
| GO:0008219 | cell death                                                       | 2232  | 0.003677466 | 1           | 1 | 1           | 1           |
| GO:0009056 | catabolic process                                                | 2490  | 1.66E-09    | 1           | 1 | 1           | 1           |
| GO:0009057 | macromolecule catabolic process                                  | 1346  | 9.85E-07    | 1           | 1 | 1           | 1           |
| GO:0009058 | biosynthetic process                                             | 6176  | 1           | 4.50E-06    | 1 | 1           | 1           |
| GO:0009059 | macromolecule biosynthetic process                               | 4998  | 1           | 1.65E-06    | 1 | 1           | 1           |

|            |                                                           |       |             |             |   |             |   |
|------------|-----------------------------------------------------------|-------|-------------|-------------|---|-------------|---|
| GO:0009251 | glucan catabolic process                                  | 19    | 0.024975729 | 1           | 1 | 1           | 1 |
| GO:0009267 | cellular response to starvation                           | 146   | 0.015656927 | 1           | 1 | 1           | 1 |
| GO:0009306 | protein secretion                                         | 550   | 0.024183556 | 1           | 1 | 1           | 1 |
| GO:0009605 | response to external stimulus                             | 2410  | 1.65E-09    | 1           | 1 | 1           | 1 |
| GO:0009607 | response to biotic stimulus                               | 1014  | 3.97E-08    | 1           | 1 | 1           | 1 |
| GO:0009611 | response to wounding                                      | 655   | 9.77E-07    | 1           | 1 | 0.876970475 | 1 |
| GO:0009615 | response to virus                                         | 315   | 0.000527109 | 1           | 1 | 1           | 1 |
| GO:0009617 | response to bacterium                                     | 683   | 0.000497498 | 1           | 1 | 1           | 1 |
| GO:0009636 | response to toxic substance                               | 513   | 0.03174739  | 1           | 1 | 1           | 1 |
| GO:0009889 | regulation of biosynthetic process                        | 4259  | 1           | 7.74E-06    | 1 | 1           | 1 |
| GO:0009890 | negative regulation of biosynthetic process               | 1625  | 1           | 1.64E-06    | 1 | 1           | 1 |
| GO:0009891 | positive regulation of biosynthetic process               | 1978  | 1           | 0.001496726 | 1 | 1           | 1 |
| GO:0009892 | negative regulation of metabolic process                  | 3395  | 1           | 0.026947894 | 1 | 1           | 1 |
| GO:0009893 | positive regulation of metabolic process                  | 3558  | 2.54E-05    | 0.065080058 | 1 | 0.796254883 | 1 |
| GO:0009894 | regulation of catabolic process                           | 875   | 5.35E-06    | 0.995169577 | 1 | 1           | 1 |
| GO:0009896 | positive regulation of catabolic process                  | 407   | 0.002076463 | 1           | 1 | 1           | 1 |
| GO:0009966 | regulation of signal transduction                         | 3183  | 8.98E-08    | 0.668982235 | 1 | 0.022834087 | 1 |
| GO:0009967 | positive regulation of signal transduction                | 1606  | 4.08E-09    | 1           | 1 | 1           | 1 |
| GO:0009987 | cellular process                                          | 16779 | 0.004881927 | 0.604011244 | 1 | 1           | 1 |
| GO:0009991 | response to extracellular stimulus                        | 513   | 0.03174739  | 0.520071834 | 1 | 1           | 1 |
| GO:0010033 | response to organic substance                             | 3172  | 1.22E-08    | 0.197199227 | 1 | 0.967833783 | 1 |
| GO:0010243 | response to organonitrogen compound                       | 950   | 5.79E-05    | 1           | 1 | 1           | 1 |
| GO:0010468 | regulation of gene expression                             | 4989  | 1           | 0.017606755 | 1 | 1           | 1 |
| GO:0010543 | regulation of platelet activation                         | 30    | 0.027236556 | 1           | 1 | 1           | 1 |
| GO:0010556 | regulation of macromolecule biosynthetic process          | 4041  | 1           | 3.35E-06    | 1 | 1           | 1 |
| GO:0010557 | positive regulation of macromolecule biosynthetic process | 1844  | 1           | 0.000674069 | 1 | 1           | 1 |
| GO:0010558 | negative regulation of macromolecule biosynthetic process | 1536  | 1           | 3.22E-07    | 1 | 1           | 1 |
| GO:0010562 | positive regulation of phosphorus metabolic process       | 1124  | 3.91E-07    | 1           | 1 | 1           | 1 |
| GO:0010604 | positive regulation of macromolecule metabolic process    | 3299  | 1.05E-05    | 0.09101847  | 1 | 0.665596251 | 1 |
| GO:0010605 | negative regulation of macromolecule metabolic process    | 3164  | 1           | 0.009382245 | 1 | 1           | 1 |
| GO:0010629 | negative regulation of gene expression                    | 2326  | 1           | 0.011891493 | 1 | 1           | 1 |

|            |                                                                |      |             |             |   |             |             |
|------------|----------------------------------------------------------------|------|-------------|-------------|---|-------------|-------------|
| GO:0010638 | positive regulation of organelle organization                  | 602  | 0.014166664 | 1           | 1 | 1           | 1           |
| GO:0010647 | positive regulation of cell communication                      | 1768 | 1.33E-08    | 1           | 1 | 0.957657142 | 1           |
| GO:0010720 | positive regulation of cell development                        | 529  | 0.026184522 | 1           | 1 | 1           | 1           |
| GO:0010821 | regulation of mitochondrion organization                       | 176  | 0.00334288  | 1           | 1 | 1           | 1           |
| GO:0010822 | positive regulation of mitochondrion organization              | 112  | 0.049884217 | 1           | 1 | 1           | 1           |
| GO:0010941 | regulation of cell death                                       | 1707 | 0.038843865 | 1           | 1 | 1           | 1           |
| GO:0010942 | positive regulation of cell death                              | 689  | 0.001270746 | 1           | 1 | 1           | 1           |
| GO:0010950 | positive regulation of endopeptidase activity                  | 171  | 0.022053268 | 1           | 1 | 0.933555354 | 1           |
| GO:0010952 | positive regulation of peptidase activity                      | 189  | 0.007469011 | 1           | 1 | 1           | 1           |
| GO:0012501 | programmed cell death                                          | 2099 | 0.002691077 | 1           | 1 | 1           | 1           |
| GO:0015031 | protein transport                                              | 1974 | 1.57E-05    | 1           | 1 | 1           | 1           |
| GO:0015669 | gas transport                                                  | 19   | 1           | 1           | 1 | 1           | 0.035229966 |
| GO:0015833 | peptide transport                                              | 2009 | 3.25E-05    | 1           | 1 | 1           | 1           |
| GO:0016043 | cellular component organization                                | 6334 | 0.034533479 | 0.905458796 | 1 | 0.489378401 | 0.102751857 |
| GO:0016045 | detection of bacterium                                         | 12   | 0.037418398 | 1           | 1 | 1           | 1           |
| GO:0016050 | vesicle organization                                           | 314  | 0.003665448 | 1           | 1 | 1           | 1           |
| GO:0016070 | RNA metabolic process                                          | 5106 | 1           | 0.001250472 | 1 | 1           | 1           |
| GO:0016192 | vesicle-mediated transport                                     | 2058 | 7.47E-19    | 1           | 1 | 1           | 1           |
| GO:0016310 | phosphorylation                                                | 2303 | 9.46E-06    | 1           | 1 | 1           | 1           |
| GO:0016477 | cell migration                                                 | 1537 | 1.08E-05    | 1           | 1 | 0.442735373 | 1           |
| GO:0018130 | heterocycle biosynthetic process                               | 4233 | 1           | 8.40E-06    | 1 | 1           | 1           |
| GO:0019219 | regulation of nucleobase-containing compound metabolic process | 4013 | 1           | 5.63E-06    | 1 | 1           | 1           |
| GO:0019220 | regulation of phosphate metabolic process                      | 1736 | 7.18E-07    | 1           | 1 | 1           | 1           |
| GO:0019221 | cytokine-mediated signaling pathway                            | 728  | 2.37E-07    | 1           | 1 | 1           | 1           |
| GO:0019222 | regulation of metabolic process                                | 7129 | 0.108871927 | 0.001496726 | 1 | 1           | 1           |
| GO:0019438 | aromatic compound biosynthetic process                         | 4242 | 1           | 9.45E-06    | 1 | 1           | 1           |
| GO:0019538 | protein metabolic process                                      | 5855 | 0.000885922 | 1           | 1 | 0.93226801  | 1           |
| GO:0022604 | regulation of cell morphogenesis                               | 474  | 0.040355298 | 1           | 1 | 1           | 1           |
| GO:0023014 | signal transduction by protein phosphorylation                 | 944  | 0.000451981 | 1           | 1 | 1           | 1           |
| GO:0023051 | regulation of signaling                                        | 3567 | 1.20E-07    | 0.918797783 | 1 | 0.00944828  | 1           |
| GO:0023056 | positive regulation of signaling                               | 1775 | 3.71E-09    | 1           | 1 | 0.984890815 | 1           |
| GO:0030097 | hemopoiesis                                                    | 819  | 0.034690044 | 0.000140896 | 1 | 1           | 0.686175641 |
| GO:0030098 | lymphocyte                                                     | 344  | 1           | 0.026584093 | 1 | 1           | 1           |

|            |                                                      |      |             |             |   |             |             |
|------------|------------------------------------------------------|------|-------------|-------------|---|-------------|-------------|
|            | differentiation                                      |      |             |             |   |             |             |
| GO:0030099 | myeloid cell differentiation                         | 405  | 0.04295607  | 0.134152259 | 1 | 1           | 1           |
| GO:0030100 | regulation of endocytosis                            | 260  | 0.013452901 | 1           | 1 | 1           | 1           |
| GO:0030155 | regulation of cell adhesion                          | 668  | 0.002919532 | 1           | 1 | 1           | 1           |
| GO:0030163 | protein catabolic process                            | 900  | 0.002021862 | 1           | 1 | 1           | 1           |
| GO:0030168 | platelet activation                                  | 152  | 4.20E-07    | 0.996446813 | 1 | 1           | 1           |
| GO:0030193 | regulation of blood coagulation                      | 77   | 0.002919532 | 1           | 1 | 1           | 1           |
| GO:0030213 | hyaluronan biosynthetic process                      | 13   | 0.049467321 | 0.93226801  | 1 | 1           | 1           |
| GO:0030218 | erythrocyte differentiation                          | 111  | 0.897478797 | 0.002200796 | 1 | 1           | 0.879865755 |
| GO:0030220 | platelet formation                                   | 20   | 1           | 0.023984508 | 1 | 1           | 1           |
| GO:0030334 | regulation of cell migration                         | 910  | 0.001353029 | 1           | 1 | 1           | 1           |
| GO:0030335 | positive regulation of cell migration                | 519  | 4.00E-06    | 1           | 1 | 1           | 1           |
| GO:0030593 | neutrophil chemotaxis                                | 101  | 0.007127455 | 1           | 1 | 1           | 1           |
| GO:0030595 | leukocyte chemotaxis                                 | 217  | 0.001379065 | 1           | 1 | 1           | 1           |
| GO:0030851 | granulocyte differentiation                          | 32   | 1           | 0.027161313 | 1 | 1           | 1           |
| GO:0031098 | stress-activated protein kinase signaling cascade    | 313  | 0.008881305 | 1           | 1 | 1           | 1           |
| GO:0031323 | regulation of cellular metabolic process             | 6127 | 0.000154745 | 5.63E-06    | 1 | 1           | 1           |
| GO:0031324 | negative regulation of cellular metabolic process    | 2571 | 0.231941565 | 3.05E-05    | 1 | 1           | 1           |
| GO:0031325 | positive regulation of cellular metabolic process    | 3260 | 1.46E-05    | 0.026184522 | 1 | 1           | 1           |
| GO:0031326 | regulation of cellular biosynthetic process          | 4184 | 1           | 6.54E-06    | 1 | 1           | 1           |
| GO:0031327 | negative regulation of cellular biosynthetic process | 1601 | 1           | 1.75E-06    | 1 | 1           | 1           |
| GO:0031328 | positive regulation of cellular biosynthetic process | 1943 | 1           | 0.000816714 | 1 | 1           | 1           |
| GO:0031329 | regulation of cellular catabolic process             | 765  | 6.52E-05    | 0.896075185 | 1 | 1           | 1           |
| GO:0031331 | positive regulation of cellular catabolic process    | 347  | 0.006173714 | 0.989561623 | 1 | 1           | 1           |
| GO:0031334 | positive regulation of protein complex assembly      | 259  | 0.029415629 | 0.973367399 | 1 | 1           | 1           |
| GO:0031347 | regulation of defense response                       | 765  | 5.92E-06    | 1           | 1 | 1           | 1           |
| GO:0031349 | positive regulation of defense response              | 427  | 5.88E-06    | 1           | 1 | 1           | 1           |
| GO:0031399 | regulation of protein modification process           | 1821 | 2.37E-07    | 1           | 1 | 1           | 1           |
| GO:0031401 | positive regulation of protein modification process  | 1220 | 8.58E-07    | 1           | 1 | 1           | 1           |
| GO:0031646 | positive regulation of neurological system process   | 58   | 1           | 1           | 1 | 0.009678209 | 1           |

|            |                                                           |      |             |             |   |   |             |
|------------|-----------------------------------------------------------|------|-------------|-------------|---|---|-------------|
| GO:0031663 | lipopolysaccharide-mediated signaling pathway             | 56   | 0.006197688 | 1           | 1 | 1 | 1           |
| GO:0031667 | response to nutrient levels                               | 481  | 0.026184522 | 0.675996209 | 1 | 1 | 1           |
| GO:0031668 | cellular response to extracellular stimulus               | 258  | 0.062580021 | 0.032811717 | 1 | 1 | 1           |
| GO:0031669 | cellular response to nutrient levels                      | 228  | 0.045842089 | 0.056922458 | 1 | 1 | 1           |
| GO:0032092 | positive regulation of protein binding                    | 94   | 0.048234344 | 1           | 1 | 1 | 1           |
| GO:0032101 | regulation of response to external stimulus               | 840  | 0.001513988 | 1           | 1 | 1 | 1           |
| GO:0032103 | positive regulation of response to external stimulus      | 297  | 0.024975729 | 1           | 1 | 1 | 1           |
| GO:0032147 | activation of protein kinase activity                     | 323  | 3.00E-05    | 1           | 1 | 1 | 1           |
| GO:0032268 | regulation of cellular protein metabolic process          | 2616 | 1.27E-07    | 1           | 1 | 1 | 1           |
| GO:0032269 | negative regulation of cellular protein metabolic process | 1083 | 0.033725236 | 1           | 1 | 1 | 1           |
| GO:0032270 | positive regulation of cellular protein metabolic process | 1584 | 8.98E-08    | 1           | 1 | 1 | 1           |
| GO:0032496 | response to lipopolysaccharide                            | 324  | 0.002200796 | 1           | 1 | 1 | 1           |
| GO:0032611 | interleukin-1 beta production                             | 73   | 0.033780469 | 1           | 1 | 1 | 1           |
| GO:0032612 | interleukin-1 production                                  | 87   | 0.029127228 | 1           | 1 | 1 | 1           |
| GO:0032637 | interleukin-8 production                                  | 73   | 0.001845049 | 1           | 1 | 1 | 1           |
| GO:0032640 | tumor necrosis factor production                          | 129  | 0.046405569 | 1           | 1 | 1 | 1           |
| GO:0032677 | regulation of interleukin-8 production                    | 66   | 0.000765005 | 1           | 1 | 1 | 1           |
| GO:0032680 | regulation of tumor necrosis factor production            | 127  | 0.041122974 | 1           | 1 | 1 | 1           |
| GO:0032757 | positive regulation of interleukin-8 production           | 46   | 0.000194198 | 1           | 1 | 1 | 1           |
| GO:0032760 | positive regulation of tumor necrosis factor production   | 73   | 0.033780469 | 1           | 1 | 1 | 1           |
| GO:0032774 | RNA biosynthetic process                                  | 3659 | 1           | 5.18E-06    | 1 | 1 | 1           |
| GO:0032880 | regulation of protein localization                        | 963  | 9.45E-06    | 1           | 1 | 1 | 1           |
| GO:0032940 | secretion by cell                                         | 1478 | 1.08E-23    | 1           | 1 | 1 | 1           |
| GO:0033036 | macromolecule localization                                | 3037 | 2.71E-05    | 1           | 1 | 1 | 1           |
| GO:0033043 | regulation of organelle organization                      | 1237 | 0.018565448 | 0.869543798 | 1 | 1 | 1           |
| GO:0033554 | cellular response to stress                               | 1928 | 0.000334829 | 1           | 1 | 1 | 1           |
| GO:0033674 | positive regulation of kinase activity                    | 552  | 1.79E-09    | 1           | 1 | 1 | 1           |
| GO:0034097 | response to cytokine                                      | 1114 | 1.30E-07    | 1           | 1 | 1 | 1           |
| GO:0034101 | erythrocyte homeostasis                                   | 120  | 1           | 0.004673466 | 1 | 1 | 0.940589364 |
| GO:0034109 | homotypic cell-cell adhesion                              | 76   | 0.04283723  | 0.996446813 | 1 | 1 | 1           |

|            |                                                             |      |             |             |   |             |             |
|------------|-------------------------------------------------------------|------|-------------|-------------|---|-------------|-------------|
| GO:0034123 | positive regulation of toll-like receptor signaling pathway | 22   | 0.043674424 | 1           | 1 | 1           | 1           |
| GO:0034134 | toll-like receptor 2 signaling pathway                      | 16   | 0.000949328 | 1           | 1 | 1           | 1           |
| GO:0034135 | regulation of toll-like receptor 2 signaling pathway        | 11   | 0.027946094 | 1           | 1 | 1           | 1           |
| GO:0034198 | cellular response to amino acid starvation                  | 45   | 0.037418398 | 1           | 1 | 1           | 1           |
| GO:0034504 | protein localization to nucleus                             | 269  | 0.042659462 | 1           | 1 | 1           | 1           |
| GO:0034613 | cellular protein localization                               | 1830 | 0.000731018 | 1           | 1 | 1           | 1           |
| GO:0034641 | cellular nitrogen compound metabolic process                | 6998 | 1           | 0.006520896 | 1 | 1           | 1           |
| GO:0034645 | cellular macromolecule biosynthetic process                 | 4853 | 1           | 8.55E-06    | 1 | 1           | 1           |
| GO:0034654 | nucleobase-containing compound biosynthetic process         | 4171 | 1           | 5.52E-06    | 1 | 1           | 1           |
| GO:0034976 | response to endoplasmic reticulum stress                    | 264  | 0.015996351 | 1           | 1 | 1           | 1           |
| GO:0035556 | intracellular signal transduction                           | 2817 | 1.30E-12    | 1           | 1 | 0.13056033  | 1           |
| GO:0036211 | protein modification process                                | 4066 | 1.66E-05    | 0.93115264  | 1 | 1           | 1           |
| GO:0036230 | granulocyte activation                                      | 505  | 4.83E-21    | 1           | 1 | 1           | 1           |
| GO:0036344 | platelet morphogenesis                                      | 21   | 1           | 0.028400502 | 1 | 1           | 1           |
| GO:0038093 | Fc receptor signaling pathway                               | 187  | 0.000173731 | 1           | 1 | 1           | 1           |
| GO:0038094 | Fc-gamma receptor signaling pathway                         | 138  | 0.02750321  | 1           | 1 | 1           | 1           |
| GO:0040012 | regulation of locomotion                                    | 1042 | 0.000435941 | 1           | 1 | 1           | 1           |
| GO:0040017 | positive regulation of locomotion                           | 570  | 6.01E-06    | 1           | 1 | 1           | 1           |
| GO:0042035 | regulation of cytokine biosynthetic process                 | 94   | 0.048234344 | 0.24587016  | 1 | 1           | 1           |
| GO:0042060 | wound healing                                               | 543  | 2.91E-08    | 1           | 1 | 1           | 1           |
| GO:0042108 | positive regulation of cytokine biosynthetic process        | 57   | 0.031006288 | 1           | 1 | 1           | 1           |
| GO:0042110 | T cell activation                                           | 451  | 0.000878164 | 1           | 1 | 1           | 1           |
| GO:0042119 | neutrophil activation                                       | 498  | 1.09E-20    | 1           | 1 | 1           | 1           |
| GO:0042221 | response to chemical                                        | 4641 | 6.82E-06    | 0.969666228 | 1 | 1           | 1           |
| GO:0042325 | regulation of phosphorylation                               | 1536 | 7.74E-07    | 1           | 1 | 1           | 1           |
| GO:0042327 | positive regulation of phosphorylation                      | 1053 | 7.48E-08    | 1           | 1 | 1           | 1           |
| GO:0042330 | taxis                                                       | 621  | 0.012287565 | 1           | 1 | 1           | 1           |
| GO:0042494 | detection of bacterial lipoprotein                          | 4    | 0.016140011 | 1           | 1 | 1           | 1           |
| GO:0042592 | homeostatic process                                         | 1867 | 0.022963874 | 1           | 1 | 0.996446813 | 0.345762208 |
| GO:0042886 | amide transport                                             | 2037 | 3.30E-05    | 1           | 1 | 1           | 1           |
| GO:0042981 | regulation of apoptotic process                             | 1572 | 0.029061136 | 1           | 1 | 1           | 1           |
| GO:0043065 | positive regulation of apoptotic process                    | 632  | 0.001982857 | 1           | 1 | 1           | 1           |

|            |                                                                                           |       |             |             |   |   |   |
|------------|-------------------------------------------------------------------------------------------|-------|-------------|-------------|---|---|---|
| GO:0043067 | regulation of programmed cell death                                                       | 1586  | 0.024126389 | 1           | 1 | 1 | 1 |
| GO:0043068 | positive regulation of programmed cell death                                              | 636   | 0.001058108 | 1           | 1 | 1 | 1 |
| GO:0043085 | positive regulation of catalytic activity                                                 | 1392  | 1.94E-09    | 1           | 1 | 1 | 1 |
| GO:0043086 | negative regulation of catalytic activity                                                 | 795   | 0.036082289 | 1           | 1 | 1 | 1 |
| GO:0043087 | regulation of GTPase activity                                                             | 481   | 0.049277258 | 1           | 1 | 1 | 1 |
| GO:0043112 | receptor metabolic process                                                                | 184   | 0.040035288 | 1           | 1 | 1 | 1 |
| GO:0043122 | regulation of I-kappaB kinase/NF-kappaB signaling                                         | 226   | 0.018065402 | 1           | 1 | 1 | 1 |
| GO:0043123 | positive regulation of I-kappaB kinase/NF-kappaB signaling                                | 181   | 0.00461387  | 1           | 1 | 1 | 1 |
| GO:0043207 | response to external biotic stimulus                                                      | 984   | 3.89E-07    | 1           | 1 | 1 | 1 |
| GO:0043249 | erythrocyte maturation                                                                    | 15    | 1           | 0.006823622 | 1 | 1 | 1 |
| GO:0043280 | positive regulation of cysteine-type endopeptidase activity involved in apoptotic process | 126   | 0.038843865 | 1           | 1 | 1 | 1 |
| GO:0043281 | regulation of cysteine-type endopeptidase activity involved in apoptotic process          | 209   | 0.007862201 | 1           | 1 | 1 | 1 |
| GO:0043299 | leukocyte degranulation                                                                   | 531   | 3.32E-21    | 1           | 1 | 1 | 1 |
| GO:0043312 | neutrophil degranulation                                                                  | 485   | 5.35E-20    | 1           | 1 | 1 | 1 |
| GO:0043405 | regulation of MAP kinase activity                                                         | 335   | 2.37E-06    | 1           | 1 | 1 | 1 |
| GO:0043406 | positive regulation of MAP kinase activity                                                | 258   | 5.07E-06    | 1           | 1 | 1 | 1 |
| GO:0043408 | regulation of MAPK cascade                                                                | 776   | 1.92E-05    | 1           | 1 | 1 | 1 |
| GO:0043412 | macromolecule modification                                                                | 4269  | 8.87E-05    | 0.680217842 | 1 | 1 | 1 |
| GO:0043434 | response to peptide hormone                                                               | 417   | 0.015891141 | 1           | 1 | 1 | 1 |
| GO:0043549 | regulation of kinase activity                                                             | 837   | 5.71E-07    | 1           | 1 | 1 | 1 |
| GO:0044093 | positive regulation of molecular function                                                 | 1736  | 5.74E-10    | 1           | 1 | 1 | 1 |
| GO:0044237 | cellular metabolic process                                                                | 11116 | 0.145299351 | 0.000447254 | 1 | 1 | 1 |
| GO:0044238 | primary metabolic process                                                                 | 11112 | 1           | 0.007170056 | 1 | 1 | 1 |
| GO:0044247 | cellular polysaccharide catabolic process                                                 | 21    | 0.004611115 | 1           | 1 | 1 | 1 |
| GO:0044248 | cellular catabolic process                                                                | 2204  | 5.16E-08    | 0.87520387  | 1 | 1 | 1 |
| GO:0044249 | cellular biosynthetic process                                                             | 6015  | 1           | 5.07E-06    | 1 | 1 | 1 |
| GO:0044260 | cellular macromolecule metabolic process                                                  | 8207  | 0.110332446 | 0.000171375 | 1 | 1 | 1 |
| GO:0044265 | cellular macromolecule catabolic process                                                  | 1118  | 0.015397049 | 0.748743161 | 1 | 1 | 1 |
| GO:0044267 | cellular protein metabolic process                                                        | 5151  | 0.000173216 | 0.901236414 | 1 | 1 | 1 |
| GO:0044271 | cellular nitrogen compound                                                                | 4905  | 1           | 1.09E-05    | 1 | 1 | 1 |

|            |                                                                         |      |             |             |   |             |             |
|------------|-------------------------------------------------------------------------|------|-------------|-------------|---|-------------|-------------|
|            | biosynthetic process                                                    |      |             |             |   |             |             |
| GO:0044275 | cellular carbohydrate catabolic process                                 | 40   | 0.021226881 | 1           | 1 | 1           | 1           |
| GO:0045055 | regulated exocytosis                                                    | 788  | 1.08E-23    | 1           | 1 | 1           | 1           |
| GO:0045087 | innate immune response                                                  | 908  | 1.30E-09    | 1           | 1 | 1           | 1           |
| GO:0045088 | regulation of innate immune response                                    | 365  | 1.57E-07    | 1           | 1 | 1           | 1           |
| GO:0045089 | positive regulation of innate immune response                           | 309  | 4.50E-06    | 1           | 1 | 1           | 1           |
| GO:0045123 | cellular extravasation                                                  | 54   | 0.000802516 | 1           | 1 | 1           | 1           |
| GO:0045184 | establishment of protein localization                                   | 2079 | 2.55E-05    | 1           | 1 | 1           | 1           |
| GO:0045321 | leukocyte activation                                                    | 1257 | 4.94E-18    | 1           | 1 | 1           | 1           |
| GO:0045597 | positive regulation of cell differentiation                             | 974  | 0.020370955 | 0.831969884 | 1 | 1           | 1           |
| GO:0045785 | positive regulation of cell adhesion                                    | 397  | 0.034129341 | 1           | 1 | 1           | 1           |
| GO:0045859 | regulation of protein kinase activity                                   | 762  | 1.59E-07    | 1           | 1 | 1           | 1           |
| GO:0045860 | positive regulation of protein kinase activity                          | 512  | 4.71E-09    | 1           | 1 | 1           | 1           |
| GO:0045862 | positive regulation of proteolysis                                      | 352  | 0.001187493 | 1           | 1 | 1           | 1           |
| GO:0045892 | negative regulation of transcription, DNA-templated                     | 1199 | 1           | 4.69E-09    | 1 | 0.469442217 | 1           |
| GO:0045932 | negative regulation of muscle contraction                               | 27   | 0.017009962 | 1           | 1 | 1           | 1           |
| GO:0045934 | negative regulation of nucleobase-containing compound metabolic process | 1457 | 1           | 6.60E-07    | 1 | 0.923274969 | 1           |
| GO:0045935 | positive regulation of nucleobase-containing compound metabolic process | 1862 | 1           | 0.001568173 | 1 | 1           | 1           |
| GO:0045937 | positive regulation of phosphate metabolic process                      | 1124 | 3.91E-07    | 1           | 1 | 1           | 1           |
| GO:0045987 | positive regulation of smooth muscle contraction                        | 32   | 0.036082289 | 1           | 1 | 1           | 1           |
| GO:0046483 | heterocycle metabolic process                                           | 6422 | 1           | 0.005792173 | 1 | 1           | 1           |
| GO:0046649 | lymphocyte activation                                                   | 713  | 0.019063382 | 0.345762208 | 1 | 1           | 1           |
| GO:0046898 | response to cycloheximide                                               | 4    | 1           | 0.013583116 | 1 | 1           | 1           |
| GO:0046903 | secretion                                                               | 1614 | 1.08E-23    | 1           | 1 | 1           | 1           |
| GO:0048010 | vascular endothelial growth factor receptor signaling pathway           | 91   | 0.038843865 | 1           | 1 | 1           | 1           |
| GO:0048013 | ephrin receptor signaling pathway                                       | 80   | 0.000841417 | 1           | 1 | 1           | 1           |
| GO:0048519 | negative regulation of biological process                               | 5698 | 0.222729944 | 0.002085165 | 1 | 0.955645847 | 1           |
| GO:0048522 | positive regulation of cellular process                                 | 5330 | 2.61E-08    | 0.01290706  | 1 | 0.892839413 | 1           |
| GO:0048523 | negative regulation of cellular process                                 | 4759 | 0.050048478 | 5.46E-05    | 1 | 0.681771571 | 1           |
| GO:0048534 | hematopoietic or lymphoid organ development                             | 861  | 0.009678209 | 0.000236607 | 1 | 1           | 0.533565531 |

|            |                                                                  |       |             |             |   |             |             |
|------------|------------------------------------------------------------------|-------|-------------|-------------|---|-------------|-------------|
| GO:0048583 | regulation of response to stimulus                               | 4234  | 2.15E-08    | 1           | 1 | 0.400677758 | 1           |
| GO:0048584 | positive regulation of response to stimulus                      | 2373  | 3.55E-10    | 1           | 1 | 1           | 1           |
| GO:0048821 | erythrocyte development                                          | 31    | 1           | 0.00036786  | 1 | 1           | 1           |
| GO:0048870 | cell motility                                                    | 1688  | 6.00E-05    | 1           | 1 | 0.629638536 | 1           |
| GO:0048872 | homeostasis of number of cells                                   | 248   | 0.019367226 | 0.052531007 | 1 | 1           | 1           |
| GO:0050663 | cytokine secretion                                               | 210   | 0.008352331 | 1           | 1 | 1           | 1           |
| GO:0050701 | interleukin-1 secretion                                          | 56    | 0.0280421   | 1           | 1 | 1           | 1           |
| GO:0050702 | interleukin-1 beta secretion                                     | 48    | 0.011788736 | 1           | 1 | 1           | 1           |
| GO:0050776 | regulation of immune response                                    | 1022  | 2.37E-08    | 1           | 1 | 1           | 1           |
| GO:0050778 | positive regulation of immune response                           | 823   | 1.39E-07    | 1           | 1 | 1           | 1           |
| GO:0050789 | regulation of biological process                                 | 11899 | 0.000110092 | 0.002209175 | 1 | 1           | 1           |
| GO:0050790 | regulation of catalytic activity                                 | 2281  | 2.61E-08    | 1           | 1 | 0.899460453 | 1           |
| GO:0050794 | regulation of cellular process                                   | 10828 | 4.85E-07    | 0.000104586 | 1 | 0.922242032 | 1           |
| GO:0050817 | coagulation                                                      | 340   | 7.31E-09    | 1           | 1 | 1           | 1           |
| GO:0050818 | regulation of coagulation                                        | 82    | 0.001058702 | 1           | 1 | 1           | 1           |
| GO:0050820 | positive regulation of coagulation                               | 26    | 0.014166664 | 1           | 1 | 1           | 1           |
| GO:0050863 | regulation of T cell activation                                  | 305   | 0.015271277 | 1           | 1 | 1           | 1           |
| GO:0050865 | regulation of cell activation                                    | 587   | 0.017981836 | 1           | 1 | 1           | 1           |
| GO:0050866 | negative regulation of cell activation                           | 184   | 0.040035288 | 1           | 1 | 1           | 1           |
| GO:0050878 | regulation of body fluid levels                                  | 493   | 1.93E-05    | 1           | 1 | 1           | 0.966588903 |
| GO:0050900 | leukocyte migration                                              | 478   | 0.000176302 | 1           | 1 | 1           | 1           |
| GO:0051050 | positive regulation of transport                                 | 936   | 0.016217447 | 1           | 1 | 1           | 1           |
| GO:0051090 | regulation of DNA-binding transcription factor activity          | 412   | 0.026984947 | 0.792082077 | 1 | 1           | 1           |
| GO:0051091 | positive regulation of DNA-binding transcription factor activity | 255   | 0.004012175 | 0.922242032 | 1 | 1           | 1           |
| GO:0051092 | positive regulation of NF-kappaB transcription factor activity   | 146   | 1.92E-05    | 0.922242032 | 1 | 1           | 1           |
| GO:0051094 | positive regulation of developmental process                     | 1395  | 0.038843865 | 0.830036129 | 1 | 1           | 1           |
| GO:0051128 | regulation of cellular component organization                    | 2457  | 3.72E-05    | 0.996446813 | 1 | 1           | 1           |
| GO:0051130 | positive regulation of cellular component organization           | 1210  | 4.29E-05    | 1           | 1 | 1           | 1           |
| GO:0051171 | regulation of nitrogen compound metabolic process                | 5907  | 0.008673409 | 5.89E-05    | 1 | 1           | 1           |
| GO:0051172 | negative regulation of nitrogen compound metabolic process       | 2410  | 0.348615674 | 8.40E-06    | 1 | 1           | 1           |

|            |                                                            |      |             |             |   |             |             |
|------------|------------------------------------------------------------|------|-------------|-------------|---|-------------|-------------|
| GO:0051173 | positive regulation of nitrogen compound metabolic process | 3140 | 2.20E-05    | 0.072497165 | 1 | 1           | 1           |
| GO:0051174 | regulation of phosphorus metabolic process                 | 1738 | 7.55E-07    | 1           | 1 | 1           | 1           |
| GO:0051222 | positive regulation of protein transport                   | 402  | 0.001684062 | 1           | 1 | 1           | 1           |
| GO:0051223 | regulation of protein transport                            | 672  | 0.023649461 | 1           | 1 | 1           | 1           |
| GO:0051246 | regulation of protein metabolic process                    | 2860 | 6.36E-08    | 1           | 1 | 1           | 1           |
| GO:0051247 | positive regulation of protein metabolic process           | 1681 | 1.05E-09    | 1           | 1 | 1           | 1           |
| GO:0051248 | negative regulation of protein metabolic process           | 1144 | 0.008981555 | 0.996446813 | 1 | 1           | 1           |
| GO:0051252 | regulation of RNA metabolic process                        | 3738 | 1           | 2.45E-06    | 1 | 1           | 1           |
| GO:0051253 | negative regulation of RNA metabolic process               | 1330 | 1           | 3.23E-08    | 1 | 0.633161182 | 1           |
| GO:0051254 | positive regulation of RNA metabolic process               | 1680 | 1           | 0.001413106 | 1 | 1           | 1           |
| GO:0051272 | positive regulation of cellular component movement         | 553  | 7.10E-06    | 1           | 1 | 1           | 1           |
| GO:0051336 | regulation of hydrolase activity                           | 1281 | 0.001796452 | 1           | 1 | 1           | 1           |
| GO:0051338 | regulation of transferase activity                         | 941  | 2.18E-06    | 1           | 1 | 1           | 1           |
| GO:0051345 | positive regulation of hydrolase activity                  | 763  | 0.002761855 | 1           | 1 | 1           | 1           |
| GO:0051347 | positive regulation of transferase activity                | 626  | 3.58E-08    | 1           | 1 | 1           | 1           |
| GO:0051607 | defense response to virus                                  | 228  | 0.007642349 | 1           | 1 | 1           | 1           |
| GO:0051641 | cellular localization                                      | 2847 | 0.024959734 | 1           | 1 | 1           | 1           |
| GO:0051674 | localization of cell                                       | 1688 | 6.00E-05    | 1           | 1 | 0.629638536 | 1           |
| GO:0051704 | multi-organism process                                     | 2485 | 3.72E-05    | 1           | 1 | 1           | 1           |
| GO:0051707 | response to other organism                                 | 982  | 3.62E-07    | 1           | 1 | 1           | 1           |
| GO:0051716 | cellular response to stimulus                              | 7432 | 3.67E-09    | 0.87520387  | 1 | 0.07488625  | 1           |
| GO:0060079 | excitatory postsynaptic potential                          | 103  | 1           | 1           | 1 | 0.026564194 | 1           |
| GO:0060218 | hematopoietic stem cell differentiation                    | 34   | 1           | 0.035278512 | 1 | 1           | 1           |
| GO:0060255 | regulation of macromolecule metabolic process              | 6630 | 0.443316572 | 0.00566515  | 1 | 1           | 1           |
| GO:0060319 | primitive erythrocyte differentiation                      | 4    | 1           | 0.013583116 | 1 | 1           | 1           |
| GO:0060326 | cell chemotaxis                                            | 295  | 0.010056469 | 1           | 1 | 1           | 1           |
| GO:0060341 | regulation of cellular localization                        | 879  | 0.024731895 | 1           | 1 | 1           | 1           |
| GO:0060627 | regulation of vesicle-mediated transport                   | 498  | 0.021966072 | 1           | 1 | 1           | 1           |
| GO:0060969 | negative regulation of gene silencing                      | 35   | 1           | 0.040035288 | 1 | 1           | 1           |
| GO:0061003 | positive regulation of dendritic spine morphogenesis       | 19   | 1           | 1           | 1 | 1           | 0.035229966 |

|            |                                                       |       |             |             |   |             |             |
|------------|-------------------------------------------------------|-------|-------------|-------------|---|-------------|-------------|
| GO:0061024 | membrane organization                                 | 846   | 0.012347546 | 1           | 1 | 1           | 1           |
| GO:0061041 | regulation of wound healing                           | 134   | 0.022218406 | 1           | 1 | 1           | 1           |
| GO:0061298 | retina vasculature development in camera-type eye     | 18    | 1           | 1           | 1 | 0.031028127 |             |
| GO:0061515 | myeloid cell development                              | 67    | 0.52528845  | 7.08E-05    | 1 | 1           | 1           |
| GO:0061900 | glial cell activation                                 | 40    | 0.003561051 | 1           | 1 | 1           | 1           |
| GO:0061919 | process utilizing autophagic mechanism                | 466   | 0.003701303 | 1           | 1 | 1           | 1           |
| GO:0065007 | biological regulation                                 | 12576 | 1.85E-06    | 0.018565448 | 1 | 0.356365961 | 1           |
| GO:0065009 | regulation of molecular function                      | 3187  | 1.56E-06    | 1           | 1 | 0.478489879 | 1           |
| GO:0070201 | regulation of establishment of protein localization   | 715   | 0.011042006 | 1           | 1 | 1           | 1           |
| GO:0070340 | detection of bacterial lipopeptide                    | 3     | 0.005055861 | 1           | 1 | 1           | 1           |
| GO:0070498 | interleukin-1-mediated signaling pathway              | 55    | 0.025766984 | 1           | 1 | 1           | 1           |
| GO:0070527 | platelet aggregation                                  | 57    | 0.031006288 | 1           | 1 | 1           | 1           |
| GO:0070727 | cellular macromolecule localization                   | 1840  | 0.00087738  | 1           | 1 | 1           | 1           |
| GO:0070887 | cellular response to chemical stimulus                | 3144  | 7.43E-11    | 0.481144832 | 1 | 1           | 0.916075135 |
| GO:0071216 | cellular response to biotic stimulus                  | 229   | 2.35E-05    | 1           | 1 | 1           | 1           |
| GO:0071219 | cellular response to molecule of bacterial origin     | 206   | 0.000693746 | 1           | 1 | 1           | 1           |
| GO:0071222 | cellular response to lipopolysaccharide               | 199   | 0.012917217 | 1           | 1 | 1           | 1           |
| GO:0071260 | cellular response to mechanical stimulus              | 78    | 1.92E-05    | 1           | 1 | 1           | 1           |
| GO:0071310 | cellular response to organic substance                | 2595  | 9.32E-10    | 0.179921038 | 1 | 1           | 0.883468397 |
| GO:0071345 | cellular response to cytokine stimulus                | 1028  | 1.59E-07    | 1           | 1 | 1           | 1           |
| GO:0071346 | cellular response to interferon-gamma                 | 178   | 0.030521352 | 1           | 1 | 1           | 1           |
| GO:0071375 | cellular response to peptide hormone stimulus         | 307   | 0.016372759 | 1           | 1 | 1           | 1           |
| GO:0071417 | cellular response to organonitrogen compound          | 555   | 7.77E-06    | 1           | 1 | 1           | 0.519887215 |
| GO:0071496 | cellular response to external stimulus                | 328   | 1.37E-05    | 0.133254818 | 1 | 1           | 1           |
| GO:0071621 | granulocyte chemotaxis                                | 120   | 0.002310269 | 1           | 1 | 1           | 1           |
| GO:0071622 | regulation of granulocyte chemotaxis                  | 42    | 0.026791027 | 1           | 1 | 1           | 1           |
| GO:0071675 | regulation of mononuclear cell migration              | 42    | 0.026791027 | 1           | 1 | 1           | 1           |
| GO:0071702 | organic substance transport                           | 2745  | 0.000324796 | 1           | 1 | 1           | 0.739725387 |
| GO:0071705 | nitrogen compound transport                           | 2335  | 0.001910279 | 1           | 1 | 1           | 1           |
| GO:0071706 | tumor necrosis factor superfamily cytokine production | 135   | 0.007547433 | 1           | 1 | 1           | 1           |

|            |                                                                 |      |             |             |   |             |             |
|------------|-----------------------------------------------------------------|------|-------------|-------------|---|-------------|-------------|
| GO:0071840 | cellular component organization or biogenesis                   | 6506 | 0.075463572 | 0.686175641 | 1 | 0.698373195 | 0.046322431 |
| GO:0071900 | regulation of protein serine/threonine kinase activity          | 496  | 1.59E-07    | 1           | 1 | 1           | 1           |
| GO:0071902 | positive regulation of protein serine/threonine kinase activity | 323  | 2.62E-08    | 1           | 1 | 1           | 1           |
| GO:0072672 | neutrophil extravasation                                        | 10   | 0.001140246 | 1           | 1 | 1           | 1           |
| GO:0080090 | regulation of primary metabolic process                         | 6069 | 0.004520227 | 9.52E-06    | 1 | 1           | 1           |
| GO:0080134 | regulation of response to stress                                | 1452 | 6.85E-08    | 1           | 1 | 1           | 1           |
| GO:0080135 | regulation of cellular response to stress                       | 684  | 0.009359443 | 1           | 1 | 1           | 1           |
| GO:0090087 | regulation of peptide transport                                 | 701  | 0.0256708   | 1           | 1 | 1           | 1           |
| GO:0090304 | nucleic acid metabolic process                                  | 5634 | 1           | 0.001513988 | 1 | 1           | 1           |
| GO:0090316 | positive regulation of intracellular protein transport          | 158  | 0.010740006 | 1           | 1 | 1           | 1           |
| GO:0097529 | myeloid leukocyte migration                                     | 199  | 0.000433484 | 1           | 1 | 1           | 1           |
| GO:0097530 | granulocyte migration                                           | 134  | 0.000500171 | 1           | 1 | 1           | 1           |
| GO:0097659 | nucleic acid-templated transcription                            | 3642 | 1           | 3.98E-06    | 1 | 1           | 1           |
| GO:0098542 | defense response to other organism                              | 548  | 0.041421832 | 1           | 1 | 1           | 1           |
| GO:0098543 | detection of other organism                                     | 13   | 0.049467321 | 1           | 1 | 1           | 1           |
| GO:0098657 | import into cell                                                | 900  | 1.17E-05    | 1           | 1 | 0.996446813 | 1           |
| GO:0098771 | inorganic ion homeostasis                                       | 722  | 0.039539873 | 1           | 1 | 0.875764979 | 1           |
| GO:0098976 | excitatory chemical synaptic transmission                       | 8    | 1           | 1           | 1 | 0.013930431 | 1           |
| GO:0099565 | chemical synaptic transmission, postsynaptic                    | 111  | 1           | 1           | 1 | 0.037418398 | 1           |
| GO:0150076 | neuroinflammatory response                                      | 47   | 0.0002357   | 1           | 1 | 1           | 1           |
| GO:1900046 | regulation of hemostasis                                        | 77   | 0.002919532 | 1           | 1 | 1           | 1           |
| GO:1901224 | positive regulation of NIK/NF-kappaB signaling                  | 70   | 0.026584093 | 1           | 1 | 1           | 1           |
| GO:1901360 | organic cyclic compound metabolic process                       | 6676 | 1           | 0.011793821 | 1 | 1           | 1           |
| GO:1901362 | organic cyclic compound biosynthetic process                    | 4387 | 1           | 1.89E-05    | 1 | 1           | 1           |
| GO:1901564 | organonitrogen compound metabolic process                       | 6899 | 9.53E-05    | 1           | 1 | 1           | 1           |
| GO:1901565 | organonitrogen compound catabolic process                       | 1253 | 0.000953023 | 1           | 1 | 1           | 1           |
| GO:1901575 | organic substance catabolic process                             | 2071 | 3.56E-07    | 1           | 1 | 1           | 1           |
| GO:1901576 | organic substance biosynthetic process                          | 6099 | 1           | 2.53E-06    | 1 | 1           | 1           |
| GO:1901652 | response to peptide                                             | 481  | 0.000512427 | 1           | 1 | 1           | 1           |

|            |                                                                               |      |             |             |   |             |             |
|------------|-------------------------------------------------------------------------------|------|-------------|-------------|---|-------------|-------------|
| GO:1901653 | cellular response to peptide                                                  | 356  | 0.000545066 | 1           | 1 | 1           | 1           |
| GO:1901698 | response to nitrogen compound                                                 | 1037 | 2.06E-05    | 1           | 1 | 1           | 1           |
| GO:1901699 | cellular response to nitrogen compound                                        | 612  | 1.40E-05    | 1           | 1 | 1           | 0.402781503 |
| GO:1901700 | response to oxygen-containing compound                                        | 1577 | 1.54E-05    | 1           | 1 | 1           | 1           |
| GO:1901701 | cellular response to oxygen-containing compound                               | 1092 | 5.13E-05    | 1           | 1 | 1           | 0.795980333 |
| GO:1902275 | regulation of chromatin organization                                          | 175  | 1           | 0.038417362 | 1 | 1           | 1           |
| GO:1902531 | regulation of intracellular signal transduction                               | 1881 | 1.13E-09    | 1           | 1 | 1           | 1           |
| GO:1902533 | positive regulation of intracellular signal transduction                      | 1077 | 3.91E-07    | 1           | 1 | 1           | 1           |
| GO:1902622 | regulation of neutrophil migration                                            | 31   | 0.03127218  | 1           | 1 | 1           | 1           |
| GO:1902679 | negative regulation of RNA biosynthetic process                               | 1251 | 1           | 1.26E-08    | 1 | 0.604011244 | 1           |
| GO:1903037 | regulation of leukocyte cell-cell adhesion                                    | 293  | 0.021687327 | 1           | 1 | 1           | 1           |
| GO:1903506 | regulation of nucleic acid-templated transcription                            | 3499 | 1           | 2.97E-06    | 1 | 1           | 1           |
| GO:1903507 | negative regulation of nucleic acid-templated transcription                   | 1249 | 1           | 1.21E-08    | 1 | 0.598967854 | 1           |
| GO:1903510 | mucopolysaccharide metabolic process                                          | 110  | 0.014483105 | 1           | 1 | 1           | 1           |
| GO:1903555 | regulation of tumor necrosis factor superfamily cytokine production           | 131  | 0.01844494  | 1           | 1 | 1           | 1           |
| GO:1903557 | positive regulation of tumor necrosis factor superfamily cytokine production  | 76   | 0.04283723  | 1           | 1 | 1           | 1           |
| GO:1903747 | regulation of establishment of protein localization to mitochondrion          | 70   | 0.026584093 | 1           | 1 | 1           | 1           |
| GO:1903749 | positive regulation of establishment of protein localization to mitochondrion | 56   | 0.0280421   | 1           | 1 | 1           | 1           |
| GO:1903827 | regulation of cellular protein localization                                   | 508  | 0.000254902 | 1           | 1 | 1           | 1           |
| GO:1903829 | positive regulation of cellular protein localization                          | 318  | 0.004402893 | 1           | 1 | 1           | 1           |
| GO:1904951 | positive regulation of establishment of protein localization                  | 437  | 0.000496601 | 1           | 1 | 1           | 1           |
| GO:1905268 | negative regulation of chromatin organization                                 | 60   | 1           | 0.028370428 | 1 | 1           | 1           |
| GO:1990266 | neutrophil migration                                                          | 112  | 0.001132309 | 1           | 1 | 1           | 1           |
| GO:1990928 | response to amino acid starvation                                             | 47   | 0.046835063 | 1           | 1 | 1           | 1           |
| GO:2000112 | regulation of cellular macromolecule                                          | 3918 | 1           | 1.43E-05    | 1 | 1           | 1           |

|            |                                                                    |      |             |          |   |             |   |
|------------|--------------------------------------------------------------------|------|-------------|----------|---|-------------|---|
|            | biosynthetic process                                               |      |             |          |   |             |   |
| GO:2000113 | negative regulation of cellular macromolecule biosynthetic process | 1459 | 1           | 3.40E-07 | 1 | 1           | 1 |
| GO:2000116 | regulation of cysteine-type endopeptidase activity                 | 232  | 0.00334288  | 1        | 1 | 1           | 1 |
| GO:2000145 | regulation of cell motility                                        | 968  | 0.00318429  | 1        | 1 | 0.995169577 | 1 |
| GO:2000147 | positive regulation of cell motility                               | 539  | 9.45E-06    | 1        | 1 | 1           | 1 |
| GO:2000377 | regulation of reactive oxygen species metabolic process            | 185  | 0.041941486 | 1        | 1 | 1           | 1 |
| GO:2000463 | positive regulation of excitatory postsynaptic potential           | 27   | 1           | 1        | 1 | 0.032162807 | 1 |
| GO:2001056 | positive regulation of cysteine-type endopeptidase activity        | 143  | 0.035857337 | 1        | 1 | 0.716801532 | 1 |
| GO:2001141 | regulation of RNA biosynthetic process                             | 3507 | 1           | 3.35E-06 | 1 | 1           | 1 |
| GO:2001233 | regulation of apoptotic signaling pathway                          | 391  | 0.014166664 | 1        | 1 | 1           | 1 |

#### [000168] Time Series Analysis of Synovial Cell Marker Genes in RA Flares

[000169] To better characterize the relevance of the clusters identified by the time series analysis to synovitis (Figure 3C), we examined them for enrichment in synovial cell subtypes characterized by scRNAseq. This analysis of 5265 single RA and osteoarthritis patient synovial cells identified four fibroblast, four B cell, six T cell, and four monocyte subpopulations (Figure 4A). We identified approximately 200 marker genes that best distinguished each of 18 synovial cell types. AC2 was enriched with naive B cell genes (Figure 4A and Figure 17), and AC3 was enriched with three sublining fibroblast genes (CD34+, HLA-DR+, and DKK3+) (Figure 4A). Two of these fibroblast subsets, CD34+ and HLA-DR+, are more abundant in inflamed synovium (20). We plotted expression of those transcripts that were common to both synovial sublining fibroblasts and AC3 over time and again noted their increased expression in blood one week prior to flare and decreased expression during flare (Figure 4B, Figure 18, and Table 5).

[000170] Overall, 622 of 625 AC3 genes decreased during flare in patient 1, and a subset (194 genes) also decreased in flares from at least 3 out of 4 RA patients (and 22 genes in 4 out of 4 patients; Figure 4C and Table 6), and permutation test indicated this overlap was greater than expected by chance ( $p=0.0001$ ). Pathway analysis of the subset of 194 overlapping genes was again enriched for extracellular matrix and secreted glycoprotein.

[000171] We further tested whether cells that expressed surface markers of synovial fibroblasts were detectable in RA blood by flow cytometry (Figures 19 and 20). CD45-/CD31-/PDPN+ cells were increased in 19 additional RA patient blood relative to healthy controls (Figure 4D). RNAseq of these

cells confirmed they were enriched with AC3 cluster genes (Figure 4E), synovial fibroblast genes (Figure 21), and expressed classic synovial fibroblast genes such as FAP, DKK3, CDH11, as well as collagens and laminins (Figure 22). Given their expression of classical mesenchymal surface markers and genes, we refer to these as PRe-Inflammatory Mesenchymal Cells (PRIME cells). Taken together, our observations suggest a model in which sequential activation of B cells activate PRIME cells just prior to flares, which are then evident at flare in inflamed synovium as inflammatory sublining fibroblasts (Figure 5).

## DISCUSSION

**[000172]** We present longitudinal genomics as a strategy to study the antecedents to RA flare that may be generalizable to autoimmune diseases associated with waxing/waning clinical courses. We developed easy-to-use tools for patients to acquire both quantifiable clinical symptoms and molecular data at home over many years. This allowed us to capture data prior to the onset of clinical flares and retrospectively analyze it, identifying different RNA signatures (AC2 and AC3) evident in peripheral blood 1-2 weeks prior to flare.

**[000173]** The RNA signature of AC3 and sorted CD45-/CD31-/PDPN+ circulating cells revealed enrichment for pathways including cartilage morphogenesis, endochondral bone growth, and extracellular matrix organization (Figure 3E) and strongly overlapped with synovial sublining fibroblasts. We therefore propose antecedent PRIME cells are the precursors to inflammatory sublining fibroblasts previously found adjacent to blood vessels in inflamed RA synovium (21).

**[000174]** Significantly, inflamed sublining fibroblasts are pathogenic in an animal model of arthritis (22). Our discovery that human AC3 genes share molecular characteristics of sublining fibroblasts, together with the observation that these cells spike prior to flare but are less detectable in blood during flare (Figure 2 and 4) support a model in which PRIME cells immigrate acutely from blood to the synovium where they contribute to the inflammatory process (Figure 5). This model is consistent with the observation that RA synovial fibroblasts can traffic to cartilage implants and are sufficient to passively transfer synovial inflammation in mice (23). Together our data suggest the mesenchymal signal detected in AC3 prior to flares represent a previously uncharacterized type of trafficking fibroblast that circulates in blood.

**[000175]** In addition, we observed a second RNA signature, AC2, activated in blood prior to the spike in AC3. AC2 bear RNA hallmarks of naive B cells. This finding is reminiscent of recent studies demonstrating autoreactive naive B cells are specifically activated in RA patients (24). While the triggers of these are unknown, infectious (for example bacterial or viral antigens), environmental or endogenous toxins (25-27) could provide a source of either specific antigens or activate pattern recognition receptors.

**[000176]** In conclusion, we demonstrate methods for densely collecting longitudinal clinical and gene expression data that can be used to discover changes in transcriptional profiles in the blood weeks prior to

symptom onset. This approach led to discovery of PRIME cells, bearing hallmarks of synovial fibroblasts, which are more common in RA patients and increase in blood just prior to flares. In modeling all our data (Figure 5), we suggest that prior to clinical flare, systemic B cell immune activation (detected as AC2) acts on PRIME cells, which traffic to the blood (detected as AC3) and subsequently to the synovial sublining during flares of disease activity. More generally, this work in RA provides an exemplar of an approach to waxing/waning inflammatory disease, suggesting a general strategy relevant to additional disorders such as lupus, multiple sclerosis, and vasculitis.

[000177] Tables 2, 5 and 6 referenced in the above are provided as follows:

**TABLE 2**

**Pathway Analysis of Differentially Expressed Genes in Flare Versus Baseline**

| ID         | TERM                                                | nGenes | sig. up.<br>ngenes | sig. down.<br>ngenes | fdr.up   | fdr.down |
|------------|-----------------------------------------------------|--------|--------------------|----------------------|----------|----------|
| GO:0002274 | myeloid leukocyte activation                        | 607    | 112                | 3                    | 1.78E-29 | 1        |
| GO:0006955 | immune response                                     | 1725   | 205                | 16                   | 8.83E-29 | 1        |
| GO:0032940 | secretion by cell                                   | 1354   | 176                | 12                   | 8.83E-29 | 1        |
| GO:0043299 | leukocyte degranulation                             | 510    | 100                | 3                    | 1.04E-28 | 1        |
| GO:0036230 | granulocyte activation                              | 486    | 97                 | 3                    | 1.74E-28 | 1        |
| GO:0001775 | cell activation                                     | 1250   | 166                | 14                   | 2.26E-28 | 1        |
| GO:0002275 | myeloid cell activation involved in immune response | 520    | 100                | 3                    | 2.26E-28 | 1        |
| GO:0002376 | immune system process                               | 2531   | 260                | 31                   | 2.26E-28 | 1        |
| GO:0002446 | neutrophil mediated immunity                        | 482    | 96                 | 3                    | 2.26E-28 | 1        |
| GO:0042119 | neutrophil activation                               | 480    | 96                 | 3                    | 2.26E-28 | 1        |
| GO:0046903 | secretion                                           | 1468   | 183                | 13                   | 2.41E-28 | 1        |
| GO:0043312 | neutrophil degranulation                            | 469    | 94                 | 3                    | 5.05E-28 | 1        |
| GO:0002444 | myeloid leukocyte mediated immunity                 | 527    | 100                | 3                    | 5.52E-28 | 1        |
| GO:0002283 | neutrophil activation involved in immune response   | 472    | 94                 | 3                    | 7.33E-28 | 1        |
| GO:0002366 | leukocyte activation involved in immune response    | 652    | 111                | 5                    | 4.28E-27 | 1        |
| GO:0002263 | cell activation involved in immune response         | 655    | 111                | 5                    | 6.10E-27 | 1        |
| GO:0045321 | leukocyte activation                                | 1111   | 150                | 10                   | 2.96E-26 | 1        |
| GO:0006887 | exocytosis                                          | 857    | 128                | 5                    | 4.51E-26 | 1        |
| GO:0002443 | leukocyte mediated immunity                         | 726    | 116                | 5                    | 5.52E-26 | 1        |
| GO:0002252 | immune effector process                             | 1063   | 145                | 7                    | 8.77E-26 | 1        |
| GO:0045055 | regulated exocytosis                                | 755    | 118                | 4                    | 1.23E-25 | 1        |
| GO:0016192 | vesicle-mediated transport                          | 1859   | 186                | 26                   | 1.74E-17 | 1        |
| GO:0006950 | response to stress                                  | 3333   | 273                | 39                   | 5.46E-15 | 1        |
| GO:0050896 | response to stimulus                                | 7448   | 500                | 104                  | 5.71E-15 | 1        |
| GO:0023052 | signaling                                           | 5257   | 380                | 73                   | 5.88E-14 | 1        |
| GO:0007165 | signal transduction                                 | 4852   | 356                | 65                   | 1.41E-13 | 1        |

|            |                                                        |       |     |     |          |             |
|------------|--------------------------------------------------------|-------|-----|-----|----------|-------------|
| GO:0007154 | cell communication                                     | 5297  | 379 | 74  | 3.76E-13 | 1           |
| GO:0009611 | response to wounding                                   | 571   | 78  | 17  | 1.05E-12 | 0.129037518 |
| GO:0002684 | positive regulation of immune system process           | 896   | 104 | 9   | 1.19E-12 | 1           |
| GO:0048584 | positive regulation of response to stimulus            | 1994  | 181 | 22  | 1.19E-12 | 1           |
| GO:0051716 | cellular response to stimulus                          | 6105  | 420 | 85  | 1.63E-12 | 1           |
| GO:0002682 | regulation of immune system process                    | 1283  | 130 | 12  | 9.76E-12 | 1           |
| GO:0002253 | activation of immune response                          | 494   | 69  | 1   | 1.47E-11 | 1           |
| GO:0050776 | regulation of immune response                          | 831   | 96  | 8   | 1.89E-11 | 1           |
| GO:0050778 | positive regulation of immune response                 | 653   | 82  | 5   | 1.89E-11 | 1           |
| GO:0070887 | cellular response to chemical stimulus                 | 2747  | 224 | 40  | 2.59E-11 | 1           |
| GO:0045087 | innate immune response                                 | 695   | 85  | 2   | 2.61E-11 | 1           |
| GO:0006952 | defense response                                       | 1291  | 129 | 6   | 3.05E-11 | 1           |
| GO:0042060 | wound healing                                          | 470   | 66  | 16  | 3.70E-11 | 0.059726283 |
| GO:0044093 | positive regulation of molecular function              | 1569  | 147 | 20  | 6.93E-11 | 1           |
| GO:0080134 | regulation of response to stress                       | 1248  | 124 | 5   | 1.45E-10 | 1           |
| GO:0048583 | regulation of response to stimulus                     | 3614  | 272 | 43  | 2.27E-10 | 1           |
| GO:0050794 | regulation of cellular process                         | 9002  | 557 | 112 | 3.98E-10 | 1           |
| GO:0002757 | immune response-activating signal transduction         | 426   | 60  | 1   | 4.31E-10 | 1           |
| GO:0048518 | positive regulation of biological process              | 5233  | 362 | 71  | 4.36E-10 | 1           |
| GO:0006810 | transport                                              | 4550  | 324 | 60  | 4.63E-10 | 1           |
| GO:0043085 | positive regulation of catalytic activity              | 1257  | 123 | 17  | 4.63E-10 | 1           |
| GO:0065007 | biological regulation                                  | 10244 | 616 | 138 | 4.63E-10 | 1           |
| GO:0051234 | establishment of localization                          | 4659  | 330 | 64  | 4.65E-10 | 1           |
| GO:0071310 | cellular response to organic substance                 | 2268  | 189 | 35  | 5.77E-10 | 1           |
| GO:0002764 | immune response-regulating signaling pathway           | 455   | 62  | 2   | 6.66E-10 | 1           |
| GO:0035556 | intracellular signal transduction                      | 2501  | 202 | 29  | 1.41E-09 | 1           |
| GO:0009605 | response to external stimulus                          | 1977  | 169 | 23  | 1.55E-09 | 1           |
| GO:0048522 | positive regulation of cellular process                | 4633  | 326 | 60  | 1.63E-09 | 1           |
| GO:0050790 | regulation of catalytic activity                       | 2027  | 171 | 24  | 3.27E-09 | 1           |
| GO:0010033 | response to organic substance                          | 2769  | 216 | 37  | 5.32E-09 | 1           |
| GO:0051179 | localization                                           | 5807  | 386 | 89  | 1.23E-08 | 1           |
| GO:0050817 | coagulation                                            | 299   | 45  | 7   | 2.98E-08 | 1           |
| GO:0042221 | response to chemical                                   | 3714  | 268 | 52  | 3.46E-08 | 1           |
| GO:0007599 | hemostasis                                             | 301   | 45  | 7   | 3.61E-08 | 1           |
| GO:0006954 | inflammatory response                                  | 616   | 71  | 5   | 3.81E-08 | 1           |
| GO:0071900 | regulation of protein serine/threonine kinase activity | 453   | 58  | 3   | 3.85E-08 | 1           |
| GO:0043549 | regulation of kinase activity                          | 765   | 82  | 4   | 4.63E-08 | 1           |
| GO:0050789 | regulation of biological process                       | 9629  | 577 | 124 | 5.25E-08 | 1           |
| GO:1902531 | regulation of intracellular signal transduction        | 1644  | 142 | 15  | 5.25E-08 | 1           |
| GO:0007596 | blood coagulation                                      | 296   | 44  | 7   | 6.48E-08 | 1           |
| GO:1990266 | neutrophil migration                                   | 80    | 21  | 3   | 1.44E-07 | 1           |

|            |                                                                    |      |     |          |          |
|------------|--------------------------------------------------------------------|------|-----|----------|----------|
| GO:0002429 | immune response-activating cell surface receptor signaling pathway | 42   | 1   | 1.54E-07 | 1        |
| GO:0033674 | positive regulation of kinase activity                             | 508  | 61  | 2        | 1.54E-07 |
| GO:0031347 | regulation of defense response                                     | 625  | 70  | 2        | 1.63E-07 |
| GO:0007166 | cell surface receptor signaling pathway                            | 2548 | 196 | 44       | 1.91E-07 |
| GO:0045859 | regulation of protein kinase activity                              | 696  | 75  | 4        | 2.14E-07 |
| GO:0097530 | granulocyte migration                                              | 99   | 23  | 3        | 2.69E-07 |
| GO:0034097 | response to cytokine                                               | 979  | 95  | 13       | 2.71E-07 |
| GO:0002768 | immune response-regulating cell surface receptor signaling pathway | 44   | 2   | 2.87E-07 | 1        |
| GO:0045088 | regulation of innate immune response                               | 335  | 46  | 0        | 3.13E-07 |
| GO:0071345 | cellular response to cytokine stimulus                             | 900  | 89  | 11       | 3.74E-07 |
| GO:0097529 | myeloid leukocyte migration                                        | 156  | 29  | 4        | 4.42E-07 |
| GO:0065009 | regulation of molecular function                                   | 2746 | 206 | 37       | 4.67E-07 |
| GO:0051338 | regulation of transferase activity                                 | 863  | 86  | 5        | 4.88E-07 |
| GO:0043405 | regulation of MAP kinase activity                                  | 306  | 43  | 2        | 5.15E-07 |
| GO:0071902 | positive regulation of protein serine/threonine kinase activity    | 296  | 42  | 1        | 5.88E-07 |
| GO:0009607 | response to biotic stimulus                                        | 775  | 79  | 4        | 8.36E-07 |
| GO:0032879 | regulation of localization                                         | 2382 | 183 | 32       | 8.36E-07 |
| GO:0045860 | positive regulation of protein kinase activity                     | 469  | 56  | 2        | 8.36E-07 |
| GO:0009967 | positive regulation of signal transduction                         | 1414 | 122 | 17       | 1.12E-06 |
| GO:0051347 | positive regulation of transferase activity                        | 578  | 64  | 3        | 1.22E-06 |
| GO:0019221 | cytokine-mediated signaling pathway                                | 619  | 67  | 9        | 1.30E-06 |
| GO:0031349 | positive regulation of defense response                            | 379  | 48  | 1        | 1.72E-06 |
| GO:1902533 | positive regulation of intracellular signal transduction           | 934  | 89  | 8        | 1.99E-06 |
| GO:0009966 | regulation of signal transduction                                  | 2771 | 204 | 36       | 2.46E-06 |
| GO:0071621 | granulocyte chemotaxis                                             | 86   | 20  | 2        | 2.75E-06 |
| GO:0030593 | neutrophil chemotaxis                                              | 70   | 18  | 2        | 2.76E-06 |
| GO:0023056 | positive regulation of signaling                                   | 1565 | 130 | 20       | 3.03E-06 |
| GO:1901700 | response to oxygen-containing compound                             | 1398 | 119 | 24       | 3.59E-06 |
| GO:0038093 | Fc receptor signaling pathway                                      | 124  | 24  | 0        | 4.29E-06 |
| GO:0010942 | positive regulation of cell death                                  | 615  | 65  | 5        | 5.18E-06 |
| GO:0023051 | regulation of signaling                                            | 3129 | 223 | 39       | 5.75E-06 |
| GO:0010647 | positive regulation of cell communication                          | 1558 | 128 | 20       | 7.38E-06 |
| GO:0051707 | response to other organism                                         | 747  | 74  | 4        | 7.77E-06 |
| GO:0043207 | response to external biotic stimulus                               | 748  | 74  | 4        | 8.13E-06 |
| GO:0008219 | cell death                                                         | 1947 | 152 | 18       | 8.16E-06 |
| GO:0043068 | positive regulation of programmed cell death                       | 569  | 61  | 5        | 8.16E-06 |
| GO:0002218 | activation of innate immune response                               | 233  | 34  | 0        | 8.37E-06 |
| GO:0051247 | positive regulation of protein metabolic process                   | 1469 | 122 | 16       | 8.56E-06 |
| GO:0010646 | regulation of cell communication                                   | 3097 | 220 | 39       | 9.07E-06 |
| GO:0042110 | T cell activation                                                  | 414  | 49  | 4        | 9.07E-06 |
| GO:0040017 | positive regulation of locomotion                                  | 481  | 54  | 8        | 1.08E-05 |

|            |                                                                |       |     |     |             |             |
|------------|----------------------------------------------------------------|-------|-----|-----|-------------|-------------|
| GO:0043406 | positive regulation of MAP kinase activity                     | 237   | 34  | 1   | 1.23E-05    | 1           |
| GO:0009987 | cellular process                                               | 13404 | 738 | 179 | 1.26E-05    | 1           |
| GO:0045089 | positive regulation of innate immune response                  | 284   | 38  | 0   | 1.31E-05    | 1           |
| GO:0043065 | positive regulation of apoptotic process                       | 565   | 60  | 5   | 1.38E-05    | 1           |
| GO:0040012 | regulation of locomotion                                       | 848   | 80  | 13  | 1.54E-05    | 1           |
| GO:0012501 | programmed cell death                                          | 1824  | 143 | 17  | 1.62E-05    | 1           |
| GO:0030335 | positive regulation of cell migration                          | 437   | 50  | 8   | 1.81E-05    | 1           |
| GO:0001816 | cytokine production                                            | 653   | 66  | 4   | 1.87E-05    | 1           |
| GO:0006915 | apoptotic process                                              | 1721  | 136 | 15  | 2.24E-05    | 1           |
| GO:0000186 | activation of MAPKK activity                                   | 49    | 14  | 0   | 2.35E-05    | 1           |
| GO:1901698 | response to nitrogen compound                                  | 931   | 85  | 12  | 2.35E-05    | 1           |
| GO:0033554 | cellular response to stress                                    | 1775  | 139 | 14  | 2.63E-05    | 1           |
| GO:0032147 | activation of protein kinase activity                          | 294   | 38  | 1   | 3.02E-05    | 1           |
| GO:0050878 | regulation of body fluid levels                                | 433   | 49  | 8   | 3.25E-05    | 1           |
| GO:0051246 | regulation of protein metabolic process                        | 2429  | 178 | 24  | 3.25E-05    | 1           |
| GO:0002758 | innate immune response-activating signal transduction          | 214   | 31  | 0   | 3.39E-05    | 1           |
| GO:0044248 | cellular catabolic process                                     | 2063  | 156 | 13  | 3.41E-05    | 1           |
| GO:0051272 | positive regulation of cellular component movement             | 462   | 51  | 8   | 3.82E-05    | 1           |
| GO:0051270 | regulation of cellular component movement                      | 855   | 79  | 14  | 3.97E-05    | 1           |
| GO:0030595 | leukocyte chemotaxis                                           | 172   | 27  | 4   | 4.04E-05    | 1           |
| GO:2000147 | positive regulation of cell motility                           | 450   | 50  | 8   | 4.04E-05    | 1           |
| GO:0051092 | positive regulation of NF-kappaB transcription factor activity | 141   | 24  | 0   | 4.12E-05    | 1           |
| GO:0016477 | cell migration                                                 | 1236  | 104 | 27  | 4.44E-05    | 0.374640189 |
| GO:0042327 | positive regulation of phosphorylation                         | 892   | 81  | 7   | 5.46E-05    | 1           |
| GO:0050900 | leukocyte migration                                            | 365   | 43  | 11  | 5.85E-05    | 0.391246998 |
| GO:0046649 | lymphocyte activation                                          | 592   | 60  | 7   | 5.94E-05    | 1           |
| GO:0038094 | Fc-gamma receptor signaling pathway                            | 78    | 17  | 0   | 6.74E-05    | 1           |
| GO:0040011 | locomotion                                                     | 1566  | 124 | 33  | 7.17E-05    | 0.318994972 |
| GO:0032268 | regulation of cellular protein metabolic process               | 2258  | 166 | 19  | 7.19E-05    | 1           |
| GO:0030168 | platelet activation                                            | 146   | 24  | 3   | 7.58E-05    | 1           |
| GO:0009056 | catabolic process                                              | 2322  | 169 | 21  | 0.000102197 | 1           |
| GO:0010562 | positive regulation of phosphorus metabolic process            | 952   | 84  | 7   | 0.000102197 | 1           |
| GO:0045937 | positive regulation of phosphate metabolic process             | 952   | 84  | 7   | 0.000102197 | 1           |
| GO:1901701 | cellular response to oxygen-containing compound                | 984   | 86  | 22  | 0.000109264 | 0.469765814 |
| GO:0030334 | regulation of cell migration                                   | 733   | 69  | 12  | 0.00011376  | 1           |
| GO:1901699 | cellular response to nitrogen compound                         | 563   | 57  | 12  | 0.000115015 | 1           |
| GO:0043408 | regulation of MAPK cascade                                     | 648   | 63  | 6   | 0.000117993 | 1           |
| GO:0010243 | response to organonitrogen compound                            | 868   | 78  | 12  | 0.000126448 | 1           |
| GO:2000145 | regulation of cell motility                                    | 780   | 72  | 13  | 0.000129242 | 1           |
| GO:0048870 | cell motility                                                  | 1366  | 110 | 28  | 0.000148918 | 0.546976326 |
| GO:0051674 | localization of cell                                           | 1366  | 110 | 28  | 0.000148918 | 0.546976326 |

|            |                                                           |      |     |    |             |             |
|------------|-----------------------------------------------------------|------|-----|----|-------------|-------------|
| GO:0071417 | cellular response to organonitrogen compound              | 513  | 53  | 12 | 0.000148943 | 0.802988607 |
| GO:0051345 | positive regulation of hydrolase activity                 | 684  | 65  | 12 | 0.000166794 | 1           |
| GO:0098657 | import into cell                                          | 757  | 70  | 16 | 0.000169245 | 0.853144703 |
| GO:0032880 | regulation of protein localization                        | 891  | 79  | 5  | 0.000173297 | 1           |
| GO:0032101 | regulation of response to external stimulus               | 686  | 65  | 4  | 0.00018111  | 1           |
| GO:0001934 | positive regulation of protein phosphorylation            | 849  | 76  | 7  | 0.00019432  | 1           |
| GO:0042325 | regulation of phosphorylation                             | 1329 | 107 | 11 | 0.000207752 | 1           |
| GO:0032270 | positive regulation of cellular protein metabolic process | 1378 | 110 | 11 | 0.000215866 | 1           |
| GO:1901652 | response to peptide                                       | 426  | 46  | 7  | 0.000230098 | 1           |
| GO:0051049 | regulation of transport                                   | 1607 | 124 | 21 | 0.000238452 | 1           |
| GO:0061024 | membrane organization                                     | 736  | 68  | 8  | 0.000239587 | 1           |
| GO:0001932 | regulation of protein phosphorylation                     | 1225 | 100 | 11 | 0.000255758 | 1           |
| GO:0007159 | leukocyte cell-cell adhesion                              | 299  | 36  | 5  | 0.000269107 | 1           |
| GO:0009306 | protein secretion                                         | 483  | 50  | 4  | 0.000269107 | 1           |
| GO:0002687 | positive regulation of leukocyte migration                | 106  | 19  | 2  | 0.000274565 | 1           |
| GO:0006468 | protein phosphorylation                                   | 1678 | 128 | 21 | 0.000274565 | 1           |
| GO:0031098 | stress-activated protein kinase signaling cascade         | 287  | 35  | 0  | 0.000274565 | 1           |
| GO:0071216 | cellular response to biotic stimulus                      | 203  | 28  | 0  | 0.000274689 | 1           |
| GO:0065008 | regulation of biological quality                          | 3483 | 233 | 50 | 0.000278675 | 1           |
| GO:0033036 | macromolecule localization                                | 2816 | 195 | 28 | 0.000293603 | 1           |
| GO:0043410 | positive regulation of MAPK cascade                       | 473  | 49  | 4  | 0.000320863 | 1           |
| GO:0007155 | cell adhesion                                             | 1250 | 101 | 32 | 0.000336573 | 0.040286053 |
| GO:0019220 | regulation of phosphate metabolic process                 | 1507 | 117 | 13 | 0.000343159 | 1           |
| GO:0031667 | response to nutrient levels                               | 421  | 45  | 3  | 0.000362009 | 1           |
| GO:0051174 | regulation of phosphorus metabolic process                | 1509 | 117 | 13 | 0.000362009 | 1           |
| GO:0006909 | phagocytosis                                              | 230  | 30  | 2  | 0.000365939 | 1           |
| GO:0002431 | Fc receptor mediated stimulatory signaling pathway        | 80   | 16  | 0  | 0.000387008 | 1           |
| GO:0022610 | biological adhesion                                       | 1257 | 101 | 32 | 0.000417147 | 0.043138    |
| GO:0050663 | cytokine secretion                                        | 185  | 26  | 1  | 0.000425866 | 1           |
| GO:0023014 | signal transduction by protein phosphorylation            | 797  | 71  | 10 | 0.000463812 | 1           |
| GO:0015031 | protein transport                                         | 1831 | 136 | 17 | 0.000473998 | 1           |
| GO:0071496 | cellular response to external stimulus                    | 308  | 36  | 4  | 0.000486676 | 1           |
| GO:0060326 | cell chemotaxis                                           | 234  | 30  | 5  | 0.0005037   | 1           |
| GO:0045184 | establishment of protein localization                     | 1934 | 142 | 19 | 0.000506381 | 1           |
| GO:0030155 | regulation of cell adhesion                               | 609  | 58  | 8  | 0.000509038 | 1           |
| GO:0045932 | negative regulation of muscle contraction                 | 20   | 8   | 0  | 0.000531728 | 1           |
| GO:0071702 | organic substance transport                               | 2515 | 176 | 27 | 0.000535431 | 1           |
| GO:0006914 | autophagy                                                 | 443  | 46  | 0  | 0.000565442 | 1           |
| GO:0061919 | process utilizing autophagic mechanism                    | 443  | 46  | 0  | 0.000565442 | 1           |
| GO:0051336 | regulation of hydrolase activity                          | 1127 | 92  | 16 | 0.000599955 | 1           |
| GO:0006897 | endocytosis                                               | 645  | 60  | 15 | 0.000695764 | 0.678522254 |

|            |                                                                  |       |     |     |             |   |
|------------|------------------------------------------------------------------|-------|-----|-----|-------------|---|
| GO:0071260 | cellular response to mechanical stimulus                         | 75    | 15  | 2   | 0.000730688 | 1 |
| GO:0042886 | amide transport                                                  | 1885  | 138 | 19  | 0.000791641 | 1 |
| GO:0032612 | interleukin-1 production                                         | 76    | 15  | 0   | 0.000859296 | 1 |
| GO:0006796 | phosphate-containing compound metabolic process                  | 2886  | 196 | 26  | 0.000875096 | 1 |
| GO:0032103 | positive regulation of response to external stimulus             | 254   | 31  | 3   | 0.000898772 | 1 |
| GO:0002790 | peptide secretion                                                | 508   | 50  | 6   | 0.000925557 | 1 |
| GO:0031401 | positive regulation of protein modification process              | 1046  | 86  | 7   | 0.000925557 | 1 |
| GO:0010952 | positive regulation of peptidase activity                        | 171   | 24  | 1   | 0.000939318 | 1 |
| GO:0015833 | peptide transport                                                | 1859  | 136 | 19  | 0.000941858 | 1 |
| GO:0009991 | response to extracellular stimulus                               | 453   | 46  | 3   | 0.000954405 | 1 |
| GO:1901653 | cellular response to peptide                                     | 319   | 36  | 5   | 0.000970827 | 1 |
| GO:0034134 | toll-like receptor 2 signaling pathway                           | 16    | 7   | 0   | 0.001002353 | 1 |
| GO:1901564 | organonitrogen compound metabolic process                        | 6040  | 367 | 60  | 0.00113986  | 1 |
| GO:0009894 | regulation of catabolic process                                  | 823   | 71  | 4   | 0.001233752 | 1 |
| GO:0000165 | MAPK cascade                                                     | 779   | 68  | 10  | 0.001302406 | 1 |
| GO:0002237 | response to molecule of bacterial origin                         | 299   | 34  | 2   | 0.001448175 | 1 |
| GO:0010950 | positive regulation of endopeptidase activity                    | 153   | 22  | 1   | 0.001467807 | 1 |
| GO:0016310 | phosphorylation                                                  | 2046  | 146 | 21  | 0.001473433 | 1 |
| GO:0006793 | phosphorus metabolic process                                     | 2913  | 196 | 26  | 0.001490737 | 1 |
| GO:0009617 | response to bacterium                                            | 490   | 48  | 3   | 0.001514023 | 1 |
| GO:0051046 | regulation of secretion                                          | 679   | 61  | 5   | 0.001556577 | 1 |
| GO:0043067 | regulation of programmed cell death                              | 1367  | 105 | 13  | 0.001586821 | 1 |
| GO:2000116 | regulation of cysteine-type endopeptidase activity               | 213   | 27  | 1   | 0.001630423 | 1 |
| GO:0030162 | regulation of proteolysis                                        | 651   | 59  | 3   | 0.001650328 | 1 |
| GO:0051091 | positive regulation of DNA-binding transcription factor activity | 238   | 29  | 0   | 0.001674787 | 1 |
| GO:0042981 | regulation of apoptotic process                                  | 1354  | 104 | 13  | 0.001724948 | 1 |
| GO:0002286 | T cell activation involved in immune response                    | 81    | 15  | 1   | 0.001731296 | 1 |
| GO:0070498 | interleukin-1-mediated signaling pathway                         | 54    | 12  | 0   | 0.001861726 | 1 |
| GO:0002685 | regulation of leukocyte migration                                | 156   | 22  | 2   | 0.001893805 | 1 |
| GO:0080135 | regulation of cellular response to stress                        | 625   | 57  | 3   | 0.001893805 | 1 |
| GO:0008150 | biological_process                                               | 14638 | 780 | 198 | 0.001926983 | 1 |
| GO:0051704 | multi-organism process                                           | 2076  | 147 | 14  | 0.001926983 | 1 |
| GO:0031399 | regulation of protein modification process                       | 1590  | 118 | 12  | 0.002015929 | 1 |
| GO:0010941 | regulation of cell death                                         | 1477  | 111 | 13  | 0.00215311  | 1 |
| GO:1903037 | regulation of leukocyte cell-cell adhesion                       | 267   | 31  | 3   | 0.00215311  | 1 |
| GO:2001056 | positive regulation of cysteine-type endopeptidase activity      | 135   | 20  | 1   | 0.002158532 | 1 |
| GO:0050867 | positive regulation of cell activation                           | 294   | 33  | 4   | 0.002322146 | 1 |
| GO:0008104 | protein localization                                             | 2517  | 172 | 25  | 0.002381633 | 1 |
| GO:0050701 | interleukin-1 secretion                                          | 47    | 11  | 0   | 0.002404685 | 1 |
| GO:0002688 | regulation of leukocyte chemotaxis                               | 94    | 16  | 2   | 0.002570483 | 1 |
| GO:0002223 | stimulatory C-type lectin receptor signaling pathway             | 56    | 12  | 0   | 0.00259536  | 1 |

|            |                                                                                             |      |     |    |             |             |
|------------|---------------------------------------------------------------------------------------------|------|-----|----|-------------|-------------|
| GO:0032611 | interleukin-1 beta production                                                               | 65   | 13  | 0  | 0.00259536  | 1           |
| GO:0001817 | regulation of cytokine production                                                           | 589  | 54  | 4  | 0.002597853 | 1           |
| GO:0002694 | regulation of leukocyte activation                                                          | 446  | 44  | 4  | 0.002664683 | 1           |
| GO:0002696 | positive regulation of leukocyte activation                                                 | 284  | 32  | 4  | 0.002776889 | 1           |
| GO:0002433 | immune response-regulating cell surface receptor signaling pathway involved in phagocytosis | 75   | 14  | 0  | 0.002791965 | 1           |
| GO:0038096 | Fc-gamma receptor signaling pathway involved in phagocytosis                                | 75   | 14  | 0  | 0.002791965 | 1           |
| GO:0051770 | positive regulation of nitric-oxide synthase biosynthetic process                           | 33   | 6   | 0  | 0.002791965 | 1           |
| GO:0050863 | regulation of T cell activation                                                             | 285  | 32  | 3  | 0.002907125 | 1           |
| GO:0098542 | defense response to other organism                                                          | 365  | 38  | 0  | 0.002907125 | 1           |
| GO:0048519 | negative regulation of biological process                                                   | 4605 | 287 | 58 | 0.003060718 | 1           |
| GO:0010604 | positive regulation of macromolecule metabolic process                                      | 2902 | 193 | 37 | 0.003155111 | 1           |
| GO:0045862 | positive regulation of proteolysis                                                          | 326  | 35  | 2  | 0.003155111 | 1           |
| GO:0051050 | positive regulation of transport                                                            | 851  | 71  | 13 | 0.003155111 | 1           |
| GO:0050851 | antigen receptor-mediated signaling pathway                                                 | 174  | 23  | 1  | 0.003171354 | 1           |
| GO:0031329 | regulation of cellular catabolic process                                                    | 715  | 62  | 0  | 0.003331165 | 1           |
| GO:0050865 | regulation of cell activation                                                               | 480  | 46  | 4  | 0.00340888  | 1           |
| GO:0052548 | regulation of endopeptidase activity                                                        | 341  | 36  | 2  | 0.003414219 | 1           |
| GO:0051223 | regulation of protein transport                                                             | 612  | 55  | 3  | 0.00355489  | 1           |
| GO:0001819 | positive regulation of cytokine production                                                  | 383  | 39  | 4  | 0.003612705 | 1           |
| GO:0051222 | positive regulation of protein transport                                                    | 370  | 38  | 2  | 0.003761834 | 1           |
| GO:0002220 | innate immune response activating cell surface receptor signaling pathway                   | 59   | 12  | 0  | 0.004134873 | 1           |
| GO:0038095 | Fc-epsilon receptor signaling pathway                                                       | 59   | 12  | 0  | 0.004134873 | 1           |
| GO:1903530 | regulation of secretion by cell                                                             | 631  | 56  | 4  | 0.004194911 | 1           |
| GO:0072672 | neutrophil extravasation                                                                    | 9    | 5   | 1  | 0.004323416 | 1           |
| GO:0051240 | positive regulation of multicellular organismal process                                     | 1506 | 111 | 22 | 0.004358097 | 1           |
| GO:0050702 | interleukin-1 beta secretion                                                                | 42   | 10  | 0  | 0.004383898 | 1           |
| GO:0002697 | regulation of immune effector process                                                       | 348  | 36  | 3  | 0.00505513  | 1           |
| GO:0002221 | pattern recognition receptor signaling pathway                                              | 168  | 22  | 0  | 0.005171898 | 1           |
| GO:0009893 | positive regulation of metabolic process                                                    | 3126 | 204 | 38 | 0.005271532 | 1           |
| GO:0051239 | regulation of multicellular organismal process                                              | 2648 | 177 | 41 | 0.005403955 | 1           |
| GO:0002755 | MyD88-dependent toll-like receptor signaling pathway                                        | 35   | 9   | 0  | 0.005460604 | 1           |
| GO:1904951 | positive regulation of establishment of protein localization                                | 405  | 40  | 3  | 0.005460604 | 1           |
| GO:0002250 | adaptive immune response                                                                    | 350  | 36  | 4  | 0.005571526 | 1           |
| GO:0016050 | vesicle organization                                                                        | 296  | 32  | 1  | 0.005571526 | 1           |
| GO:0045785 | positive regulation of cell adhesion                                                        | 364  | 37  | 4  | 0.005594484 | 1           |
| GO:0052547 | regulation of peptidase activity                                                            | 364  | 37  | 2  | 0.005594484 | 1           |
| GO:0070201 | regulation of establishment of protein localization                                         | 654  | 57  | 4  | 0.005626218 | 1           |
| GO:0006928 | movement of cell or subcellular component                                                   | 1787 | 127 | 41 | 0.005781787 | 0.054108794 |
| GO:0002367 | cytokine production involved in immune response                                             | 91   | 15  | 1  | 0.005828657 | 1           |
| GO:0071219 | cellular response to molecule of bacterial origin                                           | 182  | 23  | 0  | 0.005892329 | 1           |
| GO:0061041 | regulation of wound healing                                                                 | 113  | 17  | 0  | 0.006255149 | 1           |

|            |                                                                                                                           |      |     |    |             |             |
|------------|---------------------------------------------------------------------------------------------------------------------------|------|-----|----|-------------|-------------|
| GO:0032757 | positive regulation of interleukin-8 production                                                                           | 44   | 10  | 0  | 0.006351224 | 1           |
| GO:0071675 | regulation of mononuclear cell migration                                                                                  | 36   | 9   | 1  | 0.006679936 | 1           |
| GO:0051403 | stress-activated MAPK cascade                                                                                             | 260  | 29  | 0  | 0.006850318 | 1           |
| GO:0031323 | regulation of cellular metabolic process                                                                                  | 5315 | 322 | 54 | 0.006855097 | 1           |
| GO:0050707 | regulation of cytokine secretion                                                                                          | 160  | 21  | 1  | 0.006933616 | 1           |
| GO:0032496 | response to lipopolysaccharide                                                                                            | 287  | 31  | 2  | 0.007057627 | 1           |
| GO:0071705 | nitrogen compound transport                                                                                               | 2158 | 148 | 22 | 0.007275744 | 1           |
| GO:0010256 | endomembrane system organization                                                                                          | 384  | 38  | 3  | 0.007555502 | 1           |
| GO:0001776 | leukocyte homeostasis                                                                                                     | 83   | 14  | 3  | 0.007636898 | 1           |
| GO:0002690 | positive regulation of leukocyte chemotaxis                                                                               | 73   | 13  | 2  | 0.007690198 | 1           |
| GO:0071674 | mononuclear cell migration                                                                                                | 54   | 11  | 1  | 0.007715492 | 1           |
| GO:0098609 | cell-cell adhesion                                                                                                        | 724  | 61  | 10 | 0.007721864 | 1           |
| GO:0000187 | activation of MAPK activity                                                                                               | 138  | 19  | 0  | 0.007734155 | 1           |
| GO:1903523 | negative regulation of blood circulation                                                                                  | 29   | 8   | 0  | 0.007734155 | 1           |
| GO:0050793 | regulation of developmental process                                                                                       | 2215 | 151 | 40 | 0.007916914 | 0.781661155 |
| GO:0071622 | regulation of granulocyte chemotaxis                                                                                      | 37   | 9   | 0  | 0.008028146 | 1           |
| GO:0090087 | regulation of peptide transport                                                                                           | 635  | 55  | 4  | 0.008354822 | 1           |
| GO:0051130 | positive regulation of cellular component organization                                                                    | 1123 | 86  | 17 | 0.00860929  | 1           |
| GO:0031325 | positive regulation of cellular metabolic process                                                                         | 2873 | 188 | 31 | 0.00899248  | 1           |
| GO:0001525 | angiogenesis                                                                                                              | 445  | 42  | 6  | 0.0090508   | 1           |
| GO:0043087 | regulation of GTPase activity                                                                                             | 431  | 41  | 10 | 0.009152495 | 0.989075954 |
| GO:0071347 | cellular response to interleukin-1                                                                                        | 106  | 16  | 0  | 0.009152495 | 1           |
| GO:1903827 | regulation of cellular protein localization                                                                               | 489  | 45  | 3  | 0.009195558 | 1           |
| GO:0016236 | macroautophagy                                                                                                            | 266  | 29  | 0  | 0.00959439  | 1           |
| GO:1902622 | regulation of neutrophil migration                                                                                        | 30   | 8   | 0  | 0.009698552 | 1           |
| GO:0051249 | regulation of lymphocyte activation                                                                                       | 376  | 37  | 4  | 0.009906385 | 1           |
| GO:0050715 | positive regulation of cytokine secretion                                                                                 | 108  | 16  | 1  | 0.01128157  | 1           |
| GO:0009743 | response to carbohydrate                                                                                                  | 204  | 24  | 3  | 0.011633007 | 1           |
| GO:0070302 | regulation of stress-activated protein kinase signaling cascade                                                           | 217  | 25  | 0  | 0.011808339 | 1           |
| GO:0048013 | ephrin receptor signaling pathway                                                                                         | 77   | 13  | 1  | 0.012690739 | 1           |
| GO:0007169 | transmembrane receptor protein tyrosine kinase signaling pathway                                                          | 116  | 53  | 11 | 0.012718363 | 1           |
| GO:0006464 | cellular protein modification process                                                                                     | 3634 | 229 | 39 | 0.012821559 | 1           |
| GO:0036211 | protein modification process                                                                                              | 3634 | 229 | 39 | 0.012821559 | 1           |
| GO:0043281 | regulation of cysteine-type endopeptidase activity involved in apoptotic process                                          | 100  | 23  | 0  | 0.012949805 | 1           |
| GO:0051767 | nitric-oxide synthase biosynthetic process                                                                                | 17   | 6   | 0  | 0.013035488 | 1           |
| GO:0051769 | regulation of nitric-oxide synthase biosynthetic process                                                                  | 17   | 6   | 0  | 0.013035488 | 1           |
| GO:0070340 | detection of bacterial lipopeptide                                                                                        | 3    | 3   | 0  | 0.01315179  | 1           |
| GO:0002460 | adaptive immune response based on somatic recombination of immune receptors built from immunoglobulin superfamily domains | 280  | 26  | 1  | 0.014270364 | 1           |
| GO:0002576 | platelet degranulation                                                                                                    | 122  | 17  | 1  | 0.014503148 | 1           |
| GO:0050727 | regulation of inflammatory response                                                                                       | 314  | 32  | 2  | 0.014538693 | 1           |
| GO:0002224 | toll-like receptor signaling pathway                                                                                      | 123  | 17  | 0  | 0.01594757  | 1           |

|            |                                                               |      |     |    |             |             |
|------------|---------------------------------------------------------------|------|-----|----|-------------|-------------|
| GO:0043123 | positive regulation of I-kappaB kinase/NF-kappaB signaling    | 171  | 21  | 1  | 0.016024765 | 1           |
| GO:0045597 | positive regulation of cell differentiation                   | 858  | 68  | 15 | 0.017105336 | 1           |
| GO:0043547 | positive regulation of GTPase activity                        | 359  | 35  | 9  | 0.017159123 | 0.870477156 |
| GO:1903034 | regulation of response to wounding                            | 136  | 18  | 0  | 0.017874522 | 1           |
| GO:0051128 | regulation of cellular component organization                 | 2275 | 152 | 32 | 0.017920515 | 1           |
| GO:0030099 | myeloid cell differentiation                                  | 360  | 35  | 5  | 0.017939107 | 1           |
| GO:0051173 | positive regulation of nitrogen compound metabolic process    | 2771 | 180 | 34 | 0.01800847  | 1           |
| GO:0051094 | positive regulation of developmental process                  | 1201 | 89  | 21 | 0.018331106 | 1           |
| GO:0032677 | regulation of interleukin-8 production                        | 60   | 11  | 0  | 0.018411813 | 1           |
| GO:0070997 | neuron death                                                  | 305  | 31  | 1  | 0.018600627 | 1           |
| GO:0098543 | detection of other organism                                   | 12   | 5   | 0  | 0.018875179 | 1           |
| GO:0051048 | negative regulation of secretion                              | 186  | 22  | 2  | 0.01891199  | 1           |
| GO:0009057 | macromolecule catabolic process                               | 1269 | 93  | 10 | 0.018999165 | 1           |
| GO:0045916 | negative regulation of complement activation                  | 7    | 4   | 0  | 0.01930961  | 1           |
| GO:0051056 | regulation of small GTPase mediated signal transduction       | 306  | 31  | 6  | 0.01930961  | 1           |
| GO:0071476 | cellular hypotonic response                                   | 7    | 4   | 0  | 0.01930961  | 1           |
| GO:2000258 | negative regulation of protein activation cascade             | 7    | 4   | 0  | 0.01930961  | 1           |
| GO:0031663 | lipopolysaccharide-mediated signaling pathway                 | 51   | 10  | 0  | 0.019532324 | 1           |
| GO:0045123 | cellular extravasation                                        | 51   | 10  | 3  | 0.019532324 | 0.669150896 |
| GO:0044267 | cellular protein metabolic process                            | 4551 | 277 | 47 | 0.019796909 | 1           |
| GO:1901575 | organic substance catabolic process                           | 1934 | 132 | 16 | 0.020007773 | 1           |
| GO:0006937 | regulation of muscle contraction                              | 138  | 18  | 1  | 0.020374992 | 1           |
| GO:0043434 | response to peptide hormone                                   | 364  | 35  | 6  | 0.021070827 | 1           |
| GO:0050921 | positive regulation of chemotaxis                             | 115  | 16  | 2  | 0.02118087  | 1           |
| GO:0048523 | negative regulation of cellular process                       | 4113 | 253 | 52 | 0.021899591 | 1           |
| GO:0051051 | negative regulation of transport                              | 408  | 38  | 6  | 0.021899591 | 1           |
| GO:0010661 | positive regulation of muscle cell apoptotic process          | 26   | 7   | 1  | 0.02192505  | 1           |
| GO:0019538 | protein metabolic process                                     | 5067 | 304 | 56 | 0.022521548 | 1           |
| GO:0032872 | regulation of stress-activated MAPK cascade                   | 215  | 24  | 0  | 0.022830476 | 1           |
| GO:0035743 | CD4-positive, alpha-beta T cell cytokine production           | 19   | 6   | 0  | 0.023474679 | 1           |
| GO:0033673 | negative regulation of kinase activity                        | 216  | 24  | 2  | 0.024339447 | 1           |
| GO:0009896 | positive regulation of catabolic process                      | 382  | 36  | 4  | 0.024678993 | 1           |
| GO:0080090 | regulation of primary metabolic process                       | 5208 | 311 | 55 | 0.025290196 | 1           |
| GO:0002718 | regulation of cytokine production involved in immune response | 53   | 12  | 1  | 0.025671832 | 1           |
| GO:0070482 | response to oxygen levels                                     | 312  | 31  | 3  | 0.025671832 | 1           |
| GO:0042594 | response to starvation                                        | 166  | 20  | 0  | 0.026248102 | 1           |
| GO:0043086 | negative regulation of catalytic activity                     | 669  | 55  | 6  | 0.026248102 | 1           |
| GO:0051348 | negative regulation of transferase activity                   | 244  | 26  | 2  | 0.026248102 | 1           |
| GO:0060759 | regulation of response to cytokine stimulus                   | 154  | 19  | 0  | 0.027030672 | 1           |
| GO:0050714 | positive regulation of protein secretion                      | 218  | 24  | 1  | 0.027033414 | 1           |
| GO:0090022 | regulation of neutrophil chemotaxis                           | 27   | 7   | 0  | 0.027033414 | 1           |

|            |                                                                                                                       |      |     |    |             |   |
|------------|-----------------------------------------------------------------------------------------------------------------------|------|-----|----|-------------|---|
| GO:1904646 | cellular response to amyloid-beta                                                                                     | 27   | 7   | 1  | 0.027033414 | 1 |
| GO:0008283 | cell proliferation                                                                                                    | 1761 | 121 | 28 | 0.027213333 | 1 |
| GO:0022407 | regulation of cell-cell adhesion                                                                                      | 356  | 34  | 4  | 0.027337401 | 1 |
| GO:0006508 | proteolysis                                                                                                           | 1576 | 110 | 15 | 0.029222209 | 1 |
| GO:0072593 | reactive oxygen species metabolic process                                                                             | 246  | 26  | 3  | 0.029222209 | 1 |
| GO:0043280 | positive regulation of cysteine-type endopeptidase activity involved in apoptotic process                             | 11   | 1   | 0  | 0.029336158 | 1 |
| GO:0002526 | acute inflammatory response                                                                                           | 131  | 17  | 0  | 0.029626108 | 1 |
| GO:0032868 | response to insulin                                                                                                   | 233  | 25  | 4  | 0.029731739 | 1 |
| GO:0050708 | regulation of protein secretion                                                                                       | 387  | 36  | 2  | 0.030095053 | 1 |
| GO:0044247 | cellular polysaccharide catabolic process                                                                             | 20   | 6   | 0  | 0.03011116  | 1 |
| GO:0090025 | regulation of monocyte chemotaxis                                                                                     | 20   | 6   | 1  | 0.03011116  | 1 |
| GO:0007160 | cell-matrix adhesion                                                                                                  | 207  | 23  | 5  | 0.03037299  | 1 |
| GO:0006935 | chemotaxis                                                                                                            | 537  | 46  | 11 | 0.031747962 | 1 |
| GO:0051251 | positive regulation of lymphocyte activation                                                                          | 248  | 26  | 4  | 0.032193807 | 1 |
| GO:0035744 | T-helper 1 cell cytokine production                                                                                   | 8    | 4   | 0  | 0.032836459 | 1 |
| GO:0007264 | small GTPase mediated signal transduction                                                                             | 523  | 45  | 10 | 0.032933819 | 1 |
| GO:0019222 | regulation of metabolic process                                                                                       | 5763 | 339 | 59 | 0.032947746 | 1 |
| GO:0042330 | taxis                                                                                                                 | 539  | 46  | 11 | 0.033892587 | 1 |
| GO:0050852 | T cell receptor signaling pathway                                                                                     | 133  | 17  | 1  | 0.034161479 | 1 |
| GO:0051090 | regulation of DNA-binding transcription factor activity                                                               | 377  | 35  | 2  | 0.036224025 | 1 |
| GO:0050920 | regulation of chemotaxis                                                                                              | 184  | 21  | 2  | 0.036574118 | 1 |
| GO:0009267 | cellular response to starvation                                                                                       | 134  | 17  | 0  | 0.0368303   | 1 |
| GO:0032637 | interleukin-8 production                                                                                              | 66   | 11  | 0  | 0.0368303   | 1 |
| GO:0061025 | membrane fusion                                                                                                       | 134  | 17  | 0  | 0.0368303   | 1 |
| GO:1903901 | negative regulation of viral life cycle                                                                               | 66   | 11  | 0  | 0.0368303   | 1 |
| GO:0090026 | positive regulation of monocyte chemotaxis                                                                            | 14   | 5   | 1  | 0.037038122 | 1 |
| GO:0006469 | negative regulation of protein kinase activity                                                                        | 198  | 22  | 2  | 0.03826875  | 1 |
| GO:0006979 | response to oxidative stress                                                                                          | 408  | 37  | 3  | 0.03826875  | 1 |
| GO:0036473 | cell death in response to oxidative stress                                                                            | 77   | 12  | 0  | 0.03826875  | 1 |
| GO:0048534 | hematopoietic or lymphoid organ development                                                                           | 777  | 61  | 11 | 0.03826875  | 1 |
| GO:0050818 | regulation of coagulation                                                                                             | 77   | 12  | 0  | 0.03826875  | 1 |
| GO:1903039 | positive regulation of leukocyte cell-cell adhesion                                                                   | 198  | 22  | 3  | 0.03826875  | 1 |
| GO:0001782 | B cell homeostasis                                                                                                    | 29   | 7   | 1  | 0.039601018 | 1 |
| GO:0001999 | renal response to blood flow involved in circulatory renin-angiotensin regulation of systemic arterial blood pressure | 1    | 1   | 0  | 0.039601018 | 1 |
| GO:0002001 | renin secretion into blood stream                                                                                     | 4    | 3   | 0  | 0.039601018 | 1 |
| GO:0042494 | detection of bacterial lipoprotein                                                                                    | 4    | 3   | 0  | 0.039601018 | 1 |
| GO:1903223 | positive regulation of oxidative stress-induced neuron death                                                          | 4    | 3   | 0  | 0.039601018 | 1 |
| GO:0002720 | positive regulation of cytokine production involved in immune response                                                | 4    | 9   | 1  | 0.040286053 | 1 |
| GO:0070265 | necrotic cell death                                                                                                   | 47   | 9   | 0  | 0.040286053 | 1 |
| GO:0030888 | regulation of B cell proliferation                                                                                    | 57   | 10  | 1  | 0.041271788 | 1 |
| GO:0032729 | positive regulation of interferon-gamma production                                                                    | 57   | 10  | 1  | 0.041271788 | 1 |

|            |                                                                                           |      |     |     |             |             |
|------------|-------------------------------------------------------------------------------------------|------|-----|-----|-------------|-------------|
| GO:0070527 | platelet aggregation                                                                      | 57   | 10  | 0   | 0.041271788 | 1           |
| GO:0002822 | regulation of adaptive immune response based on somatic recombination of immune receptors | 136  | 17  | 0   | 0.041271788 | 1           |
| GO:0097300 | programmed necrotic cell death                                                            | 38   | 8   | 0   | 0.041379424 | 1           |
| GO:2000377 | regulation of reactive oxygen species metabolic process                                   | 161  | 19  | 0   | 0.041379424 | 1           |
| GO:0006629 | lipid metabolic process                                                                   | 1274 | 91  | 10  | 0.041845478 | 1           |
| GO:0043112 | receptor metabolic process                                                                | 174  | 20  | 5   | 0.041928718 | 1           |
| GO:0005976 | polysaccharide metabolic process                                                          | 101  | 14  | 1   | 0.043569205 | 1           |
| GO:0043122 | regulation of I-kappaB kinase/NF-kappaB signaling                                         | 214  | 23  | 1   | 0.043569205 | 1           |
| GO:0022603 | regulation of anatomical structure morphogenesis                                          | 912  | 69  | 18  | 0.043665082 | 1           |
| GO:0043412 | macromolecule modification                                                                | 3819 | 234 | 41  | 0.043813518 | 1           |
| GO:0071453 | cellular response to oxygen levels                                                        | 162  | 19  | 1   | 0.043846908 | 1           |
| GO:0000271 | polysaccharide biosynthetic process                                                       | 68   | 11  | 0   | 0.044145176 | 1           |
| GO:0050870 | positive regulation of T cell activation                                                  | 188  | 21  | 3   | 0.044145176 | 1           |
| GO:0071222 | cellular response to lipopolysaccharide                                                   | 175  | 20  | 0   | 0.044145176 | 1           |
| GO:1901214 | regulation of neuron death                                                                | 269  | 27  | 1   | 0.044145176 | 1           |
| GO:0070555 | response to interleukin-1                                                                 | 125  | 16  | 1   | 0.044185913 | 1           |
| GO:0032269 | negative regulation of cellular protein metabolic process                                 | 898  | 68  | 8   | 0.045826564 | 1           |
| GO:1904645 | response to amyloid-beta                                                                  | 30   | 7   | 1   | 0.045966802 | 1           |
| GO:0000272 | polysaccharide catabolic process                                                          | 22   | 6   | 0   | 0.046155493 | 1           |
| GO:0090257 | regulation of muscle system process                                                       | 202  | 22  | 2   | 0.046184075 | 1           |
| GO:0006971 | hypotonic response                                                                        | 9    | 4   | 0   | 0.049853168 | 1           |
| GO:0002673 | regulation of acute inflammatory response                                                 | 80   | 12  | 0   | 0.049885523 | 1           |
| GO:0051047 | positive regulation of secretion                                                          | 357  | 33  | 3   | 0.049885523 | 1           |
| GO:0016043 | cellular component organization                                                           | 5721 | 325 | 104 | 0.246813039 | 0.031675655 |
| GO:0006607 | NLS-bearing protein import into nucleus                                                   | 27   | 3   | 4   | 1           | 0.038603188 |
| GO:0030198 | extracellular matrix organization                                                         | 321  | 15  | 18  | 1           | 0.000116024 |
| GO:0030199 | collagen fibril organization                                                              | 47   | 2   | 7   | 1           | 0.000569572 |
| GO:0043062 | extracellular structure organization                                                      | 368  | 18  | 18  | 1           | 0.000615349 |
| GO:0060351 | cartilage development involved in endochondral bone morphogenesis                         | 4    | 1   | 5   | 1           | 0.02192505  |
| GO:0061138 | morphogenesis of a branching epithelium                                                   | 166  | 9   | 9   | 1           | 0.039793054 |
| GO:0061448 | connective tissue development                                                             | 233  | 6   | 13  | 1           | 0.002884637 |
| GO:0070208 | protein heterotrimerization                                                               | 12   | 0   | 3   | 1           | 0.040528723 |
| GO:0071229 | cellular response to acid chemical                                                        | 195  | 10  | 10  | 1           | 0.032559128 |
| GO:0071230 | cellular response to amino acid stimulus                                                  | 65   | 5   | 6   | 1           | 0.024461895 |

**TABLE 5**  
**Genes Common to Synovial Sublining Fibroblasts and AC3**

| cluster | geneset                                | ensembl         | symbol  | auc        | pct_nonzero | pct_nonzero_other |
|---------|----------------------------------------|-----------------|---------|------------|-------------|-------------------|
| SC-F1   | Fibroblast-CD34+ sublining (SC-F1)     | ENSG00000187955 | COL14A1 | 0.88699058 | 0.98347107  | 0.30535427        |
| SC-F1   | Fibroblast-CD34+ sublining (SC-F1)     | ENSG00000164692 | COL1A2  | 0.84468179 | 1           | 0.53280998        |
| SC-F1   | Fibroblast-CD34+ sublining (SC-F1)     | ENSG00000168542 | COL3A1  | 0.82353841 | 1           | 0.53301127        |
| SC-F1   | Fibroblast-CD34+ sublining (SC-F1)     | ENSG00000130635 | COL5A1  | 0.76918996 | 0.80991736  | 0.26348631        |
| SC-F1   | Fibroblast-CD34+ sublining (SC-F1)     | ENSG00000105664 | COMP    | 0.72267741 | 0.5268595   | 0.09178744        |
| SC-F1   | Fibroblast-CD34+ sublining (SC-F1)     | ENSG00000133083 | DCLK1   | 0.78673115 | 0.70041322  | 0.16807568        |
| SC-F1   | Fibroblast-CD34+ sublining (SC-F1)     | ENSG00000146648 | EGFR    | 0.76375622 | 0.72933884  | 0.23007246        |
| SC-F1   | Fibroblast-CD34+ sublining (SC-F1)     | ENSG00000120738 | EGR1    | 0.75381699 | 0.95041322  | 0.6507649         |
| SC-F1   | Fibroblast-CD34+ sublining (SC-F1)     | ENSG00000164694 | FNDC1   | 0.7526103  | 0.63842975  | 0.15116747        |
| SC-F1   | Fibroblast-CD34+ sublining (SC-F1)     | ENSG00000131386 | GALNT15 | 0.7329481  | 0.59297521  | 0.14351852        |
| SC-F1   | Fibroblast-CD34+ sublining (SC-F1)     | ENSG00000168079 | SCARA5  | 0.74916074 | 0.78512397  | 0.28965378        |
| SC-F1   | Fibroblast-CD34+ sublining (SC-F1)     | ENSG00000137573 | SULF1   | 0.73367922 | 0.67561983  | 0.23389694        |
| SC-F1   | Fibroblast-CD34+ sublining (SC-F1)     | ENSG00000091656 | ZFHX4   | 0.77838039 | 0.71487603  | 0.2071256         |
| SC-F2   | Fibroblast-HLA-DRAhi sublining (SC-F2) | ENSG00000187955 | COL14A1 | 0.91760718 | 0.99165508  | 0.27044158        |
| SC-F2   | Fibroblast-HLA-DRAhi sublining (SC-F2) | ENSG00000084636 | COL16A1 | 0.87323477 | 0.83588317  | 0.10585252        |
| SC-F2   | Fibroblast-HLA-DRAhi sublining (SC-F2) | ENSG00000164692 | COL1A2  | 0.92139483 | 1           | 0.50961335        |
| SC-F2   | Fibroblast-HLA-DRAhi sublining (SC-F2) | ENSG00000168542 | COL3A1  | 0.93074592 | 1           | 0.50982464        |
| SC-F2   | Fibroblast-HLA-DRAhi sublining (SC-F2) | ENSG00000134871 | COL4A2  | 0.84125266 | 0.86648122  | 0.18761885        |
| SC-F2   | Fibroblast-HLA-DRAhi sublining (SC-F2) | ENSG00000130635 | COL5A1  | 0.88489277 | 0.95132128  | 0.21487429        |
| SC-F2   | Fibroblast-HLA-DRAhi sublining (SC-F2) | ENSG00000133083 | DCLK1   | 0.83131283 | 0.79972184  | 0.12655821        |
| SC-F2   | Fibroblast-HLA-DRAhi sublining (SC-F2) | ENSG00000146648 | EGFR    | 0.80327353 | 0.82058414  | 0.19142193        |
| SC-F2   | Fibroblast-HLA-DRAhi sublining (SC-F2) | ENSG00000120738 | EGR1    | 0.80507545 | 0.9930459   | 0.62941052        |
| SC-F2   | Fibroblast-HLA-DRAhi sublining (SC-F2) | ENSG00000130508 | PXDN    | 0.84330642 | 0.83171071  | 0.16670188        |
| SC-F2   | Fibroblast-HLA-DRAhi sublining (SC-F2) | ENSG00000166444 | ST5     | 0.83349089 | 0.81641168  | 0.15867315        |

|       |                                    |                 |         |            |            |            |
|-------|------------------------------------|-----------------|---------|------------|------------|------------|
| SC-F3 | Fibroblast-DKK3+ sublining (SC-F3) | ENSG00000187955 | COL14A1 | 0.85231287 | 0.96929825 | 0.33920368 |
| SC-F3 | Fibroblast-DKK3+ sublining (SC-F3) | ENSG00000164692 | COL1A2  | 0.90670253 | 1          | 0.55570444 |
| SC-F3 | Fibroblast-DKK3+ sublining (SC-F3) | ENSG00000168542 | COL3A1  | 0.90184724 | 1          | 0.55589587 |
| SC-F3 | Fibroblast-DKK3+ sublining (SC-F3) | ENSG00000130635 | COL5A1  | 0.91728082 | 0.98245614 | 0.28273354 |
| SC-F3 | Fibroblast-DKK3+ sublining (SC-F3) | ENSG00000105664 | COMP    | 0.81905082 | 0.71929825 | 0.10470904 |
| SC-F3 | Fibroblast-DKK3+ sublining (SC-F3) | ENSG00000164694 | FNDC1   | 0.8072182  | 0.76315789 | 0.16960184 |
| SC-F3 | Fibroblast-DKK3+ sublining (SC-F3) | ENSG00000131386 | GALNT15 | 0.81963055 | 0.76754386 | 0.15792496 |
| SC-F3 | Fibroblast-DKK3+ sublining (SC-F3) | ENSG00000164294 | GPX8    | 0.80951068 | 0.8245614  | 0.22396631 |
| SC-F3 | Fibroblast-DKK3+ sublining (SC-F3) | ENSG00000167779 | IGFBP6  | 0.83772643 | 0.78947368 | 0.16807044 |
| SC-F3 | Fibroblast-DKK3+ sublining (SC-F3) | ENSG00000130508 | PXDN    | 0.83692715 | 0.88157895 | 0.2270291  |
| SC-F3 | Fibroblast-DKK3+ sublining (SC-F3) | ENSG00000168079 | SCARA5  | 0.81990132 | 0.89035088 | 0.3093415  |
| SC-F3 | Fibroblast-DKK3+ sublining (SC-F3) | ENSG00000137573 | SULF1   | 0.83014503 | 0.86403509 | 0.24732006 |
| SC-F3 | Fibroblast-DKK3+ sublining (SC-F3) | ENSG00000091656 | ZFXH4   | 0.78976712 | 0.80263158 | 0.22817764 |

TABLE 6  
Differential Gene Expression (Baseline versus Flare) of AC3 Genes Across Four RA Patients

| ensembl          | name    | name_source | description                                                                                          | p1.logFC     | p1.FDR      | p16.logFC    | p16.FDR | p17.logFC   | p17.FDR     | p18.logFC    | p18.FDR |
|------------------|---------|-------------|------------------------------------------------------------------------------------------------------|--------------|-------------|--------------|---------|-------------|-------------|--------------|---------|
| ENSG000000002746 | HECW1   | HGNC Symbol | "HECT, C2 and WW domain containing E3 ubiquitin protein ligase 1 [Source:HGNC Symbol;Acc:HNC:27195]" | -0.324338654 | 0.572555903 | -0.328868037 | 1       | 0.438047831 | 0.908516526 | 0.257699857  | 1       |
| ENSG000000004948 | CALCR   | HGNC Symbol | calcitonin receptor [Source:HGNC Symbol;Acc:HNC:4440]                                                | -0.383180659 | 0.45624237  | 0.278685382  | 1       | 2.855446254 | 0.69984612  | 0.32802643   | 1       |
| ENSG000000006071 | ABCC8   | HGNC Symbol | ATP binding cassette subfamily C member 8 [Source:HGNC Symbol;Acc:HNC:59]                            | -0.435216452 | 0.467869018 | -0.183143093 | 1       | -0.15172062 | 0.972940456 | 0.050166206  | 1       |
| ENSG000000006078 | TAC1    | HGNC Symbol | tachykinin precursor 1 [Source:HGNC Symbol;Acc:HNC:1517]                                             | -0.578738859 | 0.363974577 | -0.42309878  | 1       | -0.82688556 | 0.86142478  | 0.616538787  | 1       |
| ENSG000000006240 | CX3CL1  | HGNC Symbol | C-X3-C motif chemokine ligand 1 [Source:HGNC Symbol;Acc:HNC:10647]                                   | -0.47184278  | 0.450972862 | 0.394994483  | 1       | 0.142838907 | 0.984792321 | -0.105867018 | 1       |
| ENSG000000006283 | CACNA1G | HGNC Symbol | calcium voltage-gated channel subunit alpha 1G [Source:HGNC Symbol;Acc:HNC:1394]                     | -0.65282151  | 0.174301995 | -0.153595375 | 1       | 0.736365852 | 0.850652372 | 0.016389601  | 1       |
| ENSG000000006788 | MYH13   | HGNC Symbol | myosin heavy chain 13 [Source:HGNC Symbol;Acc:HNC:7571]                                              | -0.516406336 | 0.431894501 | -0.182295216 | 1       | 1.277253446 | 0.740349802 | 0.194022822  | 1       |
| ENSG000000006788 | PAX7    | HGNC Symbol | paired box 7 [Source:HGNC Symbol;Acc:HNC:10647]                                                      | -0.287556069 | 0.54217066  | -0.237365553 | 1       | 6.295166726 | 0.627668963 | 0.238426716  | 1       |

|                     |         |             |                                                                                                 |              |             |               |   |              |             |              |   |
|---------------------|---------|-------------|-------------------------------------------------------------------------------------------------|--------------|-------------|---------------|---|--------------|-------------|--------------|---|
| 009709              | GABRA3  | HGNC Symbol | Symbol/Accession:HGNC:8621                                                                      | -0.62857558  | 0.372582184 | -0.442716362  | 1 | 1.889252428  | 0.751835169 | 0.151297142  | 1 |
| ENSG0000000010677   |         |             | gamma-aminobutyric acid type A receptor alpha3 subunit [Source:HGNC Symbol/Accession:HGNC:4077] |              |             |               |   |              |             |              |   |
| ENSG00000000105520  | NPC1L1  | HGNC Symbol | NPC1 like intracellular cholesterol transporter 1 [Source:HGNC Symbol/Accession:HGNC:7898]      | -0.449755668 | 0.428701424 | -0.700785246  | 1 | -0.349773321 | 0.929542543 | 0.193503425  | 1 |
| ENSG00000000108606  | ZNF806  | HGNC Symbol | zinc finger protein 806 [Source:HGNC Symbol/Accession:HGNC:33278]                               | -0.534986692 | 0.430723959 | -0.226756688  | 1 | 0.349569946  | 0.959459365 | 0.583701654  | 1 |
| ENSG00000000108607  | ATPA2   | HGNC Symbol | ATPase Na+/K+ transporting subunit alpha 2 [Source:HGNC Symbol/Accession:HGNC:800]              | -0.380151358 | 0.49141631  | -0.323676225  | 1 | 1.616286887  | 0.772222226 | 0.102816854  | 1 |
| ENSG00000000108625  | SYT13   | HGNC Symbol | synaptotagmin 13 [Source:HGNC Symbol/Accession:HGNC:14562]                                      | -0.846107945 | 0.185236167 | 0.192851682   | 1 | 1.7666610549 | 0.735101059 | -0.059221871 | 1 |
| ENSG00000000109505  | DNAH5   | HGNC Symbol | dyanein axonemal heavy chain 5 [Source:HGNC Symbol/Accession:HGNC:2950]                         | -0.56914692  | 0.367219403 | -0.3510782091 | 1 | 0.33657337   | 0.929444672 | 0.374918338  | 1 |
| ENSG00000000103929  | BEST2   | HGNC Symbol | bestrophin 2 [Source:HGNC Symbol/Accession:HGNC:1107]                                           | -0.461098164 | 0.486868005 | -0.266358455  | 1 | -0.702919573 | 0.879866057 | -0.349787212 | 1 |
| ENSG000000001039987 | PTPRN   | HGNC Symbol | "protein tyrosine phosphatase, receptor type N [Source:HGNC Symbol/Accession:HGNC:9676]"        | -0.476009808 | 0.238645395 | 0.117452397   | 1 | -0.42869871  | 0.839974197 | -0.036104409 | 1 |
| ENSG000000001054356 | PTPRU   | HGNC Symbol | "protein tyrosine phosphatase, receptor type U [Source:HGNC Symbol/Accession:HGNC:9683]"        | -0.440932203 | 0.365704058 | -0.2104603501 | 1 | 0.38553287   | 0.883612752 | 0.052221341  | 1 |
| ENSG000000001050556 | RIMBP2  | HGNC Symbol | RMS binding protein 2 [Source:HGNC Symbol/Accession:HGNC:30339]                                 | -0.486388539 | 0.318754361 | -0.14886622   | 1 | 0.267280913  | 0.953466793 | -0.023574473 | 1 |
| ENSG000000001050709 | FBF3    | HGNC Symbol | fibroblast growth factor receptor 3 [Source:HGNC Symbol/Accession:HGNC:3690]                    | -0.474403299 | 0.318084941 | 0.779778588   | 1 | 0.6655050568 | 0.860481624 | -0.338667178 | 1 |
| ENSG000000001068078 | ABCC9   | HGNC Symbol | ATP binding cassette subfamily C member 9 [Source:HGNC Symbol/Accession:HGNC:60]                | -0.755222404 | 0.20328346  | -0.658467219  | 1 | 1.50464862   | 0.754933936 | 0.427108144  | 1 |
| ENSG000000001069431 | EPHA8   | HGNC Symbol | EPH receptor A8 [Source:HGNC Symbol/Accession:HGNC:3391]                                        | -0.506558126 | 0.338093351 | 0.037142847   | 1 | 0.618732016  | 0.876857452 | -0.036880882 | 1 |
| ENSG000000001070886 | SLC6A15 | HGNC Symbol | solute carrier family 6 member 15 [Source:HGNC Symbol/Accession:HGNC:1652]                      | -0.23655442  | 0.738227188 | -0.029174812  | 1 | 0.598327652  | 0.919139163 | 0.218044555  | 1 |
| ENSG000000001072041 | PAX2    | HGNC Symbol | paired box 2 [Source:HGNC Symbol/Accession:HGNC:8616]                                           | -0.768916818 | 0.140101294 | -0.139681455  | 1 | 0.666537779  | 0.859477376 | 0.023401093  | 1 |
| ENSG000000001075891 | ACTL6B  | HGNC Symbol | actin like 6B [Source:HGNC Symbol/Accession:HGNC:160]                                           | -0.59184773  | 0.349654075 | -0.291947443  | 1 | 2.05248954   | 0.734558921 | -0.579843889 | 1 |
| ENSG000000001077081 | ACTN2   | HGNC Symbol | actinin alpha 2 [Source:HGNC Symbol/Accession:HGNC:164]                                         | -0.42322874  | 0.461775497 | -0.359543665  | 1 | 1.055057551  | 0.816563802 | 0.056205006  | 1 |
| ENSG000000001077522 | ADCY2   | HGNC Symbol | adenylate cyclase 2 [Source:HGNC Symbol/Accession:HGNC:2233]                                    | -0.361085034 | 0.538385903 | -0.153032167  | 1 | 0.090300816  | 0.919623026 | -0.60763243  | 1 |
| ENSG000000001078295 | ADCYAP1 | HGNC Symbol | ADCYAP receptor type 1 [Source:HGNC Symbol/Accession:HGNC:242]                                  | -0.253394484 | 0.715971682 | -0.548781659  | 1 | 0.436615106  | 0.919671237 | 0.282001957  | 1 |
| ENSG000000001078549 | BPIFB2  | HGNC Symbol | BPI fold containing family B member 2 [Source:HGNC Symbol/Accession:HGNC:1677]                  | -0.586529177 | 0.353356504 | -0.186330302  | 1 | 0.617904762  | 0.87446638  | 0.447655654  | 1 |
| ENSG000000001078898 | CDH17   | HGNC Symbol | cadherin 17 [Source:HGNC Symbol/Accession:HGNC:1756]                                            | -0.61532191  | 0.280210348 | -0.17451018   | 1 | 1.291358643  | 0.794377353 | -0.24687928  | 1 |
| ENSG000000001079102 | RIMS1   | HGNC Symbol | regulating synaptic membrane exocytosis 1 [Source:HGNC Symbol/Accession:HGNC:17282]             | -0.387854778 | 0.537171359 | -0.220371451  | 1 | 0.261822706  | 0.957654277 | 0.360367388  | 1 |
| ENSG000000001079841 | CACNA1S | HGNC Symbol | calcium voltage-gated channel subunit alpha 1S [Source:HGNC Symbol/Accession:HGNC:1397]         | -0.562402388 | 0.274521043 | -0.185575362  | 1 | -0.292283267 | 0.939917429 | 0.087334946  | 1 |
| ENSG000000001081248 |         |             |                                                                                                 |              |             |               |   |              |             |              |   |

|                  |         |             |                                                                                     |               |              |               |   |              |             |              |   |
|------------------|---------|-------------|-------------------------------------------------------------------------------------|---------------|--------------|---------------|---|--------------|-------------|--------------|---|
| ENSG000000081800 | SLC3A1  | HGNC Symbol | solute carrier family 13 member 1 [Source:HGNC Symbol;Acc:HGNC:10916]               | -0.71148359   | 0.288085754  | -0.315731689  | 1 | 0.415484856  | 0.928558195 | -0.122942855 | 1 |
| ENSG000000082175 | PGR     | HGNC Symbol | progesterone receptor [Source:HGNC Symbol;Acc:HGNC:8910]                            | -0.458379398  | 0.41160075   | -0.172803447  | 1 | 1.97789718   | 0.699435544 | -0.170595574 | 1 |
| ENSG000000084635 | COL6A1  | HGNC Symbol | collagen type XI alpha 1 chain [Source:HGNC Symbol;Acc:HGNC:2193]                   | -0.798050487  | 0.055725925  | -0.166089061  | 1 | 0.586078349  | 0.853985444 | -0.126623098 | 1 |
| ENSG000000088340 | FER1L4  | HGNC Symbol | "fer-1 like family member 4, pseudogene [Source:HGNC Symbol;Acc:HGNC:45801]"        | -0.6167873    | 0.656310461  | -0.078004571  | 1 | 0.349186341  | 0.910714926 | -0.239607349 | 1 |
| ENSG000000089106 | LHX5    | HGNC Symbol | LIM homeobox 5 [Source:HGNC Symbol;Acc:HGNC:14216]                                  | -0.803770537  | 0.087896409  | 0.065318066   | 1 | 0.185916509  | 0.972840456 | 0.479888913  | 1 |
| ENSG000000089189 | CH6B    | HGNC Symbol | chromogranin B [Source:HGNC Symbol;Acc:HGNC:1950]                                   | -0.637146342  | 0.2553573795 | -0.3270202315 | 1 | 0.377523248  | 0.925166542 | -0.124040006 | 1 |
| ENSG000000089225 | TBX5    | HGNC Symbol | T-box 5 [Source:HGNC Symbol;Acc:HGNC:11604]                                         | -0.56322196   | 0.348101747  | -0.1865556677 | 1 | 0.5867101642 | 0.888551048 | 0.187810501  | 1 |
| ENSG00000009128  | LAMB4   | HGNC Symbol | laminin subunit beta 4 [Source:HGNC Symbol;Acc:HGNC:6491]                           | -0.48817715   | 0.358139517  | 0.074590997   | 1 | 1.1348410911 | 0.766091016 | 0.591653405  | 1 |
| ENSG00000009137  | SLC26A4 | HGNC Symbol | solute carrier family 26 member 4 [Source:HGNC Symbol;Acc:HGNC:8818]                | -0.554256056  | 0.184723389  | -0.379948372  | 1 | 0.990897518  | 0.77694729  | 0.18408228   | 1 |
| ENSG000000091656 | ZFX4    | HGNC Symbol | zinc finger homeobox 4 [Source:HGNC Symbol;Acc:HGNC:31939]                          | -0.447229074  | 0.37818144   | 0.068987085   | 1 | 0.573719306  | 0.878468837 | -0.178950263 | 1 |
| ENSG000000095587 | TLL2    | HGNC Symbol | taloid like 2 [Source:HGNC Symbol;Acc:HGNC:11844]                                   | -0.408359463  | 0.40882038   | -0.26381606   | 1 | 1.33832395   | 0.748037903 | 0.086688368  | 1 |
| ENSG000000095637 | SORBS1  | HGNC Symbol | sorbin and SH3 domain containing 1 [Source:HGNC Symbol;Acc:HGNC:14565]              | -0.32424573   | 0.08491354   | -0.08682706   | 1 | 0.07212715   | 0.980464761 | 0.233872426  | 1 |
| ENSG000000098675 | C8ARP   | HGNC Symbol | CACN beta subunit associated regulatory protein [Source:HGNC Symbol;Acc:HGNC:28617] | -0.61658751   | 0.305918323  | 0.924708632   | 1 | 4.510500591  | 0.630714789 | -0.556807911 | 1 |
| ENSG00000010033  | PRODH   | HGNC Symbol | proline dehydrogenase 1 [Source:HGNC Symbol;Acc:HGNC:9453]                          | -0.729953766  | 0.14187223   | 0.3926102047  | 1 | 0.416465918  | 0.927256163 | 0.074209613  | 1 |
| ENSG00000010065  | CARD10  | HGNC Symbol | cardiac recruitment domain family member 10 [Source:HGNC Symbol;Acc:HGNC:16427]     | -0.704322375  | 0.16976682   | -0.094316814  | 1 | 1.184451362  | 0.737781088 | 0.010459367  | 1 |
| ENSG00000010078  | PLA2G3  | HGNC Symbol | phospholipase A2 group III [Source:HGNC Symbol;Acc:HGNC:19334]                      | -0.639107104  | 0.855150771  | 0.366462718   | 1 | -0.819130599 | 0.880905808 | 0.273159772  | 1 |
| ENSG00000010132  | ACR     | HGNC Symbol | acrosin [Source:HGNC Symbol;Acc:HGNC:426]                                           | -0.5855590525 | 0.367166088  | -0.436425953  | 1 | -0.816265078 | 0.843731985 | 0.905100759  | 1 |
| ENSG00000010104  | NNL     | HGNC Symbol | ninin like [Source:HGNC Symbol;Acc:HGNC:2963]                                       | -0.461697247  | 0.104557083  | -0.1393393033 | 1 | 0.111085893  | 0.958051922 | 0.007374673  | 1 |
| ENSG00000010157  | MYB12   | HGNC Symbol | MYB proto-oncogene like 2 [Source:HGNC Symbol;Acc:HGNC:7548]                        | -0.34828275   | 0.63757922   | 0.0655592977  | 1 | -0.316761009 | 0.853985444 | -0.363993202 | 1 |
| ENSG00000010203  | COL20A1 | HGNC Symbol | collagen type XI alpha 1 chain [Source:HGNC Symbol;Acc:HGNC:14670]                  | -0.611271042  | 0.6216506    | 0.172380322   | 1 | 1.371012438  | 0.716501857 | 0.256710081  | 1 |
| ENSG00000010276  | SLC52A3 | HGNC Symbol | solute carrier family 52 member 3 [Source:HGNC Symbol;Acc:HGNC:16187]               | -0.619771881  | 0.3181117    | 0.082884294   | 1 | 1.903327866  | 0.760815797 | -0.182594116 | 1 |
| ENSG00000010680  | LAMA1   | HGNC Symbol | laminin subunit alpha 1 [Source:HGNC Symbol;Acc:HGNC:648]                           | -0.361627167  | 0.534718981  | -0.2103871279 | 1 | 0.4010062263 | 0.922861341 | 0.571294866  | 1 |
| ENSG00000010671  | MID1    | HGNC Symbol | midline 1 [Source:HGNC Symbol;Acc:HGNC:7095]                                        | -0.530388862  | 0.1602105439 | 0.209637567   | 1 | -0.268716891 | 0.951054633 | -0.136170874 | 1 |
| ENSG00000010287  | GABRE   | HGNC Symbol | gamma-aminobutyric acid type A receptor epsilon subunit [Source:HGNC]               | -0.6719752592 | 0.062885559  | -0.178338056  | 1 | 0.533972134  | 0.910752728 | 0.371680991  | 1 |

|                 |         |             |                             |                                                                                                  |               |              |               |   |              |              |              |   |
|-----------------|---------|-------------|-----------------------------|--------------------------------------------------------------------------------------------------|---------------|--------------|---------------|---|--------------|--------------|--------------|---|
| ENSG00000102290 | PCDH1X  | HGNC Symbol | Symbol/Accession:HGNC:4085  | protocadherin IX-linked [Source:HGNC Symbol/Accession:HGNC:8656]                                 | -0.6469727871 | 0.279252696  | -0.633443604  | I | 0.887626644  | 0.84830486   | 0.35306708   | I |
| ENSG00000102452 | NALCN   | HGNC Symbol | Symbol/Accession:HGNC:8656  | "sodium leak channel, non-selective" [Source:HGNC Symbol/Accession:HGNC:40852]"                  | -0.587200069  | 0.346930169  | -0.228025142  | I | 0.395274547  | 0.920775245  | 0.236838494  | I |
| ENSG00000103647 | CORO2B  | HGNC Symbol | Symbol/Accession:HGNC:2256  | coronin 2B [Source:HGNC Symbol/Accession:HGNC:2256]                                              | -0.36456868   | 0.361292957  | 0.479287145   | I | 0.16146607   | 0.954367943  | 0.394858842  | I |
| ENSG00000103855 | C0276   | HGNC Symbol | Symbol/Accession:HGNC:4937  | C0276 molecule [Source:HGNC Symbol/Accession:HGNC:4937]                                          | -0.786482702  | 0.123893703  | -0.043746659  | I | 2.891670875  | 0.1655801493 | 0.339884759  | I |
| ENSG00000104055 | TGM5    | HGNC Symbol | Symbol/Accession:HGNC:4780  | transglutaminase 5 [Source:HGNC Symbol/Accession:HGNC:4780]                                      | -0.744478896  | 0.16612955   | 0.346888998   | I | 2.8575116    | 0.169458936  | 0.48659696   | I |
| ENSG00000104313 | EYAI    | HGNC Symbol | Symbol/Accession:HGNC:3519  | EYA transcriptional coactivator and phosphatase I [Source:HGNC Symbol/Accession:HGNC:3519]       | -0.54795624   | 0.332328891  | -0.089328093  | I | 0.90438457   | 0.874940952  | -0.145400561 | I |
| ENSG00000104435 | STMN2   | HGNC Symbol | Symbol/Accession:HGNC:10577 | stathmin 2 [Source:HGNC Symbol/Accession:HGNC:10577]                                             | -0.538148899  | 0.37773554   | -0.070271779  | I | 2.13874005   | 0.743863355  | 0.679714458  | I |
| ENSG00000104537 | ANXA3   | HGNC Symbol | Symbol/Accession:HGNC:538   | annexin A3 [Source:HGNC Symbol/Accession:HGNC:538]                                               | -0.296697524  | 0.666104371  | -0.197734314  | I | 0.962189734  | 0.845260843  | 0.15906724   | I |
| ENSG00000104657 | NOVA2   | HGNC Symbol | Symbol/Accession:HGNC:7887  | NOVA alternative splicing regulator 2 [Source:HGNC Symbol/Accession:HGNC:7887]                   | -0.905429895  | 0.09600687   | -0.408162724  | I | -0.248666658 | 0.967431863  | -0.288237016 | I |
| ENSG00000105290 | APIP1   | HGNC Symbol | Symbol/Accession:HGNC:597   | anyloid beta precursor like protein 1 [Source:HGNC Symbol/Accession:HGNC:597]                    | -0.6268897604 | 0.28126695   | 0.239914511   | I | 0.16123374   | 0.884845783  | -0.023517235 | I |
| ENSG00000105357 | MYH14   | HGNC Symbol | Symbol/Accession:HGNC:2322  | myosin heavy chain 14 [Source:HGNC Symbol/Accession:HGNC:2322]                                   | -0.396112836  | 0.4893919147 | -0.105194384  | I | -0.286257636 | 0.937722107  | 0.12225136   | I |
| ENSG00000105392 | CRX     | HGNC Symbol | Symbol/Accession:HGNC:2383  | cone-rod homeobox [Source:HGNC Symbol/Accession:HGNC:2383]                                       | -0.652077771  | 0.2956697    | -0.140180995  | I | 1.350403461  | 0.782183897  | 0.12132333   | I |
| ENSG00000105549 | THEG    | HGNC Symbol | Symbol/Accession:HGNC:13705 | theig spermatid protein [Source:HGNC Symbol/Accession:HGNC:13705]                                | -0.567300418  | 0.345650275  | -0.1675865699 | I | 0.43424405   | 0.933776275  | -0.01546944  | I |
| ENSG00000105605 | CACNG7  | HGNC Symbol | Symbol/Accession:HGNC:2227  | calcium voltage-gated channel auxiliary subunit gamma 7 [Source:HGNC Symbol/Accession:HGNC:2227] | -0.825334915  | 0.173466676  | -0.044046243  | I | -0.078830301 | 0.997233628  | -0.364251039 | I |
| ENSG00000105654 | COMP    | HGNC Symbol | Symbol/Accession:HGNC:2219  | cartilage oligomeric matrix protein [Source:HGNC Symbol/Accession:HGNC:2219]                     | -0.799182187  | 0.027432398  | 0.234763584   | I | 0.107592469  | 0.973220719  | -0.169205599 | I |
| ENSG00000106078 | C0BL    | HGNC Symbol | Symbol/Accession:HGNC:2219  | cardion-bleu WH2 repeat protein [Source:HGNC Symbol/Accession:HGNC:2219]                         | -0.492882326  | 0.263675181  | -0.596346691  | I | 1.300744474  | 0.75103015   | 0.037709932  | I |
| ENSG00000106304 | SPAM1   | HGNC Symbol | Symbol/Accession:HGNC:4217  | sperm adhesion molecule 1 [Source:HGNC Symbol/Accession:HGNC:4217]                               | -0.294698557  | 0.697359656  | -0.454356675  | I | 1.278780312  | 0.800133595  | 0.772079094  | I |
| ENSG00000106648 | GALNTL5 | HGNC Symbol | Symbol/Accession:HGNC:2725  | polypeptide N-acetylglucosaminyltransferase like 5 [Source:HGNC Symbol/Accession:HGNC:2725]      | -0.610689222  | 0.369270393  | -0.116446058  | I | 1.570956079  | 0.742949496  | 0.243774247  | I |
| ENSG00000106689 | LHX2    | HGNC Symbol | Symbol/Accession:HGNC:5594  | LHX homeobox 2 [Source:HGNC Symbol/Accession:HGNC:5594]                                          | -0.630789543  | 0.278439847  | 0.428190081   | I | -0.07571984  | 0.995803452  | 0.046816551  | I |
| ENSG00000107295 | SH3GL2  | HGNC Symbol | Symbol/Accession:HGNC:10831 | "SH3 domain containing GRB2 like 2, endophilin A1 [Source:HGNC Symbol/Accession:HGNC:10831]"     | -0.633805457  | 0.3501655788 | -0.774258486  | I | 2.464703425  | 0.168994444  | -0.082666666 | I |
| ENSG00000107807 | TLX1    | HGNC Symbol | Symbol/Accession:HGNC:5056  | T cell leukemia homeobox 1 [Source:HGNC Symbol/Accession:HGNC:5056]                              | -0.773774408  | 0.166228514  | 0.137827715   | I | 0.544587691  | 0.9119798    | 0.23211497   | I |
| ENSG00000108018 | SORCS1  | HGNC Symbol | Symbol/Accession:HGNC:16597 | sortilin related VPSID domain containing receptor 1 [Source:HGNC Symbol/Accession:HGNC:16597]    | -0.57187073   | 0.324225606  | -0.547468752  | I | 0.85269341   | 0.843439811  | 0.729297049  | I |
| ENSG00000109101 | FOXN1   | HGNC Symbol | Symbol/Accession:HGNC:12765 | forkhead box N1 [Source:HGNC Symbol/Accession:HGNC:12765]                                        | -0.551457548  | 0.309062169  | 0.538410693   | I | -0.082464276 | 0.993535942  | -0.47244805  | I |

|                |         |             |                                                                                                |               |              |               |   |               |             |               |   |
|----------------|---------|-------------|------------------------------------------------------------------------------------------------|---------------|--------------|---------------|---|---------------|-------------|---------------|---|
| ENSG0000010786 | PTPNS   | HGNC Symbol | "protein tyrosine phosphatase, non-receptor type 5 [Source:HGNC Symbol;Acc:HGNC:9657]"         | -0.733454811  | 0.20453453   | 0.191507596   | 1 | 0.06886557    | 0.99765152  | -0.238985372  | 1 |
| ENSG0000010887 | DAO     | HGNC Symbol | D-amino acid oxidase [Source:HGNC Symbol;Acc:HGNC:2571]                                        | -0.59549208   | 0.394229719  | 0.13111108    | 1 | -0.1444679    | 0.97995314  | 0.597447393   | 1 |
| ENSG0000010975 | SYT10   | HGNC Symbol | synaptotagmin 10 [Source:HGNC Symbol;Acc:HGNC:19766]                                           | -0.94217722   | 0.209970599  | -0.251499943  | 1 | -0.31391037   | 0.946363384 | -0.995079899  | 1 |
| ENSG0000011262 | KCNMA1  | HGNC Symbol | potassium voltage-gated channel subfamily A member 1 [Source:HGNC Symbol;Acc:HGNC:6218]        | -0.777520439  | 0.155026428  | -0.46562427   | 1 | 1.142878791   | 0.805478894 | 0.642729197   | 1 |
| ENSG0000011739 | COL12A1 | HGNC Symbol | collagen type XII alpha 1 chain [Source:HGNC Symbol;Acc:HGNC:2188]                             | -0.950476274  | 0.050128873  | -0.14911957   | 1 | 0.782188184   | 0.832135161 | 0.238165895   | 1 |
| ENSG0000012066 | CAP2    | HGNC Symbol | cyclase associated actin cytoskeleton regulatory protein 2 [Source:HGNC Symbol;Acc:HGNC:21039] | -0.98733845   | 0.075743598  | -0.074260504  | 1 | 0.733866999   | 0.867584445 | 0.324661966   | 1 |
| ENSG0000012238 | PROM1B  | HGNC Symbol | PR/SET domain 18 [Source:HGNC Symbol;Acc:HGNC:18998]                                           | -0.7185787    | 0.166103748  | 0.393701014   | 1 | 0.320967557   | 0.953891446 | 1.15377245    | 1 |
| ENSG0000012337 | SLC7A2  | HGNC Symbol | solute carrier family 7 member 2 [Source:HGNC Symbol;Acc:HGNC:10930]                           | -0.701065633  | 0.275381592  | -0.333294833  | 1 | 0.738233667   | 0.881825991 | 0.694827888   | 1 |
| ENSG0000012495 | SLC22A2 | HGNC Symbol | solute carrier family 22 member 2 [Source:HGNC Symbol;Acc:HGNC:10966]                          | -0.585273919  | 0.28351069   | -0.305955711  | 1 | 0.00100383    | 1           | 0.402578655   | 1 |
| ENSG0000014019 | AMOTL2  | HGNC Symbol | angiotensin like 2 [Source:HGNC Symbol;Acc:HGNC:17812]                                         | -0.638655464  | 0.2108142203 | 0.119358618   | 1 | 0.925741653   | 0.7871604   | -0.086135098  | 1 |
| ENSG0000015041 | KCNIP3  | HGNC Symbol | potassium voltage-gated channel interacting protein 3 [Source:HGNC Symbol;Acc:HGNC:15523]      | -0.3910671123 | 0.447854968  | -9.28E-106    | 1 | -0.126754251  | 0.980723343 | 0.216502642   | 1 |
| ENSG0000015155 | OTOF    | HGNC Symbol | otofelin [Source:HGNC Symbol;Acc:HGNC:8516]                                                    | -0.549744866  | 0.21106939   | 0.197643374   | 1 | -0.204895956  | 0.934184441 | -0.265355542  | 1 |
| ENSG0000015648 | MLPH    | HGNC Symbol | melanophilin [Source:HGNC Symbol;Acc:HGNC:29543]                                               | -0.344672976  | 0.077643704  | -0.639406576  | 1 | -0.152231941  | 0.978305518 | 0.334010625   | 1 |
| ENSG0000016176 | TPSG1   | HGNC Symbol | tryptase gamma 1 [Source:HGNC Symbol;Acc:HGNC:14134]                                           | -0.696648839  | 0.249497404  | 0.76791399    | 1 | -1.7348835    | 0.61629741  | 0.133366927   | 1 |
| ENSG0000016721 | PRAMEF1 | HGNC Symbol | PRAME family member 1 [Source:HGNC Symbol;Acc:HGNC:28840]                                      | -0.903335599  | 0.148992939  | -0.251960328  | 1 | 2.472757959   | 0.726218184 | 0.947232758   | 1 |
| ENSG0000016748 | AMPD1   | HGNC Symbol | adenosine monophosphate deaminase 1 [Source:HGNC Symbol;Acc:HGNC:468]                          | -0.630797468  | 0.331507314  | -0.218155016  | 1 | -0.621451573  | 0.885080104 | 0.618256343   | 1 |
| ENSG0000016833 | NR5A2   | HGNC Symbol | nuclear receptor subfamily 5 group A member 2 [Source:HGNC Symbol;Acc:HGNC:7984]               | -0.795732503  | 0.0697955635 | -0.31274377   | 1 | -0.114723584  | 0.991823026 | -0.210882797  | 1 |
| ENSG0000017114 | ADGR12  | HGNC Symbol | adhesion G protein-coupled receptor 12 [Source:HGNC Symbol;Acc:HGNC:18582]                     | -0.80941013   | 0.08058928   | 0.580532431   | 1 | 1.383108381   | 0.725470307 | 0.382752752   | 1 |
| ENSG0000017501 | MRDH9   | HGNC Symbol | meastro heat like repeat family member 9 [Source:HGNC Symbol;Acc:HGNC:26287]                   | -0.710918244  | 0.189731062  | -0.242525931  | 1 | -0.356711873  | 0.923537499 | -0.1094478934 | 1 |
| ENSG0000018194 | TNNI7   | HGNC Symbol | "Troponin T2, cardiac type [Source:HGNC Symbol;Acc:HGNC:11949]"                                | -0.546314355  | 0.341882105  | -0.1194780553 | 1 | -0.0450145649 | 1           | -0.028707775  | 1 |
| ENSG0000018733 | OLFM3   | HGNC Symbol | olfactomedin 3 [Source:HGNC Symbol;Acc:HGNC:17990]                                             | -0.801008321  | 0.20328346   | -0.168316891  | 1 | 0.457073761   | 0.9262162   | 0.31727164    | 1 |
| ENSG0000019125 | GDA     | HGNC Symbol | guanine deaminase [Source:HGNC Symbol;Acc:HGNC:4212]                                           | -0.747333668  | 0.215788278  | -0.247436947  | 1 | 0.000299093   | 1           | 0.467310142   | 1 |
| ENSG0000019283 | TRIM67  | HGNC Symbol | tripartite motif containing 67 [Source:HGNC Symbol;Acc:HGNC:31859]                             | -0.692548587  | 0.18978734   | -0.304232098  | 1 | 0.887258927   | 0.818798586 | 0.26282956    | 1 |
| ENSG0000019301 | ONECUT2 | HGNC Symbol | one cut homeobox 2 [Source:HGNC Symbol;Acc:HGNC:10966]                                         | -0.364094999  | 0.566818453  | -0.24466557   | 1 | 1.784782386   | 0.723496808 | 0.103628364   | 1 |

|       |                  |          |             |                                                                                               |               |              |               |   |               |              |              |   |
|-------|------------------|----------|-------------|-----------------------------------------------------------------------------------------------|---------------|--------------|---------------|---|---------------|--------------|--------------|---|
| 9547  | ENSG000001000001 | GRIA2    | H6NC Symbol | Symbol:Acc:H6NC:81839                                                                         | -0.536759703  | 0.3336339567 | -0.09033807   | 1 | 1.488077153   | 0.724767358  | 0.04642107   | 1 |
| 20251 | ENSG000001000001 | TNN      | H6NC Symbol | glutamate ionotropic receptor AMPA type subunit 2 [Source:H6NC Symbol:Acc:H6NC:4572]          | -0.7973018943 | 0.154902439  | -0.518957551  | 1 | 0.742351698   | 0.858958348  | 0.1659739349 | 1 |
| 20332 | ENSG000001000001 | EGR1     | H6NC Symbol | tenascin N [Source:H6NC Symbol:Acc:H6NC:23942]                                                | 0.387004274   | 0.467739752  | -0.097555102  | 1 | -1.3688358877 | 0.6271668963 | 0.333462255  | 1 |
| 20738 | ENSG000001000001 | LRAT     | H6NC Symbol | early growth response 1 [Source:H6NC Symbol:Acc:H6NC:32238]                                   | -0.478677249  | 0.448668849  | -0.855301435  | 1 | 0.23718596    | 0.989503557  | 0.00862707   | 1 |
| 22107 | ENSG000001000001 | XPNPEP2  | H6NC Symbol | lecithin retinol acyltransferase [Source:H6NC Symbol:Acc:H6NC:66855]                          | -0.787898058  | 0.044847173  | -0.09623373   | 1 | 0.894693822   | 0.777250738  | -0.249093554 | 1 |
| 22701 | ENSG000001000001 | KIAA1549 | H6NC Symbol | X-prolyl aminopeptidase 2 [Source:H6NC Symbol:Acc:H6NC:12823]                                 | -0.5166930518 | 0.188827673  | -0.07755628   | 1 | 0.2106228029  | 0.957773266  | 0.2183627019 | 1 |
| 22778 | ENSG000001000001 | ITIH5    | H6NC Symbol | KIAA1549 [Source:H6NC Symbol:Acc:H6NC:22218]                                                  | -0.57168831   | 0.310810591  | -0.505623699  | 1 | 1.247465012   | 0.732735655  | 0.1955676108 | 1 |
| 22243 | ENSG000001000001 | NRK      | H6NC Symbol | inter-alpha-trypsin inhibitor heavy chain family member-5 [Source:H6NC Symbol:Acc:H6NC:21449] | -0.468349518  | 0.420910239  | -0.203352014  | 1 | 0.683557554   | 0.88816233   | 0.605103071  | 1 |
| 23572 | ENSG000001000001 | DAWI     | H6NC Symbol | Nik related kinase [Source:H6NC Symbol:Acc:H6NC:25391]                                        | -0.65449876   | 0.276598737  | 0.4887195569  | 1 | 1.5035592086  | 0.7879879108 | -0.29079265  | 1 |
| 23977 | ENSG000001000001 | CTCF1    | H6NC Symbol | dynein assembly factor with WD repeats 1 [Source:H6NC Symbol:Acc:H6NC:26383]                  | -0.443303842  | 0.467030393  | 0.002752214   | 1 | 0.80865262    | 0.8405330754 | -0.019073803 | 1 |
| 24092 | ENSG000001000001 | PCX1     | H6NC Symbol | CCCTC-binding factor like [Source:H6NC Symbol:Acc:H6NC:86234]                                 | -0.720216315  | 0.251094538  | 0.279193916   | 1 | 0.276714095   | 0.916167576  | 0.2847674529 | 1 |
| 24253 | ENSG000001000001 | HIF3A    | H6NC Symbol | phosphoenolpyruvate carboxykinase 1 [Source:H6NC Symbol:Acc:H6NC:8724]                        | -0.743934584  | 0.170170786  | -0.772828945  | 1 | 1.389567585   | 0.762736348  | 0.14892327   | 1 |
| 24440 | ENSG000001000001 | LYPD3    | H6NC Symbol | hypoxia inducible factor 3 alpha subunit [Source:H6NC Symbol:Acc:H6NC:15825]                  | -0.753607242  | 0.045770183  | 0.288985975   | 1 | 0.763945067   | 0.840373914  | -0.097673747 | 1 |
| 24466 | ENSG000001000001 | COL21A1  | H6NC Symbol | LY6/PLAUR domain containing 3 [Source:H6NC Symbol:Acc:H6NC:24880]                             | -0.382103802  | 0.594356444  | -0.514235569  | 1 | 1.4181074     | 0.7627693024 | 0.0826652892 | 1 |
| 24743 | ENSG000001000001 | SLC10A2  | H6NC Symbol | collagen type XXI alpha 1 chain [Source:H6NC Symbol:Acc:H6NC:7025]                            | -0.168555575  | 0.262927554  | -0.0271827102 | 1 | 0.044483879   | 1            | 0.555402919  | 1 |
| 25235 | ENSG000001000001 | BARHL1   | H6NC Symbol | solute carrier family 10 member 2 [Source:H6NC Symbol:Acc:H6NC:10506]                         | -0.153912437  | 0.823410461  | 0.879844413   | 1 | 0.899121028   | 0.8558827107 | -0.754557485 | 1 |
| 25492 | ENSG000001000001 | FUSB     | H6NC Symbol | Bat1 like homeobox 1 [Source:H6NC Symbol:Acc:H6NC:9553]                                       | 0.1684910461  | 0.82332541   | -0.208014548  | 1 | -0.7729399164 | 0.752973556  | -0.122863284 | 1 |
| 25740 | ENSG000001000001 | EDN2     | H6NC Symbol | "FusB proto-oncogene, AP-1 transcription factor subunit" [Source:H6NC Symbol:Acc:H6NC:3797]"  | -0.396163266  | 0.500439556  | 0.552589146   | 1 | 0.492727351   | 0.9301807704 | -0.35565941  | 1 |
| 27129 | ENSG000001000001 | FDPX2    | H6NC Symbol | endothelin 2 [Source:H6NC Symbol:Acc:H6NC:3177]                                               | -0.4256278055 | 0.496663487  | -0.633652169  | 1 | 1.2045104792  | 0.787794769  | -0.19108142  | 1 |
| 28573 | ENSG000001000001 | DL14     | H6NC Symbol | forkhead box P2 [Source:H6NC Symbol:Acc:H6NC:18875]                                           | -0.702456843  | 0.136145207  | -0.165547246  | 1 | -0.27626558   | 0.951033574  | 0.219555916  | 1 |
| 28917 | ENSG000001000001 | SHC2     | H6NC Symbol | delta like canonical Notch ligand 4 [Source:H6NC Symbol:Acc:H6NC:2910]                        | -0.843357896  | 0.0814031    | 0.430826667   | 1 | 0.9860168391  | 0.754933936  | 0.4432710016 | 1 |
| 29946 | ENSG000001000001 | SYT5     | H6NC Symbol | SHC adaptor protein 2 [Source:H6NC Symbol:Acc:H6NC:29869]                                     | -0.818710587  | 0.165777371  | -0.01528682   | 1 | 1.631732318   | 0.745077552  | -0.06149728  | 1 |

|                 |          |             |                                                                                    |               |              |              |   |              |             |              |   |
|-----------------|----------|-------------|------------------------------------------------------------------------------------|---------------|--------------|--------------|---|--------------|-------------|--------------|---|
| ENSG00000130226 | DPP6     | HGNC Symbol | dipeptidyl peptidase like 6 [Source:HGNC Symbol;Acc:HGNC:30100]                    | -0.086732477  | 0.915560052  | -0.491632363 | 1 | 0.40102019   | 0.9715457   | 0.04935884   | 1 |
| ENSG00000130287 | NCAN     | HGNC Symbol | neurexin [Source:HGNC Symbol;Acc:HGNC:2465]                                        | -0.655557898  | 0.28766504   | 0.36905074   | 1 | 0.427018875  | 0.92077063  | -0.642008684 | 1 |
| ENSG00000130477 | UNC13A   | HGNC Symbol | unc-13 homolog A [Source:HGNC Symbol;Acc:HGNC:23650]                               | -0.49344944   | 0.309175629  | -0.044819609 | 1 | 0.39454009   | 0.905148092 | -0.28674943  | 1 |
| ENSG00000130508 | PXDN     | HGNC Symbol | peroxidasin [Source:HGNC Symbol;Acc:HGNC:14966]                                    | -0.703310686  | 0.23499449   | -0.472985684 | 1 | 0.226774267  | 0.954203705 | -0.18172062  | 1 |
| ENSG00000130528 | HRC      | HGNC Symbol | histidine rich calcium binding protein [Source:HGNC Symbol;Acc:HGNC:5178]          | -0.69248487   | 0.295913641  | 0.225433939  | 1 | 1.995649839  | 0.722740931 | -0.363636866 | 1 |
| ENSG00000130540 | SULT4A1  | HGNC Symbol | sulfatransferase family 4A member 1 [Source:HGNC Symbol;Acc:HGNC:14903]            | -0.672278031  | 0.247255807  | 0.10638129   | 1 | 2.178253808  | 0.722717784 | 0.071276285  | 1 |
| ENSG00000130635 | COL5A1   | HGNC Symbol | collagen type V alpha 1 chain [Source:HGNC Symbol;Acc:HGNC:2209]                   | -1.0595386259 | 0.005145777  | -0.01150205  | 1 | -0.056854342 | 0.990946263 | 0.076799389  | 1 |
| ENSG00000130144 | TTL9     | HGNC Symbol | tubulin tyrosine ligase like 9 [Source:HGNC Symbol;Acc:HGNC:1618]                  | -0.6465555965 | 0.081577407  | -0.183372839 | 1 | 0.74810611   | 0.828000591 | 0.086100403  | 1 |
| ENSG00000130183 | SLC34A1  | HGNC Symbol | solute carrier family 34 member 1 [Source:HGNC Symbol;Acc:HGNC:1016]               | -0.5536018699 | 0.222662062  | 0.032988094  | 1 | -0.784903911 | 0.832983886 | 0.137278528  | 1 |
| ENSG00000130386 | GALNT15  | HGNC Symbol | polypeptide N-acetylglucosaminyltransferase 15 [Source:HGNC Symbol;Acc:HGNC:21531] | -0.249199422  | 0.57938334   | -0.012465071 | 1 | -0.275997847 | 0.960788648 | 0.18571653   | 1 |
| ENSG00000132797 | HHLA1    | HGNC Symbol | HERV-H LTR-associating 1 [Source:HGNC Symbol;Acc:HGNC:4804]                        | -0.569303097  | 0.342618221  | -0.45037748  | 1 | 0.335686986  | 0.946406426 | 0.544916255  | 1 |
| ENSG00000132821 | IQCA1    | HGNC Symbol | IQ motif containing with AAA domain 1 [Source:HGNC Symbol;Acc:HGNC:26195]          | -0.491444835  | 0.307219735  | -0.329452064 | 1 | 0.488440298  | 0.910758277 | 0.37551855   | 1 |
| ENSG00000132839 | SNAP25   | HGNC Symbol | synaptosome associated protein 25 [Source:HGNC Symbol;Acc:HGNC:1182]               | -0.484371596  | 0.393579181  | -0.408665796 | 1 | 1.905967427  | 0.726386579 | 0.425545535  | 1 |
| ENSG00000132972 | RNF7     | HGNC Symbol | ring finger protein 7 [Source:HGNC Symbol;Acc:HGNC:10060]                          | -0.539876442  | 0.323658258  | -0.231290586 | 1 | 0.046100411  | 1           | 0.196976455  | 1 |
| ENSG00000132975 | GPR12    | HGNC Symbol | G protein-coupled receptor 12 [Source:HGNC Symbol;Acc:HGNC:4466]                   | -0.559671607  | 0.3810271581 | -0.229055585 | 1 | 0.861729873  | 0.878558735 | 0.035899532  | 1 |
| ENSG00000133083 | DCLK1    | HGNC Symbol | doublecortin like kinase 1 [Source:HGNC Symbol;Acc:HGNC:27100]                     | -0.693023499  | 0.188550204  | -0.20329481  | 1 | 0.45301812   | 0.90855876  | 0.023846382  | 1 |
| ENSG00000133110 | POSTN    | HGNC Symbol | perostatin [Source:HGNC Symbol;Acc:HGNC:16553]                                     | -1.95711401   | 0.0014871    | -0.34938544  | 1 | -0.086735544 | 0.992429838 | -0.345362803 | 1 |
| ENSG00000133124 | IRS4     | HGNC Symbol | insulin receptor substrate 4 [Source:HGNC Symbol;Acc:HGNC:6128]                    | -0.486576537  | 0.45362956   | -0.72052378  | 1 | 5.343239343  | 0.627668963 | 0.002775328  | 1 |
| ENSG00000133454 | MYO18B   | HGNC Symbol | myosin XVIIIb [Source:HGNC Symbol;Acc:HGNC:1860]                                   | -0.556047442  | 0.18461856   | -0.273389213 | 1 | 0.397760747  | 0.892320091 | 0.190816003  | 1 |
| ENSG00000134240 | HMGC2    | HGNC Symbol | 3-hydroxy-3-methylglutaryl-CoA synthase 2 [Source:HGNC Symbol;Acc:HGNC:5018]       | -0.558866518  | 0.222794501  | 0.097873954  | 1 | -0.238140625 | 0.963271892 | 0.02438912   | 1 |
| ENSG00000134871 | COL4A2   | HGNC Symbol | collagen type IV alpha 2 chain [Source:HGNC Symbol;Acc:HGNC:2203]                  | -0.723558351  | 0.079843824  | 0.140639269  | 1 | -0.42555673  | 0.85038998  | -0.091086456 | 1 |
| ENSG00000135097 | MSI1     | HGNC Symbol | mucash RNA binding protein 1 [Source:HGNC Symbol;Acc:HGNC:7330]                    | -0.681488708  | 0.233945897  | -0.20335644  | 1 | 0.49731089   | 0.937722107 | -0.056538922 | 1 |
| ENSG00000135409 | AMHR2    | HGNC Symbol | anti-Müllerian hormone receptor type 2 [Source:HGNC Symbol;Acc:HGNC:465]           | -0.36590271   | 0.57936334   | 0.204280771  | 1 | -0.27558101  | 0.956707132 | -0.438149866 | 1 |
| ENSG00000135454 | B4GALNT1 | HGNC Symbol | "beta-1,4-N-acetyl-galactosaminyltransferase 1 [Source:HGNC Symbol;Acc:HGNC:4107]" | -0.83916247   | 0.09476195   | 0.299571806  | 1 | 0.64545358   | 0.867558968 | -0.208851705 | 1 |

|                 |         |             |                                                                                                             |              |              |              |   |              |             |              |   |
|-----------------|---------|-------------|-------------------------------------------------------------------------------------------------------------|--------------|--------------|--------------|---|--------------|-------------|--------------|---|
| ENSG00000135472 | FAIM2   | HGNC Symbol | Fas apoptotic inhibitory molecule 2 [Source:HGNC Symbol;Acc:HGNC:70167]                                     | -0.88324772  | 0.166816589  | 0.202004682  | 1 | 0.818056333  | 0.844324446 | -0.2451895   | 1 |
| ENSG00000135917 | SLC9A3  | HGNC Symbol | solute carrier family 9 member 3 [Source:HGNC Symbol;Acc:HGNC:16265]                                        | -0.940946251 | 0.097071433  | -0.392103408 | 1 | 1.852245487  | 0.724400969 | -0.403065239 | 1 |
| ENSG00000135931 | ARMC9   | HGNC Symbol | armadillo repeat containing 9 [Source:HGNC Symbol;Acc:HGNC:27030]                                           | -0.671965301 | 0.140773449  | -0.131277483 | 1 | 0.804318724  | 0.819067405 | 0.374946273  | 1 |
| ENSG00000136352 | NKX2-1  | HGNC Symbol | NK2 homeobox 1 [Source:HGNC Symbol;Acc:HGNC:11825]                                                          | -0.828072024 | 0.143100566  | 1.366181821  | 1 | 1.261855582  | 0.759162726 | 0.316716709  | 1 |
| ENSG00000136353 | TBR1    | HGNC Symbol | "T-box brain 1 [Source:HGNC Symbol;Acc:HGNC:14590]"                                                         | -0.569543876 | 0.29481016   | -0.306732866 | 1 | 1.986072677  | 0.725297356 | 0.258942535  | 1 |
| ENSG00000136574 | GATA4   | HGNC Symbol | GATA binding protein 4 [Source:HGNC Symbol;Acc:HGNC:4473]                                                   | -0.43785431  | 0.456883716  | -0.085495591 | 1 | -0.352812935 | 0.937737302 | 0.61877166   | 1 |
| ENSG00000136595 | IL36RN  | HGNC Symbol | interleukin 36 receptor antagonist [Source:HGNC Symbol;Acc:HGNC:15561]                                      | -0.11115253  | 0.887785479  | -0.281913506 | 1 | 0.461088841  | 0.936821903 | -0.051266805 | 1 |
| ENSG00000137203 | TFAP2A  | HGNC Symbol | transcription factor AP-2 alpha [Source:HGNC Symbol;Acc:HGNC:1742]                                          | -0.718616178 | 0.197925578  | -0.53802252  | 1 | -0.210705526 | 0.966677784 | -0.033229666 | 1 |
| ENSG00000137573 | SULF1   | HGNC Symbol | sulfatase 1 [Source:HGNC Symbol;Acc:HGNC:20391]                                                             | -0.721090487 | 0.155372588  | -0.087328771 | 1 | 0.825205342  | 0.843454046 | 0.191859508  | 1 |
| ENSG00000137648 | TMPPSS4 | HGNC Symbol | transmembrane serine protease 4 [Source:HGNC Symbol;Acc:HGNC:11878]                                         | -0.697399948 | 0.003019089  | -0.536995553 | 1 | 1.978852165  | 0.690920831 | -0.033994499 | 1 |
| ENSG00000137766 | UNC18C  | HGNC Symbol | unc-18 homolog C [Source:HGNC Symbol;Acc:HGNC:22349]                                                        | -0.245910067 | 0.592753582  | -0.800818916 | 1 | 0.083665679  | 0.99633075  | 0.528354487  | 1 |
| ENSG00000137819 | PAQR5   | HGNC Symbol | progesterin and adipoR1 receptor family member 5 [Source:HGNC Symbol;Acc:HGNC:29845]                        | -0.465198504 | 0.254871322  | -0.26719588  | 1 | -0.022161664 | 1           | -0.150321984 | 1 |
| ENSG00000138162 | TACC2   | HGNC Symbol | transforming acidic coiled-coil containing protein 2 [Source:HGNC Symbol;Acc:HGNC:1623]                     | -0.598272168 | 0.215716557  | -0.394014657 | 1 | 0.050343402  | 0.988800576 | -0.138236443 | 1 |
| ENSG00000138650 | PCDH10  | HGNC Symbol | protocadherin 10 [Source:HGNC Symbol;Acc:HGNC:16404]                                                        | -0.339310016 | 0.614591273  | 0.042302016  | 1 | 0.227487401  | 0.96989385  | 0.091491003  | 1 |
| ENSG00000138675 | FGF5    | HGNC Symbol | fibroblast growth factor 5 [Source:HGNC Symbol;Acc:HGNC:35833]                                              | -0.605345738 | 0.3627579738 | 0.09432516   | 1 | 1.669289062  | 0.754933936 | 0.390565845  | 1 |
| ENSG00000138759 | FRS1    | HGNC Symbol | Fraser extracellular matrix complex subunit 1 [Source:HGNC Symbol;Acc:HGNC:19185]                           | -0.222394616 | 0.747027813  | -0.230470196 | 1 | 0.716331438  | 0.828463409 | 0.168376931  | 1 |
| ENSG00000138892 | TTL18   | HGNC Symbol | tubulin tyrosine ligase like 8 [Source:HGNC Symbol;Acc:HGNC:34100]                                          | -0.887768688 | 0.092191936  | 0.314040376  | 1 | -0.418379105 | 0.92963834  | 0.177510233  | 1 |
| ENSG00000139144 | PIK3C2G | HGNC Symbol | phosphatidylinositol-4-phosphate 3-kinase catalytic subunit type 2 gamma [Source:HGNC Symbol;Acc:HGNC:8973] | -0.165595171 | 0.833030165  | 0.29979692   | 1 | 1.47351311   | 0.75410684  | 0.429551463  | 1 |
| ENSG00000139220 | PPFA2   | HGNC Symbol | PTPRF interacting protein alpha 2 [Source:HGNC Symbol;Acc:HGNC:5246]                                        | -0.378470282 | 0.536515358  | -0.068663108 | 1 | 0.235756127  | 0.956688515 | -0.194979109 | 1 |
| ENSG00000139367 | SRRM4   | HGNC Symbol | serine/arginine repetitive matrix 4 [Source:HGNC Symbol;Acc:HGNC:29389]                                     | -0.3343885   | 0.80876368   | -0.194960482 | 1 | 0.885758938  | 0.818749145 | 0.11423744   | 1 |
| ENSG00000139865 | TTC6    | HGNC Symbol | tetratricopeptide repeat domain 6 [Source:HGNC Symbol;Acc:HGNC:19739]                                       | -0.5461875   | 0.377281018  | 0.138883348  | 1 | 0.239059125  | 0.964093129 | 0.4413004    | 1 |
| ENSG00000140279 | DIOX2   | HGNC Symbol | dual oxidase 2 [Source:HGNC Symbol;Acc:HGNC:18773]                                                          | -0.60618929  | 0.67197775   | 0.347497074  | 1 | 0.453255659  | 0.910383337 | -0.067628419 | 1 |
| ENSG00000140527 | WDR93   | HGNC Symbol | WD repeat domain 93 [Source:HGNC Symbol;Acc:HGNC:21924]                                                     | -0.51239896  | 0.363801238  | 0.121581454  | 1 | 0.32761064   | 0.945240895 | 0.342334255  | 1 |
| ENSG00000141361 | SH3GL3  | HGNC Symbol | "SH3 domain containing G6B2 like 3, endophilin                                                              | -0.346680711 | 0.576550131  | -0.050610896 | 1 | 0.773782722  | 0.86617857  | 0.265942406  | 1 |

|                 |         |             |                                                                                                       |               |              |              |   |              |             |               |   |
|-----------------|---------|-------------|-------------------------------------------------------------------------------------------------------|---------------|--------------|--------------|---|--------------|-------------|---------------|---|
| 40600           | MEPIB   | HGNC Symbol | A3 [Source:HGNC Symbol;Acc:HGNC:108321]<br>nepirin A subunit beta [Source:HGNC Symbol;Acc:HGNC:70720] | -0.835498908  | 0.100858384  | -0.724970362 | 1 | 1.075438474  | 0.800861697 | 0.454970747   | 1 |
| ENSG00000014434 |         |             |                                                                                                       |               |              |              |   |              |             |               |   |
| ENSG00000014658 | CELN2   | HGNC Symbol | ceratulin 2 precursor [Source:HGNC Symbol;Acc:HGNC:1544]                                              | -0.408916792  | 0.515136432  | 0.075867803  | 1 | 1.63570017   | 0.76543823  | 0.04591254    | 1 |
| ENSG00000014945 | ZIM3    | HGNC Symbol | zinc finger imprinted 3 [Source:HGNC Symbol;Acc:HGNC:16366]                                           | -0.553169901  | 0.418027916  | -0.091028345 | 1 | 0.082223031  | 0.936460723 | 0.18197706    | 1 |
| ENSG00000014946 | CACNG8  | HGNC Symbol | calcium voltage-gated channel auxiliary subunit gamma 8 [Source:HGNC Symbol;Acc:HGNC:13678]           | -0.654089337  | 0.014843597  | -0.003238868 | 1 | 0.6559651868 | 0.750144627 | 0.047494152   | 1 |
| ENSG00000014948 |         |             |                                                                                                       |               |              |              |   |              |             |               |   |
| ENSG00000014949 | FBXN3   | HGNC Symbol | fibroblast 3 [Source:HGNC Symbol;Acc:HGNC:18794]                                                      | -0.447182655  | 0.423778352  | -0.470497888 | 1 | -0.030000224 | 1           | 0.027609401   | 1 |
| ENSG00000014950 | IGLON5  | HGNC Symbol | IgLO family member 5 [Source:HGNC Symbol;Acc:HGNC:33450]                                              | -0.544479383  | 0.395566456  | -0.00560726  | 1 | 0.73291036   | 0.889236595 | -0.165464006  | 1 |
| ENSG00000014951 | PROM6   | HGNC Symbol | PR SET domain 16 [Source:HGNC Symbol;Acc:HGNC:14000]                                                  | -0.743776119  | 0.100743572  | -0.21025678  | 1 | 0.541607842  | 0.876575598 | -0.107893595  | 1 |
| ENSG00000014951 |         |             |                                                                                                       |               |              |              |   |              |             |               |   |
| ENSG00000014952 | PADI1   | HGNC Symbol | peptidyl arginine deiminase 1 [Source:HGNC Symbol;Acc:HGNC:18567]                                     | -0.616881627  | 0.333844866  | -0.681545599 | 1 | 0.648194613  | 0.880022596 | -0.307236278  | 1 |
| ENSG00000014953 | CNKSR1  | HGNC Symbol | connector enhancer of kinase suppressor of Ras 1 [Source:HGNC Symbol;Acc:HGNC:19700]                  | -0.498623814  | 0.138710312  | 0.280272134  | 1 | -0.617257919 | 0.810652354 | 0.640584658   | 1 |
| ENSG00000014954 | TINAGL1 | HGNC Symbol | tubulin-interstitial nephritis antigen like 1 [Source:HGNC Symbol;Acc:HGNC:1918]                      | -0.695391691  | 0.158108486  | 0.16987273   | 1 | -0.809803802 | 0.814581081 | 0.016307454   | 1 |
| ENSG00000014954 |         |             |                                                                                                       |               |              |              |   |              |             |               |   |
| ENSG00000014955 | FNDC7   | HGNC Symbol | fibronectin type II domain containing 7 [Source:HGNC Symbol;Acc:HGNC:26688]                           | -0.533451774  | 0.237273415  | -0.671664787 | 1 | 1.05958764   | 0.781988535 | 0.1675159527  | 1 |
| ENSG00000014955 |         |             |                                                                                                       |               |              |              |   |              |             |               |   |
| ENSG00000014956 | LHX8    | HGNC Symbol | LIM homeobox 8 [Source:HGNC Symbol;Acc:HGNC:14272]                                                    | -0.481719357  | 0.356710059  | 0.142033448  | 1 | 2.142940272  | 0.665274436 | 0.633424086   | 1 |
| ENSG00000014956 |         |             |                                                                                                       |               |              |              |   |              |             |               |   |
| ENSG00000014957 | DAZ3    | HGNC Symbol | ornithine decarboxylase antizyme 3 [Source:HGNC Symbol;Acc:HGNC:8197]                                 | -0.731310388  | 0.04678294   | -0.004524812 | 1 | 0.16530747   | 0.977890656 | -0.210681852  | 1 |
| ENSG00000014957 |         |             |                                                                                                       |               |              |              |   |              |             |               |   |
| ENSG00000014958 | SYT14   | HGNC Symbol | synaptotagmin 14 [Source:HGNC Symbol;Acc:HGNC:23943]                                                  | -0.5295771675 | 0.429195839  | -0.447510986 | 1 | -0.956862615 | 0.814421207 | 0.457714936   | 1 |
| ENSG00000014958 |         |             |                                                                                                       |               |              |              |   |              |             |               |   |
| ENSG00000014959 | OSR1    | HGNC Symbol | odd-skipped related transcription factor 1 [Source:HGNC Symbol;Acc:HGNC:8110]                         | -0.350186152  | 0.5930327035 | -0.581637838 | 1 | 1.277349941  | 0.767398121 | -0.246555505  | 1 |
| ENSG00000014959 |         |             |                                                                                                       |               |              |              |   |              |             |               |   |
| ENSG00000014960 | THNSL2  | HGNC Symbol | threonine synthase like 2 [Source:HGNC Symbol;Acc:HGNC:25602]                                         | -0.37376109   | 0.532109313  | 0.08695122   | 1 | 1.406766298  | 0.677688963 | -0.0931330536 | 1 |
| ENSG00000014960 |         |             |                                                                                                       |               |              |              |   |              |             |               |   |
| ENSG00000014961 | ESPNL   | HGNC Symbol | espin like [Source:HGNC Symbol;Acc:HGNC:27837]                                                        | -0.577831971  | 0.2533652718 | 0.12286329   | 1 | 0.183671314  | 0.98468271  | -0.472455254  | 1 |
| ENSG00000014961 |         |             |                                                                                                       |               |              |              |   |              |             |               |   |
| ENSG00000014962 | ACKR2   | HGNC Symbol | atypical chemokine receptor 2 [Source:HGNC Symbol;Acc:HGNC:1565]                                      | -0.471303908  | 0.045940057  | 0.031375673  | 1 | -0.106830853 | 1           | 0.289480869   | 1 |
| ENSG00000014962 |         |             |                                                                                                       |               |              |              |   |              |             |               |   |
| ENSG00000014963 | STAC    | HGNC Symbol | SH3 and cysteine rich domain [Source:HGNC Symbol;Acc:HGNC:14353]                                      | -0.560150605  | 0.182021883  | -0.063462505 | 1 | 2.4427386048 | 0.655810493 | -0.1901358616 | 1 |
| ENSG00000014963 |         |             |                                                                                                       |               |              |              |   |              |             |               |   |
| ENSG00000014964 | IL17RD  | HGNC Symbol | interleukin 17 receptor D [Source:HGNC Symbol;Acc:HGNC:17616]                                         | -0.581607198  | 0.294688324  | -0.325294976 | 1 | -0.187758877 | 0.965332755 | 0.080723396   | 1 |
| ENSG00000014964 |         |             |                                                                                                       |               |              |              |   |              |             |               |   |
| ENSG00000014965 | ADGRG7  | HGNC Symbol | adhesion G protein-coupled receptor G7 [Source:HGNC Symbol;Acc:HGNC:19241]                            | -0.492313851  | 0.43613712   | -0.373239237 | 1 | 1.0547197057 | 0.807095259 | -0.065816535  | 1 |
| ENSG00000014965 |         |             |                                                                                                       |               |              |              |   |              |             |               |   |
| ENSG00000014966 | ALDH1L1 | HGNC Symbol | aldehyde dehydrogenase 1 family member 1 [Source:HGNC Symbol;Acc:HGNC:39718]                          | -0.472941982  | 0.451051268  | 0.073431053  | 1 | 0.618763387  | 0.869975678 | 0.034578065   | 1 |
| ENSG00000014966 |         |             |                                                                                                       |               |              |              |   |              |             |               |   |
| ENSG00000014967 | EPHA5   | HGNC Symbol | EPH receptor A5 [Source:HGNC Symbol;Acc:HGNC:3389]                                                    | -0.50828279   | 0.3978103557 | -0.091518359 | 1 | 0.91278704   | 0.85881037  | 0.146271744   | 1 |
| ENSG00000014967 |         |             |                                                                                                       |               |              |              |   |              |             |               |   |

|                 |           |             |                                                                                   |               |              |              |   |               |              |               |   |
|-----------------|-----------|-------------|-----------------------------------------------------------------------------------|---------------|--------------|--------------|---|---------------|--------------|---------------|---|
| ENSG00000145526 | CDH8      | HGNC Symbol | cadherin 8 [Source:HGNC Symbol;Acc:HGNC:1757]                                     | -0.1470705064 | 0.255000028  | -0.802285847 | 1 | 1.00099442    | 0.843439811  | 0.179252073   | 1 |
| ENSG00000145542 | SHISA2B   | HGNC Symbol | shisa like 2B [Source:HGNC Symbol;Acc:HGNC:34238]                                 | -1.490085497  | 0.001461516  | 0.2706508322 | 1 | 0.854782399   | 0.897785147  | 1.025590395   | 1 |
| ENSG00000145832 | SLC25A48  | HGNC Symbol | solute carrier family 25 member 48 [Source:HGNC Symbol;Acc:HGNC:30451]            | -0.382607037  | 0.565480846  | -0.280573959 | 1 | 1.518959271   | 0.770970716  | 0.10267202    | 1 |
| ENSG00000146005 | PSD2      | HGNC Symbol | pleckstrin and Sec7 domain containing 2 [Source:HGNC Symbol;Acc:HGNC:48092]       | -0.474391279  | 0.322395181  | 0.021403556  | 1 | 0.480468991   | 0.905793309  | -0.1064177    | 1 |
| ENSG00000146521 | LINC01558 | HGNC Symbol | long intergenic non-protein coding RNA 1558 [Source:HGNC Symbol;Acc:HGNC:29235]   | -0.930731064  | 0.104990162  | -0.374380824 | 1 | 1.0660197068  | 0.840197873  | 0.248763858   | 1 |
| ENSG00000146948 | EGFR      | HGNC Symbol | epidermal growth factor receptor [Source:HGNC Symbol;Acc:HGNC:3236]               | -0.464347302  | 0.3223063336 | -0.33233532  | 1 | 0.9510729589  | 0.797043771  | 0.272516644   | 1 |
| ENSG00000146939 | ZAN       | HGNC Symbol | zonadhesin (gene/pseudogene) [Source:HGNC Symbol;Acc:HGNC:12857]                  | -0.501601018  | 0.397563388  | -0.125191006 | 1 | 0.079846162   | 0.992989633  | -0.189812795  | 1 |
| ENSG00000146950 | SHROOM2   | HGNC Symbol | shroom family member 2 [Source:HGNC Symbol;Acc:HGNC:6301]                         | -0.547481274  | 0.163040816  | 0.202718038  | 1 | 0.778222778   | 0.849102793  | -0.06543539   | 1 |
| ENSG00000147573 | TRIM55    | HGNC Symbol | tripartite motif containing 55 [Source:HGNC Symbol;Acc:HGNC:4216]                 | -0.406221036  | 0.529220394  | -0.594055397 | 1 | 1.095002077   | 0.799860378  | -0.162457891  | 1 |
| ENSG00000147655 | RSP02     | HGNC Symbol | R-spondin 2 [Source:HGNC Symbol;Acc:HGNC:28583]                                   | -0.425816624  | 0.480190964  | -0.332530076 | 1 | 1.2719102     | 0.79452482   | 0.50470696    | 1 |
| ENSG00000147689 | FAM63A    | HGNC Symbol | family with sequence similarity 83 member A [Source:HGNC Symbol;Acc:HGNC:28210]   | -0.470463683  | 0.295555482  | 0.16948171   | 1 | -0.9103228622 | 0.77316391   | 0.066442976   | 1 |
| ENSG00000148357 | HMCN2     | HGNC Symbol | hemicentin 2 [Source:HGNC Symbol;Acc:HGNC:27293]                                  | -0.5355566286 | 0.290997361  | 0.264805329  | 1 | 1.3216010301  | 0.732397555  | -0.187042982  | 1 |
| ENSG00000148408 | CACNA1B   | HGNC Symbol | calcium voltage-gated channel subunit alpha 1B [Source:HGNC Symbol;Acc:HGNC:1389] | -0.504688836  | 0.28487302   | 0.048380959  | 1 | 0.530191495   | 0.874658309  | -0.0310898439 | 1 |
| ENSG00000148518 | ANKRD30A  | HGNC Symbol | ankyrin repeat domain 30A [Source:HGNC Symbol;Acc:HGNC:17234]                     | -0.871448013  | 0.164735594  | -0.305026977 | 1 | 0.953450107   | 0.839264767  | 0.371091001   | 1 |
| ENSG00000148702 | HABP2     | HGNC Symbol | hyaluronan binding protein 2 [Source:HGNC Symbol;Acc:HGNC:4798]                   | -0.563571725  | 0.372582084  | -0.70168564  | 1 | 0.6916165189  | 0.891304498  | -0.267218198  | 1 |
| ENSG00000148942 | SLC5A12   | HGNC Symbol | solute carrier family 5 member 12 [Source:HGNC Symbol;Acc:HGNC:28750]             | -0.603891229  | 0.317483763  | 0.589091602  | 1 | 2.02107846    | 0.724655033  | 0.288605968   | 1 |
| ENSG00000149533 | KIAA1755  | HGNC Symbol | KIAA1755 [Source:HGNC Symbol;Acc:HGNC:29372]                                      | -0.626269466  | 0.2955555482 | -0.102950944 | 1 | 0.845177883   | 0.84263985   | 0.07008457    | 1 |
| ENSG00000149554 | CDH22     | HGNC Symbol | cadherin 22 [Source:HGNC Symbol;Acc:HGNC:18251]                                   | -0.36181649   | 0.564754244  | 0.48594264   | 1 | 1.642451251   | 0.704650879  | 0.373083932   | 1 |
| ENSG00000149976 | FAM57B    | HGNC Symbol | family with sequence similarity 57 member B [Source:HGNC Symbol;Acc:HGNC:25295]   | -0.826512075  | 0.147540268  | 0.338790838  | 1 | 0.63666601    | 0.87726176   | 0.22332443    | 1 |
| ENSG00000150086 | NA        | NA          | NA                                                                                | -0.387891929  | 0.543943649  | 0.101883742  | 1 | 0.09254319    | 0.993023802  | 0.01920446    | 1 |
| ENSG00000150893 | FREM2     | HGNC Symbol | FRAS1 related extracellular matrix protein 2 [Source:HGNC Symbol;Acc:HGNC:25396]  | -0.27918432   | 0.68553075   | -0.016022791 | 1 | 0.68399736    | 0.858353069  | 0.230897523   | 1 |
| ENSG00000151274 | MAT1A     | HGNC Symbol | methionine adenosyltransferase 1A [Source:HGNC Symbol;Acc:HGNC:6903]              | -0.695879857  | 0.25715468   | 0.197653903  | 1 | 2.604150819   | 0.1699467056 | 0.028446108   | 1 |
| ENSG00000151474 | FRMD4A    | HGNC Symbol | FERM domain containing 4A [Source:HGNC Symbol;Acc:HGNC:25491]                     | -0.266779579  | 0.183727706  | 0.076464676  | 1 | -1.188547325  | 0.525549357  | 0.101780987   | 1 |
| ENSG00000151572 | ANO4      | HGNC Symbol | anoctamin 4 [Source:HGNC Symbol;Acc:HGNC:23837]                                   | -0.427488162  | 0.474520364  | -0.114230143 | 1 | 1.195495335   | 0.73198104   | 0.34018558    | 1 |

|                 |            |                            |                                                                                      |              |             |               |   |               |              |              |   |
|-----------------|------------|----------------------------|--------------------------------------------------------------------------------------|--------------|-------------|---------------|---|---------------|--------------|--------------|---|
| ENSG00000152872 | GRM1       | HGNC Symbol                | glutamate metabotropic receptor 1 [Source:HGNC Symbol;Acc:HGNC:4593]                 | -0.56020862  | 0.32066526  | 0.09857202    | 1 | 0.9505538     | 0.84902793   | 0.35777006   | 1 |
| ENSG00000152910 | CNTNAP4    | HGNC Symbol                | contactin associated protein like 4 [Source:HGNC Symbol;Acc:HGNC:18747]              | -0.144263925 | 0.859543976 | -0.42488097   | 1 | 0.369465713   | 0.93772207   | -0.2837856   | 1 |
| ENSG00000153065 | RBP3       | HGNC Symbol                | RANBP2-like and GRP domain containing 3 [Source:HGNC Symbol;Acc:HGNC:32416]          | -0.869466335 | 0.003638752 | -0.224684905  | 1 | 2.095595953   | 0.62766963   | -0.26547248  | 1 |
| ENSG00000154099 | DNAH1      | HGNC Symbol                | dynein axonemal assembly factor 1 [Source:HGNC Symbol;Acc:HGNC:30539]                | -0.616204423 | 0.27095494  | 0.345094508   | 1 | 1.56795966    | 0.738962739  | -0.424945152 | 1 |
| ENSG00000154478 | GRP26      | HGNC Symbol                | 6 protein-coupled receptor 26 [Source:HGNC Symbol;Acc:HGNC:4481]                     | -0.494806205 | 0.406550218 | -0.603462454  | 1 | 3.14725066    | 0.63230269   | 0.299335738  | 1 |
| ENSG00000155806 | FMN2       | HGNC Symbol                | formin 2 [Source:HGNC Symbol;Acc:HGNC:4074]                                          | -0.41873015  | 0.328656826 | -0.266666973  | 1 | -0.1932320828 | 0.97265979   | 0.394876442  | 1 |
| ENSG00000156076 | WIF1       | HGNC Symbol                | WNT inhibitory factor 1 [Source:HGNC Symbol;Acc:HGNC:16081]                          | -0.701695845 | 0.246971053 | -0.291654074  | 1 | -0.119197606  | 0.992675307  | 0.39962807   | 1 |
| ENSG00000156103 | MMP16      | HGNC Symbol                | matrix metalloproteinase 16 [Source:HGNC Symbol;Acc:HGNC:7162]                       | -0.612940918 | 0.354953307 | 0.785584644   | 1 | 1.561003497   | 0.737781088  | 0.049120893  | 1 |
| ENSG00000156222 | SLC28A1    | HGNC Symbol                | solute carrier family 28 member 1 [Source:HGNC Symbol;Acc:HGNC:4001]                 | -0.484780444 | 0.394310444 | 0.027974247   | 1 | -0.178812362  | 0.97374933   | 0.083144459  | 1 |
| ENSG00000156413 | FUT6       | HGNC Symbol                | lucosyltransferase 6 [Source:HGNC Symbol;Acc:HGNC:4077]                              | -0.59042874  | 0.29769914  | 0.04077306    | 1 | 1.916994434   | 0.76035827   | -0.126102335 | 1 |
| ENSG00000156687 | UNC5D      | HGNC Symbol                | unc-5 netrin receptor 5 [Source:HGNC Symbol;Acc:HGNC:16634]                          | -0.678558816 | 0.21927459  | -0.175857955  | 1 | -0.04494555   | 1            | 0.372334005  | 1 |
| ENSG00000157274 | STAP2      | HGNC Symbol                | STAP2 metalloproteinase [Source:HGNC Symbol;Acc:HGNC:17885]                          | -0.751247183 | 0.64094301  | -0.138333013  | 1 | 3.283888998   | 0.62766963   | 0.194259     | 1 |
| ENSG00000157423 | HYDIN      | HGNC Symbol                | "HYDIN, axonemal central pair apparatus protein [Source:HGNC Symbol;Acc:HGNC:19368]" | -0.33931962  | 0.501656392 | -0.307482345  | 1 | 0.77155018    | 0.82495196   | 0.345889545  | 1 |
| ENSG00000157827 | RADIL      | HGNC Symbol                | Ran associating with DIL domain [Source:HGNC Symbol;Acc:HGNC:22226]                  | -0.542930542 | 0.218274573 | 0.749636554   | 1 | 0.477550274   | 0.905148092  | -0.16547528  | 1 |
| ENSG00000158077 | NLRP14     | HGNC Symbol                | NLR family pyrin domain containing 14 [Source:HGNC Symbol;Acc:HGNC:22389]            | -0.399561024 | 0.501606622 | 0.06840817    | 1 | 0.259016203   | 0.96631639   | 0.259994409  | 1 |
| ENSG00000158125 | XDH        | HGNC Symbol                | xanthine dehydrogenase [Source:HGNC Symbol;Acc:HGNC:12805]                           | -0.856880361 | 0.18494762  | -0.505018354  | 1 | 1.29103073018 | 0.756996807  | 0.187029284  | 1 |
| ENSG00000158258 | CLSTN2     | HGNC Symbol                | calystinin 2 [Source:HGNC Symbol;Acc:HGNC:17448]                                     | -0.472745595 | 0.46827728  | -0.4393559401 | 1 | 1.26103511    | 0.752978057  | 0.225483257  | 1 |
| ENSG00000159251 | ACT1       | HGNC Symbol                | "actin, alpha, cardiac muscle 1 [Source:HGNC Symbol;Acc:HGNC:143]"                   | -0.407779393 | 0.500035053 | -0.391085345  | 1 | 1.56186689    | 0.749009777  | 0.188962838  | 1 |
| ENSG00000159337 | PLA2G4D    | HGNC Symbol                | phospholipase A2 group IV [Source:HGNC Symbol;Acc:HGNC:30038]                        | -0.62384411  | 0.222267482 | 0.452714015   | 1 | 0.95816216    | 0.824640952  | -0.148948276 | 1 |
| ENSG00000159650 | URDC1      | HGNC Symbol                | uracinate hydratase 1 [Source:HGNC Symbol;Acc:HGNC:28444]                            | -0.59260834  | 0.295239234 | -0.050143865  | 1 | 1.289104367   | 0.750144627  | -0.127652982 | 1 |
| ENSG00000160460 | SPTBN4     | HGNC Symbol                | "spectrin beta, non-erythrocytic 4 [Source:HGNC Symbol;Acc:HGNC:14896]"              | -0.68223524  | 0.093882704 | 0.00048346    | 1 | 0.227969832   | 0.9554991    | -0.204422386 | 1 |
| ENSG00000160994 | CDC0105    | HGNC Symbol                | coiled-coil domain containing 105 [Source:HGNC Symbol;Acc:HGNC:26866]                | -0.455466684 | 0.442646097 | 0.124559299   | 1 | 4.22482034    | 0.1676125287 | 0.347165754  | 1 |
| ENSG00000161003 | AC008127.1 | Clone-based (Ensembl) gene |                                                                                      | -0.528229433 | 0.317152409 | -0.608562688  | 1 | 1.675951687   | 0.727991986  | 0.130918148  | 1 |
| ENSG00000161243 | FBXO27     | HGNC Symbol                | F-box protein 27 [Source:HGNC Symbol;Acc:HGNC:18753]                                 | -0.817434469 | 0.165930422 | -0.622240471  | 1 | 2.046982131   | 0.708026594  | 0.753324058  | 1 |

|                  |         |             |                                                                                                      |              |             |              |   |              |              |              |   |
|------------------|---------|-------------|------------------------------------------------------------------------------------------------------|--------------|-------------|--------------|---|--------------|--------------|--------------|---|
| ENSG0000016170   | NPHS1   | HGNC Symbol | "NPHS1, nephrin [Source:HGNC Symbol;Acc:HGNC:7908]"                                                  | -0.59448236  | 0.3042161   | -0.677560856 | 1 | -0.316527889 | 0.93627297   | -0.164586694 | 1 |
| ENSG0000016109   | CDC155  | HGNC Symbol | coiled-coil domain containing 155 [Source:HGNC Symbol;Acc:HGNC:26520]                                | -0.559664333 | 0.31845888  | 0.321856534  | 1 | 1.27876212   | 0.776886286  | -0.254407597 | 1 |
| ENSG0000016182   | FAM71A2 | HGNC Symbol | family with sequence similarity 71 member 42 [Source:HGNC Symbol;Acc:HGNC:30480]                     | -0.83708843  | 0.064801456 | 0.26730244   | 1 | 0.789426772  | 0.876517598  | 0.09403063   | 1 |
| ENSG0000016140   | BCL6B   | HGNC Symbol | B cell CLL/lymphoma 6B [Source:HGNC Symbol;Acc:HGNC:1002]                                            | -0.733676229 | 0.061835527 | 0.3066629089 | 1 | 1.015597853  | 0.82066818   | 0.229086895  | 1 |
| ENSG0000016206   | MSLN    | HGNC Symbol | mesothelin-like [Source:HGNC Symbol;Acc:HGNC:1470]                                                   | -0.82468169  | 0.09146457  | 1.067686879  | 1 | 0.162688447  | 0.974864202  | -0.300137609 | 1 |
| ENSG00000162062  | TFDZ2   | HGNC Symbol | tubulin epsilon and delta complex 2 [Source:HGNC Symbol;Acc:HGNC:25849]                              | -0.659329887 | 0.16097424  | 0.450095579  | 1 | -0.0462343   | 1            | 0.29562575   | 1 |
| ENSG0000016250   | MATN1   | HGNC Symbol | "matrilin 1, cartilage matrix protein [Source:HGNC Symbol;Acc:HGNC:6907]"                            | -0.622999455 | 0.185310976 | -0.101984244 | 1 | -0.576816273 | 0.8546897053 | 0.272474864  | 1 |
| ENSG00000162631  | NTNG1   | HGNC Symbol | netrin 61 [Source:HGNC Symbol;Acc:HGNC:23318]                                                        | -0.620321047 | 0.18727621  | -0.401679035 | 1 | 0.274332455  | 0.948978235  | 0.539361847  | 1 |
| ENSG00000162706  | CAOM3   | HGNC Symbol | cell adhesion molecule 3 [Source:HGNC Symbol;Acc:HGNC:17601]                                         | -0.682331042 | 0.208106324 | 0.3713010869 | 1 | -0.555096936 | 0.875775045  | 0.05757637   | 1 |
| ENSG00000162738  | VANGL2  | HGNC Symbol | VANG1, planar cell polarity protein 2 [Source:HGNC Symbol;Acc:HGNC:15510]                            | -0.666370045 | 0.256539503 | -0.14701686  | 1 | 0.10993908   | 0.985016079  | -0.16276741  | 1 |
| ENSG0000016335   | IGF1N   | HGNC Symbol | immunoglobulin-like and fibronectin type III domain containing 1 [Source:HGNC Symbol;Acc:HGNC:24607] | -0.426568352 | 0.487780556 | -0.487480191 | 1 | 0.663264747  | 0.84902793   | 0.2100522973 | 1 |
| ENSG00000163689  | C3orf67 | HGNC Symbol | chromosome 3 open reading frame 67 [Source:HGNC Symbol;Acc:HGNC:24763]                               | -0.465955576 | 0.282307208 | -0.21641276  | 1 | 1.02748208   | 0.773447218  | 0.232500831  | 1 |
| ENSG00000163914  | RHO     | HGNC Symbol | Rhodopsin [Source:HGNC Symbol;Acc:HGNC:10012]                                                        | -0.91549882  | 0.333797586 | -0.71360021  | 1 | 0.41523755   | 0.916153867  | -0.848474498 | 1 |
| ENSG00000163975  | MELT    | HGNC Symbol | melanotransferrin [Source:HGNC Symbol;Acc:HGNC:7037]                                                 | -0.48778144  | 0.261507627 | 0.159834765  | 1 | -0.25102074  | 0.933291917  | 0.020651785  | 1 |
| ENSG00000163995  | ABLIM2  | HGNC Symbol | actin binding LIM protein family member 2 [Source:HGNC Symbol;Acc:HGNC:18195]                        | -0.520186403 | 0.063442539 | -0.105526095 | 1 | 0.51085722   | 0.773755142  | 0.233221699  | 1 |
| ENSG00000164093  | PITY2   | HGNC Symbol | paired like homeodomain 2 [Source:HGNC Symbol;Acc:HGNC:9005]                                         | -0.857868402 | 0.05730592  | 0.083391752  | 1 | 0.19335448   | 0.984650234  | 0.039253213  | 1 |
| ENSG0000016407   | HAND2   | HGNC Symbol | heart and neural crest derivatives expressed 2 [Source:HGNC Symbol;Acc:HGNC:4808]                    | -0.753644576 | 0.223874451 | -0.314074481 | 1 | 5.38018532   | 0.627688963  | 0.16433772   | 1 |
| ENSG0000016422   | ASB5    | HGNC Symbol | ankyrin repeat and SOCS box containing 5 [Source:HGNC Symbol;Acc:HGNC:7180]                          | 0.079831425  | 0.916328605 | 0.03521823   | 1 | 1.371358167  | 0.769405357  | -0.108086449 | 1 |
| ENSG00000164255  | SCGB3A2 | HGNC Symbol | secretoglobulin family 3A member 2 [Source:HGNC Symbol;Acc:HGNC:16391]                               | -0.5161464   | 0.003838842 | -1.103984543 | 1 | 0.4074356031 | 0.910756217  | 0.088276728  | 1 |
| ENSG00000164294  | GPX8    | HGNC Symbol | glutathione peroxidase 8 (putative) [Source:HGNC Symbol;Acc:HGNC:33100]                              | -0.656518063 | 0.28965417  | -0.219928588 | 1 | 2.0946910441 | 0.725943889  | 0.279465544  | 1 |
| ENSG00000164393  | AOC12   | HGNC Symbol | adhesion G protein-coupled receptor 12 [Source:HGNC Symbol;Acc:HGNC:18990]                           | -0.3870263   | 0.551201043 | -0.075720464 | 1 | 1.22944626   | 0.79424038   | 0.276302456  | 1 |
| ENSG00000164692  | COL1A2  | HGNC Symbol | collagen type I alpha 2 chain [Source:HGNC Symbol;Acc:HGNC:2198]                                     | -1.329100825 | 0.002055054 | -0.18773057  | 1 | -0.192726392 | 0.949746122  | 0.1461589    | 1 |
| ENSG00000164694  | FNDC1   | HGNC Symbol | fibronectin type III domain containing 1 [Source:HGNC Symbol;Acc:HGNC:21184]                         | -0.656127373 | 0.21872787  | -0.150125663 | 1 | 0.35156973   | 0.91831034   | 0.00936716   | 1 |
| ENSG0000016471A1 | ALDH1A1 | HGNC Symbol | aldehyde dehydrogenase 7 family member A1                                                            | -0.491810368 | 0.202719915 | -0.45949142  | 1 | 0.519367578  | 0.857601614  | -0.173250351 | 1 |

|       |               |         |             |                                                                                                                                              |              |              |              |              |              |               |   |
|-------|---------------|---------|-------------|----------------------------------------------------------------------------------------------------------------------------------------------|--------------|--------------|--------------|--------------|--------------|---------------|---|
| 64904 | ENSG000000001 | SLITRK5 | HGNC Symbol | [Source:HGNC Symbol;Acc:HGNC:877]<br>SLIT and NTRK like family member-5                                                                      | -0.67519097  | 0.028500813  | 0.2704575242 | 0.567555607  | 0.839716003  | -0.5671934478 | I |
| 65300 | ENSG000000001 | FAT3    | HGNC Symbol | [Source:HGNC Symbol;Acc:HGNC:20295]<br>FAT atypical cadherin 3 [Source:HGNC Symbol;Acc:HGNC:23812]                                           | -0.385540325 | 0.505923328  | -0.069846908 | 0.929543197  | 0.819610241  | 0.01656038    | I |
| 65323 | ENSG000000001 | LRFN5   | HGNC Symbol | [Source:HGNC Symbol;Acc:HGNC:23812]<br>leucine rich repeat and fibronectin type III domain containing 5 [Source:HGNC Symbol;Acc:HGNC:210360] | -0.642766127 | 0.318351819  | -0.357859717 | 0.9925363648 | 0.854865024  | 0.002427      | I |
| 65379 | ENSG000000001 | PNKD2   | HGNC Symbol | [Source:HGNC Symbol;Acc:HGNC:16744]<br>PBX/knotted 1 homeobox 2 [Source:HGNC Symbol;Acc:HGNC:16744]                                          | -0.072065851 | 0.813551285  | -0.364534906 | 2.475038628  | 0.6271668953 | 0.013822717   | I |
| 65495 | ENSG000000001 | AMER2   | HGNC Symbol | [Source:HGNC Symbol;Acc:HGNC:26360]<br>APD membrane recruitment protein 2 [Source:HGNC Symbol;Acc:HGNC:26360]                                | -0.383500908 | 0.550047859  | -0.326252538 | 2.2137462735 | 0.6989448    | -0.055804664  | I |
| 65566 | ENSG000000001 | JCAD    | HGNC Symbol | [Source:HGNC Symbol;Acc:HGNC:29283]<br>junctional cadherin 5 associated [Source:HGNC Symbol;Acc:HGNC:29283]                                  | -0.687536783 | 0.0530334    | -0.072388796 | 0.743888409  | 0.791276686  | 0.488556874   | I |
| 65816 | ENSG000000001 | WNA2    | HGNC Symbol | [Source:HGNC Symbol;Acc:HGNC:24709]<br>von Willebrand factor A domain containing 2 [Source:HGNC Symbol;Acc:HGNC:24709]                       | -0.616956529 | 0.228018995  | -0.077404904 | 0.917070948  | 0.973827049  | 0.3450810658  | I |
| 65866 | ENSG000000001 | PDLRN4  | HGNC Symbol | [Source:HGNC Symbol;Acc:HGNC:30552]<br>PDZ domain containing ring finger 4 [Source:HGNC Symbol;Acc:HGNC:30552]                               | -0.710133651 | 0.283637569  | -0.285064687 | 0.808503061  | 0.853575665  | 0.07166123    | I |
| 65970 | ENSG000000001 | SUC6A5  | HGNC Symbol | [Source:HGNC Symbol;Acc:HGNC:40501]<br>solute carrier family 6 member 5 [Source:HGNC Symbol;Acc:HGNC:40501]                                  | -0.446556406 | 0.467030383  | -0.374632483 | 0.402947708  | 0.939106996  | 0.6071693059  | I |
| 65970 | ENSG000000001 | NELL1   | HGNC Symbol | [Source:HGNC Symbol;Acc:HGNC:77501]<br>neural EF1 like 1 [Source:HGNC Symbol;Acc:HGNC:77501]                                                 | -0.775652603 | 0.220165101  | -0.007894805 | 0.550064836  | 0.913766503  | 0.368089989   | I |
| 65973 | ENSG000000001 | SPA1A9  | HGNC Symbol | [Source:HGNC Symbol;Acc:HGNC:30614]<br>spermatogenesis associated 19 [Source:HGNC Symbol;Acc:HGNC:30614]                                     | -0.778014279 | 0.27315445   | 0.064397127  | 0.773848003  | 0.865671698  | 0.035744334   | I |
| 6618  | ENSG000000001 | LRTM2   | HGNC Symbol | [Source:HGNC Symbol;Acc:HGNC:32443]<br>leucine rich repeats and transmembrane domains 2 [Source:HGNC Symbol;Acc:HGNC:32443]                  | -0.85389222  | 0.085585789  | 0.378309904  | 0.7257163036 | 0.871916627  | -0.0845978    | I |
| 66169 | ENSG000000001 | TWEM10  | HGNC Symbol | [Source:HGNC Symbol;Acc:HGNC:25607]<br>transmembrane protein 100 [Source:HGNC Symbol;Acc:HGNC:25607]                                         | -0.25098468  | 0.758168139  | -0.406454556 | 5.310152728  | 0.6271668953 | 0.517986656   | I |
| 66292 | ENSG000000001 | MOGAT2  | HGNC Symbol | [Source:HGNC Symbol;Acc:HGNC:23248]<br>monoacylglycerol O-acyltransferase 2 [Source:HGNC Symbol;Acc:HGNC:23248]                              | -0.648731495 | 0.319053284  | -0.609899388 | 0.02785553   | 0.98444518   | 0.44502466    | I |
| 66391 | ENSG000000001 | ST5     | HGNC Symbol | [Source:HGNC Symbol;Acc:HGNC:10501]<br>suppression of tumorigenicity 5 [Source:HGNC Symbol;Acc:HGNC:10501]                                   | -0.623989828 | 0.08234925   | -0.216220169 | 0.919970837  | 0.96970837   | -0.025992347  | I |
| 66444 | ENSG000000001 | PQOIL2  | HGNC Symbol | [Source:HGNC Symbol;Acc:HGNC:27115]<br>polyoystin 1 like 2 (gene/psudogene) [Source:HGNC Symbol;Acc:HGNC:27115]                              | -0.291071825 | 0.668316557  | 0.069479882  | 0.803294813  | 0.8255652858 | 0.035579592   | I |
| 66473 | ENSG000000001 | SUC3B48 | HGNC Symbol | [Source:HGNC Symbol;Acc:HGNC:32434]<br>solute carrier family 38 member 8 [Source:HGNC Symbol;Acc:HGNC:32434]                                 | -0.565390451 | 0.349528978  | 0.028492019  | 0.460310781  | 0.9272604678 | 0.043250087   | I |
| 66558 | ENSG000000001 | CFAP52  | HGNC Symbol | [Source:HGNC Symbol;Acc:HGNC:16053]<br>cilium and flagella associated protein 52 [Source:HGNC Symbol;Acc:HGNC:16053]                         | -0.378333127 | 0.5657527075 | -0.716740317 | 0.9693849716 | 0.827355425  | -0.073516986  | I |
| 66596 | ENSG000000001 | PLEKHA7 | HGNC Symbol | [Source:HGNC Symbol;Acc:HGNC:27049]<br>pleckstrin homology domain containing A7 [Source:HGNC Symbol;Acc:HGNC:27049]                          | -0.295527396 | 0.24102465   | -0.210446306 | 0.6564545013 | 0.733544265  | -0.086057803  | I |
| 66689 | ENSG000000001 | TAC3    | HGNC Symbol | [Source:HGNC Symbol;Acc:HGNC:10520]<br>tachykinin 3 [Source:HGNC Symbol;Acc:HGNC:10520]                                                      | -0.725563817 | 0.198940702  | 0.276320889  | 2.053024881  | 0.70133644   | 0.327595963   | I |
| 66683 | ENSG000000001 | CHP2    | HGNC Symbol | [Source:HGNC Symbol;Acc:HGNC:24927]<br>caldesmon like EF-hand protein 2 [Source:HGNC Symbol;Acc:HGNC:24927]                                  | -0.947768021 | 0.0220394    | -0.35384617  | 0.055580641  | 0.999535068  | 0.32322593    | I |
| 66869 | ENSG000000001 | TOPD12  | HGNC Symbol | [Source:HGNC Symbol;Acc:HGNC:24927]<br>t-complex 10 like 2 [Source:HGNC Symbol;Acc:HGNC:24927]                                               | -0.754572409 | 0.150377424  | -0.437351638 | -0.57447192  | 0.867158445  | -0.21288731   | I |
| 66984 | ENSG000000001 | AT1AY   | HGNC Symbol | [Source:HGNC Symbol;Acc:HGNC:21234]<br>"AT1AY" radixin [Source:HGNC Symbol;Acc:HGNC:21234]                                                   | -0.919559213 | 0.089473958  | 0.929551767  | 2.883854099  | 0.656595383  | 0.00042742    | I |

|                 |          |             |                                                                                                    |              |             |              |   |              |             |              |   |
|-----------------|----------|-------------|----------------------------------------------------------------------------------------------------|--------------|-------------|--------------|---|--------------|-------------|--------------|---|
| 67654           |          |             | Symbol:Acc:HNC:779"                                                                                | -0.553018449 | 0.047202728 | -0.152316762 | 1 | 0.359307054  | 0.88017288  | 0.051735039  | 1 |
| ENSG00000167723 | TRPV3    | HGNC Symbol | transient receptor potential cation channel subfamily V member 3 [Source:HNC Symbol:Acc:HNC:18084] | -0.877178887 | 0.265229199 | 0.07732329   | 1 | 2.144333068  | 0.74956272  | 0.0416241    | 1 |
| ENSG00000167757 | KLK11    | HGNC Symbol | kallikrein related peptidase 11 [Source:HNC Symbol:Acc:HNC:6359]                                   | -0.444806942 | 0.307549599 | 0.49440126   | 1 | 0.84301591   | 0.840244238 | -0.149057284 | 1 |
| ENSG00000167779 | IGFBP6   | HGNC Symbol | insulin like growth factor binding protein 6 [Source:HNC Symbol:Acc:HNC:5475]                      | -0.397404693 | 0.575036428 | -0.69180716  | 1 | 1.232456505  | 0.79452482  | 0.047198354  | 1 |
| ENSG00000167798 | C3P1     | HGNC Symbol | complement component 3 precursor isoologene [Source:HNC Symbol:Acc:HNC:3444]                       | -0.633708326 | 0.239072641 | 0.155387518  | 1 | 0.283530465  | 0.945342734 | -0.03127047  | 1 |
| ENSG00000168077 | SCARA3   | HGNC Symbol | scavenger receptor class A member 3 [Source:HNC Symbol:Acc:HNC:19000]                              | -0.678863321 | 0.11887496  | 0.304909506  | 1 | 0.842542483  | 0.79237154  | 0.109013922  | 1 |
| ENSG00000168079 | SCARA5   | HGNC Symbol | scavenger receptor class A member 5 [Source:HNC Symbol:Acc:HNC:28701]                              | -0.41877904  | 0.366781722 | -0.610944587 | 1 | -0.263924959 | 0.944798487 | 0.35100504   | 1 |
| ENSG00000168356 | SCN1A    | HGNC Symbol | sodium voltage-gated channel alpha subunit 1 [Source:HNC Symbol:Acc:HNC:10583]                     | -0.1663307   | 0.89274309  | -0.593665591 | 1 | 1.742787077  | 0.74059294  | 0.058945896  | 1 |
| ENSG00000168367 | UNC00917 | HGNC Symbol | long intergenic non-protein coding RNA 917 [Source:HNC Symbol:Acc:HNC:48607]                       | -0.573256523 | 0.30228903  | -0.17768002  | 1 | -0.176057427 | 0.97521881  | -0.361933393 | 1 |
| ENSG00000168481 | LG13     | HGNC Symbol | leucine rich repeat L1 family member 3 [Source:HNC Symbol:Acc:HNC:18710]                           | -0.37382046  | 0.06332935  | -0.55159713  | 1 | -0.306770833 | 0.950916899 | 0.177687701  | 1 |
| ENSG00000168484 | SFTPC    | HGNC Symbol | surfactant protein C [Source:HNC Symbol:Acc:HNC:10807]                                             | -0.37382046  | 0.06332935  | -0.55159713  | 1 | -0.306770833 | 0.950916899 | 0.177687701  | 1 |
| ENSG00000168542 | COL3A1   | HGNC Symbol | collagen type III alpha 1 chain [Source:HNC Symbol:Acc:HNC:2701]                                   | -0.37382046  | 0.06332935  | -0.55159713  | 1 | -0.306770833 | 0.950916899 | 0.177687701  | 1 |
| ENSG00000168597 | PLA2G4F  | HGNC Symbol | phospholipase A2 group IV [Source:HNC Symbol:Acc:HNC:27396]                                        | -0.587140167 | 0.29544708  | -0.344346884 | 1 | 0.027716324  | 1           | 0.0595854026 | 1 |
| ENSG00000168599 | GRM5     | HGNC Symbol | glutamate metabotropic receptor 5 [Source:HNC Symbol:Acc:HNC:4597]                                 | -0.453653069 | 0.441910603 | -0.377363911 | 1 | 0.590871081  | 0.88200771  | 0.094617918  | 1 |
| ENSG0000016925  | ARMC4    | HGNC Symbol | armadillo repeat containing 4 [Source:HNC Symbol:Acc:HNC:25583]                                    | -0.575622875 | 0.29544708  | -0.488364348 | 1 | 1.816920531  | 0.732815758 | 0.904302929  | 1 |
| ENSG0000016969  | CPT1C    | HGNC Symbol | carnitine palmitoyltransferase 1C [Source:HNC Symbol:Acc:HNC:16540]                                | -0.341610466 | 0.476106903 | 0.631079872  | 1 | -0.095662355 | 0.98993439  | -0.345407026 | 1 |
| ENSG00000169344 | UMOD     | HGNC Symbol | uromodulin [Source:HNC Symbol:Acc:HNC:12559]                                                       | -0.76971658  | 0.18187865  | -0.135743663 | 1 | 0.408154074  | 0.931976942 | -0.17551803  | 1 |
| ENSG00000169436 | COL2A1   | HGNC Symbol | collagen type XII alpha 1 chain [Source:HNC Symbol:Acc:HNC:22989]                                  | -0.374487855 | 0.528626826 | -0.280059254 | 1 | 0.74748695   | 0.82188312  | 0.140488858  | 1 |
| ENSG00000169862 | CTNND2   | HGNC Symbol | catenin delta 2 [Source:HNC Symbol:Acc:HNC:27516]                                                  | -0.350914798 | 0.520102355 | -0.072724035 | 1 | 0.690029393  | 0.84076646  | 0.284817064  | 1 |
| ENSG00000169876 | MUC17    | HGNC Symbol | "mucin 17, cell surface associated [Source:HNC Symbol:Acc:HNC:16800]"                              | -0.566443746 | 0.387167501 | 0.684807971  | 1 | 1.393210612  | 0.747487389 | 0.615964856  | 1 |
| ENSG00000170381 | SEMA3E   | HGNC Symbol | semaphorin 3E [Source:HNC Symbol:Acc:HNC:10727]                                                    | -0.598756051 | 0.385408727 | 0.07568161   | 1 | 0.356729287  | 0.943406874 | 0.074345074  | 1 |
| ENSG00000170426 | SDR9C7   | HGNC Symbol | short chain dehydrogenase/reductase family 9C member 7 [Source:HNC Symbol:Acc:HNC:29558]           | -0.669644519 | 0.163673446 | -0.50740439  | 1 | 0.508730318  | 0.915138245 | 0.170350896  | 1 |
| ENSG00000170442 | KRT66    | HGNC Symbol | keratin 66 [Source:HNC Symbol:Acc:HNC:3463]                                                        | -0.370773529 | 0.370892028 | 0.67524677   | 1 | 0.47253793   | 0.91690397  | -0.700899984 | 1 |
| ENSG00000170442 | TTL16    | HGNC Symbol | tubulin tyrosine ligase like 6 [Source:HNC Symbol:Acc:HNC:3463]                                    | -0.589944567 | 0.344781215 | -0.056072488 | 1 | 0.735266638  | 0.899343886 | 0.301559858  | 1 |

[illegible]

[illegible]

|                 |         |             |                                                                                                 |               |              |              |   |              |             |              |   |
|-----------------|---------|-------------|-------------------------------------------------------------------------------------------------|---------------|--------------|--------------|---|--------------|-------------|--------------|---|
| ENSG00000179863 | FAM218B | HGNC Symbol | Symbol/Accession:HGNC:272451                                                                    | -0.305849787  | 0.705076551  | -0.056443991 | 1 | 1.17423548   | 0.855882707 | 0.51048003   | 1 |
| ENSG00000180291 | SLC9A4  | HGNC Symbol | [Source:HGNC Symbol/Accession:HGNC:26883] solute carrier family 9 member A4                     | -0.349423486  | 0.580672041  | 0.354022333  | 1 | 1.853862748  | 0.729903191 | 0.137552884  | 1 |
| ENSG00000181443 | MUC16   | HGNC Symbol | "mucin 16, cell surface associated [Source:HGNC Symbol/Accession:HGNC:45582]"                   | -0.329348592  | 0.430361654  | 0.265140388  | 1 | -0.610345242 | 0.829807444 | 0.370527471  | 1 |
| ENSG00000181555 | DFEC1   | HGNC Symbol | orofacial cleft 1 candidate 1 [Source:HGNC Symbol/Accession:HGNC:21007]                         | -0.532362428  | 0.43784601   | -0.65169174  | 1 | 0.495357778  | 0.913357086 | -0.37543806  | 1 |
| ENSG00000181978 | CFAP55  | HGNC Symbol | cilia and flagella associated protein 55 [Source:HGNC Symbol/Accession:HGNC:25325]              | -0.434847926  | 0.442594607  | -0.142589287 | 1 | -0.442095465 | 0.88530895  | -0.140868213 | 1 |
| ENSG00000182756 | GABRG3  | HGNC Symbol | gamma-aminobutyric acid type A receptor gamma3 subunit [Source:HGNC Symbol/Accession:HGNC:4088] | -0.256233297  | 0.696478261  | 0.0016151    | 1 | 1.678376167  | 0.74180575  | 0.537162329  | 1 |
| ENSG00000183016 | NA      | NA          | NA                                                                                              | -0.301665823  | 0.66144616   | -0.409663712 | 1 | 0.214059907  | 0.963151207 | 0.164903336  | 1 |
| ENSG00000183067 | IGSF5   | HGNC Symbol | immunoglobulin superfamily member 5 [Source:HGNC Symbol/Accession:HGNC:5952]                    | -0.513102971  | 0.457242584  | 0.01001437   | 1 | 5.552457083  | 0.677668963 | 0.610657118  | 1 |
| ENSG00000183206 | POTEC   | HGNC Symbol | POTE ankyrin domain family member C [Source:HGNC Symbol/Accession:HGNC:33894]                   | -0.327870746  | 0.614565385  | 0.288269994  | 1 | 1.44511872   | 0.715714746 | 0.09740365   | 1 |
| ENSG00000183242 | W1AS    | HGNC Symbol | W1 antisense RNA [Source:HGNC Symbol/Accession:HGNC:1835]                                       | -0.327487007  | 0.635303035  | -0.24901635  | 1 | 2.83449092   | 0.689965785 | 0.22893402   | 1 |
| ENSG00000183287 | CCBE1   | HGNC Symbol | collagen and calcium binding EGF domains 1 [Source:HGNC Symbol/Accession:HGNC:29426]            | -0.590879294  | 0.238072641  | -0.108476557 | 1 | 0.67769926   | 0.88616233  | 0.102473963  | 1 |
| ENSG00000183304 | FAM8A   | HGNC Symbol | family with sequence similarity 9 member A [Source:HGNC Symbol/Accession:HGNC:18403]            | -0.338058237  | 0.0955036375 | 0.787981855  | 1 | 1.285285772  | 0.817952528 | -0.064655496 | 1 |
| ENSG00000183317 | EPHA10  | HGNC Symbol | EPH receptor A10 [Source:HGNC Symbol/Accession:HGNC:19587]                                      | -0.4659592797 | 0.372910195  | -0.320481618 | 1 | 0.884261146  | 0.820489984 | 0.118204369  | 1 |
| ENSG00000183580 | FBX17   | HGNC Symbol | F-box and leucine rich repeat protein 7 [Source:HGNC Symbol/Accession:HGNC:13604]               | -0.591833897  | 0.3651077842 | -0.524894371 | 1 | 0.925469737  | 0.860534878 | 0.671873557  | 1 |
| ENSG00000183668 | PSG9    | HGNC Symbol | pregnancy specific beta-1-glycoprotein 9 [Source:HGNC Symbol/Accession:HGNC:9526]               | -0.78121682   | 0.216746846  | -0.250813779 | 1 | -0.395330668 | 0.939971429 | 0.58544285   | 1 |
| ENSG00000183778 | B3GALT5 | HGNC Symbol | "beta-1,3-galactosyltransferase 5 [Source:HGNC Symbol/Accession:HGNC:920]"                      | -0.49369755   | 0.401627772  | -0.981318157 | 1 | 2.317782559  | 0.722505857 | 0.663167198  | 1 |
| ENSG00000183780 | SLC35F3 | HGNC Symbol | solute carrier family 35 member F3 [Source:HGNC Symbol/Accession:HGNC:23616]                    | -0.289076993  | 0.42216105   | 0.083035636  | 1 | 0.842283744  | 0.692730659 | -0.242552512 | 1 |
| ENSG00000183856 | IQGAP3  | HGNC Symbol | IQ motif containing GTPase activating protein 3 [Source:HGNC Symbol/Accession:HGNC:21669]       | -0.465335464  | 0.302087891  | -0.18178081  | 1 | -0.43815854  | 0.859665429 | 0.161670003  | 1 |
| ENSG00000183876 | ARSI    | HGNC Symbol | arylsulfatase family member 1 [Source:HGNC Symbol/Accession:HGNC:37521]                         | -0.487563606  | 0.40321661   | 0.27777532   | 1 | 1.2888661    | 0.787336888 | -0.216444352 | 1 |
| ENSG00000183908 | LRRCS5  | HGNC Symbol | leucine rich repeat containing 55 [Source:HGNC Symbol/Accession:HGNC:32924]                     | -0.30823165   | 0.60477643   | 0.04564564   | 1 | 2.382195282  | 0.713135474 | 0.020004922  | 1 |
| ENSG00000184012 | TMPPSS2 | HGNC Symbol | transmembrane serine protease 2 [Source:HGNC Symbol/Accession:HGNC:1876]                        | -0.918034548  | 0.037008563  | -0.246437402 | 1 | 0.101566228  | 0.919823026 | -0.089842719 | 1 |
| ENSG00000184227 | ACOT11  | HGNC Symbol | acyl-CoA thioesterase 1 [Source:HGNC Symbol/Accession:HGNC:33128]                               | -0.665249244  | 0.162555375  | 0.52223814   | 1 | -0.626385273 | 0.794524132 | -0.442718998 | 1 |
| ENSG00000184302 | SIX6    | HGNC Symbol | SIX homeobox 6 [Source:HGNC Symbol/Accession:HGNC:10892]                                        | -0.504018881  | 0.441451067  | 0.558283399  | 1 | -0.045859523 | 1           | 0.231671606  | 1 |

|                 |             |             |                                                                                   |               |              |   |              |             |              |   |
|-----------------|-------------|-------------|-----------------------------------------------------------------------------------|---------------|--------------|---|--------------|-------------|--------------|---|
| ENSG00000184304 | PRK01       | HGNC Symbol | protein kinase D1 [Source:HGNC Symbol;Acc:HGNC:94077]                             | 0.45595988    | -0.063709292 | 1 | 1.432135626  | 0.74753926  | 0.035035921  | 1 |
| ENSG00000184809 | B3GALT5-AS1 | HGNC Symbol | B3GALT5 antisense RNA 1 [Source:HGNC Symbol;Acc:HGNC:16424]                       | -0.339454299  | 0.140091076  | 1 | -0.05616504  | 0.99937713  | 0.744086602  | 1 |
| ENSG00000184908 | CLCNK8      | HGNC Symbol | chloride voltage-gated channel K1b [Source:HGNC Symbol;Acc:HGNC:27027]            | -0.357691839  | 0.540451079  | 1 | -0.836321916 | 0.799148915 | 0.134333106  | 1 |
| ENSG00000185038 | MROH2A      | HGNC Symbol | maestro heat like repeat family member 2A [Source:HGNC Symbol;Acc:HGNC:27836]     | -0.38431913   | 0.3273839541 | 1 | 0.857416789  | 0.82438292  | -0.165235359 | 1 |
| ENSG00000185069 | KRT76       | HGNC Symbol | keratin 76 [Source:HGNC Symbol;Acc:HGNC:24430]                                    | -0.5580061    | 0.3653389935 | 1 | -0.69532548  | 0.855426705 | -0.323886971 | 1 |
| ENSG00000185303 | SFTPA2      | HGNC Symbol | surfactant protein A2 [Source:HGNC Symbol;Acc:HGNC:10799]                         | -0.803359583  | 0.189636469  | 1 | 2.140859914  | 0.727990986 | 0.3194447    | 1 |
| ENSG00000185333 | SCN10A      | HGNC Symbol | sodium voltage-gated channel alpha subunit 10 [Source:HGNC Symbol;Acc:HGNC:10582] | -0.230551689  | 0.73625037   | 1 | 0.167482957  | 0.973318649 | 0.143181925  | 1 |
| ENSG00000185467 | KPNA7       | HGNC Symbol | karyopherin subunit alpha 7 [Source:HGNC Symbol;Acc:HGNC:21839]                   | -0.69440359   | 0.827997131  | 1 | -0.3087587   | 0.948255578 | 0.278772356  | 1 |
| ENSG00000185686 | PRAME       | HGNC Symbol | preferentially expressed antigen in melanoma [Source:HGNC Symbol;Acc:HGNC:9336]   | -0.683189263  | 0.23879249   | 1 | -0.34640386  | 0.94835771  | 0.819682549  | 1 |
| ENSG00000185737 | NRG3        | HGNC Symbol | neuregulin 3 [Source:HGNC Symbol;Acc:HGNC:7899]                                   | -0.33707231   | 0.60833718   | 1 | -0.202080434 | 0.974607748 | 0.39711249   | 1 |
| ENSG00000185739 | SRL         | HGNC Symbol | sarcosine [Source:HGNC Symbol;Acc:HGNC:11295]                                     | -0.78970248   | 0.82833474   | 1 | 1.1010047    | 0.794748396 | 0.040317772  | 1 |
| ENSG00000185823 | NPAPI       | HGNC Symbol | nuclear pore associated protein 1 [Source:HGNC Symbol;Acc:HGNC:1180]              | -0.709460544  | 0.239778807  | 1 | 0.3799295    | 0.939780849 | 0.780350439  | 1 |
| ENSG00000185974 | GRK1        | HGNC Symbol | G protein-coupled receptor kinase 1 [Source:HGNC Symbol;Acc:HGNC:10013]           | -0.524877614  | 0.365633163  | 1 | 0.84577371   | 0.816513218 | 0.105802313  | 1 |
| ENSG00000186065 | KIF18B      | HGNC Symbol | kinesin family member 18B [Source:HGNC Symbol;Acc:HGNC:27102]                     | -0.5339102601 | 0.08735557   | 1 | 1.659755026  | 0.627658963 | -0.043354427 | 1 |
| ENSG00000186393 | KRT26       | HGNC Symbol | keratin 26 [Source:HGNC Symbol;Acc:HGNC:30840]                                    | -0.510861904  | 0.3935531656 | 1 | -0.273830863 | 0.967516048 | -0.245635919 | 1 |
| ENSG00000186487 | MYT1L       | HGNC Symbol | myelin transcription factor 1 like [Source:HGNC Symbol;Acc:HGNC:1623]             | -0.551259763  | 0.323477526  | 1 | 1.185653359  | 0.773755142 | 0.2734510958 | 1 |
| ENSG00000186526 | CYP4F8      | HGNC Symbol | cytochrome P450 family 4 subfamily F member 8 [Source:HGNC Symbol;Acc:HGNC:2648]  | -0.633956341  | 0.284297086  | 1 | -0.29164062  | 0.976008317 | 0.046648148  | 1 |
| ENSG00000186862 | P0ZD7       | HGNC Symbol | P0Z domain containing 7 [Source:HGNC Symbol;Acc:HGNC:26257]                       | -0.554675047  | 0.16405126   | 1 | 0.2230154668 | 0.933489898 | 0.072854071  | 1 |
| ENSG00000187058 | C3orf70     | HGNC Symbol | chromosome 3 open reading frame 70 [Source:HGNC Symbol;Acc:HGNC:33731]            | -0.883227104  | 0.73981403   | 1 | -0.039299772 | 0.919823026 | 0.304445715  | 1 |
| ENSG00000187094 | CLK         | HGNC Symbol | cholecystikinin [Source:HGNC Symbol;Acc:HGNC:1669]                                | -0.803919388  | 0.14982169   | 1 | 1.13454822   | 1           | -0.258457511 | 1 |
| ENSG0000018723  | LYPD5       | HGNC Symbol | LY6/PLAUR domain containing 5 [Source:HGNC Symbol;Acc:HGNC:28751]                 | -0.508808838  | 0.40101895   | 1 | 0.866181631  | 0.820882968 | 0.56627688   | 1 |
| ENSG00000187527 | ATP13A5     | HGNC Symbol | ATPase 13A5 [Source:HGNC Symbol;Acc:HGNC:31789]                                   | -0.4675455019 | 0.428173196  | 1 | -0.41275252  | 0.786877233 | 0.279380903  | 1 |
| ENSG00000187772 | LINC28B     | HGNC Symbol | lin-28 homolog B [Source:HGNC Symbol;Acc:HGNC:32207]                              | -0.234471087  | 0.763770257  | 1 | -0.019347151 | 1           | 0.066218621  | 1 |
| ENSG00000187905 | LRRIC74B    | HGNC Symbol | leucine rich repeat containing 74B [Source:HGNC Symbol;Acc:HGNC:34301]            | -0.461043362  | 0.4745351    | 1 | 1.2448556    | 0.78516312  | 0.048322593  | 1 |

|                 |            |                            |                                                                                 |               |             |               |   |              |             |              |   |
|-----------------|------------|----------------------------|---------------------------------------------------------------------------------|---------------|-------------|---------------|---|--------------|-------------|--------------|---|
| ENSG00000187955 | COL14A1    | HCNC Symbol                | collagen type XIV alpha 1 chain [Source:HGNC Symbol;Acc:HGNC:2191]              | -0.80264294   | 0.060883822 | -0.101877235  | 1 | 0.493543     | 0.886962045 | 0.083906397  | 1 |
| ENSG00000187957 | C17orf99   | HCNC Symbol                | chromosome 17 open reading frame 99 [Source:HGNC Symbol;Acc:HGNC:34490]         | -0.54593757   | 0.228439083 | 0.090918915   | 1 | -0.722809509 | 0.7736391   | 0.292391541  | 1 |
| ENSG00000188086 | PRSS45     | HCNC Symbol                | serine protease 45 [Source:HGNC Symbol;Acc:HGNC:330717]                         | -0.5810610502 | 0.385562603 | -0.219462299  | 1 | 2.05884047   | 0.71491936  | 0.036388504  | 1 |
| ENSG0000018812  | C6orf132   | HCNC Symbol                | chromosome 6 open reading frame 132 [Source:HGNC Symbol;Acc:HGNC:21288]         | -0.912928908  | 0.0832644   | -0.3093550842 | 1 | 1.835030788  | 0.69783232  | -0.543290658 | 1 |
| ENSG00000188162 | OTOG       | HCNC Symbol                | otogelin [Source:HGNC Symbol;Acc:HGNC:8516]                                     | -0.501929759  | 0.34669837  | -0.014039957  | 1 | 0.595459788  | 0.858968348 | 0.036693298  | 1 |
| ENSG00000188338 | SLC38A3    | HCNC Symbol                | solute carrier family 38 member 3 [Source:HGNC Symbol;Acc:HGNC:48144]           | -0.761738167  | 0.152108524 | -0.516375224  | 1 | 0.918485421  | 0.81317296  | 0.112758653  | 1 |
| ENSG00000188488 | SERPINA5   | HCNC Symbol                | serpin family A member 5 [Source:HGNC Symbol;Acc:HGNC:9723]                     | -0.692734776  | 0.248884109 | -0.398827099  | 1 | -0.066986093 | 0.99928282  | 0.034654676  | 1 |
| ENSG00000188706 | ZDHHC9     | HCNC Symbol                | zinc finger DHHC-type containing 9 [Source:HGNC Symbol;Acc:HGNC:18475]          | -0.385110334  | 0.030930967 | 0.055051422   | 1 | 0.707442896  | 0.705378609 | 0.084978724  | 1 |
| ENSG00000188782 | CATSPER4   | HCNC Symbol                | cation channel sperm associated 4 [Source:HGNC Symbol;Acc:HGNC:23220]           | -0.829338746  | 0.157963233 | 0.37862979    | 1 | -0.078094345 | 0.995880337 | 0.022895997  | 1 |
| ENSG00000188803 | SHISA6     | HCNC Symbol                | shisa family member 6 [Source:HGNC Symbol;Acc:HGNC:3449]                        | -0.516218657  | 0.482783    | 0.142754216   | 1 | 0.753257185  | 0.86191853  | 0.190594903  | 1 |
| ENSG00000188886 | ASTL       | HCNC Symbol                | astacin like metalloendopeptidase [Source:HGNC Symbol;Acc:HGNC:31704]           | -1.18762195   | 0.005079261 | -0.606540007  | 1 | 0.948025586  | 0.78067562  | -0.02126839  | 1 |
| ENSG00000196091 | MYBPC1     | HCNC Symbol                | "myosin binding protein C, slow type [Source:HGNC Symbol;Acc:HGNC:7549]"        | -0.430673258  | 0.437393542 | -0.626720148  | 1 | 0.309888777  | 0.933370884 | -0.01044474  | 1 |
| ENSG00000196136 | SERPINA3   | HCNC Symbol                | serpin family A member 3 [Source:HGNC Symbol;Acc:HGNC:16]                       | -0.909089758  | 0.016147674 | -0.356107603  | 1 | 0.19141925   | 0.97700852  | -0.282370334 | 1 |
| ENSG00000196381 | ELAVL3     | HCNC Symbol                | ELAV like RNA binding protein 3 [Source:HGNC Symbol;Acc:HGNC:3314]              | -0.75893849   | 0.14285189  | 0.301465434   | 1 | 1.953337262  | 0.706499236 | -0.235289109 | 1 |
| ENSG0000019645  | PRIN3      | HCNC Symbol                | proteinase 3 [Source:HGNC Symbol;Acc:HGNC:5495]                                 | -1.443754633  | 0.007256568 | -0.30167112   | 1 | 1.102437354  | 0.834571278 | -0.376208763 | 1 |
| ENSG00000196565 | HBB2       | HCNC Symbol                | hemoglobin subunit gamma 2 [Source:HGNC Symbol;Acc:HGNC:4832]                   | -0.531424276  | 0.01465659  | -0.512995497  | 1 | -0.260328339 | 0.915188245 | -0.54792429  | 1 |
| ENSG00000196862 | RGP04      | HCNC Symbol                | RANBP2-like and GRIP domain containing 4 [Source:HGNC Symbol;Acc:HGNC:32417]    | -0.694018274  | 0.03331637  | -0.376146102  | 1 | 6.58910869   | 0.402387206 | 0.140028962  | 1 |
| ENSG00000197078 | KRT35      | HCNC Symbol                | keratin 35 [Source:HGNC Symbol;Acc:HGNC:6453]                                   | -0.658605824  | 0.248428762 | -0.090695231  | 1 | 2.158446723  | 0.69783232  | -0.532102814 | 1 |
| ENSG00000197085 | NPSRI-AS1  | HCNC Symbol                | NPSRI antisense RNA 1 [Source:HGNC Symbol;Acc:HGNC:22128]                       | -0.47682751   | 0.385383826 | -0.320908913  | 1 | 6.218739468  | 0.627668963 | 0.68986278   | 1 |
| ENSG00000197406 | DIO3       | HCNC Symbol                | iodothyronine dioxygenase 3 [Source:HGNC Symbol;Acc:HGNC:2885]                  | -0.582483897  | 0.278225713 | 0.404297609   | 1 | 0.46384897   | 0.935206684 | -0.223986968 | 1 |
| ENSG00000197408 | CYP2B6     | HCNC Symbol                | cytochrome P450 family 2 subfamily B member 6 [Source:HGNC Symbol;Acc:HGNC:296] | -0.59880912   | 0.38510274  | -0.63253654   | 1 | 0.912421099  | 0.83757431  | -0.55716613  | 1 |
| ENSG00000197853 | NRAP       | HCNC Symbol                | nebulin related anchoring protein [Source:HGNC Symbol;Acc:HGNC:7988]            | -0.32566386   | 0.63782184  | -0.271689128  | 1 | 0.792610765  | 0.853462632 | 0.153165007  | 1 |
| ENSG00000197991 | AL592490.1 | Clone-based (Ensembl) gene |                                                                                 | -0.605428218  | 0.343101516 | 0.070232584   | 1 | -0.41372368  | 0.916194501 | -0.158852377 | 1 |
| ENSG00000198010 | DLGAP2     | HCNC Symbol                | DLG associated protein 2 [Source:HGNC Symbol;Acc:HGNC:2916]                     | -0.462914925  | 0.40374714  | 0.068714495   | 1 | 1.089410281  | 0.791327824 | 0.185394349  | 1 |

|                 |            |                            |                                                                                 |              |             |               |   |              |             |               |   |
|-----------------|------------|----------------------------|---------------------------------------------------------------------------------|--------------|-------------|---------------|---|--------------|-------------|---------------|---|
| ENSG00000198597 | ZNF536     | HGNC Symbol                | zinc finger protein 536 [Source:HGNC Symbol;Acc:HGNC:29025]                     | -0.38101583  | 0.81244809  | -0.44524094   | 1 | 0.631864973  | 0.872919273 | 0.365147069   | 1 |
| ENSG00000198765 | SYCP1      | HGNC Symbol                | synaptonemal complex protein 1 [Source:HGNC Symbol;Acc:HGNC:1487]               | -0.47425869  | 0.46558509  | 0.08200108    | 1 | -0.44549802  | 0.938883645 | 0.59365793    | 1 |
| ENSG00000198788 | MUC2       | HGNC Symbol                | "mucin 2, oligomeric mucus/gel-forming [Source:HGNC Symbol;Acc:HGNC:7502]"      | -0.556584229 | 0.527492504 | 0.28921894    | 1 | 0.760795909  | 0.824640952 | -0.243937903  | 1 |
| ENSG00000198914 | POLR33     | HGNC Symbol                | POLR class 3 homeobox 3 [Source:HGNC Symbol;Acc:HGNC:3216]                      | -0.566373551 | 0.328222585 | -0.01918062   | 1 | 2.501307942  | 0.707562018 | 0.163345574   | 1 |
| ENSG00000198929 | NOS1AP     | HGNC Symbol                | nitric oxide synthase 1 adaptor protein [Source:HGNC Symbol;Acc:HGNC:16859]     | -0.572447538 | 0.233601559 | -0.482556569  | 1 | 2.16810226   | 0.640552142 | 0.142426268   | 1 |
| ENSG00000193805 | PIPP4      | HGNC Symbol                | phospholipid phosphatase 4 [Source:HGNC Symbol;Acc:HGNC:23531]                  | -0.645887167 | 0.225621278 | -0.402456377  | 1 | -0.697779625 | 0.843165524 | -0.1465716451 | 1 |
| ENSG00000193900 | ALU1827.1  | Clone-based (Ensembl) gene |                                                                                 | -0.907580244 | 0.058168339 | 0.238165065   | 1 | -0.168928987 | 0.978937783 | 0.297866886   | 1 |
| ENSG00000194055 | ALU5815.1  | Clone-based (Ensembl) gene |                                                                                 | -0.301965968 | 0.531561049 | -0.010051871  | 1 | 0.074072995  | 0.992895239 | -0.246765108  | 1 |
| ENSG00000194241 | AP000911.1 | Clone-based (Ensembl) gene |                                                                                 | -0.52422921  | 0.04789169  | -0.228333883  | 1 | 0.294018453  | 0.908182547 | 0.165088872   | 1 |
| ENSG00000194283 | LINC01873  | HGNC Symbol                | long intergenic non-protein coding RNA 1873 [Source:HGNC Symbol;Acc:HGNC:52801] | -0.68301921  | 0.054758167 | -0.228084457  | 1 | 0.638359883  | 0.869751079 | 0.435875025   | 1 |
| ENSG00000194635 | SP5        | HGNC Symbol                | SP5 transcription factor [Source:HGNC Symbol;Acc:HGNC:14529]                    | -0.78601025  | 0.095082729 | -0.683704258  | 1 | 3.816503481  | 0.654405468 | -0.629007298  | 1 |
| ENSG00000194674 | DISP3      | HGNC Symbol                | dispatched RND transporter family member 3 [Source:HGNC Symbol;Acc:HGNC:29251]  | -0.556105174 | 0.021630159 | 0.072435123   | 1 | 0.368182964  | 0.908517399 | -0.01202324   | 1 |
| ENSG00000194681 | C5orf60    | HGNC Symbol                | chromosome 5 open reading frame 60 [Source:HGNC Symbol;Acc:HGNC:27753]          | -0.728340381 | 0.247150568 | 0.228008501   | 1 | 1.464324816  | 0.818753547 | 0.320835884   | 1 |
| ENSG00000194829 | AGO07389.1 | Clone-based (Ensembl) gene |                                                                                 | -0.64685442  | 0.282661756 | -0.866338929  | 1 | 0.579187938  | 0.896714972 | 0.775627303   | 1 |
| ENSG00000194941 | PS65       | HGNC Symbol                | pregnancy specific beta-1-glycoprotein 5 [Source:HGNC Symbol;Acc:HGNC:9522]     | -0.381745163 | 0.571866572 | -0.013942807  | 1 | 0.2343910505 | 0.969012561 | 0.627451691   | 1 |
| ENSG00000195054 | LINC01021  | HGNC Symbol                | long intergenic non-protein coding RNA 1021 [Source:HGNC Symbol;Acc:HGNC:49266] | -0.287245288 | 0.691210517 | -1.02585252   | 1 | 1.432981369  | 0.762363148 | 0.219446559   | 1 |
| ENSG00000195176 | REX10P     | HGNC Symbol                | "REX10 like 1, pseudogene [Source:HGNC Symbol;Acc:HGNC:24560]"                  | -0.633446922 | 0.361284725 | -0.149338523  | 1 | 1.708370547  | 0.729530842 | 0.03288074    | 1 |
| ENSG00000195312 | KRT7P4     | HGNC Symbol                | keratin 17 pseudogene 4 [Source:HGNC Symbol;Acc:HGNC:50722]                     | -0.74632956  | 0.271010304 | -0.895607246  | 1 | 4.115403356  | 0.627668963 | -0.339892563  | 1 |
| ENSG00000195396 | LINC00661  | HGNC Symbol                | long intergenic non-protein coding RNA 661 [Source:HGNC Symbol;Acc:HGNC:27002]  | -0.690094698 | 0.181892869 | -0.726364765  | 1 | -0.158146417 | 0.979462675 | 0.016687252   | 1 |
| ENSG00000195592 | MUC19      | HGNC Symbol                | "mucin 19, oligomeric [Source:HGNC Symbol;Acc:HGNC:14362]"                      | -0.30661845  | 0.552328817 | -0.434340209  | 1 | 0.994766625  | 0.787682192 | 0.298495845   | 1 |
| ENSG00000195667 | ARSH       | HGNC Symbol                | arylsulfatase family member H [Source:HGNC Symbol;Acc:HGNC:32488]               | -0.537559532 | 0.388914638 | -0.055380476  | 1 | 4.99427166   | 0.634030703 | 0.001757458   | 1 |
| ENSG00000195922 | ONECUT3    | HGNC Symbol                | one cut homeobox 3 [Source:HGNC Symbol;Acc:HGNC:16399]                          | -0.673544588 | 0.250050423 | -0.5856716548 | 1 | -0.724910149 | 0.849102793 | -0.305046492  | 1 |
| ENSG00000195976 | AC091651.1 | Clone-based (Ensembl) gene |                                                                                 | -0.72071846  | 0.22466354  | 0.261966231   | 1 | 0.948880524  | 0.86678933  | -0.38218884   | 1 |
| ENSG00000196027 | MT-1A      | HGNC Symbol                | mitochondrially encoded tRNA alanine [Source:HGNC Symbol;Acc:HGNC:7475]         | -0.730149542 | 0.078668146 | -0.731653603  | 1 | 0.561716026  | 0.861305803 | -0.161620037  | 1 |

|                |            |                            |                                                                                                   |               |              |               |   |              |             |              |   |
|----------------|------------|----------------------------|---------------------------------------------------------------------------------------------------|---------------|--------------|---------------|---|--------------|-------------|--------------|---|
| ENSG0000023467 | HMBBP37    | HGNC Symbol                | high mobility group box 1 pseudogene 37 [Source:HGNC Symbol;Acc:HGNC:39184]                       | -1.143333307  | 0.002787608  | 0.64533241    | 1 | 5.3291463    | 0.677668963 | 0.130234386  | 1 |
| ENSG0000023864 | EEF1B2P2   | HGNC Symbol                | eukaryotic translation elongation factor 1 beta 2 pseudogene 2 [Source:HGNC Symbol;Acc:HGNC:3209] | -1.164370093  | 0.00450201   | 0.0985276     | 1 | 0.67118195   | 0.884405435 | 0.38807784   | 1 |
| ENSG0000023934 | HBB1       | HGNC Symbol                | hemoglobin subunit gamma 1 [Source:HGNC Symbol;Acc:HGNC:4831]                                     | -1.501612934  | 0.00753409   | 0.51785763    | 1 | -1.318199497 | 0.687959091 | -0.59732425  | 1 |
| ENSG0000024428 | TMEM213    | HGNC Symbol                | transmembrane protein 213 [Source:HGNC Symbol;Acc:HGNC:27220]                                     | -0.72103795   | 0.16025378   | 0.01367688    | 1 | 0.834709087  | 0.852992821 | 0.07268621   | 1 |
| ENSG0000024481 | NA         | NA                         | NA                                                                                                | -0.970789027  | 0.013222867  | -0.0244144    | 1 | 1.472777831  | 0.68127884  | 0.54401043   | 1 |
| ENSG0000024402 | LCN11      | HGNC Symbol                | lipocalin like 1 [Source:HGNC Symbol;Acc:HGNC:34436]                                              | -0.706465394  | 0.073719528  | 0.34446807    | 1 | 1.403831004  | 0.74059294  | -0.2044238   | 1 |
| ENSG0000024429 | SPATA3D1   | HGNC Symbol                | SPATA3 subfamily D member 1 [Source:HGNC Symbol;Acc:HGNC:37283]                                   | -0.6516278    | 0.36627033   | 0.231067225   | 1 | -0.18457317  | 0.972105264 | 0.513786884  | 1 |
| ENSG0000024505 | NA         | NA                         | NA                                                                                                | -0.671865475  | 0.352456865  | -1.37257253   | 1 | 5.455210646  | 0.635517964 | 0.730636605  | 1 |
| ENSG0000024564 | NBP1       | HGNC Symbol                | NBP1 member 1 [Source:HGNC Symbol;Acc:HGNC:31989]                                                 | -0.90843358   | 0.018653866  | -0.6033307235 | 1 | 0.7591065108 | 0.832879845 | -0.266125165 | 1 |
| ENSG0000024595 | AL354702.1 | Clone-based (Ensembl) gene | NA                                                                                                | -0.782838755  | 0.075665055  | 0.169581062   | 1 | 2.642918942  | 0.628866264 | 0.087726662  | 1 |
| ENSG0000024704 | PPIAP31    | HGNC Symbol                | peptidylprolyl isomerase A pseudogene 31 [Source:HGNC Symbol;Acc:HGNC:44962]                      | -0.998868816  | 0.000348277  | 0.018169781   | 1 | -0.084258883 | 0.969781315 | 0.327827165  | 1 |
| ENSG0000024858 | AC006971.1 | Clone-based (Ensembl) gene | NA                                                                                                | -0.954548418  | 0.015850348  | 0.048631386   | 1 | 0.377677976  | 0.92688302  | 0.346082982  | 1 |
| ENSG0000024872 | AC008060.1 | Clone-based (Ensembl) gene | NA                                                                                                | -0.770845732  | 0.16404204   | 0.360545772   | 1 | 4.503237831  | 0.637377141 | 0.128436775  | 1 |
| ENSG0000024823 | PAPOLB     | HGNC Symbol                | poly(A) polymerase beta [Source:HGNC Symbol;Acc:HGNC:16970]                                       | -0.18493482   | 0.27787886   | -0.146279628  | 1 | 0.370878195  | 0.938546531 | -0.058926155 | 1 |
| ENSG0000024826 | PSS3       | HGNC Symbol                | pregnancy specific beta-1-glycoprotein 3 [Source:HGNC Symbol;Acc:HGNC:9520]                       | -0.240003956  | 0.750637339  | -0.905913781  | 1 | 0.468930195  | 0.922861341 | -0.168206699 | 1 |
| ENSG0000024878 | PSS7       | HGNC Symbol                | pregnancy specific beta-1-glycoprotein 7 (gene/pseudogene) [Source:HGNC Symbol;Acc:HGNC:9524]     | -0.453232662  | 0.540259029  | -0.3345147    | 1 | 0.794876697  | 0.875275045 | -0.56392725  | 1 |
| ENSG0000024344 | LINC00473  | HGNC Symbol                | long intergenic non-protein coding RNA 473 [Source:HGNC Symbol;Acc:HGNC:21160]                    | -1.017484945  | 0.084276877  | 0.398876949   | 1 | 2.170444123  | 0.747425557 | 0.340358512  | 1 |
| ENSG0000024366 | TNRC18P2   | HGNC Symbol                | trinucleotide repeat containing 18 pseudogene 2 [Source:HGNC Symbol;Acc:HGNC:34014]               | -0.65314849   | 0.205565205  | -0.033255387  | 1 | 1.255469251  | 0.773820479 | 0.165805354  | 1 |
| ENSG0000024394 | ROR1-AS1   | HGNC Symbol                | ROR1 antisense RNA 1 [Source:HGNC Symbol;Acc:HGNC:44508]                                          | -0.645751828  | 0.29094527   | 0.17177254    | 1 | 0.363654551  | 0.944019028 | 0.785033547  | 1 |
| ENSG0000024459 | HSPA8P16   | HGNC Symbol                | heat shock protein family A (Hsp70) member 8 pseudogene 16 [Source:HGNC Symbol;Acc:HGNC:44931]    | -1.139741884  | 0.025824728  | 0.085744611   | 1 | 1.119588857  | 0.816513218 | -0.287957535 | 1 |
| ENSG0000024409 | LINC00466  | HGNC Symbol                | long intergenic non-protein coding RNA 466 [Source:HGNC Symbol;Acc:HGNC:27294]                    | -1.176248621  | 0.0398720431 | -0.329952707  | 1 | 4.996989997  | 0.63590801  | 1.016744481  | 1 |
| ENSG0000024471 | ALUJ329.1  | Clone-based (Ensembl) gene | NA                                                                                                | -0.6639936339 | 0.277648202  | 0.307895578   | 1 | 0.668981691  | 0.905148092 | 0.475804817  | 1 |
| ENSG0000024471 | DACY1P     | HGNC Symbol                | "D"-acyltransferase like, pseudogene                                                              | -0.601815549  | 0.296095547  | -0.312440554  | 1 | -0.11814356  | 0.990883948 | 0.288576794  | 1 |

|       |               |            |                               |                                                                                                            |               |              |               |   |               |              |              |   |
|-------|---------------|------------|-------------------------------|------------------------------------------------------------------------------------------------------------|---------------|--------------|---------------|---|---------------|--------------|--------------|---|
| 24367 | ENSG000000002 | NFIP6      | HGNC Symbol                   | [Source:HGNC Symbol;Acc:HGNC:44362"]<br>neurofibromin 1 pseudogene 6 [Source:HGNC<br>Symbol;Acc:HGNC:7771] | -0.897662927  | 0.07500142   | -0.465472953  | 1 | 2.806924373   | 0.70172189   | 0.467138001  | 1 |
| 24435 | ENSG000000002 | IP08PI     | HGNC Symbol                   | importin 8 pseudogene 1 [Source:HGNC<br>Symbol;Acc:HGNC:49555]                                             | -0.694695462  | 0.0493383688 | 0.021954815   | 1 | 2.07297623    | 0.68882163   | 0.145327081  | 1 |
| 24688 | ENSG000000002 | TEX2B-AS1  | HGNC Symbol                   | TEX2B antisense RNA 1 [Source:HGNC<br>Symbol;Acc:HGNC:42784]                                               | -0.610821916  | 0.281832209  | -0.442966632  | 1 | 5.789138398   | 0.627668963  | 0.1542710252 | 1 |
| 24743 | ENSG000000002 | AP001046.1 | Clone-based<br>(Ensembl) gene |                                                                                                            | -0.681940896  | 0.281821655  | -0.627749272  | 1 | 1.545301662   | 0.794521432  | -0.165724687 | 1 |
| 25637 | ENSG000000002 | AC064875.1 | Clone-based<br>(Ensembl) gene |                                                                                                            | -0.6987910548 | 0.3263216466 | -0.296958899  | 1 | 2.053521976   | 0.74016481   | 0.717587026  | 1 |
| 25649 | ENSG000000002 | AC009299.1 | Clone-based<br>(Ensembl) gene |                                                                                                            | -0.210655195  | 0.744295555  | -0.127561246  | 1 | 3.104297109   | 0.6389275887 | -0.044905566 | 1 |
| 25813 | ENSG000000002 | SA192-AS1  | HGNC Symbol                   | SA192 antisense RNA 1 [Source:HGNC<br>Symbol;Acc:HGNC:26480]                                               | -0.527452078  | 0.3102410719 | -0.1071165886 | 1 | -0.1055927318 | 0.9910101886 | 0.108270165  | 1 |
| 25953 | ENSG000000002 | PHF2P2     | HGNC Symbol                   | PHF2 finger protein 2 pseudogene 2<br>[Source:HGNC Symbol;Acc:HGNC:38908]                                  | -0.3373269658 | 0.356181552  | -0.06126026   | 1 | -0.683305773  | 0.794521432  | 0.065891047  | 1 |
| 26057 | ENSG000000002 | HNRNPA3P4  | HGNC Symbol                   | heterogeneous nuclear ribonucleoprotein A3<br>pseudogene 4 [Source:HGNC<br>Symbol;Acc:HGNC:38773]          | -1.210089183  | 0.013553682  | -0.686854837  | 1 | 0.7651075801  | 0.86439314   | 0.359560736  | 1 |
| 26068 | ENSG000000002 | AL365214.2 | Clone-based<br>(Ensembl) gene |                                                                                                            | -0.699416502  | 0.2877810065 | -0.357778931  | 1 | 1.048188407   | 0.839325295  | -0.182057491 | 1 |
| 26440 | ENSG000000002 | LINC02554  | HGNC Symbol                   | long intergenic non-protein coding RNA 2554<br>[Source:HGNC Symbol;Acc:HGNC:53594]                         | -0.684878038  | 0.2733216765 | -0.0126955967 | 1 | 5.855442377   | 0.627668963  | 0.158850168  | 1 |
| 26741 | ENSG000000002 | HNRNPA3P1  | HGNC Symbol                   | heterogeneous nuclear ribonucleoprotein A3<br>pseudogene 1 [Source:HGNC<br>Symbol;Acc:HGNC:18729]          | -1.384734034  | 0.000189579  | -0.396590339  | 1 | 0.30165281    | 0.9104741007 | 0.482916358  | 1 |
| 26790 | ENSG000000002 | LINC00511  | HGNC Symbol                   | long intergenic non-protein coding RNA 511<br>[Source:HGNC Symbol;Acc:HGNC:43564]                          | -0.5088310938 | 0.1537571922 | -0.081842392  | 1 | 1.073510076   | 0.756531946  | 0.1340199004 | 1 |
| 27036 | ENSG000000002 | AKR1B5     | HGNC Symbol                   | aldo-keto reductase family 1 member-B15<br>[Source:HGNC Symbol;Acc:HGNC:37281]                             | -0.827071435  | 0.071895362  | -0.1878719279 | 1 | 0.646340303   | 0.91047395   | -0.166716865 | 1 |
| 27471 | ENSG000000002 | RP17P6     | HGNC Symbol                   | ribosomal protein L7 pseudogene 6<br>[Source:HGNC Symbol;Acc:HGNC:37430]                                   | -1.210918266  | 0.0130330406 | 0.176827018   | 1 | 0.140151631   | 0.980905392  | 0.636393422  | 1 |
| 27525 | ENSG000000002 | LINC01940  | HGNC Symbol                   | long intergenic non-protein coding RNA 1940<br>[Source:HGNC Symbol;Acc:HGNC:52783]                         | -0.6106198906 | 0.3104216394 | -0.768704495  | 1 | 2.498837138   | 0.731089271  | -0.334768949 | 1 |
| 27744 | ENSG000000002 | AC138969.2 | Clone-based<br>(Ensembl) gene |                                                                                                            | -0.5928106597 | 0.1667183813 | 0.3474551004  | 1 | -0.893239125  | 0.689965785  | 0.0372210014 | 1 |
| 27827 | ENSG000000002 | BX284688.2 | Clone-based<br>(Ensembl) gene |                                                                                                            | -0.6810105559 | 0.067244282  | -0.0669591016 | 1 | 1.5501659524  | 0.6635464    | 0.142348654  | 1 |
| 28549 | ENSG000000002 | SLC47A1P1  | HGNC Symbol                   | solitaire carrier family 47 member 1 pseudogene 1<br>[Source:HGNC Symbol;Acc:HGNC:51849]                   | -0.8109148556 | 0.2081298    | -0.078571477  | 1 | 0.159271054   | 0.988052109  | -0.315269274 | 1 |
| 28983 | ENSG000000002 | SMPD4P2    | HGNC Symbol                   | sphingomyelin phosphodiesterase 4 pseudogene 2<br>[Source:HGNC Symbol;Acc:HGNC:38674]                      | -0.546121346  | 0.3681213078 | 0.163672911   | 1 | 4.59874887    | 0.674133395  | 0.03574788   | 1 |
| 29447 | ENSG000000002 | LINC00710  | HGNC Symbol                   | long intergenic non-protein coding RNA 710<br>[Source:HGNC Symbol;Acc:HGNC:27386]                          | -0.3486963104 | 0.636769038  | -0.463376599  | 1 | 2.389547223   | 0.723566719  | 0.81962187   | 1 |
| 2947  | ENSG000000002 | AL13242.1  | Clone-based<br>(Ensembl) gene |                                                                                                            | -1.134015271  | 0.03106855   | -1.461237915  | 1 | 5.01959101    | 0.627668963  | 0.574333178  | 1 |
| 29817 | ENSG000000002 | IQCF3      | HGNC Symbol                   | IQ motif containing E3 [Source:HGNC<br>Symbol;Acc:HGNC:44776]                                              | -0.7107465438 | 0.2388644776 | 0.0957456375  | 1 | 4.84144143    | 0.657456375  | -0.01510723  | 1 |

|       |               |             |                                                                        |                                                                                 |               |              |               |   |              |              |              |   |
|-------|---------------|-------------|------------------------------------------------------------------------|---------------------------------------------------------------------------------|---------------|--------------|---------------|---|--------------|--------------|--------------|---|
| 29972 | ENSG000000002 | LINC02028   | SymbolAcc:HGNC:30816                                                   | long intergenic non-protein coding RNA 2028 [Source:HGNC Symbol;Acc:HGNC:27718] | -0.84959372   | 0.15659487   | 0.08073864    | 1 | 0.129736847  | 0.98819763   | -0.097566507 | 1 |
| 30002 | ENSG000000002 | LINC00721   | HGNC Symbol                                                            | long intergenic non-protein coding RNA 1721 [Source:HGNC Symbol;Acc:HGNC:52508] | -0.269403043  | 0.71003504   | -0.336765938  | 1 | 4.60075983   | 0.67154129   | 0.054222063  | 1 |
| 30063 | ENSG000000002 | AC0046835.1 | Clone-based (Ensembl) gene                                             | -0.84709631                                                                     | 0.10286431    | 0.10286431   | -0.67554528   | 1 | 1.884314398  | 0.75297145   | -0.466467709 | 1 |
| 30392 | ENSG000000002 | AC092162.2  | Clone-based (Ensembl) gene                                             | -0.369167666                                                                    | 0.571101565   | 0.571101565  | -0.477976855  | 1 | 2.786389729  | 0.657456325  | 0.10748725   | 1 |
| 30552 | ENSG000000002 | AL139270.2  | Clone-based (Ensembl) gene                                             | -0.52204036                                                                     | 0.382707592   | 0.382707592  | -0.0775818    | 1 | 2.277546357  | 0.701343297  | 0.278838325  | 1 |
| 30615 | ENSG000000002 | STIND1      | stathmin domain containing 1 [Source:HGNC Symbol;Acc:HGNC:44658]       | -0.361799128                                                                    | 0.61243915    | 0.61243915   | -0.601677596  | 1 | 1.869643521  | 0.749476591  | -0.08916797  | 1 |
| 30873 | ENSG000000002 | LINC01468   | HGNC Symbol                                                            | long intergenic non-protein coding RNA 1468 [Source:HGNC Symbol;Acc:HGNC:50913] | -0.5393334563 | 0.42259164   | -0.717745459  | 1 | 4.703090151  | 0.634030703  | -0.018039325 | 1 |
| 31422 | ENSG000000002 | LINC01516   | HGNC Symbol                                                            | long intergenic non-protein coding RNA 1516 [Source:HGNC Symbol;Acc:HGNC:51211] | -0.5564643466 | 0.39546555   | -0.448623675  | 1 | 1.46146418   | 0.750080465  | 0.58919716   | 1 |
| 32061 | ENSG000000002 | AC002365.1  | Clone-based (Ensembl) gene                                             | -0.5104617303                                                                   | 0.318754361   | 0.318754361  | -0.140152029  | 1 | -0.415515591 | 0.937722107  | 0.304983976  | 1 |
| 32392 | ENSG000000002 | AC004862.1  | Clone-based (Ensembl) gene                                             | -0.377427732                                                                    | 0.617985726   | 0.617985726  | -1.08261087   | 1 | 1.003284752  | 0.858966348  | -0.087710074 | 1 |
| 32667 | ENSG000000002 | AC004690.1  | Clone-based (Ensembl) gene                                             | -0.532711499                                                                    | 0.428875064   | 0.428875064  | -0.325138065  | 1 | 5.470227099  | 0.638925887  | 0.24855089   | 1 |
| 32756 | ENSG000000002 | AL138889.1  | Clone-based (Ensembl) gene                                             | -0.6444340746                                                                   | 0.293569058   | 0.293569058  | -0.460286874  | 1 | 1.142684211  | 0.755594359  | -0.057403209 | 1 |
| 33063 | ENSG000000002 | LINC00841   | HGNC Symbol                                                            | long intergenic non-protein coding RNA 841 [Source:HGNC Symbol;Acc:HGNC:27430]  | -0.755094485  | 0.24458107   | -0.3016590217 | 1 | 2.1641616494 | 0.727991986  | 0.345511188  | 1 |
| 33395 | ENSG000000002 | AL03283.2   | Clone-based (Ensembl) gene                                             | -0.6391007269                                                                   | 0.295175271   | 0.295175271  | 0.180714248   | 1 | -0.844030822 | 0.823278306  | -0.398102734 | 1 |
| 33465 | ENSG000000002 | AC010294.1  | Clone-based (Ensembl) gene                                             | -0.7072716432                                                                   | 0.262324375   | 0.262324375  | -0.342714764  | 1 | 0.7990106026 | 0.895729958  | -0.143595171 | 1 |
| 33539 | ENSG000000002 | LINC01360   | HGNC Symbol                                                            | long intergenic non-protein coding RNA 1360 [Source:HGNC Symbol;Acc:HGNC:50593] | -0.427339916  | 0.5465910871 | -0.516750537  | 1 | 0.105701038  | 0.994504436  | 0.818352419  | 1 |
| 33973 | ENSG000000002 | AC099681.3  | Clone-based (Ensembl) gene                                             | -12.09772617                                                                    | 0.027629442   | 0.027629442  | -0.38786505   | 1 | 4.91323959   | 0.677666963  | -0.085503463 | 1 |
| 33977 | ENSG000000002 | NA          | NA                                                                     | -0.525566632                                                                    | 0.310260093   | 0.310260093  | -0.158599656  | 1 | 0.70789114   | 0.879160351  | -0.066786642 | 1 |
| 33991 | ENSG000000002 | AL359263.1  | Clone-based (Ensembl) gene                                             | -0.9830100141                                                                   | 0.004471167   | 0.004471167  | -0.116467879  | 1 | -1.060329506 | 0.682140373  | -0.006454574 | 1 |
| 34160 | ENSG000000002 | LINC01114   | HGNC Symbol                                                            | long intergenic non-protein coding RNA 1114 [Source:HGNC Symbol;Acc:HGNC:49245] | -0.49846577   | 0.434856109  | 0.684663308   | 1 | 5.391063483  | 0.6771668963 | 0.749376614  | 1 |
| 34177 | ENSG000000002 | TLR2P       | "Toll like receptor 2, pseudogene [Source:HGNC Symbol;Acc:HGNC:31754]" | -0.514877503                                                                    | 0.44103354    | 0.44103354   | 1.365371669   | 1 | 0.390273719  | 0.942400392  | 0.42350419   | 1 |
| 34512 | ENSG000000002 | AL354751.1  | Clone-based (Ensembl) gene                                             | -0.384649992                                                                    | 0.532855014   | 0.532855014  | -0.239733974  | 1 | 5.219577926  | 0.6271668963 | 0.10072621   | 1 |
| 34537 | ENSG000000002 | IQCM        | IQ motif containing M [Source:HGNC Symbol;Acc:HGNC:55443]              | -0.6772714946                                                                   | 0.33150019    | 0.33150019   | -0.035140174  | 1 | 0.70765966   | 0.886973057  | 0.272391707  | 1 |
| 34828 | ENSG000000002 | ANKRD34C    | ankyrin repeat domain 34C [Source:HGNC Symbol;Acc:HGNC:336549]         | -0.6796646373                                                                   | 0.321694729   | 0.321694729  | 0.0341172649  | 1 | 0.7910336549 | 0.863105109  | 0.604716661  | 1 |

|       |                 |             |                            |                                                                                    |               |              |               |   |               |             |              |   |
|-------|-----------------|-------------|----------------------------|------------------------------------------------------------------------------------|---------------|--------------|---------------|---|---------------|-------------|--------------|---|
| 35711 | ENSG00000235881 | AC14776.1   | Clone-based (Ensembl) gene | Symbol:Acc:HNC.33888                                                               | -0.557508401  | 0.40045344   | 0.125604823   | 1 | 4.342310827   | 0.641655872 | 0.439379883  | 1 |
| 35712 | ENSG00000235881 | LINC01447   | HGNC Symbol                | long intergenic non-protein coding RNA 1447 [Source:HGNC Symbol;Acc:HNC.50783]     | -0.901815564  | 0.105956615  | -1.304003166  | 1 | -0.52242853   | 0.898407207 | 0.03274802   | 1 |
| 35713 | ENSG00000235881 | VEZFP1      | HGNC Symbol                | vascular endothelial zinc finger 1 pseudogene 1 [Source:HGNC Symbol;Acc:HNC.32320] | -0.741631818  | 0.120281854  | 0.160105502   | 1 | 0.253042553   | 0.946405426 | -0.405474523 | 1 |
| 35714 | ENSG00000235881 | SLC25A3P1   | HGNC Symbol                | solute carrier family 25 member 3 pseudogene 1 [Source:HGNC Symbol;Acc:HNC.26869]  | -0.817459523  | 0.156535514  | -0.231683569  | 1 | -0.23797832   | 0.969107561 | 0.84186377   | 1 |
| 35715 | ENSG00000235881 | VDLR-AS1    | HGNC Symbol                | VDLR antisense RNA 1 [Source:HGNC Symbol;Acc:HNC.49521]                            | -0.817831635  | 0.28098976   | -0.43102737   | 1 | -0.474971558  | 0.93512862  | 0.324321098  | 1 |
| 35716 | ENSG00000235881 | LINC00608   | HGNC Symbol                | long intergenic non-protein coding RNA 608 [Source:HGNC Symbol;Acc:HNC.27719]      | -0.743359785  | 0.28126595   | -0.270795514  | 1 | 5.432857932   | 0.627668963 | 0.644630745  | 1 |
| 35717 | ENSG00000235881 | BCYRN1      | HGNC Symbol                | brain cytoplasmic RNA 1 (head to head) [Source:HGNC Symbol;Acc:HNC.1072]           | -0.556526317  | 0.083153215  | 0.057989767   | 1 | 0.34810967    | 0.915148192 | -0.088910462 | 1 |
| 35718 | ENSG00000235881 | HAND2-AS1   | HGNC Symbol                | HAND2 antisense RNA 1 (head to head) [Source:HGNC Symbol;Acc:HNC.48872]            | -0.621343361  | 0.261507627  | -0.355425825  | 1 | 0.959425342   | 0.8349487   | 0.11462542   | 1 |
| 35719 | ENSG00000235881 | LINC01958   | HGNC Symbol                | long intergenic non-protein coding RNA 1958 [Source:HGNC Symbol;Acc:HNC.52794]     | -0.672454358  | 0.2777710947 | -0.63479436   | 1 | 5.771289152   | 0.628886787 | -0.121549704 | 1 |
| 35720 | ENSG00000235881 | AL35992.4.1 | Clone-based (Ensembl) gene | "creatine kinase, mitochondrial 18 [Source:HGNC Symbol;Acc:HNC.1955]"              | -0.844197088  | 0.225502335  | -0.12360104   | 1 | 0.180846578   | 0.981354954 | 0.160552494  | 1 |
| 35721 | ENSG00000235881 | CKMT1B      | HGNC Symbol                | "creatine kinase, mitochondrial 18 [Source:HGNC Symbol;Acc:HNC.1955]"              | -0.216491018  | 0.195077893  | -0.294426419  | 1 | 1.7877610281  | 0.752827393 | 0.548281539  | 1 |
| 35722 | ENSG00000235881 | SHISA9      | Clone-based (Ensembl) gene | shisa family member 9 [Source:HGNC Symbol;Acc:HNC.37231]                           | -0.809100055  | 0.06410732   | -0.060656577  | 1 | -0.125757547  | 0.984792321 | -0.034481521 | 1 |
| 35723 | ENSG00000235881 | ANKRD26P3   | HGNC Symbol                | ankyrin repeat domain 26 pseudogene 3 [Source:HGNC Symbol;Acc:HNC.39689]           | -0.387705186  | 0.56180253   | -0.6523619    | 1 | 1.235736516   | 0.785004308 | -0.203879103 | 1 |
| 35724 | ENSG00000235881 | ZNF527.1    | Clone-based (Ensembl) gene | long intergenic non-protein coding RNA 1471 [Source:HGNC Symbol;Acc:HNC.51106]     | -0.432460557  | 0.515402598  | 0.03107749    | 1 | 5.195146623   | 0.627668963 | 0.324780279  | 1 |
| 35725 | ENSG00000235881 | TEX35       | HGNC Symbol                | testis expressed 35 [Source:HGNC Symbol;Acc:HNC.25366]                             | -0.374959793  | 0.565054774  | 0.083015195   | 1 | -0.457221847  | 0.911339121 | 0.205779558  | 1 |
| 35726 | ENSG00000235881 | PNMA2       | HGNC Symbol                | PNMA family member 2 [Source:HGNC Symbol;Acc:HNC.9159]                             | -0.5378910532 | 0.01844862   | -0.057174748  | 1 | 0.82751444    | 0.842124589 | -0.225122808 | 1 |
| 35727 | ENSG00000235881 | LINC01068   | HGNC Symbol                | long intergenic non-protein coding RNA 1068 [Source:HGNC Symbol;Acc:HNC.49537]     | -0.8438355897 | 0.088801762  | 0.45768823    | 1 | 1.563106698   | 0.754669401 | -0.165990548 | 1 |
| 35728 | ENSG00000235881 | ADAMTS3-AS1 | HGNC Symbol                | ADAMTS3 antisense RNA 1 [Source:HGNC Symbol;Acc:HNC.4025]                          | -0.416654485  | 0.588233437  | -0.1201041533 | 1 | 0.91083501636 | 0.844324446 | 0.688461522  | 1 |
| 35729 | ENSG00000235881 | LINC01206   | HGNC Symbol                | long intergenic non-protein coding RNA 1206 [Source:HGNC Symbol;Acc:HNC.49537]     | -0.706615823  | 0.298614872  | -0.52038982   | 1 | 2.09559188    | 0.718736978 | 0.480753033  | 1 |
| 35730 | ENSG00000235881 | STRC        | HGNC Symbol                | stereocilin [Source:HGNC Symbol;Acc:HNC.16035]                                     | -0.378462807  | 0.423980174  | -0.271882673  | 1 | 0.218329488   | 0.95266024  | 0.47492962   | 1 |
| 35731 | ENSG00000235881 | PSSH        | HGNC Symbol                | pregnancy specific beta-1-glycoprotein II [Source:HGNC Symbol;Acc:HNC.9516]        | -0.54081905   | 0.355755564  | 0.2156966     | 1 | 0.420866737   | 0.936408883 | 0.456415159  | 1 |
| 35732 | ENSG00000235881 | PTCHD4      | HGNC Symbol                | patched domain containing 4 [Source:HGNC Symbol;Acc:HNC.16035]                     | -0.5616310256 | 0.019326576  | -0.585265938  | 1 | 0.281016262   | 0.957471614 | -0.053184384 | 1 |

|                 |            |                                                                         |                                                                                                                        |              |              |               |   |              |              |              |   |
|-----------------|------------|-------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------|--------------|--------------|---------------|---|--------------|--------------|--------------|---|
| 4494            | USP2-AS1   | HGNC Symbol                                                             | Symbol/Accession:HGNC:21345                                                                                            | -0.52076811  | 0.390756677  | -0.512445862  | I | 2.757269299  | 0.717228729  | -0.305885654 | I |
| ENSG00000245748 |            | USP2 antisense RNA 1 (head to head) [Source:HGNC Symbol;Acc:HGNC:48673] |                                                                                                                        | -0.54469632  | 0.389457898  | -0.0435949133 | I | 4.637420367  | 0.64365872   | 0.080391919  | I |
| 4551            | AC083805.1 | Clone-based (Ensembl) gene                                              |                                                                                                                        | -0.61682121  | 0.3102219736 | -0.356653621  | I | 5.168032109  | 0.631753875  | -0.020381824 | I |
| ENSG00000245551 |            | RASSF8 antisense RNA 1 [Source:HGNC Symbol;Acc:HGNC:48637]              |                                                                                                                        | -0.955409124 | 0.07623748   | -0.016315976  | I | 0.91481357   | 0.836563776  | -0.04697474  | I |
| 45955           | LINC01498  | HGNC Symbol                                                             | long intergenic non-protein coding RNA 1498 [Source:HGNC Symbol;Acc:HGNC:51164]                                        | -0.050991069 | 0.073837393  | -0.163855722  | I | 4.403825386  | 0.630714789  | 0.238209542  | I |
| 47213           | AC008609.1 | Clone-based (Ensembl) gene                                              |                                                                                                                        | -0.698157573 | 0.2408791    | -0.270935153  | I | 1.525731524  | 0.778988681  | -0.027239838 | I |
| ENSG00000247699 |            | GNDF antisense RNA 1 (head to head) [Source:HGNC Symbol;Acc:HGNC:43592] |                                                                                                                        | -0.540718726 | 0.305645261  | -0.16925333   | I | -0.560389013 | 0.859477376  | 0.271840562  | I |
| 48587           | AC083902.2 | Clone-based (Ensembl) gene                                              | "Homo sapiens uncharacterized LOC285556 (LOC285556): mRNA. [Source:RefSeq mRNA;Acc:NM_003544351]"                      | -0.833558399 | 0.085185005  | 0.56472696    | I | -0.464953446 | 0.884053868  | 0.124065725  | I |
| ENSG00000248746 | ACTN3      | HGNC Symbol                                                             | actinin alpha 3 (gene/pseudogene) [Source:HGNC Symbol;Acc:HGNC:165]                                                    | -0.90954794  | 0.00542621   | -0.3637616    | I | 0.606226987  | 0.80060544   | -0.394401901 | I |
| ENSG00000248966 | BCLAF1P1   | HGNC Symbol                                                             | BCL2 associated transcription factor 1 pseudogene 1 [Source:HGNC Symbol;Acc:HGNC:51829]                                | -0.655164585 | 0.316522442  | -0.696722695  | I | 0.734788549  | 0.906091083  | 0.544431614  | I |
| ENSG00000248975 | AL133372.2 | Clone-based (Ensembl) gene                                              |                                                                                                                        | -1255534276  | 0.007510713  | -0.628092072  | I | 2.8954301913 | 0.654655709  | 0.516230804  | I |
| ENSG00000249119 | MTN06P4    | HGNC Symbol                                                             | mitochondrially encoded NADH-ubiquinone oxidoreductase core subunit 6 pseudogene 4 [Source:HGNC Symbol;Acc:HGNC:39467] | -129709171   | 0.000137132  | 0.154736731   | I | -1.04023217  | 0.6271668963 | 0.421347089  | I |
| ENSG00000249215 | NC0A4P4    | HGNC Symbol                                                             | nuclear receptor coactivator 4 pseudogene 4 [Source:HGNC Symbol;Acc:HGNC:52405]                                        | -0.755105061 | 0.228670526  | -0.256125279  | I | 6.3371647595 | 0.6271668963 | -0.491599301 | I |
| 49257           | LINC00939  | HGNC Symbol                                                             | long intergenic non-protein coding RNA 939 [Source:HGNC Symbol;Acc:HGNC:48631]                                         | -0.839158018 | 0.18019435   | -0.880234432  | I | 0.98818147   | 0.865396845  | -0.229478865 | I |
| ENSG00000249341 | AC12407.1  | Clone-based (Ensembl) gene                                              |                                                                                                                        | -0.927878847 | 0.088706109  | -0.514600069  | I | 1.191897515  | 0.800335595  | 0.297158453  | I |
| 49464           | LINC01091  | HGNC Symbol                                                             | long intergenic non-protein coding RNA 1091 [Source:HGNC Symbol;Acc:HGNC:27721]                                        | -0.580988221 | 0.346216369  | -0.582748024  | I | 0.905397905  | 0.853001039  | 0.662950073  | I |
| ENSG00000249584 | LINC02225  | HGNC Symbol                                                             | long intergenic non-protein coding RNA 2225 [Source:HGNC Symbol;Acc:HGNC:53194]                                        | -0.99469738  | 0.18925447   | -0.722916516  | I | 5.291010405  | 0.6271668963 | 0.977525841  | I |
| ENSG00000249618 | LINC02465  | HGNC Symbol                                                             | long intergenic non-protein coding RNA 2465 [Source:HGNC Symbol;Acc:HGNC:53403]                                        | -0.734378499 | 0.27927591   | 0.565567149   | I | 4.638749643  | 0.649773207  | -0.025657469 | I |
| ENSG00000250049 | AC14316.2  | Clone-based (Ensembl) gene                                              |                                                                                                                        | -1.010449463 | 0.073333123  | -0.704591533  | I | 4.538861217  | 0.637153875  | 0.181526143  | I |
| 50230           | AP007754.1 | Clone-based (Ensembl) gene                                              |                                                                                                                        | -0.8564176   | 0.188525408  | 0.006459177   | I | 1.165649249  | 0.805758306  | 0.299943939  | I |
| ENSG00000250420 | AACSP1     | HGNC Symbol                                                             | acetylacetyl-CoA synthetase pseudogene 1 [Source:HGNC Symbol;Acc:HGNC:18226]                                           | -0.616623881 | 0.3102589969 | -0.592559414  | I | 0.361772621  | 0.936402935  | 0.459665173  | I |
| 50423           | KIAA1210   | HGNC Symbol                                                             | KIAA1210 [Source:HGNC Symbol;Acc:HGNC:29218]                                                                           | -0.423508937 | 0.487573965  | -0.290397732  | I | 1.178346789  | 0.835185817  | 0.221818975  | I |
| ENSG00000250493 | AP004147.1 | Clone-based (Ensembl) gene                                              |                                                                                                                        |              |              |               |   |              |              |              |   |

|                 |            |                            |                                                                                                                                                             |              |             |              |   |             |             |              |   |
|-----------------|------------|----------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------|-------------|--------------|---|-------------|-------------|--------------|---|
| ENSG00000250519 | AP002784.1 | Clone-based (Ensembl) gene |                                                                                                                                                             | -0.66865269  | 0.300298544 | -0.524459048 | 1 | 0.714452444 | 0.88692804  | 0.294333525  | 1 |
| ENSG00000250546 | AC079160.1 | Clone-based (Ensembl) gene |                                                                                                                                                             | -0.594876334 | 0.407475799 | -0.546662826 | 1 | 0.645898296 | 0.908465718 | 0.158608765  | 1 |
| ENSG00000251557 | HNRNP33    | HGNC Symbol                | heterogeneous nuclear ribonucleoprotein K pseudogene 3 [Source:HGNC Symbol;Acc:HGNC:42376]                                                                  | -0.98325003  | 0.165739901 | 0.173767605  | 1 | 4.903073168 | 0.636992081 | 0.360350496  | 1 |
| ENSG00000251596 | H4DHAPI    | HGNC Symbol                | "hydroxyacyl-CoA dehydrogenase/3-ketoacyl-CoA thiolase/enoyl-CoA hydratase (mitochondrial), alpha subunit pseudogene 1 [Source:HGNC Symbol;Acc:HGNC:48027]" | -0.7483099   | 0.215472986 | -0.876623306 | 1 | 5.588638432 | 0.627668963 | -0.06327841  | 1 |
| ENSG00000251705 | RNA5-5SP6  | HGNC Symbol                | "RNA 5.5S ribosomal pseudogene 5 [Source:HGNC Symbol;Acc:HGNC:48601]"                                                                                       | -0.425991495 | 0.294278305 | -0.480692863 | 1 | 0.605480991 | 0.935148092 | 0.973551682  | 1 |
| ENSG00000253230 | LINC00559  | HGNC Symbol                | long intergenic non-protein coding RNA 559 [Source:HGNC Symbol;Acc:HGNC:27231]                                                                              | -0.761456332 | 0.165073382 | 0.653376032  | 1 | 5.30777447  | 0.627668963 | 0.485127664  | 1 |
| ENSG00000253288 | AC046195.1 | Clone-based (Ensembl) gene |                                                                                                                                                             | -0.709937786 | 0.305188446 | -0.79818447  | 1 | 1.76778886  | 0.760843839 | -0.45060209  | 1 |
| ENSG00000253301 | LINC01606  | HGNC Symbol                | long intergenic non-protein coding RNA 1606 [Source:HGNC Symbol;Acc:HGNC:51656]                                                                             | -0.71659914  | 0.234542306 | -0.266149016 | 1 | 1.768597236 | 0.74687395  | 0.10795721   | 1 |
| ENSG00000253864 | NA         | NA                         | NA                                                                                                                                                          | -0.88918236  | 0.11585236  | -0.32564569  | 1 | 1.06881022  | 0.853001139 | -0.14030064  | 1 |
| ENSG00000253871 | AC068075.1 | Clone-based (Ensembl) gene |                                                                                                                                                             | -1.1237045   | 0.07614677  | -1.27840073  | 1 | 4.899864919 | 0.634030703 | -0.12847863  | 1 |
| ENSG00000253974 | NRG1-IT1   | HGNC Symbol                | NRG1 intronic transcript 1 [Source:HGNC Symbol;Acc:HGNC:43533]                                                                                              | -0.501373766 | 0.471813581 | -0.494066938 | 1 | 0.695380138 | 0.905537291 | 0.183664543  | 1 |
| ENSG00000254042 | AC01365.1  | Clone-based (Ensembl) gene |                                                                                                                                                             | -0.60224259  | 0.364960528 | -0.386727632 | 1 | 1.459720166 | 0.770874694 | 0.278099271  | 1 |
| ENSG0000025401  | LINC02055  | HGNC Symbol                | long intergenic non-protein coding RNA 2055 [Source:HGNC Symbol;Acc:HGNC:52895]                                                                             | -0.503549507 | 0.165220672 | 0.59458364   | 1 | 1.424825    | 0.8377714   | 0.60553371   | 1 |
| ENSG00000254561 | AP003393.1 | Clone-based (Ensembl) gene |                                                                                                                                                             | -0.734816559 | 0.197377124 | -1.139245326 | 1 | 1.50840068  | 0.754933936 | 0.05932753   | 1 |
| ENSG00000255343 | AC095350.1 | Clone-based (Ensembl) gene |                                                                                                                                                             | -0.895073552 | 0.169037894 | -0.537186458 | 1 | 1.275718507 | 0.828463409 | 0.618599755  | 1 |
| ENSG00000255612 | CYP28P     | HGNC Symbol                | "cytochrome P450 family 2 subfamily B member 7, pseudogene [Source:HGNC Symbol;Acc:HGNC:27616]"                                                             | -0.489184845 | 0.20391081  | -0.117590576 | 1 | 0.23156174  | 0.944880397 | -0.02046101  | 1 |
| ENSG00000256616 | AP00244.2  | Clone-based (Ensembl) gene |                                                                                                                                                             | -0.53380034  | 0.435483446 | 0.345935051  | 1 | 5.003784955 | 0.64365872  | -0.366243561 | 1 |
| ENSG00000257008 | GPR142     | HGNC Symbol                | 6 protein-coupled receptor 142 [Source:HGNC Symbol;Acc:HGNC:20088]                                                                                          | -0.88548094  | 0.103049732 | 0.848934248  | 1 | -0.10277109 | 0.991463557 | -0.769158893 | 1 |
| ENSG00000257175 | CR383656.1 | Clone-based (Ensembl) gene |                                                                                                                                                             | -0.64668034  | 0.142758994 | -0.023027297 | 1 | 0.488729454 | 0.870273599 | -0.046325545 | 1 |
| ENSG00000257576 | HSPD1P4    | HGNC Symbol                | heat shock protein family D (Hsp60) member 1 pseudogene 4 [Source:HGNC Symbol;Acc:HGNC:35146]                                                               | -0.870496882 | 0.027959144 | -0.488873297 | 1 | 2.343052713 | 0.646773142 | -0.636576554 | 1 |
| ENSG00000257907 | EEF1A1P7   | HGNC Symbol                | eukaryotic translation elongation factor 1 alpha 1 pseudogene 17 [Source:HGNC Symbol;Acc:HGNC:37890]                                                        | -1.061636051 | 0.02387251  | -0.512436099 | 1 | 0.588424968 | 0.88207703  | -0.175387446 | 1 |

|                 |            |                            |              |             |               |   |              |              |              |   |
|-----------------|------------|----------------------------|--------------|-------------|---------------|---|--------------|--------------|--------------|---|
| ENSG00000258678 | AC126803.1 | Clone-based (Ensembl) gene | -0.495394087 | 0.38894088  | -0.07230517   | 1 | 2.13674904   | 0.669487849  | -0.047239297 | 1 |
| ENSG00000258679 | AC12758.1  | Clone-based (Ensembl) gene | -0.057256137 | 0.26627188  | -0.525392969  | 1 | 0.183775694  | 0.979491691  | -0.287680838 | 1 |
| ENSG00000259010 | AL049669.1 | Clone-based (Ensembl) gene | -1.06237153  | 0.004353922 | -0.240255224  | 1 | 0.197786861  | 0.956870658  | 0.060147849  | 1 |
| ENSG00000259456 | CHEK2P2    | HGNC Symbol                | -0.816052698 | 0.007260967 | -0.56304076   | 1 | 0.6762214    | 0.863255934  | 0.73375248   | 1 |
| ENSG00000259716 | NA         | NA                         | -0.68972052  | 0.24300017  | -0.530044663  | 1 | 2.106754077  | 0.722808749  | 1.540016541  | 1 |
| ENSG00000259800 | AC087473.1 | Clone-based (Ensembl) gene | -0.259518718 | 0.707119428 | -0.58933832   | 1 | 5.1815559    | 0.6271688963 | 0.287497897  | 1 |
| ENSG00000259458 | AC100839.1 | Clone-based (Ensembl) gene | -0.71262016  | 0.226889647 | 0.44725309    | 1 | 0.442861703  | 0.946558275  | 0.559307634  | 1 |
| ENSG00000259790 | ANP32BP1   | HGNC Symbol                | -0.99159785  | 0.00791058  | -0.210937874  | 1 | -1.346501099 | 0.655801493  | 0.633164315  | 1 |
| ENSG00000259841 | LINC01566  | HGNC Symbol                | -0.459757166 | 0.519493356 | -0.79107658   | 1 | 1.107914278  | 0.836986961  | 0.765989445  | 1 |
| ENSG00000260027 | H0XB7      | HGNC Symbol                | -0.542434326 | 0.225372277 | 0.660163746   | 1 | 0.476035227  | 0.906333972  | -0.095631653 | 1 |
| ENSG00000260072 | AC008938.1 | Clone-based (Ensembl) gene | -0.666966682 | 0.313455888 | -0.789539115  | 1 | 0.86310797   | 0.827508914  | 0.128280001  | 1 |
| ENSG00000260290 | AC092115.1 | Clone-based (Ensembl) gene | -0.846632607 | 0.007989568 | 0.104471538   | 1 | -0.836870858 | 0.675458806  | 0.197375256  | 1 |
| ENSG00000260305 | NTRK3-AS1  | HGNC Symbol                | -0.409045013 | 0.529909289 | -1.028600501  | 1 | 4.7440723953 | 0.628886787  | 0.698875009  | 1 |
| ENSG00000260441 | NA         | NA                         | -0.518027268 | 0.393639567 | -0.128473671  | 1 | 0.046107103  | 1            | -0.12690723  | 1 |
| ENSG00000260759 | AP010120.1 | Clone-based (Ensembl) gene | -0.787270245 | 0.25023019  | -0.192880296  | 1 | 0.94955643   | 0.867746032  | -0.05104077  | 1 |
| ENSG00000261004 | AC083904.4 | Clone-based (Ensembl) gene | -0.334778367 | 0.600661825 | -1.123431613  | 1 | 4.880266739  | 0.657456325  | 0.120349508  | 1 |
| ENSG00000261165 | TNEM1788   | HGNC Symbol                | -0.352100285 | 0.265283771 | -0.234381639  | 1 | 1.51747564   | 0.661458936  | 0.462069476  | 1 |
| ENSG00000261777 | AC135012.1 | Clone-based (Ensembl) gene | -0.994275816 | 0.048314645 | -0.081233144  | 1 | 1.187537332  | 0.817387218  | -0.310065734 | 1 |
| ENSG00000261725 | AC092447.8 | Clone-based (Ensembl) gene | -0.812472764 | 0.203816116 | -0.4281869    | 1 | 0.786323262  | 0.890183171  | 0.732924735  | 1 |
| ENSG00000264466 | AC136944.4 | Clone-based (Ensembl) gene | -1.095339774 | 0.04757833  | -0.0910787283 | 1 | 4.851894871  | 0.638396538  | -0.094510196 | 1 |
| ENSG0000026623  | LINC02179  | HGNC Symbol                | -0.14470784  | 0.908308893 | -0.095785762  | 1 | 1.080068661  | 0.844324446  | 0.864825115  | 1 |
| ENSG00000261649 | G0104617   | HGNC Symbol                | -1.0822245   | 0.087301492 | -0.660353888  | 1 | 2.043392484  | 0.73954672   | -0.33000743  | 1 |
| ENSG00000261949 | GFY        | HGNC Symbol                | -0.816057864 | 0.078504736 | -0.47525606   | 1 | -0.763663955 | 0.850814909  | 0.089947054  | 1 |
| ENSG00000262001 | AC040160.1 | Clone-based                | -0.538786924 | 0.387929125 | 0.252943534   | 1 | 5.08134361   | 0.6271688963 | -0.401503894 | 1 |

[illegible]

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## EXAMPLE 2

### AC2 and AC3 Genes and PRIME Cell Markers

#### **[000179]** RNAs and Markers

**[000180]** As detailed above, RNA analysis of fingerstick blood samples from RA patients has identified RNAs suitable as markers of RA flares. A first set of markers and RNAs, denoted AC2, is increased 2 weeks prior to flare. AC2 RNAs are enriched with developmental pathways for naïve B cells and leukocytes. A second set of markers, denoted AC3, is increased the week prior to flare and is then decreased for the duration of the flare. AC3 is enriched for pathways not typical of blood samples, particularly cartilage morphogenesis, endochondral bone growth, extracellular matrix organization. AC3 is enriched with sublining fibroblast genes (CD34+HLADR+DKK3+). The AC2 markers are listed below in Table 7. AC3 gene markers are listed below in Table 8.

TABLE 7

#### AC2 GENES

| <u>Ensembl</u>  | <u>Symbol</u> | <u>Description</u>                                                                                      | <u>Score/AUC</u> |
|-----------------|---------------|---------------------------------------------------------------------------------------------------------|------------------|
| ENSG00000204632 | HLA-G         | "major histocompatibility complex, class I, G<br>[Source:HGNC Symbol;Acc:HGNC:4964]"                    | 5.77E-05         |
| ENSG00000184792 | OSBP2         | oxysterol binding protein 2<br>[Source:HGNC Symbol;Acc:HGNC:8504]                                       | 6.39E-05         |
| ENSG00000198892 | SHISA4        | shisa family member 4<br>[Source:HGNC Symbol;Acc:HGNC:27139]                                            | 0.00012762       |
| ENSG00000187017 | ESPN          | espin<br>[Source:HGNC Symbol;Acc:HGNC:13281]                                                            | 0.000131036      |
| ENSG00000233762 | MARCKSL1      | MARCKS like 1                                                                                           | 0.000323289      |
| ENSG00000175130 |               | [Source:HGNC Symbol;Acc:HGNC:7142]                                                                      | 0.000358619      |
| ENSG00000125534 | PPDPF         | pancreatic progenitor cell differentiation and proliferation factor [Source:HGNC Symbol;Acc:HGNC:16142] | 0.00037025       |
| ENSG00000158856 | DMTN          | dematin actin binding protein<br>[Source:HGNC Symbol;Acc:HGNC:3382]                                     | 0.000376535      |
| ENSG00000121413 | ZSCAN18       | zinc finger and SCAN domain containing 18<br>[Source:HGNC Symbol;Acc:HGNC:21037]                        | 0.000443873      |
| ENSG00000230715 | RPL13P12      | ribosomal protein L13 pseudogene 12                                                                     | 0.000528797      |
| ENSG00000215030 |               |                                                                                                         | 0.000588454      |

|                 |            |                                                                                                |             |
|-----------------|------------|------------------------------------------------------------------------------------------------|-------------|
| ENSG00000146540 | C7orf50    | [Source:HGNC Symbol;Acc:HGNC:35701]<br>chromosome 7 open reading frame 50                      | 0.000639272 |
| ENSG00000029534 | ANK1       | [Source:HGNC Symbol;Acc:HGNC:22421]<br>ankyrin 1                                               | 0.000697583 |
| ENSG00000121104 | FAM117A    | [Source:HGNC Symbol;Acc:HGNC:492]<br>family with sequence similarity 117 member A              | 0.000697583 |
| ENSG00000260231 | JHDM1D-AS1 | [Source:HGNC Symbol;Acc:HGNC:24179]<br>JHDM1D antisense RNA 1 (head to head)                   | 0.00070319  |
| ENSG00000211895 | IGHA1      | [Source:HGNC Symbol;Acc:HGNC:48959]<br>immunoglobulin heavy constant alpha 1                   | 0.000707226 |
| ENSG00000173581 | CCDC106    | [Source:HGNC Symbol;Acc:HGNC:5478]<br>coiled-coil domain containing 106                        | 0.000730947 |
| ENSG00000008441 | NFIX       | [Source:HGNC Symbol;Acc:HGNC:30181]<br>nuclear factor I X                                      | 0.000837162 |
| ENSG00000105701 | FKBP8      | [Source:HGNC Symbol;Acc:HGNC:7788]<br>FK506 binding protein 8                                  | 0.000994972 |
| ENSG00000079308 | TNS1       | [Source:HGNC Symbol;Acc:HGNC:3724]<br>tensin 1                                                 | 0.00113151  |
| ENSG00000264063 | MIR3687-2  | [Source:HGNC Symbol;Acc:HGNC:11973]<br>microRNA 3687-2                                         | 0.001218296 |
| ENSG00000049089 | COL9A2     | [Source:HGNC Symbol;Acc:HGNC:50835]<br>collagen type IX alpha 2 chain                          | 0.001236713 |
| ENSG00000126461 | SCAF1      | [Source:HGNC Symbol;Acc:HGNC:2218]<br>SR-related CTD associated factor 1                       | 0.00126185  |
| ENSG00000243679 |            | [Source:HGNC Symbol;Acc:HGNC:30403]<br>activating transcription factor 5                       | 0.001292673 |
| ENSG00000169136 | ATF5       | [Source:HGNC Symbol;Acc:HGNC:790]<br>mex-3 RNA binding family member D                         | 0.001421682 |
| ENSG00000181588 | MEX3D      | [Source:HGNC Symbol;Acc:HGNC:16734]<br>solute carrier family 7 member 5                        | 0.001421682 |
| ENSG00000103257 | SLC7A5     | [Source:HGNC Symbol;Acc:HGNC:11063]<br>ubiquitin conjugating enzyme E2 O                       | 0.001574737 |
| ENSG00000175931 | UBE2O      | [Source:HGNC Symbol;Acc:HGNC:29554]<br>WD repeat domain 18                                     | 0.001669619 |
| ENSG00000065268 | WDR18      | [Source:HGNC Symbol;Acc:HGNC:17956]<br>plasmalemma vesicle associated protein                  | 0.001764407 |
| ENSG00000130300 | PLVAP      | [Source:HGNC Symbol;Acc:HGNC:13635]<br>apical junction component 1 homolog                     | 0.001779673 |
| ENSG00000232434 | AJM1       | [Source:HGNC Symbol;Acc:HGNC:37284]<br>KN motif and ankyrin repeat domains 2                   | 0.001937905 |
| ENSG00000197256 | KANK2      | [Source:HGNC Symbol;Acc:HGNC:29300]<br>zinc finger protein 688                                 | 0.001945859 |
| ENSG00000229809 | ZNF688     | [Source:HGNC Symbol;Acc:HGNC:30489]<br>calcium voltage-gated channel auxiliary subunit gamma 6 | 0.002041059 |
| ENSG00000130433 | CACNG6     | [Source:HGNC Symbol;Acc:HGNC:13625]<br>RNA binding motif protein 42                            | 0.002327494 |
| ENSG00000126254 | RBM42      | [Source:HGNC Symbol;Acc:HGNC:28117]<br>solute carrier family 25 member 39                      | 0.002342133 |
| ENSG00000013306 | SLC25A39   | [Source:HGNC Symbol;Acc:HGNC:24279]<br>NA                                                      | 0.002354141 |
| ENSG00000179837 | NA         | NA                                                                                             | 0.002482976 |
| ENSG00000265714 | NA         | NA                                                                                             | 0.002482976 |
| ENSG00000172460 | PRSS30P    | "serine protease 30, pseudogene<br>[Source:HGNC Symbol;Acc:HGNC:28753]"                        | 0.002490713 |
| ENSG00000104983 | CCDC61     | [Source:HGNC Symbol;Acc:HGNC:33629]<br>coiled-coil domain containing 61                        | 0.002565172 |
| ENSG00000211898 | IGHD       | [Source:HGNC Symbol;Acc:HGNC:5480]<br>immunoglobulin heavy constant delta                      | 0.002565172 |
| ENSG00000055118 | KCNH2      | [Source:HGNC Symbol;Acc:HGNC:6251]<br>potassium voltage-gated channel subfamily H member 2     | 0.002637584 |
| ENSG00000260335 |            |                                                                                                | 0.002639596 |
| ENSG00000104903 | LYL1       | "LYL1, basic helix-loop-helix family member<br>[Source:HGNC Symbol;Acc:HGNC:6734]"             | 0.002696079 |
| ENSG00000099958 | DERL3      | [Source:HGNC Symbol;Acc:HGNC:14236]<br>derlin 3                                                | 0.002709927 |
| ENSG00000179526 | SHARPIN    | [Source:HGNC Symbol;Acc:HGNC:25321]<br>SHANK associated RH domain interactor                   | 0.002709927 |

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|-----------------|-----------|----------------------------------------------------------------------------------------------------------|-------------|
| ENSG00000133069 | TMCC2     | transmembrane and coiled-coil domain family 2<br>[Source:HGNC Symbol;Acc:HGNC:24239]                     | 0.002940811 |
| ENSG00000240342 | RPS2P5    | ribosomal protein S2 pseudogene 5<br>[Source:HGNC Symbol;Acc:HGNC:31386]                                 | 0.002940811 |
| ENSG00000264462 | MIR3648-2 | microRNA 3648-2<br>[Source:HGNC Symbol;Acc:HGNC:50843]                                                   | 0.003313878 |
| ENSG00000256576 | LINC02361 | long intergenic non-protein coding RNA 2361<br>[Source:HGNC Symbol;Acc:HGNC:53283]                       | 0.003383286 |
| ENSG00000007968 | E2F2      | E2F transcription factor 2<br>[Source:HGNC Symbol;Acc:HGNC:3114]                                         | 0.003400809 |
| ENSG00000141858 | SAMD1     | sterile alpha motif domain containing 1<br>[Source:HGNC Symbol;Acc:HGNC:17958]                           | 0.003623721 |
| ENSG00000126705 | AHDC1     | AT-hook DNA binding motif containing 1<br>[Source:HGNC Symbol;Acc:HGNC:25230]                            | 0.004035577 |
| ENSG00000141456 | PELP1     | "proline, glutamate and leucine rich protein 1<br>[Source:HGNC Symbol;Acc:HGNC:30134]"                   | 0.00422876  |
| ENSG00000159713 | TPPP3     | tubulin polymerization promoting protein family member 3<br>[Source:HGNC Symbol;Acc:HGNC:24162]          | 0.004525344 |
| ENSG00000104897 | SF3A2     | splicing factor 3a subunit 2<br>[Source:HGNC Symbol;Acc:HGNC:10766]                                      | 0.004539725 |
| ENSG00000063245 | EPN1      | epsin 1<br>[Source:HGNC Symbol;Acc:HGNC:21604]                                                           | 0.004540184 |
| ENSG00000162783 | IER5      | immediate early response 5<br>[Source:HGNC Symbol;Acc:HGNC:5393]                                         | 0.004549021 |
| ENSG00000141582 | CBX4      | chromobox 4<br>[Source:HGNC Symbol;Acc:HGNC:1554]                                                        | 0.004686524 |
| ENSG00000168159 | RNF187    | ring finger protein 187<br>[Source:HGNC Symbol;Acc:HGNC:27146]                                           | 0.004686524 |
| ENSG00000136826 | KLF4      | Kruppel like factor 4<br>[Source:HGNC Symbol;Acc:HGNC:6348]                                              | 0.004891089 |
| ENSG00000237214 |           |                                                                                                          | 0.004891089 |
| ENSG00000066336 | SPI1      | Spi-1 proto-oncogene<br>[Source:HGNC Symbol;Acc:HGNC:11241]                                              | 0.005082358 |
| ENSG00000172270 | BSG       | basigin (Ok blood group)<br>[Source:HGNC Symbol;Acc:HGNC:1116]                                           | 0.005082358 |
| ENSG00000173868 | PHOSPHO1  | phosphoethanolamine/phosphocholine phosphatase<br>[Source:HGNC Symbol;Acc:HGNC:16815]                    | 0.005082358 |
| ENSG00000167182 | SP2       | Sp2 transcription factor<br>[Source:HGNC Symbol;Acc:HGNC:11207]                                          | 0.005118791 |
| ENSG00000104805 | NUCB1     | nucleobindin 1<br>[Source:HGNC Symbol;Acc:HGNC:8043]                                                     | 0.005119064 |
| ENSG00000099381 | SETD1A    | SET domain containing 1A<br>[Source:HGNC Symbol;Acc:HGNC:29010]                                          | 0.00514547  |
| ENSG00000185340 | GAS2L1    | growth arrest specific 2 like 1<br>[Source:HGNC Symbol;Acc:HGNC:16955]                                   | 0.00514547  |
| ENSG00000007541 | PIGQ      | phosphatidylinositol glycan anchor biosynthesis class Q<br>[Source:HGNC Symbol;Acc:HGNC:14135]           | 0.005166641 |
| ENSG00000105610 | KLF1      | Kruppel like factor 1<br>[Source:HGNC Symbol;Acc:HGNC:6345]                                              | 0.005217627 |
| ENSG00000137193 | PIM1      | "Pim-1 proto-oncogene, serine/threonine kinase<br>[Source:HGNC Symbol;Acc:HGNC:8986]"                    | 0.005247531 |
| ENSG00000171552 | BCL2L1    | BCL2 like 1<br>[Source:HGNC Symbol;Acc:HGNC:992]                                                         | 0.005530506 |
| ENSG00000172889 | EGFL7     | EGF like domain multiple 7<br>[Source:HGNC Symbol;Acc:HGNC:20594]                                        | 0.005530506 |
| ENSG00000213402 | PTPRCAP   | "protein tyrosine phosphatase, receptor type C associated protein<br>[Source:HGNC Symbol;Acc:HGNC:9667]" | 0.00560032  |
| ENSG00000099330 | OCEL1     | occludin/ELL domain containing 1<br>[Source:HGNC Symbol;Acc:HGNC:26221]                                  | 0.005671418 |
| ENSG00000147443 | DOK2      | docking protein 2<br>[Source:HGNC Symbol;Acc:HGNC:2991]                                                  | 0.005857886 |
| ENSG00000182240 | BACE2     | beta-site APP-cleaving enzyme 2<br>[Source:HGNC Symbol;Acc:HGNC:934]                                     | 0.005857886 |
| ENSG00000170128 | GPR25     | G protein-coupled receptor 25<br>[Source:HGNC Symbol;Acc:HGNC:4480]                                      | 0.006101348 |
| ENSG00000140406 | TLNRD1    | talin rod domain containing 1<br>[Source:HGNC Symbol;Acc:HGNC:13519]                                     | 0.0061541   |

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| ENSG00000117394 | SLC2A1    | solute carrier family 2 member 1<br>[Source:HGNC Symbol;Acc:HGNC:11005]                       | 0.006158727 |
| ENSG00000141854 | MISP3     | MISP family member 3<br>[Source:HGNC Symbol;Acc:HGNC:26963]                                   | 0.006204755 |
| ENSG00000129757 | CDKN1C    | cyclin dependent kinase inhibitor 1C<br>[Source:HGNC Symbol;Acc:HGNC:1786]                    | 0.006380434 |
| ENSG00000186891 | TNFRSF18  | TNF receptor superfamily member 18<br>[Source:HGNC Symbol;Acc:HGNC:11914]                     | 0.006421961 |
| ENSG00000184897 | H1FX      | H1 histone family member X<br>[Source:HGNC Symbol;Acc:HGNC:4722]                              | 0.006465512 |
| ENSG00000185236 | RAB11B    | "RAB11B, member RAS oncogene family<br>[Source:HGNC Symbol;Acc:HGNC:9761]"                    | 0.006602734 |
| ENSG00000030582 | GRN       | granulin precursor<br>[Source:HGNC Symbol;Acc:HGNC:4601]                                      | 0.006751675 |
| ENSG00000071564 | TCF3      | transcription factor 3<br>[Source:HGNC Symbol;Acc:HGNC:11633]                                 | 0.006772165 |
| ENSG00000267749 |           |                                                                                               | 0.006848491 |
| ENSG00000105373 | NOP53     | NOP53 ribosome biogenesis factor<br>[Source:HGNC Symbol;Acc:HGNC:4333]                        | 0.006952696 |
| ENSG00000240445 | FOXO3B    | forkhead box O3B pseudogene<br>[Source:HGNC Symbol;Acc:HGNC:3822]                             | 0.006952696 |
| ENSG00000127528 | KLF2      | Kruppel like factor 2<br>[Source:HGNC Symbol;Acc:HGNC:6347]                                   | 0.00698206  |
| ENSG00000254858 | MPV17L2   | MPV17 mitochondrial inner membrane protein like 2<br>[Source:HGNC Symbol;Acc:HGNC:28177]      | 0.006997113 |
| ENSG00000130595 | TNNT3     | "tropomyosin T3, fast skeletal type<br>[Source:HGNC Symbol;Acc:HGNC:11950]"                   | 0.007133196 |
| ENSG00000130749 | ZC3H4     | zinc finger CCCH-type containing 4<br>[Source:HGNC Symbol;Acc:HGNC:17808]                     | 0.007141116 |
| ENSG00000132819 | RBM38     | RNA binding motif protein 38<br>[Source:HGNC Symbol;Acc:HGNC:15818]                           | 0.007141116 |
| ENSG00000135925 | WNT10A    | Wnt family member 10A<br>[Source:HGNC Symbol;Acc:HGNC:13829]                                  | 0.007141116 |
| ENSG00000205639 | MFS2B     | major facilitator superfamily domain containing 2B<br>[Source:HGNC Symbol;Acc:HGNC:37207]     | 0.007141116 |
| ENSG00000213763 | ACTBP2    | "actin, beta pseudogene 2<br>[Source:HGNC Symbol;Acc:HGNC:135]"                               | 0.007141116 |
| ENSG00000261221 | ZNF865    | zinc finger protein 865<br>[Source:HGNC Symbol;Acc:HGNC:38705]                                | 0.007141116 |
| ENSG00000171611 | PTCRA     | pre T cell antigen receptor alpha<br>[Source:HGNC Symbol;Acc:HGNC:21290]                      | 0.007255358 |
| ENSG00000161642 | ZNF385A   | zinc finger protein 385A<br>[Source:HGNC Symbol;Acc:HGNC:17521]                               | 0.007304748 |
| ENSG00000226608 | FTLP3     | ferritin light chain pseudogene 3<br>[Source:HGNC Symbol;Acc:HGNC:4000]                       | 0.007304748 |
| ENSG00000170684 | ZNF296    | zinc finger protein 296<br>[Source:HGNC Symbol;Acc:HGNC:15981]                                | 0.007327997 |
| ENSG00000213638 | ADAT3     | "adenosine deaminase, tRNA specific 3<br>[Source:HGNC Symbol;Acc:HGNC:25151]"                 | 0.007343983 |
| ENSG00000179262 | RAD23A    | "RAD23 homolog A, nucleotide excision repair protein<br>[Source:HGNC Symbol;Acc:HGNC:9812]"   | 0.0073448   |
| ENSG00000196126 | HLA-DRB1  | "major histocompatibility complex, class II, DR beta 1<br>[Source:HGNC Symbol;Acc:HGNC:4948]" | 0.00745996  |
| ENSG00000197149 |           |                                                                                               | 0.007535198 |
| ENSG00000213820 | RPL13P2   | ribosomal protein L13 pseudogene 2<br>[Source:HGNC Symbol;Acc:HGNC:16342]                     | 0.007619923 |
| ENSG00000225331 | LINC01678 | long intergenic non-protein coding RNA 1678<br>[Source:HGNC Symbol;Acc:HGNC:52466]            | 0.007619923 |
| ENSG00000235605 |           |                                                                                               | 0.007619923 |
| ENSG00000183092 | BEGAIN    | brain enriched guanylate kinase associated<br>[Source:HGNC Symbol;Acc:HGNC:24163]             | 0.007755013 |
| ENSG00000105369 | CD79A     | CD79a molecule<br>[Source:HGNC Symbol;Acc:HGNC:1698]                                          | 0.007835589 |
| ENSG00000160256 | FAM207A   | family with sequence similarity 207 member A<br>[Source:HGNC Symbol;Acc:HGNC:15811]           | 0.007901726 |
| ENSG00000105516 | DBP       | D-box binding PAR bZIP transcription factor<br>[Source:HGNC Symbol;Acc:HGNC:2697]             | 0.00795596  |

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| ENSG00000179094 | PER1     | period circadian regulator 1<br>[Source:HGNC Symbol;Acc:HGNC:8845]                           | 0.008010463 |
| ENSG00000154146 | NRGN     | neurogranin<br>[Source:HGNC Symbol;Acc:HGNC:8000]                                            | 0.008019602 |
| ENSG00000160813 | PPP1R35  | protein phosphatase 1 regulatory subunit 35<br>[Source:HGNC Symbol;Acc:HGNC:28320]           | 0.008019602 |
| ENSG00000152082 | MZT2B    | mitotic spindle organizing protein 2B<br>[Source:HGNC Symbol;Acc:HGNC:25886]                 | 0.008149414 |
| ENSG00000115274 | INO80B   | INO80 complex subunit B<br>[Source:HGNC Symbol;Acc:HGNC:13324]                               | 0.008388785 |
| ENSG00000185112 | FAM43A   | family with sequence similarity 43 member A<br>[Source:HGNC Symbol;Acc:HGNC:26888]           | 0.008409751 |
| ENSG00000130592 | LSP1     | lymphocyte-specific protein 1<br>[Source:HGNC Symbol;Acc:HGNC:6707]                          | 0.00866593  |
| ENSG00000077348 | EXOSC5   | exosome component 5<br>[Source:HGNC Symbol;Acc:HGNC:24662]                                   | 0.008679008 |
| ENSG00000196498 | NCOR2    | nuclear receptor corepressor 2<br>[Source:HGNC Symbol;Acc:HGNC:7673]                         | 0.008729326 |
| ENSG00000132382 | MYBBP1A  | MYB binding protein 1a<br>[Source:HGNC Symbol;Acc:HGNC:7546]                                 | 0.008886691 |
| ENSG00000104885 | DOT1L    | DOT1 like histone lysine methyltransferase<br>[Source:HGNC Symbol;Acc:HGNC:24948]            | 0.008912378 |
| ENSG00000153443 | UBALD1   | UBA like domain containing 1<br>[Source:HGNC Symbol;Acc:HGNC:29576]                          | 0.008912378 |
| ENSG00000070182 | SPTB     | "spectrin beta, erythrocytic<br>[Source:HGNC Symbol;Acc:HGNC:11274]"                         | 0.008927471 |
| ENSG00000168517 | HEXIM2   | hexamethylene bisacetamide inducible 2<br>[Source:HGNC Symbol;Acc:HGNC:28591]                | 0.008959412 |
| ENSG00000090674 | MCOLN1   | mucolipin 1<br>[Source:HGNC Symbol;Acc:HGNC:13356]                                           | 0.009327518 |
| ENSG00000198816 | ZNF358   | zinc finger protein 358<br>[Source:HGNC Symbol;Acc:HGNC:16838]                               | 0.009506451 |
| ENSG00000175334 | BANF1    | barrier to autointegration factor 1<br>[Source:HGNC Symbol;Acc:HGNC:17397]                   | 0.009647997 |
| ENSG00000125520 | SLC2A4RG | SLC2A4 regulator<br>[Source:HGNC Symbol;Acc:HGNC:15930]                                      | 0.009686596 |
| ENSG00000141084 | RANBP10  | RAN binding protein 10<br>[Source:HGNC Symbol;Acc:HGNC:29285]                                | 0.009715508 |
| ENSG00000149016 | TUT1     | "terminal uridylyl transferase 1, U6 snRNA-specific<br>[Source:HGNC Symbol;Acc:HGNC:26184]"  | 0.009768686 |
| ENSG00000178951 | ZBTB7A   | zinc finger and BTB domain containing 7A<br>[Source:HGNC Symbol;Acc:HGNC:18078]              | 0.009810065 |
| ENSG00000186111 | PIP5K1C  | phosphatidylinositol-4-phosphate 5-kinase type 1 gamma<br>[Source:HGNC Symbol;Acc:HGNC:8996] | 0.009810065 |
| ENSG00000184481 | FOXO4    | forkhead box O4<br>[Source:HGNC Symbol;Acc:HGNC:7139]                                        | 0.009820284 |
| ENSG00000064961 | HMG20B   | high mobility group 20B<br>[Source:HGNC Symbol;Acc:HGNC:5002]                                | 0.009858965 |
| ENSG00000108309 | RUNDC3A  | RUN domain containing 3A<br>[Source:HGNC Symbol;Acc:HGNC:16984]                              | 0.010055443 |
| ENSG00000130165 | ELOF1    | elongation factor 1 homolog<br>[Source:HGNC Symbol;Acc:HGNC:28691]                           | 0.010212535 |
| ENSG00000130159 | ECSIT    | ECSIT signalling integrator<br>[Source:HGNC Symbol;Acc:HGNC:29548]                           | 0.010245658 |
| ENSG00000244560 |          |                                                                                              | 0.010245658 |
| ENSG00000125148 | MT2A     | metallothionein 2A<br>[Source:HGNC Symbol;Acc:HGNC:7406]                                     | 0.01061889  |
| ENSG00000131116 | ZNF428   | zinc finger protein 428<br>[Source:HGNC Symbol;Acc:HGNC:20804]                               | 0.010712491 |
| ENSG00000105617 | LENG1    | leukocyte receptor cluster member 1<br>[Source:HGNC Symbol;Acc:HGNC:15502]                   | 0.010999325 |
| ENSG00000139718 | SETD1B   | SET domain containing 1B<br>[Source:HGNC Symbol;Acc:HGNC:29187]                              | 0.011038344 |
| ENSG00000106665 | CLIP2    | CAP-Gly domain containing linker protein 2<br>[Source:HGNC Symbol;Acc:HGNC:2586]             | 0.011064297 |
| ENSG00000130821 | SLC6A8   | solute carrier family 6 member 8<br>[Source:HGNC Symbol;Acc:HGNC:11055]                      | 0.011213055 |

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| ENSG00000184232 | OAF      | out at first homolog                                         |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:28752]                          | 0.011286635 |
| ENSG00000179820 | MYADM    | myeloid associated differentiation marker                    |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:7544]                           | 0.011330192 |
| ENSG00000127580 | WDR24    | WD repeat domain 24                                          |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:20852]                          | 0.011570001 |
| ENSG00000004939 | SLC4A1   | solute carrier family 4 member 1 (Diego blood group)         |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:11027]                          | 0.011732314 |
| ENSG00000130522 | JUND     | "JunD proto-oncogene, AP-1 transcription factor subunit      |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:6206]"                          | 0.011813745 |
| ENSG00000148362 | PAXX     | "PAXX, non-homologous end joining factor                     |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:27849]"                         | 0.011821074 |
| ENSG00000262902 | MTCO1P40 | mitochondrially encoded cytochrome c oxidase I pseudogene 40 |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:52105]                          | 0.011821074 |
| ENSG00000167671 | UBXN6    | UBX domain protein 6                                         |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:14928]                          | 0.011831088 |
| ENSG00000125457 | MIF4GD   | MIF4G domain containing                                      |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:24030]                          | 0.011851589 |
| ENSG00000146066 | HIGD2A   | HIG1 hypoxia inducible domain family member 2A               |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:28311]                          | 0.011914767 |
| ENSG00000184221 | OLIG1    | oligodendrocyte transcription factor 1                       |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:16983]                          | 0.011914767 |
| ENSG00000260316 |          |                                                              | 0.0119947   |
| ENSG00000124762 | CDKN1A   | cyclin dependent kinase inhibitor 1A                         |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:1784]                           | 0.012077375 |
| ENSG00000103148 | NPRL3    | "NPR3 like, GATOR1 complex subunit                           |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:14124]"                         | 0.012137266 |
| ENSG00000179115 | FARSA    | phenylalanyl-tRNA synthetase alpha subunit                   |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:3592]                           | 0.012137266 |
| ENSG00000120896 | SORBS3   | sorbin and SH3 domain containing 3                           |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:30907]                          | 0.012150664 |
| ENSG00000174886 | NDUFA11  | NADH:ubiquinone oxidoreductase subunit A11                   |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:20371]                          | 0.012268883 |
| ENSG00000102145 | GATA1    | GATA binding protein 1                                       |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:4170]                           | 0.012285964 |
| ENSG00000166428 | PLD4     | phospholipase D family member 4                              |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:23792]                          | 0.012401569 |
| ENSG00000213015 | ZNF580   | zinc finger protein 580                                      |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:29473]                          | 0.012630003 |
| ENSG00000142544 | CTU1     | cytosolic thiouridylase subunit 1                            |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:29590]                          | 0.012676606 |
| ENSG00000085644 | ZNF213   | zinc finger protein 213                                      |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:13005]                          | 0.012935817 |
| ENSG00000003249 | DBNDD1   | dysbindin domain containing 1                                |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:28455]                          | 0.013109402 |
| ENSG00000221288 | MIR663B  | microRNA 663b                                                |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:35270]                          | 0.013333238 |
| ENSG00000042062 | RIPOR3   | RIPOR family member 3                                        |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:16168]                          | 0.013356858 |
| ENSG00000105329 | TGFB1    | transforming growth factor beta 1                            |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:11766]                          | 0.013356858 |
| ENSG00000116871 | MAP7D1   | MAP7 domain containing 1                                     |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:25514]                          | 0.013356858 |
| ENSG00000168298 | HIST1H1E | histone cluster 1 H1 family member e                         |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:4718]                           | 0.013400191 |
| ENSG00000127666 | TICAM1   | toll like receptor adaptor molecule 1                        |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:18348]                          | 0.013447765 |
| ENSG00000166886 | NAB2     | NGFI-A binding protein 2                                     |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:7627]                           | 0.013572419 |
| ENSG00000112787 | FBRSL1   | fibrosin like 1                                              |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:29308]                          | 0.013760569 |
| ENSG00000100243 | CYB5R3   | cytochrome b5 reductase 3                                    |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:2873]                           | 0.013883197 |
| ENSG00000197457 | STMN3    | stathmin 3                                                   |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:15926]                          | 0.013964273 |
| ENSG00000255441 |          |                                                              | 0.013965194 |
| ENSG00000173801 | JUP      | junction plakoglobin                                         |             |

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|-----------------|-----------|---------------------------------------------------------------------------------------------------|-------------|
| ENSG00000224614 | TNK2-AS1  | [Source:HGNC Symbol;Acc:HGNC:6207]<br>TNK2 antisense RNA 1                                        | 0.014437619 |
| ENSG00000058453 | CROCC     | [Source:HGNC Symbol;Acc:HGNC:49093]<br>"ciliary rootlet coiled-coil, rootletin                    | 0.014437619 |
| ENSG00000079313 | REXO1     | [Source:HGNC Symbol;Acc:HGNC:21299]"<br>RNA exonuclease 1 homolog                                 | 0.014522615 |
| ENSG00000154102 | C16orf74  | [Source:HGNC Symbol;Acc:HGNC:24616]<br>chromosome 16 open reading frame 74                        | 0.014579462 |
| ENSG00000172650 | AGAP5     | [Source:HGNC Symbol;Acc:HGNC:23362]<br>"ArfGAP with GTPase domain, ankyrin repeat and PH domain 5 | 0.014732236 |
| ENSG00000159733 | ZFYVE28   | [Source:HGNC Symbol;Acc:HGNC:23467]"<br>zinc finger FYVE-type containing 28                       | 0.014761715 |
| ENSG00000019582 | CD74      | [Source:HGNC Symbol;Acc:HGNC:29334]<br>CD74 molecule                                              | 0.014792652 |
| ENSG00000211771 | TRBJ2-7   | [Source:HGNC Symbol;Acc:HGNC:1697]<br>T cell receptor beta joining 2-7                            | 0.014946895 |
| ENSG00000214309 | MBLAC1    | [Source:HGNC Symbol;Acc:HGNC:12175]<br>metallo-beta-lactamase domain containing 1                 | 0.014961068 |
| ENSG00000187266 | EPOR      | [Source:HGNC Symbol;Acc:HGNC:22180]<br>erythropoietin receptor                                    | 0.014976932 |
| ENSG00000108106 | UBE2S     | [Source:HGNC Symbol;Acc:HGNC:3416]<br>ubiquitin conjugating enzyme E2 S                           | 0.015342955 |
| ENSG00000185838 | GNB1L     | [Source:HGNC Symbol;Acc:HGNC:17895]<br>G protein subunit beta 1 like                              | 0.015459542 |
| ENSG00000228594 | FNDC10    | [Source:HGNC Symbol;Acc:HGNC:4397]<br>fibronectin type III domain containing 10                   | 0.015552452 |
| ENSG00000126464 | PRR12     | [Source:HGNC Symbol;Acc:HGNC:42951]<br>proline rich 12                                            | 0.015552452 |
| ENSG00000084092 | NOA1      | [Source:HGNC Symbol;Acc:HGNC:29217]<br>nitric oxide associated 1                                  | 0.015622838 |
| ENSG00000105227 | PRX       | [Source:HGNC Symbol;Acc:HGNC:28473]<br>periaxin                                                   | 0.015753463 |
| ENSG00000260401 |           | [Source:HGNC Symbol;Acc:HGNC:13797]<br>zyxin                                                      | 0.015787169 |
| ENSG00000159840 | ZYX       | [Source:HGNC Symbol;Acc:HGNC:13200]<br>zyxin                                                      | 0.015787169 |
| ENSG00000197483 | ZNF628    | [Source:HGNC Symbol;Acc:HGNC:28054]<br>zinc finger protein 628                                    | 0.015829354 |
| ENSG00000182572 | NA        | [Source:HGNC Symbol;Acc:HGNC:28114]<br>NA                                                         | 0.015834462 |
| ENSG00000154035 | NA        | [Source:HGNC Symbol;Acc:HGNC:4717]<br>NA                                                          | 0.015908819 |
| ENSG00000161618 | ALDH16A1  | [Source:HGNC Symbol;Acc:HGNC:28114]<br>aldehyde dehydrogenase 16 family member A1                 | 0.015942034 |
| ENSG00000124575 | HIST1H1D  | [Source:HGNC Symbol;Acc:HGNC:4717]<br>histone cluster 1 H1 family member d                        | 0.015948868 |
| ENSG00000196092 | PAX5      | [Source:HGNC Symbol;Acc:HGNC:8619]<br>paired box 5                                                | 0.01597311  |
| ENSG00000105429 | MEGF8     | [Source:HGNC Symbol;Acc:HGNC:3233]<br>multiple EGF like domains 8                                 | 0.015986308 |
| ENSG00000213753 | CENPBD1P1 | [Source:HGNC Symbol;Acc:HGNC:28421]<br>CENPB DNA-binding domains containing 1 pseudogene 1        | 0.016008143 |
| ENSG00000179627 | ZBTB42    | [Source:HGNC Symbol;Acc:HGNC:32550]<br>zinc finger and BTB domain containing 42                   | 0.016166469 |
| ENSG00000107816 | LZTS2     | [Source:HGNC Symbol;Acc:HGNC:29381]<br>leucine zipper tumor suppressor 2                          | 0.016243979 |
| ENSG00000183779 | ZNF703    | [Source:HGNC Symbol;Acc:HGNC:25883]<br>zinc finger protein 703                                    | 0.016243979 |
| ENSG00000203950 | RTL8A     | [Source:HGNC Symbol;Acc:HGNC:24514]<br>retrotransposon Gag like 8A                                | 0.01630694  |
| ENSG00000088826 | SMOX      | [Source:HGNC Symbol;Acc:HGNC:15862]<br>spermine oxidase                                           | 0.016416472 |
| ENSG00000105298 | CACTIN    | [Source:HGNC Symbol;Acc:HGNC:29938]"<br>"cactin, spliceosome C complex subunit                    | 0.016416472 |
| ENSG00000137218 | FRS3      | [Source:HGNC Symbol;Acc:HGNC:16970]<br>fibroblast growth factor receptor substrate 3              | 0.016416472 |
| ENSG00000175550 | DRAP1     | [Source:HGNC Symbol;Acc:HGNC:3019]<br>DR1 associated protein 1                                    | 0.016587059 |

|                 |            |                                                                                                           |             |
|-----------------|------------|-----------------------------------------------------------------------------------------------------------|-------------|
| ENSG00000166165 | CKB        | creatine kinase B<br>[Source:HGNC Symbol;Acc:HGNC:1991]                                                   | 0.01659925  |
| ENSG00000162366 | PDZK1IP1   | PDZK1 interacting protein 1<br>[Source:HGNC Symbol;Acc:HGNC:16887]                                        | 0.016705327 |
| ENSG00000184428 | TOP1MT     | DNA topoisomerase I mitochondrial<br>[Source:HGNC Symbol;Acc:HGNC:29787]                                  | 0.016722415 |
| ENSG00000130479 | MAP1S      | microtubule associated protein 1S<br>[Source:HGNC Symbol;Acc:HGNC:15715]                                  | 0.016796937 |
| ENSG00000171222 | SCAND1     | SCAN domain containing 1<br>[Source:HGNC Symbol;Acc:HGNC:10566]                                           | 0.016821415 |
| ENSG00000171223 | JUNB       | "JunB proto-oncogene, AP-1 transcription factor subunit<br>[Source:HGNC Symbol;Acc:HGNC:6205]"            | 0.016966042 |
| ENSG00000107902 | LHPP       | phospholysine phosphohistidine inorganic pyrophosphate phosphatase<br>[Source:HGNC Symbol;Acc:HGNC:30042] | 0.017052413 |
| ENSG00000170271 | FAXDC2     | fatty acid hydroxylase domain containing 2<br>[Source:HGNC Symbol;Acc:HGNC:1334]                          | 0.017052413 |
| ENSG00000100325 | ASCC2      | activating signal cointegrator 1 complex subunit 2<br>[Source:HGNC Symbol;Acc:HGNC:24103]                 | 0.017132234 |
| ENSG00000142694 | EVA1B      | eva-1 homolog B<br>[Source:HGNC Symbol;Acc:HGNC:25558]                                                    | 0.017132234 |
| ENSG00000064201 | TSPAN32    | tetraspanin 32<br>[Source:HGNC Symbol;Acc:HGNC:13410]                                                     | 0.017210927 |
| ENSG00000157911 | PEX10      | peroxisomal biogenesis factor 10<br>[Source:HGNC Symbol;Acc:HGNC:8851]                                    | 0.017211726 |
| ENSG00000079432 | CIC        | capicua transcriptional repressor<br>[Source:HGNC Symbol;Acc:HGNC:14214]                                  | 0.017339051 |
| ENSG00000188825 | LINC00910  | long intergenic non-protein coding RNA 910<br>[Source:HGNC Symbol;Acc:HGNC:44361]                         | 0.017339051 |
| ENSG00000196961 | AP2A1      | adaptor related protein complex 2 alpha 1 subunit<br>[Source:HGNC Symbol;Acc:HGNC:561]                    | 0.017339051 |
| ENSG00000214279 | SCART1     | scavenger receptor family member expressed on T cells 1<br>[Source:HGNC Symbol;Acc:HGNC:32411]            | 0.017339051 |
| ENSG00000272449 |            |                                                                                                           |             |
| ENSG00000104973 | MED25      | mediator complex subunit 25<br>[Source:HGNC Symbol;Acc:HGNC:28845]                                        | 0.017392388 |
| ENSG00000180767 | CHST13     | carbohydrate sulfotransferase 13<br>[Source:HGNC Symbol;Acc:HGNC:21755]                                   | 0.017392388 |
| ENSG00000227232 | WASH7P     | WAS protein family homolog 7 pseudogene<br>[Source:HGNC Symbol;Acc:HGNC:38034]                            | 0.017392388 |
| ENSG00000162302 | RPS6KA4    | ribosomal protein S6 kinase A4<br>[Source:HGNC Symbol;Acc:HGNC:10433]                                     | 0.017767827 |
| ENSG00000136840 | ST6GALNAC4 | "ST6 N-acetylgalactosaminide alpha-2,6-sialyltransferase 4<br>[Source:HGNC Symbol;Acc:HGNC:17846]"        | 0.017832974 |
| ENSG00000160404 | TOR2A      | torsin family 2 member A<br>[Source:HGNC Symbol;Acc:HGNC:11996]                                           | 0.018020454 |
| ENSG00000233038 |            |                                                                                                           | 0.018071818 |
| ENSG00000243449 | C4orf48    | chromosome 4 open reading frame 48<br>[Source:HGNC Symbol;Acc:HGNC:34437]                                 | 0.018116836 |
| ENSG00000160050 | CCDC28B    | coiled-coil domain containing 28B<br>[Source:HGNC Symbol;Acc:HGNC:28163]                                  | 0.01812987  |
| ENSG00000138623 | SEMA7A     | semaphorin 7A (John Milton Hagen blood group)<br>[Source:HGNC Symbol;Acc:HGNC:10741]                      | 0.01834001  |
| ENSG00000101439 | CST3       | cystatin C<br>[Source:HGNC Symbol;Acc:HGNC:2475]                                                          | 0.018421259 |
| ENSG00000100368 | CSF2RB     | colony stimulating factor 2 receptor beta common subunit<br>[Source:HGNC Symbol;Acc:HGNC:2436]            | 0.01865112  |
| ENSG00000006015 | REX1BD     | required for excision 1-B domain containing<br>[Source:HGNC Symbol;Acc:HGNC:26098]                        | 0.01871477  |
| ENSG00000011451 | WIZ        | widely interspaced zinc finger motifs<br>[Source:HGNC Symbol;Acc:HGNC:30917]                              | 0.018812736 |
| ENSG00000160888 | IER2       | immediate early response 2<br>[Source:HGNC Symbol;Acc:HGNC:28871]                                         | 0.018812736 |
| ENSG00000174807 | CD248      | CD248 molecule<br>[Source:HGNC Symbol;Acc:HGNC:18219]                                                     | 0.018812736 |
| ENSG00000099821 | POLRMT     | RNA polymerase mitochondrial<br>[Source:HGNC Symbol;Acc:HGNC:9200]                                        | 0.018832922 |
| ENSG00000211899 | IGHM       | immunoglobulin heavy constant mu                                                                          |             |

|                 |          |                                                                                              |             |
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| ENSG00000130313 | PGLS     | [Source:HGNC Symbol;Acc:HGNC:5541]<br>6-phosphogluconolactonase                              | 0.018832922 |
| ENSG00000165702 | GFI1B    | [Source:HGNC Symbol;Acc:HGNC:8903]<br>growth factor independent 1B transcriptional repressor | 0.019015294 |
| ENSG00000196557 | CACNA1H  | [Source:HGNC Symbol;Acc:HGNC:4238]<br>calcium voltage-gated channel subunit alpha1 H         | 0.019015294 |
| ENSG00000188486 | H2AFX    | [Source:HGNC Symbol;Acc:HGNC:1395]<br>H2A histone family member X                            | 0.019108077 |
| ENSG00000103260 | METRN    | [Source:HGNC Symbol;Acc:HGNC:4739]<br>"meteorin, glial cell differentiation regulator        | 0.019120708 |
| ENSG00000166925 | TSC22D4  | [Source:HGNC Symbol;Acc:HGNC:14151]"<br>TSC22 domain family member 4                         | 0.01915234  |
| ENSG00000106266 | SNX8     | [Source:HGNC Symbol;Acc:HGNC:21696]<br>sorting nexin 8                                       | 0.01920241  |
| ENSG00000110400 | NECTIN1  | [Source:HGNC Symbol;Acc:HGNC:14972]<br>nectin cell adhesion molecule 1                       | 0.019236897 |
| ENSG00000088992 | TESC     | [Source:HGNC Symbol;Acc:HGNC:9706]<br>tescalcin                                              | 0.01926502  |
| ENSG00000126368 | NR1D1    | [Source:HGNC Symbol;Acc:HGNC:26065]<br>nuclear receptor subfamily 1 group D member 1         | 0.019687862 |
| ENSG00000103202 | NME4     | [Source:HGNC Symbol;Acc:HGNC:7962]<br>NME/NM23 nucleoside diphosphate kinase 4               | 0.019740714 |
| ENSG00000213626 | LBH      | [Source:HGNC Symbol;Acc:HGNC:7852]<br>limb bud and heart development                         | 0.019829586 |
| ENSG00000138629 | UBL7     | [Source:HGNC Symbol;Acc:HGNC:29532]<br>ubiquitin like 7                                      | 0.019900152 |
| ENSG00000254614 |          | [Source:HGNC Symbol;Acc:HGNC:28221]<br>ecretory carrier membrane protein 3                   | 0.019916102 |
| ENSG00000116521 | SCAMP3s  | [Source:HGNC Symbol;Acc:HGNC:10565]<br>tripartite motif containing 47                        | 0.019953714 |
| ENSG00000132481 | TRIM47   | [Source:HGNC Symbol;Acc:HGNC:19020]<br>lipolysis stimulated lipoprotein receptor             | 0.019989295 |
| ENSG00000105699 | LSR      | [Source:HGNC Symbol;Acc:HGNC:29572]<br>protein phosphatase 1 regulatory subunit 12C          | 0.019999965 |
| ENSG00000125503 | PPP1R12C | [Source:HGNC Symbol;Acc:HGNC:14947]<br>sphingomyelin phosphodiesterase 3                     | 0.020063533 |
| ENSG00000103056 | SMPD3    | [Source:HGNC Symbol;Acc:HGNC:14240]<br>ankyrin repeat domain 9                               | 0.020115844 |
| ENSG00000156381 | ANKRD9   | [Source:HGNC Symbol;Acc:HGNC:20096]<br>sialophorin                                           | 0.020225168 |
| ENSG00000197471 | SPN      | [Source:HGNC Symbol;Acc:HGNC:11249]<br>sialophorin                                           | 0.020225168 |
| ENSG00000197471 | SPN      | [Source:HGNC Symbol;Acc:HGNC:11249]<br>hydroxyacylglutathione hydrolase                      | 0.020225168 |
| ENSG00000063854 | HAGH     | [Source:HGNC Symbol;Acc:HGNC:4805]<br>sterile alpha motif domain containing 10               | 0.020247513 |
| ENSG00000130590 | SAMD10   | [Source:HGNC Symbol;Acc:HGNC:16129]<br>transmembrane and immunoglobulin domain containing 2  | 0.020258063 |
| ENSG00000167664 | TMIGD2   | [Source:HGNC Symbol;Acc:HGNC:28324]<br>ring finger protein 44                                | 0.020258063 |
| ENSG00000146083 | RNF44    | [Source:HGNC Symbol;Acc:HGNC:19180]<br>TAP binding protein                                   | 0.020327471 |
| ENSG00000231925 | TAPBP    | [Source:HGNC Symbol;Acc:HGNC:11566]<br>R3H domain containing 4                               | 0.020387859 |
| ENSG00000198858 | R3HDM4   | [Source:HGNC Symbol;Acc:HGNC:28270]<br>DnaJ heat shock protein family (Hsp40) member B2      | 0.020462672 |
| ENSG00000135924 | DNAJB2   | [Source:HGNC Symbol;Acc:HGNC:5228]<br>toll like receptor 9                                   | 0.020505106 |
| ENSG00000239732 | TLR9     | [Source:HGNC Symbol;Acc:HGNC:15633]<br>ribosomal protein S15                                 | 0.02065324  |
| ENSG00000115268 | RPS15    | [Source:HGNC Symbol;Acc:HGNC:10388]<br>ABI family member 3                                   | 0.020839375 |
| ENSG00000108798 | ABI3     | [Source:HGNC Symbol;Acc:HGNC:29859]<br>interferon regulatory factor 2 binding protein like   | 0.02085252  |
| ENSG00000119669 | IRF2BPL  | [Source:HGNC Symbol;Acc:HGNC:14282]<br>zinc finger DHHC-type containing 12                   | 0.02099734  |
| ENSG00000160446 | ZDHHC12  |                                                                                              |             |

|                 |          |                                                                                                         |             |
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| ENSG00000063169 | BICRA    | [Source:HGNC Symbol;Acc:HGNC:19159]<br>BRD4 interacting chromatin remodeling complex associated protein | 0.02150253  |
| ENSG00000141933 | TPGS1    | [Source:HGNC Symbol;Acc:HGNC:4332]<br>tubulin polyglutamylase complex subunit 1                         | 0.021525887 |
| ENSG00000088256 | GNA11    | [Source:HGNC Symbol;Acc:HGNC:25058]<br>G protein subunit alpha 11                                       | 0.021539966 |
| ENSG00000169583 | CLIC3    | [Source:HGNC Symbol;Acc:HGNC:4379]<br>chloride intracellular channel 3                                  | 0.021557835 |
| ENSG00000188511 | C22orf34 | [Source:HGNC Symbol;Acc:HGNC:2064]<br>chromosome 22 open reading frame 34                               | 0.021557835 |
| ENSG00000165406 | 8-Mar    | [Source:HGNC Symbol;Acc:HGNC:28010]<br>membrane associated ring-CH-type finger 8                        | 0.021557835 |
| ENSG00000173762 | CD7      | [Source:HGNC Symbol;Acc:HGNC:23356]<br>CD7 molecule                                                     | 0.021577416 |
| ENSG00000188322 | SBK1     | [Source:HGNC Symbol;Acc:HGNC:1695]<br>SH3 domain binding kinase 1                                       | 0.021879276 |
| ENSG00000204310 | AGPAT1   | [Source:HGNC Symbol;Acc:HGNC:17699]<br>1-acylglycerol-3-phosphate O-acyltransferase 1                   | 0.021879276 |
| ENSG00000167797 | CDK2AP2  | [Source:HGNC Symbol;Acc:HGNC:324]<br>cyclin dependent kinase 2 associated protein 2                     | 0.021879276 |
| ENSG00000142669 | SH3BGR13 | [Source:HGNC Symbol;Acc:HGNC:30833]<br>SH3 domain binding glutamate rich protein like 3                 | 0.021895705 |
| ENSG00000155034 | FBXL18   | [Source:HGNC Symbol;Acc:HGNC:15568]<br>F-box and leucine rich repeat protein 18                         | 0.022007819 |
| ENSG00000187840 | EIF4EBP1 | [Source:HGNC Symbol;Acc:HGNC:21874]<br>eukaryotic translation initiation factor 4E binding protein 1    | 0.022133956 |
| ENSG00000185187 | SIGIRR   | [Source:HGNC Symbol;Acc:HGNC:3288]<br>single Ig and TIR domain containing                               | 0.02227554  |
| ENSG00000158545 | ZC3H18   | [Source:HGNC Symbol;Acc:HGNC:30575]<br>zinc finger CCCH-type containing 18                              | 0.022615882 |
| ENSG00000184730 | APOBR    | [Source:HGNC Symbol;Acc:HGNC:25091]<br>polipoprotein B receptor                                         | 0.022649486 |
| ENSG00000204463 | BAG6     | [Source:HGNC Symbol;Acc:HGNC:24087]<br>BCL2 associated athanogene 6                                     | 0.022689972 |
| ENSG00000071242 | RPS6KA2  | [Source:HGNC Symbol;Acc:HGNC:13919]<br>ribosomal protein S6 kinase A2                                   | 0.022689972 |
| ENSG00000146701 | MDH2     | [Source:HGNC Symbol;Acc:HGNC:10431]<br>malate dehydrogenase 2                                           | 0.022776502 |
| ENSG00000180155 | LYNX1    | [Source:HGNC Symbol;Acc:HGNC:6971]<br>Ly6/neurotoxin 1                                                  | 0.02289018  |
| ENSG00000213563 | C8orf82  | [Source:HGNC Symbol;Acc:HGNC:29604]<br>chromosome 8 open reading frame 82                               | 0.02289018  |
| ENSG00000105281 | SLC1A5   | [Source:HGNC Symbol;Acc:HGNC:33826]<br>solute carrier family 1 member 5                                 | 0.023112388 |
| ENSG00000162882 | HAAO     | [Source:HGNC Symbol;Acc:HGNC:10943]<br>"3-hydroxyanthranilate 3,4-dioxygenase                           | 0.023356543 |
| ENSG00000181513 | ACBD4    | [Source:HGNC Symbol;Acc:HGNC:4796]<br>acyl-CoA binding domain containing 4                              | 0.02337834  |
| ENSG00000185730 | ZNF696   | [Source:HGNC Symbol;Acc:HGNC:23337]<br>zinc finger protein 696                                          | 0.02337834  |
| ENSG00000007520 | TSR3     | [Source:HGNC Symbol;Acc:HGNC:25872]<br>"TSR3, acp transferase ribosome maturation factor                | 0.02337834  |
| ENSG00000090006 | LTBP4    | [Source:HGNC Symbol;Acc:HGNC:14175]<br>latent transforming growth factor beta binding protein 4         | 0.023637109 |
| ENSG00000146535 | GNA12    | [Source:HGNC Symbol;Acc:HGNC:6717]<br>G protein subunit alpha 12                                        | 0.023637109 |
| ENSG00000141965 | FEM1A    | [Source:HGNC Symbol;Acc:HGNC:4380]<br>fem-1 homolog A                                                   | 0.023652058 |
| ENSG00000160957 | RECQL4   | [Source:HGNC Symbol;Acc:HGNC:16934]<br>RecQ like helicase 4                                             | 0.023707215 |
| ENSG00000135916 | ITM2C    | [Source:HGNC Symbol;Acc:HGNC:9949]<br>integral membrane protein 2C                                      | 0.023710452 |
| ENSG00000177732 | SOX12    | [Source:HGNC Symbol;Acc:HGNC:6175]<br>SRY-box 12                                                        | 0.023733416 |
| ENSG00000184508 | HDDC3    | [Source:HGNC Symbol;Acc:HGNC:11198]<br>HD domain containing 3                                           | 0.023733416 |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:30522]                                                                     | 0.023802652 |

|                 |          |                                                                  |             |
|-----------------|----------|------------------------------------------------------------------|-------------|
| ENSG00000175591 | P2RY2    | purinergic receptor P2Y2                                         |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:8541]                               | 0.023918507 |
| ENSG00000127903 | ZNF835   | zinc finger protein 835                                          |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:34332]                              | 0.023926586 |
| ENSG00000176022 | B3GALT6  | "beta-1,3-galactosyltransferase 6                                |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:17978]"                             | 0.023926586 |
| ENSG00000255319 | ENPP7P8  | ectonucleotide pyrophosphatase/phosphodiesterase                 |             |
|                 |          | 7 pseudogene 8                                                   |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:48691]                              | 0.02392953  |
| ENSG00000105479 | CCDC114  | coiled-coil domain containing 114                                |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:26560]                              | 0.02398767  |
| ENSG00000130529 | TRPM4    | transient receptor potential cation channel subfamily M member 4 |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:17993]                              | 0.024020687 |
| ENSG00000133250 | ZNF414   | zinc finger protein 414                                          |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:20630]                              | 0.024020687 |
| ENSG00000215908 | CROCCP2  | "ciliary rootlet coiled-coil, rootletin pseudogene 2             |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:28170]"                             | 0.024052859 |
| ENSG00000118046 | STK11    | serine/threonine kinase 11                                       |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:11389]                              | 0.024056107 |
| ENSG00000034152 | MAP2K3   | mitogen-activated protein kinase kinase 3                        |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:6843]                               | 0.024155164 |
| ENSG00000142453 | CARM1    | coactivator associated arginine methyltransferase 1              |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:23393]                              | 0.024155164 |
| ENSG00000256323 | NA       | NA                                                               | 0.024155164 |
| ENSG00000160094 | ZNF362   | zinc finger protein 362                                          |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:18079]                              | 0.024171066 |
| ENSG00000104884 | ERCC2    | "ERCC excision repair 2, TFIIH core complex helicase subunit     |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:3434]"                              | 0.024345083 |
| ENSG00000149257 | SERPINH1 | serpin family H member 1                                         |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:1546]                               | 0.024345083 |
| ENSG00000169635 | HIC2     | HIC ZBTB transcriptional repressor 2                             |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:18595]                              | 0.024354637 |
| ENSG00000143416 | SELENBP1 | selenium binding protein 1                                       |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:10719]                              | 0.024421599 |
| ENSG00000148411 | NACC2    | NACC family member 2                                             |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:23846]                              | 0.02443315  |
| ENSG00000085872 | CHERP    | calcium homeostasis endoplasmic reticulum protein                |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:16930]                              | 0.024463522 |
| ENSG00000176182 | MYPOP    | "Myb related transcription factor, partner of profiling          |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:20178]"                             | 0.024477311 |
| ENSG00000160113 | NR2F6    | nuclear receptor subfamily 2 group F member 6                    |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:7977]                               | 0.024505177 |
| ENSG00000108262 | GIT1     | GIT ArfGAP 1                                                     |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:4272]                               | 0.024614621 |
| ENSG00000161395 | PGAP3    | post-GPI attachment to proteins 3                                |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:23719]                              | 0.024705126 |
| ENSG00000142089 | IFITM3   | interferon induced transmembrane protein 3                       |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:5414]                               | 0.024765171 |
| ENSG00000070444 | MNT      | MAX network transcriptional repressor                            |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:7188]                               | 0.025148395 |
| ENSG00000112514 | CUTA     | cutA divalent cation tolerance homolog                           |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:21101]                              | 0.025148395 |
| ENSG00000167394 | ZNF668   | zinc finger protein 668                                          |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:25821]                              | 0.025148395 |
| ENSG00000167965 | MLST8    | "MTOR associated protein, LST8 homolog                           |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:24825]"                             | 0.025148395 |
| ENSG00000244187 | TMEM141  | transmembrane protein 141                                        |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:28211]                              | 0.025148395 |
| ENSG00000218175 |          |                                                                  | 0.02527518  |
| ENSG00000110063 | DCPS     | "decapping enzyme, scavenger                                     |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:29812]"                             | 0.025300524 |
| ENSG00000128805 | ARHGAP22 | Rho GTPase activating protein 22                                 |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:30320]                              | 0.025318552 |
| ENSG00000148400 | NOTCH1   | notch 1                                                          |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:7881]                               | 0.025506427 |
| ENSG00000186076 |          |                                                                  | 0.0257616   |
| ENSG00000167470 | MIDN     | midnolin                                                         |             |

|                 |           |                                                                                                        |             |
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| ENSG00000188305 | PEAK3     | [Source:HGNC Symbol;Acc:HGNC:16298]<br>PEAK family member 3                                            | 0.02580767  |
| ENSG00000181396 | OGFOD3    | [Source:HGNC Symbol;Acc:HGNC:24793]<br>2-oxoglutarate and iron dependent oxygenase domain containing 3 | 0.02580767  |
| ENSG00000240877 | RN7SL521P | [Source:HGNC Symbol;Acc:HGNC:26174]<br>"RNA, 7SL, cytoplasmic 521, pseudogene                          | 0.026198035 |
| ENSG00000130511 | SSBP4     | [Source:HGNC Symbol;Acc:HGNC:46537]"<br>single stranded DNA binding protein 4                          | 0.026492508 |
| ENSG00000063177 | RPL18     | [Source:HGNC Symbol;Acc:HGNC:15676]<br>ribosomal protein L18                                           | 0.026588317 |
| ENSG00000172663 | TMEM134   | [Source:HGNC Symbol;Acc:HGNC:10310]<br>transmembrane protein 134                                       | 0.026698079 |
| ENSG00000130706 | ADRM1     | [Source:HGNC Symbol;Acc:HGNC:26142]<br>adhesion regulating molecule 1                                  | 0.026698079 |
| ENSG00000214063 | TSPAN4    | [Source:HGNC Symbol;Acc:HGNC:15759]<br>tetraspanin 4                                                   | 0.026721536 |
| ENSG00000161677 | JOSD2     | [Source:HGNC Symbol;Acc:HGNC:11859]<br>Josephin domain containing 2                                    | 0.026759131 |
| ENSG00000189060 | H1FO      | [Source:HGNC Symbol;Acc:HGNC:28853]<br>H1 histone family member 0                                      | 0.026798474 |
| ENSG00000256811 |           | [Source:HGNC Symbol;Acc:HGNC:4714]<br>0.027109095                                                      | 0.027109095 |
| ENSG00000133317 | LGALS12   | galectin 12                                                                                            |             |
| ENSG00000012061 | ERCC1     | [Source:HGNC Symbol;Acc:HGNC:15788]<br>"ERCC excision repair 1, endonuclease non-catalytic subunit     | 0.027164347 |
| ENSG00000007376 | RPUSD1    | [Source:HGNC Symbol;Acc:HGNC:3433]"<br>RNA pseudouridylate synthase domain containing 1                | 0.027196959 |
| ENSG00000108175 | ZMIZ1     | [Source:HGNC Symbol;Acc:HGNC:14173]<br>zinc finger MIZ-type containing 1                               | 0.027275974 |
| ENSG00000132003 | ZSWIM4    | [Source:HGNC Symbol;Acc:HGNC:16493]<br>zinc finger SWIM-type containing 4                              | 0.027331142 |
| ENSG00000148296 | SURF6     | [Source:HGNC Symbol;Acc:HGNC:25704]<br>surfeit 6                                                       | 0.027331142 |
| ENSG00000186056 | MATN1-AS1 | [Source:HGNC Symbol;Acc:HGNC:11478]<br>MATN1 antisense RNA 1                                           | 0.027362837 |
| ENSG00000115649 | CNPPD1    | [Source:HGNC Symbol;Acc:HGNC:40364]<br>cyclin Pas1/PHO80 domain containing 1                           | 0.02742002  |
| ENSG00000065057 | NTHL1     | [Source:HGNC Symbol;Acc:HGNC:25220]<br>nth like DNA glycosylase 1                                      | 0.027574972 |
| ENSG00000272098 | NA        | [Source:HGNC Symbol;Acc:HGNC:8028]<br>NA                                                               | 0.027763734 |
| ENSG00000011009 | LYPLA2    | [Source:HGNC Symbol;Acc:HGNC:6738]<br>lysophospholipase II                                             | 0.027825114 |
| ENSG00000110025 | SNX15     | [Source:HGNC Symbol;Acc:HGNC:14978]<br>sorting nexin 15                                                | 0.028071412 |
| ENSG00000095321 | CRAT      | [Source:HGNC Symbol;Acc:HGNC:2342]<br>carnitine O-acetyltransferase                                    | 0.028074538 |
| ENSG00000108515 | ENO3      | [Source:HGNC Symbol;Acc:HGNC:3354]<br>enolase 3                                                        | 0.028133383 |
| ENSG00000123064 | DDX54     | [Source:HGNC Symbol;Acc:HGNC:20084]<br>DEAD-box helicase 54                                            | 0.028133383 |
| ENSG00000169564 | PCBP1     | [Source:HGNC Symbol;Acc:HGNC:8647]<br>poly(rC) binding protein 1                                       | 0.028358899 |
| ENSG00000171045 | TSNARE1   | [Source:HGNC Symbol;Acc:HGNC:26437]<br>t-SNARE domain containing 1                                     | 0.028645846 |
| ENSG00000225978 | HAR1A     | [Source:HGNC Symbol;Acc:HGNC:33117]<br>highly accelerated region 1A (non-protein coding)               | 0.028645846 |
| ENSG00000128283 | CDC42EP1  | [Source:HGNC Symbol;Acc:HGNC:17014]<br>CDC42 effector protein 1                                        | 0.028675863 |
| ENSG00000174282 | ZBTB4     | [Source:HGNC Symbol;Acc:HGNC:23847]<br>zinc finger and BTB domain containing 4                         | 0.028871519 |
| ENSG00000167685 | ZNF444    | [Source:HGNC Symbol;Acc:HGNC:16052]<br>zinc finger protein 444                                         | 0.028919683 |
| ENSG00000110104 | CCDC86    | [Source:HGNC Symbol;Acc:HGNC:28359]<br>coiled-coil domain containing 86                                | 0.028929404 |
| ENSG00000171703 | TCEA2     | transcription elongation factor A2                                                                     |             |

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| ENSG00000177600 | RPLP2     | [Source:HGNC Symbol;Acc:HGNC:11614]<br>ribosomal protein lateral stalk subunit P2                      | 0.029117009 |
| ENSG00000182095 | TNRC18    | [Source:HGNC Symbol;Acc:HGNC:10377]<br>trinucleotide repeat containing 18                              | 0.029298722 |
| ENSG00000167106 | FAM102A   | [Source:HGNC Symbol;Acc:HGNC:11962]<br>family with sequence similarity 102 member A                    | 0.029299181 |
| ENSG00000126458 | RRAS      | [Source:HGNC Symbol;Acc:HGNC:31419]<br>RAS related                                                     | 0.029415219 |
| ENSG00000105063 | PPP6R1    | [Source:HGNC Symbol;Acc:HGNC:10447]<br>protein phosphatase 6 regulatory subunit 1                      | 0.02952737  |
| ENSG00000125730 | C3        | [Source:HGNC Symbol;Acc:HGNC:29195]<br>complement C3                                                   | 0.02959944  |
| ENSG00000237973 | MTCO1P12  | [Source:HGNC Symbol;Acc:HGNC:1318]<br>mitochondrially encoded cytochrome c oxidase I pseudogene 12     | 0.029997906 |
| ENSG00000267412 |           | [Source:HGNC Symbol;Acc:HGNC:52014]                                                                    | 0.030144659 |
| ENSG00000185813 | PCYT2     | "phosphate cytidyltransferase 2, ethanolamine<br>[Source:HGNC Symbol;Acc:HGNC:8756]"                   | 0.030317293 |
| ENSG00000163462 | TRIM46    | tripartite motif containing 46<br>[Source:HGNC Symbol;Acc:HGNC:19019]                                  | 0.030614393 |
| ENSG00000157933 | SKI       | SKI proto-oncogene<br>[Source:HGNC Symbol;Acc:HGNC:10896]                                              | 0.030701411 |
| ENSG00000161091 | MFSD12    | major facilitator superfamily domain containing 12<br>[Source:HGNC Symbol;Acc:HGNC:28299]              | 0.030704292 |
| ENSG00000185163 | DDX51     | DEAD-box helicase 51<br>[Source:HGNC Symbol;Acc:HGNC:20082]                                            | 0.030735268 |
| ENSG00000171813 | PWWP2B    | PWWP domain containing 2B<br>[Source:HGNC Symbol;Acc:HGNC:25150]                                       | 0.030810478 |
| ENSG00000137267 | TUBB2A    | tubulin beta 2A class IIa<br>[Source:HGNC Symbol;Acc:HGNC:12412]                                       | 0.030847037 |
| ENSG00000188747 | NOXA1     | NADPH oxidase activator 1<br>[Source:HGNC Symbol;Acc:HGNC:10668]                                       | 0.030853611 |
| ENSG00000108557 | RAI1      | retinoic acid induced 1<br>[Source:HGNC Symbol;Acc:HGNC:9834]                                          | 0.030977697 |
| ENSG00000137166 | FOXP4     | forkhead box P4<br>[Source:HGNC Symbol;Acc:HGNC:20842]                                                 | 0.030977697 |
| ENSG00000204420 | MPIG6B    | megakaryocyte and platelet inhibitory receptor G6b<br>[Source:HGNC Symbol;Acc:HGNC:13937]              | 0.031369168 |
| ENSG00000133265 | HSPBP1    | HSPA (Hsp70) binding protein 1<br>[Source:HGNC Symbol;Acc:HGNC:24989]                                  | 0.031442624 |
| ENSG00000008710 | PKD1      | "polycystin 1, transient receptor potential channel interacting<br>[Source:HGNC Symbol;Acc:HGNC:9008]" | 0.031566582 |
| ENSG00000099624 | ATP5F1D   | ATP synthase F1 subunit delta<br>[Source:HGNC Symbol;Acc:HGNC:837]                                     | 0.031657927 |
| ENSG00000108819 | PPP1R9B   | protein phosphatase 1 regulatory subunit 9B<br>[Source:HGNC Symbol;Acc:HGNC:9298]                      | 0.031695534 |
| ENSG00000158292 | GPR153    | G protein-coupled receptor 153<br>[Source:HGNC Symbol;Acc:HGNC:23618]                                  | 0.031750316 |
| ENSG00000130382 | MLLT1     | "MLLT1, super elongation complex subunit<br>[Source:HGNC Symbol;Acc:HGNC:7134]"                        | 0.031828022 |
| ENSG00000269352 | PTOV1-AS2 | PTOV1 antisense RNA 2<br>[Source:HGNC Symbol;Acc:HGNC:51284]                                           | 0.031850457 |
| ENSG00000162585 | FAAP20    | Fanconi anemia core complex associated protein 20<br>[Source:HGNC Symbol;Acc:HGNC:26428]               | 0.0320507   |
| ENSG00000157240 | FZD1      | frizzled class receptor 1<br>[Source:HGNC Symbol;Acc:HGNC:4038]                                        | 0.032151732 |
| ENSG00000135736 | CCDC102A  | coiled-coil domain containing 102A<br>[Source:HGNC Symbol;Acc:HGNC:28097]                              | 0.032302006 |
| ENSG00000020181 | ADGRA2    | adhesion G protein-coupled receptor A2<br>[Source:HGNC Symbol;Acc:HGNC:17849]                          | 0.032424937 |
| ENSG00000198546 | ZNF511    | zinc finger protein 511<br>[Source:HGNC Symbol;Acc:HGNC:28445]                                         | 0.032576231 |
| ENSG00000123144 | TRIR      | telomerase RNA component interacting RNase<br>[Source:HGNC Symbol;Acc:HGNC:28424]                      | 0.032671184 |
| ENSG00000156860 | FBRS      | fibrosin<br>[Source:HGNC Symbol;Acc:HGNC:20442]                                                        | 0.032671184 |
| ENSG00000162910 | MRPL55    | mitochondrial ribosomal protein L55                                                                    |             |

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| ENSG00000130731 | METTL26     | [Source:HGNC Symbol;Acc:HGNC:16686]<br>methyltransferase like 26                                          | 0.032697662 |
| ENSG00000101986 | ABCD1       | [Source:HGNC Symbol;Acc:HGNC:14141]<br>ATP binding cassette subfamily D member 1                          | 0.032833764 |
| ENSG00000020633 | RUNX3       | [Source:HGNC Symbol;Acc:HGNC:61]<br>runt related transcription factor 3                                   | 0.032886018 |
| ENSG00000184640 | 9-Sep       | [Source:HGNC Symbol;Acc:HGNC:10473]<br>septin 9                                                           | 0.033016587 |
| ENSG00000260521 | NA          | [Source:HGNC Symbol;Acc:HGNC:7323]<br>NA                                                                  | 0.033101928 |
| ENSG00000125787 | GNRH2       | gonadotropin releasing hormone 2                                                                          | 0.033101928 |
| ENSG00000229391 | HLA-DRB6    | [Source:HGNC Symbol;Acc:HGNC:4420]<br>"major histocompatibility complex, class II, DR beta 6 (pseudogene) | 0.033349502 |
| ENSG00000160223 | ICOSLG      | [Source:HGNC Symbol;Acc:HGNC:4954]"<br>inducible T cell costimulator ligand                               | 0.033349502 |
| ENSG00000105204 | DYRK1B      | [Source:HGNC Symbol;Acc:HGNC:17087]<br>dual specificity tyrosine phosphorylation regulated kinase 1B      | 0.033394348 |
| ENSG00000142173 | COL6A2      | [Source:HGNC Symbol;Acc:HGNC:3092]<br>collagen type VI alpha 2 chain                                      | 0.033465567 |
| ENSG00000169710 | FASN        | [Source:HGNC Symbol;Acc:HGNC:2212]<br>fatty acid synthase                                                 | 0.033483825 |
| ENSG00000176533 | GNG7        | [Source:HGNC Symbol;Acc:HGNC:3594]<br>G protein subunit gamma 7                                           | 0.033483825 |
| ENSG00000179253 |             | [Source:HGNC Symbol;Acc:HGNC:4410]<br>pseudouridylate synthase-like 1                                     | 0.033483825 |
| ENSG00000169972 | PUSL1       | [Source:HGNC Symbol;Acc:HGNC:26914]<br>G protein signaling modulator 1                                    | 0.033509544 |
| ENSG00000160360 | GPSM1       | [Source:HGNC Symbol;Acc:HGNC:17858]<br>chromosome 9 open reading frame 16                                 | 0.033771567 |
| ENSG00000171159 | C9orf16     | [Source:HGNC Symbol;Acc:HGNC:17823]<br>myosin light chain 5                                               | 0.033853634 |
| ENSG00000215375 | MYL5        | [Source:HGNC Symbol;Acc:HGNC:7586]<br>NSF attachment protein alpha                                        | 0.033853634 |
| ENSG00000105402 | NAPA        | [Source:HGNC Symbol;Acc:HGNC:7641]<br>C-type lectin domain containing 16A                                 | 0.034044441 |
| ENSG00000038532 | CLEC16A     | [Source:HGNC Symbol;Acc:HGNC:29013]<br>MID1 interacting protein 1                                         | 0.034108157 |
| ENSG00000165175 | MID1IP1     | [Source:HGNC Symbol;Acc:HGNC:20715]<br>erythrocyte membrane protein band 4.2                              | 0.03418982  |
| ENSG00000166947 | EPB42       | [Source:HGNC Symbol;Acc:HGNC:3381]<br>THAP domain containing 11                                           | 0.03418982  |
| ENSG00000168286 | THAP11      | [Source:HGNC Symbol;Acc:HGNC:23194]<br>receptor accessory protein 4                                       | 0.03418982  |
| ENSG00000168476 | REEP4       | [Source:HGNC Symbol;Acc:HGNC:26176]<br>"HPS1, biogenesis of lysosomal organelles complex 3 subunit 1      | 0.034591261 |
| ENSG00000107521 | HPS1        | [Source:HGNC Symbol;Acc:HGNC:5163]"<br>calcineurin binding protein 1                                      | 0.034688533 |
| ENSG00000267436 |             | [Source:HGNC Symbol;Acc:HGNC:24187]<br>dihydrouridine synthase 1 like                                     | 0.034821851 |
| ENSG00000099991 | CABIN1      | [Source:HGNC Symbol;Acc:HGNC:30086]<br>fizzy and cell division cycle 20 related 1                         | 0.034858474 |
| ENSG00000169718 | DUS1L       | [Source:HGNC Symbol;Acc:HGNC:24824]<br>TBC1 domain family member 16                                       | 0.034980702 |
| ENSG00000105325 | FZR1        | [Source:HGNC Symbol;Acc:HGNC:28356]<br>carbohydrate sulfotransferase 2                                    | 0.035034499 |
| ENSG00000167291 | TBC1D16     | [Source:HGNC Symbol;Acc:HGNC:1970]<br>CCDC183 antisense RNA 1                                             | 0.035082388 |
| ENSG00000213399 | CHST2       | [Source:HGNC Symbol;Acc:HGNC:44105]<br>eukaryotic translation elongation factor 2                         | 0.035085538 |
| ENSG00000175040 | CCDC183-AS1 | [Source:HGNC Symbol;Acc:HGNC:3214]<br>yippee like 3                                                       | 0.035106231 |
| ENSG00000228544 | EEF2        | [Source:HGNC Symbol;Acc:HGNC:18327]<br>carnosine synthase 1                                               | 0.035154264 |
| ENSG00000167658 | EEF2        | [Source:HGNC Symbol;Acc:HGNC:29268]<br>carosine synthase 1                                                | 0.03521308  |
| ENSG00000090238 | YPEL3       |                                                                                                           | 0.035223199 |
| ENSG00000172508 | CARNS1      |                                                                                                           | 0.03555645  |

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| ENSG00000173272 | MZT2A    | mitotic spindle organizing protein 2A<br>[Source:HGNC Symbol;Acc:HGNC:33187]                          | 0.035664739 |
| ENSG00000141522 | ARHGDIA  | Rho GDP dissociation inhibitor alpha<br>[Source:HGNC Symbol;Acc:HGNC:678]                             | 0.03575577  |
| ENSG00000149541 | B3GAT3   | "beta-1,3-glucuronyltransferase 3<br>[Source:HGNC Symbol;Acc:HGNC:923]"                               | 0.03575577  |
| ENSG00000171206 | TRIM8    | tripartite motif containing 8<br>[Source:HGNC Symbol;Acc:HGNC:15579]                                  | 0.035790036 |
| ENSG00000027869 | SH2D2A   | SH2 domain containing 2A<br>[Source:HGNC Symbol;Acc:HGNC:10821]                                       | 0.035871776 |
| ENSG00000149823 | VPS51    | "VPS51, GARP complex subunit<br>[Source:HGNC Symbol;Acc:HGNC:1172]"                                   | 0.035906645 |
| ENSG00000196355 | NA       | NA                                                                                                    | 0.035938935 |
| ENSG00000165804 | ZNF219   | zinc finger protein 219<br>[Source:HGNC Symbol;Acc:HGNC:13011]                                        | 0.035996581 |
| ENSG00000177542 | SLC25A22 | solute carrier family 25 member 22<br>[Source:HGNC Symbol;Acc:HGNC:19954]                             | 0.035996581 |
| ENSG00000130202 | NECTIN2  | nectin cell adhesion molecule 2<br>[Source:HGNC Symbol;Acc:HGNC:9707]                                 | 0.036025366 |
| ENSG00000006638 | TBXA2R   | thromboxane A2 receptor<br>[Source:HGNC Symbol;Acc:HGNC:11608]                                        | 0.036065767 |
| ENSG00000025770 | NCAPH2   | non-SMC condensin II complex subunit H2<br>[Source:HGNC Symbol;Acc:HGNC:25071]                        | 0.036065767 |
| ENSG00000100316 | RPL3     | ribosomal protein L3<br>[Source:HGNC Symbol;Acc:HGNC:10332]                                           | 0.036065767 |
| ENSG00000110665 | C11orf21 | chromosome 11 open reading frame 21<br>[Source:HGNC Symbol;Acc:HGNC:13231]                            | 0.036065767 |
| ENSG00000160445 | ZER1     | zyg-11 related cell cycle regulator<br>[Source:HGNC Symbol;Acc:HGNC:30960]                            | 0.036065767 |
| ENSG00000173786 | CNP      | "2',3'-cyclic nucleotide 3' phosphodiesterase<br>[Source:HGNC Symbol;Acc:HGNC:2158]"                  | 0.036065767 |
| ENSG00000229368 |          |                                                                                                       | 0.036065767 |
| ENSG00000160789 | LMNA     | lamin A/C<br>[Source:HGNC Symbol;Acc:HGNC:6636]                                                       | 0.036188381 |
| ENSG00000166189 | HPS6     | "HPS6, biogenesis of lysosomal organelles complex 2 subunit 3<br>[Source:HGNC Symbol;Acc:HGNC:18817]" | 0.036188381 |
| ENSG00000261226 |          |                                                                                                       | 0.036342968 |
| ENSG00000185049 | NELFA    | negative elongation factor complex member A<br>[Source:HGNC Symbol;Acc:HGNC:12768]                    | 0.036383164 |
| ENSG00000005882 | PDK2     | pyruvate dehydrogenase kinase 2<br>[Source:HGNC Symbol;Acc:HGNC:8810]                                 | 0.036423123 |
| ENSG00000163050 | COQ8A    | coenzyme Q8A<br>[Source:HGNC Symbol;Acc:HGNC:16812]                                                   | 0.036459828 |
| ENSG00000060138 | YBX3     | Y-box binding protein 3<br>[Source:HGNC Symbol;Acc:HGNC:2428]                                         | 0.03651176  |
| ENSG00000122971 | ACADS    | acyl-CoA dehydrogenase short chain<br>[Source:HGNC Symbol;Acc:HGNC:90]                                | 0.036511776 |
| ENSG00000205927 | OLIG2    | oligodendrocyte transcription factor 2<br>[Source:HGNC Symbol;Acc:HGNC:9398]                          | 0.036582868 |
| ENSG00000092096 | SLC22A17 | solute carrier family 22 member 17<br>[Source:HGNC Symbol;Acc:HGNC:23095]                             | 0.036619295 |
| ENSG00000090554 | FLT3LG   | fms related tyrosine kinase 3 ligand<br>[Source:HGNC Symbol;Acc:HGNC:3766]                            | 0.036780281 |
| ENSG00000078902 | TOLLIP   | toll interacting protein<br>[Source:HGNC Symbol;Acc:HGNC:16476]                                       | 0.036796695 |
| ENSG00000136802 | LRRC8A   | leucine rich repeat containing 8 VRAC subunit A<br>[Source:HGNC Symbol;Acc:HGNC:19027]                | 0.036860551 |
| ENSG00000236976 |          |                                                                                                       | 0.036972133 |
| ENSG00000100908 | EMC9     | ER membrane protein complex subunit 9<br>[Source:HGNC Symbol;Acc:HGNC:20273]                          | 0.037054085 |
| ENSG00000105364 | MRPL4    | mitochondrial ribosomal protein L4<br>[Source:HGNC Symbol;Acc:HGNC:14276]                             | 0.03712252  |
| ENSG00000157184 | CPT2     | carnitine palmitoyltransferase 2<br>[Source:HGNC Symbol;Acc:HGNC:2330]                                | 0.03712252  |

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| ENSG00000168056 | LTBP3     | latent transforming growth factor beta binding protein 3<br>[Source:HGNC Symbol;Acc:HGNC:6716]              | 0.037135417 |
| ENSG00000196313 | POM121    | POM121 transmembrane nucleoporin<br>[Source:HGNC Symbol;Acc:HGNC:19702]                                     | 0.037140956 |
| ENSG00000170604 | IRF2BP1   | interferon regulatory factor 2 binding protein 1<br>[Source:HGNC Symbol;Acc:HGNC:21728]                     | 0.037222007 |
| ENSG00000110697 | PITPNM1   | phosphatidylinositol transfer protein membrane associated 1<br>[Source:HGNC Symbol;Acc:HGNC:9003]           | 0.037374978 |
| ENSG00000100348 | TXN2      | thioredoxin 2<br>[Source:HGNC Symbol;Acc:HGNC:17772]                                                        | 0.037546969 |
| ENSG00000102007 | PLP2      | proteolipid protein 2<br>[Source:HGNC Symbol;Acc:HGNC:9087]                                                 | 0.037630556 |
| ENSG00000132005 | RFX1      | regulatory factor X1<br>[Source:HGNC Symbol;Acc:HGNC:9982]                                                  | 0.037671165 |
| ENSG00000141499 | WRAP53    | WD repeat containing antisense to TP53<br>[Source:HGNC Symbol;Acc:HGNC:25522]                               | 0.037678229 |
| ENSG00000189114 | BLOC1S3   | biogenesis of lysosomal organelles complex 1 subunit 3<br>[Source:HGNC Symbol;Acc:HGNC:20914]               | 0.037963219 |
| ENSG00000123154 | WDR83     | WD repeat domain 83<br>[Source:HGNC Symbol;Acc:HGNC:32672]                                                  | 0.038059131 |
| ENSG00000127663 | KDM4B     | lysine demethylase 4B<br>[Source:HGNC Symbol;Acc:HGNC:29136]                                                | 0.038059131 |
| ENSG00000175274 | TP53I11   | tumor protein p53 inducible protein 11<br>[Source:HGNC Symbol;Acc:HGNC:16842]                               | 0.038059131 |
| ENSG00000249115 | HAUS5     | HAUS augmin like complex subunit 5<br>[Source:HGNC Symbol;Acc:HGNC:29130]                                   | 0.038059131 |
| ENSG00000130764 | LRRC47    | leucine rich repeat containing 47<br>[Source:HGNC Symbol;Acc:HGNC:29207]                                    | 0.038286929 |
| ENSG00000176946 | THAP4     | THAP domain containing 4<br>[Source:HGNC Symbol;Acc:HGNC:23187]                                             | 0.038286929 |
| ENSG00000137497 | NUMA1     | nuclear mitotic apparatus protein 1<br>[Source:HGNC Symbol;Acc:HGNC:8059]                                   | 0.038678067 |
| ENSG00000143761 | ARF1      | ADP ribosylation factor 1<br>[Source:HGNC Symbol;Acc:HGNC:652]                                              | 0.038678067 |
| ENSG00000198931 | APRT      | adenine phosphoribosyltransferase<br>[Source:HGNC Symbol;Acc:HGNC:626]                                      | 0.038678067 |
| ENSG00000186174 | BCL9L     | B cell CLL/lymphoma 9 like<br>[Source:HGNC Symbol;Acc:HGNC:23688]                                           | 0.039375488 |
| ENSG00000104894 | CD37      | CD37 molecule<br>[Source:HGNC Symbol;Acc:HGNC:1666]                                                         | 0.039523734 |
| ENSG00000235314 | LINC00957 | long intergenic non-protein coding RNA 957<br>[Source:HGNC Symbol;Acc:HGNC:22332]                           | 0.039534059 |
| ENSG00000076864 | RAP1GAP   | RAP1 GTPase activating protein<br>[Source:HGNC Symbol;Acc:HGNC:9858]                                        | 0.039534171 |
| ENSG00000179348 | GATA2     | GATA binding protein 2<br>[Source:HGNC Symbol;Acc:HGNC:4171]                                                | 0.039644975 |
| ENSG00000223496 | EXOSC6    | exosome component 6<br>[Source:HGNC Symbol;Acc:HGNC:19055]                                                  | 0.039646513 |
| ENSG00000174004 | NRROS     | negative regulator of reactive oxygen species<br>[Source:HGNC Symbol;Acc:HGNC:24613]                        | 0.039697731 |
| ENSG00000185736 | ADARB2    | "adenosine deaminase, RNA specific B2 (inactive)<br>[Source:HGNC Symbol;Acc:HGNC:227]"                      | 0.039813584 |
| ENSG00000177595 | PIDD1     | p53-induced death domain protein 1<br>[Source:HGNC Symbol;Acc:HGNC:16491]                                   | 0.039841437 |
| ENSG00000114767 | RRP9      | "ribosomal RNA processing 9, U3 small nucleolar RNA binding protein<br>[Source:HGNC Symbol;Acc:HGNC:16829]" | 0.039852243 |
| ENSG00000198336 | MYL4      | myosin light chain 4<br>[Source:HGNC Symbol;Acc:HGNC:7585]                                                  | 0.040061329 |
| ENSG00000267427 | NA        | NA                                                                                                          | 0.040061329 |
| ENSG00000123159 | GIPC1     | GIPC PDZ domain containing family member 1<br>[Source:HGNC Symbol;Acc:HGNC:1226]                            | 0.040207239 |
| ENSG00000139405 | RITA1     | RBPJ interacting and tubulin associated 1<br>[Source:HGNC Symbol;Acc:HGNC:25925]                            | 0.040571361 |
| ENSG00000149929 | HIRIP3    | HIRA interacting protein 3<br>[Source:HGNC Symbol;Acc:HGNC:4917]                                            | 0.040590193 |
| ENSG00000198517 | MAFK      | MAF bZIP transcription factor K<br>[Source:HGNC Symbol;Acc:HGNC:6782]                                       | 0.040590193 |

|                 |          |                                                              |             |
|-----------------|----------|--------------------------------------------------------------|-------------|
| ENSG00000164897 | TMUB1    | transmembrane and ubiquitin like domain containing 1         |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:21709]                          | 0.040938395 |
| ENSG00000070047 | PHRF1    | PHD and ring finger domains 1                                |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:24351]                          | 0.041015111 |
| ENSG00000100403 | ZC3H7B   | zinc finger CCCH-type containing 7B                          |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:30869]                          | 0.041151359 |
| ENSG00000205147 | NA       | NA                                                           | 0.041207854 |
| ENSG00000184470 | TXNRD2   | thioredoxin reductase 2                                      |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:18155]                          | 0.04134465  |
| ENSG00000103145 | HCFC1R1  | host cell factor C1 regulator 1                              |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:21198]                          | 0.041366672 |
| ENSG00000087086 | FTL      | ferritin light chain                                         |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:3999]                           | 0.041631474 |
| ENSG00000102870 | ZNF629   | zinc finger protein 629                                      |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:29008]                          | 0.041631474 |
| ENSG00000181444 | ZNF467   | zinc finger protein 467                                      |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:23154]                          | 0.041868067 |
| ENSG00000142444 | TIMM29   | translocase of inner mitochondrial membrane 29               |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:25152]                          | 0.041933219 |
| ENSG00000204252 | HLA-DOA  | "major histocompatibility complex, class II, DO alpha        |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:4936]"                          | 0.041944166 |
| ENSG00000224051 | CPTP     | ceramide-1-phosphate transfer protein                        |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:28116]                          | 0.041944166 |
| ENSG00000103253 | HAGHL    | hydroxyacylglutathione hydrolase like                        |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:14177]                          | 0.042027801 |
| ENSG00000011590 | ZBTB32   | zinc finger and BTB domain containing 32                     |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:16763]                          | 0.042101327 |
| ENSG00000182566 | CLEC4G   | C-type lectin domain family 4 member G                       |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:24591]                          | 0.042114834 |
| ENSG00000244165 | P2RY11   | purinergic receptor P2Y11                                    |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:8540]                           | 0.042114834 |
| ENSG00000267275 |          |                                                              | 0.042114834 |
| ENSG00000173327 | MAP3K11  | mitogen-activated protein kinase kinase kinase 11            |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:6850]                           | 0.042395519 |
| ENSG00000149418 | ST14     | suppression of tumorigenicity 14                             |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:11344]                          | 0.04243773  |
| ENSG00000112658 | SRF      | serum response factor                                        |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:11291]                          | 0.042440717 |
| ENSG00000106003 | LFNG     | LFNG O-fucosylpeptide 3-beta-N-acetylglucosaminyltransferase |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:6560]                           | 0.042450091 |
| ENSG00000164896 | FASTK    | Fas activated serine/threonine kinase                        |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:24676]                          | 0.042450091 |
| ENSG00000196544 | BORCS6   | BLOC-1 related complex subunit 6                             |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:25939]                          | 0.042514351 |
| ENSG00000134107 | BHLHE40  | basic helix-loop-helix family member e40                     |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:1046]                           | 0.042517218 |
| ENSG00000151176 | PLBD2    | phospholipase B domain containing 2                          |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:27283]                          | 0.042582368 |
| ENSG00000183397 | C19orf71 | chromosome 19 open reading frame 71                          |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:34496]                          | 0.042902315 |
| ENSG00000105738 | SIPA1L3  | signal induced proliferation associated 1 like 3             |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:23801]                          | 0.043052047 |
| ENSG00000157353 | FUK      | fucokinase                                                   |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:29500]                          | 0.043381308 |
| ENSG00000126062 | TMEM115  | transmembrane protein 115                                    |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:30055]                          | 0.043382452 |
| ENSG00000179632 | MAF1     | "MAF1 homolog, negative regulator of RNA polymerase III      |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:24966]"                         | 0.043386409 |
| ENSG00000254910 |          |                                                              | 0.043544967 |
| ENSG00000073111 | MCM2     | minichromosome maintenance complex component 2               |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:6944]                           | 0.043556269 |
| ENSG00000105698 | USF2     | "upstream transcription factor 2, c-fos interacting          |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:12594]"                         | 0.043737282 |
| ENSG00000261043 |          |                                                              | 0.043870446 |
| ENSG00000078808 | SDF4     | stromal cell derived factor 4                                |             |
|                 |          | [Source:HGNC Symbol;Acc:HGNC:24188]                          | 0.043914575 |
| ENSG00000182154 | MRPL41   | mitochondrial ribosomal protein L41                          |             |

|                 |           |                                                                                                         |             |
|-----------------|-----------|---------------------------------------------------------------------------------------------------------|-------------|
| ENSG00000237476 | LINC01637 | [Source:HGNC Symbol;Acc:HGNC:14492]<br>long intergenic non-protein coding RNA 1637                      | 0.044022575 |
| ENSG00000264577 |           | [Source:HGNC Symbol;Acc:HGNC:52424]                                                                     | 0.044022575 |
| ENSG00000160877 | NACC1     | nucleus accumbens associated 1                                                                          | 0.044022575 |
| ENSG00000162032 | SPSB3     | [Source:HGNC Symbol;Acc:HGNC:20967]<br>splA/ryanodine receptor domain and SOCS box containing 3         | 0.044046233 |
| ENSG00000123933 | MXD4      | [Source:HGNC Symbol;Acc:HGNC:30629]<br>MAX dimerization protein 4                                       | 0.044046233 |
| ENSG00000149260 | CAPN5     | [Source:HGNC Symbol;Acc:HGNC:13906]<br>calpain 5                                                        | 0.044146857 |
| ENSG00000197324 | LRP10     | [Source:HGNC Symbol;Acc:HGNC:1482]<br>LDL receptor related protein 10                                   | 0.044146857 |
| ENSG00000128011 | LRFN1     | [Source:HGNC Symbol;Acc:HGNC:14553]<br>leucine rich repeat and fibronectin type III domain containing 1 | 0.044146857 |
| ENSG00000103126 | AXIN1     | [Source:HGNC Symbol;Acc:HGNC:29290]<br>axin 1                                                           | 0.044424476 |
| ENSG00000183134 | PTGDR2    | [Source:HGNC Symbol;Acc:HGNC:903]<br>prostaglandin D2 receptor 2                                        | 0.044490553 |
| ENSG00000185905 | C16orf54  | [Source:HGNC Symbol;Acc:HGNC:4502]<br>chromosome 16 open reading frame 54                               | 0.044490553 |
| ENSG00000185905 | C16orf54  | [Source:HGNC Symbol;Acc:HGNC:26649]<br>chromosome 16 open reading frame 54                              | 0.044574634 |
| ENSG00000176974 | SHMT1     | [Source:HGNC Symbol;Acc:HGNC:26649]<br>serine hydroxymethyltransferase 1                                | 0.044574634 |
| ENSG00000105327 | BBC3      | [Source:HGNC Symbol;Acc:HGNC:10850]<br>BCL2 binding component 3                                         | 0.044717969 |
| ENSG00000212123 | PRR22     | [Source:HGNC Symbol;Acc:HGNC:17868]<br>proline rich 22                                                  | 0.044899327 |
| ENSG00000171798 | KNDC1     | [Source:HGNC Symbol;Acc:HGNC:28354]<br>kinase non-catalytic C-lobe domain containing 1                  | 0.044899327 |
| ENSG00000073150 | PANX2     | [Source:HGNC Symbol;Acc:HGNC:29374]<br>pannexin 2                                                       | 0.045139854 |
| ENSG00000126453 | BCL2L12   | [Source:HGNC Symbol;Acc:HGNC:8600]<br>BCL2 like 12                                                      | 0.045237232 |
| ENSG00000159692 | CTBP1     | [Source:HGNC Symbol;Acc:HGNC:13787]<br>C-terminal binding protein 1                                     | 0.04527356  |
| ENSG00000105248 | CCDC94    | [Source:HGNC Symbol;Acc:HGNC:2494]<br>coiled-coil domain containing 94                                  | 0.04527356  |
| ENSG00000101220 | C20orf27  | [Source:HGNC Symbol;Acc:HGNC:25518]<br>chromosome 20 open reading frame 27                              | 0.045450088 |
| ENSG00000188735 | TMEM120B  | [Source:HGNC Symbol;Acc:HGNC:15873]<br>transmembrane protein 120B                                       | 0.045474144 |
| ENSG00000149476 | TKFC      | [Source:HGNC Symbol;Acc:HGNC:32008]<br>triokinase and FMN cyclase                                       | 0.045474144 |
| ENSG00000100105 | PATZ1     | [Source:HGNC Symbol;Acc:HGNC:24552]<br>POZ/BTB and AT hook containing zinc finger 1                     | 0.045497488 |
| ENSG00000136295 | TTYH3     | [Source:HGNC Symbol;Acc:HGNC:13071]<br>tweety family member 3                                           | 0.045500961 |
| ENSG00000104823 | ECH1      | [Source:HGNC Symbol;Acc:HGNC:22222]<br>enoyl-CoA hydratase 1                                            | 0.045528908 |
| ENSG00000167930 | FAM234A   | [Source:HGNC Symbol;Acc:HGNC:3149]<br>family with sequence similarity 234 member A                      | 0.045555559 |
| ENSG00000125505 | MBOAT7    | [Source:HGNC Symbol;Acc:HGNC:14163]<br>membrane bound O-acyltransferase domain containing 7             | 0.045584551 |
| ENSG00000136720 | HS6ST1    | [Source:HGNC Symbol;Acc:HGNC:15505]<br>heparan sulfate 6-O-sulfotransferase 1                           | 0.045601783 |
| ENSG00000156853 | ZNF689    | [Source:HGNC Symbol;Acc:HGNC:5201]<br>zinc finger protein 689                                           | 0.045601783 |
| ENSG00000176108 | CHMP6     | [Source:HGNC Symbol;Acc:HGNC:25173]<br>charged multivesicular body protein 6                            | 0.045601783 |
| ENSG00000205336 | ADGRG1    | [Source:HGNC Symbol;Acc:HGNC:25675]<br>adhesion G protein-coupled receptor G1                           | 0.045601783 |
| ENSG00000186350 | RXRA      | [Source:HGNC Symbol;Acc:HGNC:4512]<br>retinoid X receptor alpha                                         | 0.045601783 |
| ENSG00000164849 | GPR146    | [Source:HGNC Symbol;Acc:HGNC:10477]<br>G protein-coupled receptor 146                                   | 0.045691236 |
| ENSG00000124313 | IQSEC2    | [Source:HGNC Symbol;Acc:HGNC:21718]<br>IQ motif and Sec7 domain 2                                       | 0.045781    |

|                 |              |                                                                                                        |             |
|-----------------|--------------|--------------------------------------------------------------------------------------------------------|-------------|
| ENSG00000148341 | SH3GLB2      | [Source:HGNC Symbol;Acc:HGNC:29059]<br>"SH3 domain containing GRB2 like, endophilin B2"                | 0.045921742 |
| ENSG00000213654 | GPSM3        | [Source:HGNC Symbol;Acc:HGNC:10834]"<br>G protein signaling modulator 3                                | 0.045931004 |
| ENSG00000171219 | CDC42BPG     | [Source:HGNC Symbol;Acc:HGNC:13945]<br>CDC42 binding protein kinase gamma                              | 0.045963746 |
| ENSG00000125741 | OPA3         | [Source:HGNC Symbol;Acc:HGNC:29829]<br>"OPA3, outer mitochondrial membrane lipid metabolism regulator" | 0.046017697 |
| ENSG00000089693 | MLF2         | [Source:HGNC Symbol;Acc:HGNC:8142]"<br>myeloid leukemia factor 2                                       | 0.046210538 |
| ENSG00000267283 |              | [Source:HGNC Symbol;Acc:HGNC:7126]                                                                     | 0.046269835 |
| ENSG00000238164 | TNFRSF14-AS1 | 0.046536749<br>TNFRSF14 antisense RNA 1                                                                |             |
| ENSG00000167815 | PRDX2        | [Source:HGNC Symbol;Acc:HGNC:26966]<br>peroxiredoxin 2                                                 | 0.046584081 |
| ENSG00000140564 | FURIN        | [Source:HGNC Symbol;Acc:HGNC:9353]<br>"furin, paired basic amino acid cleaving enzyme"                 | 0.046640005 |
| ENSG00000059122 | FLYWCH1      | [Source:HGNC Symbol;Acc:HGNC:8568]"<br>FLYWCH-type zinc finger 1                                       | 0.046653045 |
| ENSG00000070423 | RNF126       | [Source:HGNC Symbol;Acc:HGNC:25404]<br>ring finger protein 126                                         | 0.046934685 |
| ENSG00000027847 | B4GALT7      | [Source:HGNC Symbol;Acc:HGNC:21151]<br>"beta-1,4-galactosyltransferase 7"                              | 0.047070015 |
| ENSG00000108518 | PFN1         | [Source:HGNC Symbol;Acc:HGNC:930]"<br>profilin 1                                                       | 0.047130774 |
| ENSG00000110711 | AIP          | [Source:HGNC Symbol;Acc:HGNC:8881]<br>aryl hydrocarbon receptor interacting protein                    | 0.047157356 |
| ENSG00000164068 | RNF123       | [Source:HGNC Symbol;Acc:HGNC:358]<br>ring finger protein 123                                           | 0.04721490  |
| ENSG00000137216 | TMEM63B      | [Source:HGNC Symbol;Acc:HGNC:21148]<br>transmembrane protein 63B                                       | 0.047214902 |
| ENSG00000179588 | ZFPM1        | [Source:HGNC Symbol;Acc:HGNC:17735]<br>"zinc finger protein, FOG family member 1"                      | 0.047244731 |
| ENSG00000188070 | C11orf95     | [Source:HGNC Symbol;Acc:HGNC:19762]"<br>chromosome 11 open reading frame 95                            | 0.047461433 |
| ENSG00000162722 | TRIM58       | [Source:HGNC Symbol;Acc:HGNC:28449]<br>tripartite motif containing 58                                  | 0.047461433 |
| ENSG00000068724 | TTC7A        | [Source:HGNC Symbol;Acc:HGNC:24150]<br>tetratricopeptide repeat domain 7A                              | 0.047475759 |
| ENSG00000142227 | EMP3         | [Source:HGNC Symbol;Acc:HGNC:19750]<br>epithelial membrane protein 3                                   | 0.0476766   |
| ENSG00000159714 | ZDHHC1       | [Source:HGNC Symbol;Acc:HGNC:3335]<br>zinc finger DHHC-type containing 1                               | 0.0476766   |
| ENSG00000196182 | STK40        | [Source:HGNC Symbol;Acc:HGNC:17916]<br>serine/threonine kinase 40                                      | 0.04772167  |
| ENSG00000099875 | MKNK2        | [Source:HGNC Symbol;Acc:HGNC:21373]<br>MAP kinase interacting serine/threonine kinase 2                | 0.047779011 |
| ENSG00000132514 | CLEC10A      | [Source:HGNC Symbol;Acc:HGNC:7111]"<br>C-type lectin domain containing 10A                             | 0.047824795 |
| ENSG00000197982 | C1orf122     | [Source:HGNC Symbol;Acc:HGNC:16916]<br>chromosome 1 open reading frame 122                             | 0.047824795 |
| ENSG00000204348 | DXO          | [Source:HGNC Symbol;Acc:HGNC:24789]<br>decapping exoribonuclease                                       | 0.047824795 |
| ENSG00000259856 | RAB43P1      | [Source:HGNC Symbol;Acc:HGNC:2992]<br>RAB43 pseudogene 1                                               | 0.047913021 |
| ENSG00000103254 | FAM173A      | [Source:HGNC Symbol;Acc:HGNC:33153]<br>family with sequence similarity 173 member A                    | 0.048194625 |
| ENSG00000196453 | ZNF777       | [Source:HGNC Symbol;Acc:HGNC:14152]"<br>zinc finger protein 777                                        | 0.048206847 |
| ENSG00000167173 | C15orf39     | [Source:HGNC Symbol;Acc:HGNC:22213]<br>chromosome 15 open reading frame 39                             | 0.048246269 |
| ENSG00000172534 | HCFC1        | [Source:HGNC Symbol;Acc:HGNC:24497]<br>host cell factor C1                                             | 0.048259142 |
| ENSG00000198804 | MT-CO1       | [Source:HGNC Symbol;Acc:HGNC:4839]<br>mitochondrially encoded cytochrome c oxidase I                   | 0.04840783  |
| ENSG00000244486 | SCARF2       | [Source:HGNC Symbol;Acc:HGNC:7419]<br>scavenger receptor class F member 2                              | 0.048409706 |

|                 |         |                                                                                           |             |
|-----------------|---------|-------------------------------------------------------------------------------------------|-------------|
| ENSG00000125652 | ALKBH7  | [Source:HGNC Symbol;Acc:HGNC:19869]<br>alkB homolog 7                                     | 0.048617065 |
| ENSG00000176101 | SSNA1   | [Source:HGNC Symbol;Acc:HGNC:21306]<br>SS nuclear autoantigen 1                           | 0.048746819 |
| ENSG00000129103 | SUMF2   | [Source:HGNC Symbol;Acc:HGNC:11321]<br>sulfatase modifying factor 2                       | 0.048934402 |
| ENSG00000115756 | HPCAL1  | [Source:HGNC Symbol;Acc:HGNC:20415]<br>hippocalcin like 1                                 | 0.048950286 |
| ENSG00000243566 | UPK3B   | [Source:HGNC Symbol;Acc:HGNC:5145]<br>uroplakin 3B                                        | 0.049011448 |
| ENSG00000149150 | SLC43A1 | [Source:HGNC Symbol;Acc:HGNC:21444]<br>solute carrier family 43 member 1                  | 0.049012128 |
| ENSG00000103227 | LMF1    | [Source:HGNC Symbol;Acc:HGNC:9225]<br>lipase maturation factor 1                          | 0.049128197 |
| ENSG00000271959 |         | [Source:HGNC Symbol;Acc:HGNC:14154]<br>MCF.2 cell line derived transforming sequence like | 0.049193782 |
| ENSG00000261222 |         |                                                                                           | 0.049311473 |
| ENSG00000126217 | MCF2L   |                                                                                           | 0.049471704 |
| ENSG00000104964 | AES     | [Source:HGNC Symbol;Acc:HGNC:14576]<br>amino-terminal enhancer of split                   | 0.049648177 |
| ENSG00000127831 | VIL1    | [Source:HGNC Symbol;Acc:HGNC:307]<br>villin 1                                             | 0.049726662 |
| ENSG00000169738 | DCXR    | [Source:HGNC Symbol;Acc:HGNC:12690]<br>dicarbonyl and L-xylulose reductase                | 0.049726662 |
| ENSG00000086015 | MAST2   | [Source:HGNC Symbol;Acc:HGNC:18985]<br>microtubule associated serine/threonine kinase 2   | 0.049760492 |
|                 |         | [Source:HGNC Symbol;Acc:HGNC:19035]                                                       | 0.04998097  |

**TABLE 8**  
**AC3 GENES**

| <u>Ensembl</u>  | <u>Symbol</u> | <u>Description</u>                                                                         | <u>Score/AUC</u> |
|-----------------|---------------|--------------------------------------------------------------------------------------------|------------------|
| ENSG00000251705 | RNA5-8SP6     | "RNA, 5.8S ribosomal pseudogene 6<br>[Source:HGNC Symbol;Acc:HGNC:41960]"                  | 5.29E-67         |
| ENSG00000133110 | POSTN         | periostin<br>[Source:HGNC Symbol;Acc:HGNC:16953]                                           | 1.78E-06         |
| ENSG00000142449 | FBN3          | fibrillin 3<br>[Source:HGNC Symbol;Acc:HGNC:18794]                                         | 2.85E-05         |
| ENSG00000183668 | PSG9          | pregnancy specific beta-1-glycoprotein 9<br>[Source:HGNC Symbol;Acc:HGNC:9526]             | 9.26E-05         |
| ENSG00000258628 |               |                                                                                            | 0.000107247      |
| ENSG00000260290 |               |                                                                                            | 0.000163871      |
| ENSG00000224367 | OACYLP        | "O-acyltransferase like, pseudogene<br>[Source:HGNC Symbol;Acc:HGNC:44362]"                | 0.000275943      |
| ENSG00000108018 | SORCS1        | sortilin related VPS10 domain containing receptor 1<br>[Source:HGNC Symbol;Acc:HGNC:16697] | 0.000366056      |
| ENSG00000135454 | B4GALNT1      | "beta-1,4-N-acetyl-galactosaminyltransferase 1<br>[Source:HGNC Symbol;Acc:HGNC:4117]"      | 0.000429017      |
| ENSG00000266172 | NA            | NA                                                                                         | 0.000574378      |
| ENSG00000173769 | TOPAZ1        | testis and ovary specific PAZ domain containing 1<br>[Source:HGNC Symbol; Acc:HGNC:24746]  | 0.00059023       |
| ENSG00000181378 | CFAP65        | cilia and flagella associated protein 65<br>[Source:HGNC Symbol;Acc:HGNC:25325]            | 0.000602774      |
| ENSG00000174498 | IGDCC3        | immunoglobulin superfamily DCC subclass member 3<br>[Source:HGNC Symbol;Acc:HGNC:9700]     | 0.00062895       |
| ENSG00000089116 | LHX5          | LIM homeobox 5<br>[Source:HGNC Symbol;Acc:HGNC:14216]                                      | 0.000639272      |
| ENSG00000161270 | NPHS1         | "NPHS1, nephrin<br>[Source:HGNC Symbol;Acc:HGNC:7908]"                                     | 0.000697583      |
| ENSG00000006210 | CX3CL1        | C-X3-C motif chemokine ligand 1<br>[Source:HGNC Symbol;Acc:HGNC:10647]                     | 0.000730947      |
| ENSG00000249618 | LINC02465     | long intergenic non-protein coding RNA 2465<br>[Source:HGNC Symbol;Acc:HGNC:53403]         | 0.000730947      |
| ENSG00000253871 |               |                                                                                            | 0.000789684      |

|                  |           |                                                         |             |
|------------------|-----------|---------------------------------------------------------|-------------|
| ENSG00000130540  | SULT4A1   | sulfotransferase family 4A member 1                     |             |
|                  |           | [Source:HGNC Symbol;Acc:HGNC:14903]                     | 0.000791019 |
| ENSG00000148942  | SLC5A12   | solute carrier family 5 member 12                       |             |
|                  |           | [Source:HGNC Symbol;Acc:HGNC:28750]                     | 0.000819378 |
| ENSG00000226790  | HNRNPA3P1 | heterogeneous nuclear ribonucleoprotein A3 pseudogene 1 |             |
|                  |           | [Source:HGNC Symbol;Acc:HGNC:13729]                     | 0.000826721 |
| ENSG00000160460  | SPTBN4    | "spectrin beta, non-erythrocytic 4                      |             |
|                  |           | [Source:HGNC Symbol;Acc:HGNC:14896]"                    | 0.000837162 |
| ENSG00000243130  | PSG11     | pregnancy specific beta-1-glycoprotein 11               |             |
|                  |           | [Source:HGNC Symbol;Acc:HGNC:9516]                      | 0.000837162 |
| ENSG00000244694  | PTCHD4    | patched domain containing 4                             |             |
|                  |           | [Source:HGNC Symbol;Acc:HGNC:21345]                     | 0.000837162 |
| ENSG00000249464  | LINC01091 | long intergenic non-protein coding RNA 1091             |             |
|                  |           | [Source:HGNC Symbol;Acc:HGNC:27721]                     | 0.000837162 |
| ENSG00000011677  | GABRA3    | gamma-aminobutyric acid type A receptor alpha3 subunit  |             |
|                  |           | [Source:HGNC Symbol;Acc:HGNC:4077]                      | 0.000896018 |
| ENSG00000256343  |           |                                                         | 0.00097441  |
| ENSG00000039139  | DNAH5     | dynein axonemal heavy chain 5                           |             |
|                  |           | [Source:HGNC Symbol;Acc:HGNC:2950]                      | 0.001236713 |
| ENSG00000130635  | COL5A1    | collagen type V alpha 1 chain                           |             |
|                  |           | [Source:HGNC Symbol;Acc:HGNC:2209]                      | 0.001236713 |
| ENSG00000242512  | LINC01206 | long intergenic non-protein coding RNA 1206             |             |
|                  |           | [Source:HGNC Symbol;Acc:HGNC:49637]                     | 0.001253551 |
| ENSG00000164692  | COL1A2    | collagen type I alpha 2 chain                           |             |
|                  |           | [Source:HGNC Symbol;Acc:HGNC:2198]                      | 0.00126185  |
| ENSG00000259841  | LINC01566 | long intergenic non-protein coding RNA 1566             |             |
|                  |           | [Source:HGNC Symbol;Acc:HGNC:27555]                     | 0.001274332 |
| ENSG00000170777  | TPD52L3   | tumor protein D52 like 3                                |             |
|                  |           | [Source:HGNC Symbol;Acc:HGNC:23382]                     | 0.001484087 |
| ENSG00000186487  | MYT1L     | myelin transcription factor 1 like                      |             |
|                  |           | [Source:HGNC Symbol;Acc:HGNC:7623]                      | 0.001774703 |
| ENSG00000082175  | PGR       | progesterone receptor                                   |             |
|                  |           | [Source:HGNC Symbol;Acc:HGNC:8910]                      | 0.001879127 |
| ENSG00000205922  | ONECUT3   | one cut homeobox 3                                      |             |
|                  |           | [Source:HGNC Symbol;Acc:HGNC:13399]                     | 0.001993667 |
| ENSG00000249341  |           |                                                         | 0.002126073 |
| ENSG00000139865  | TTC6      | tetratricopeptide repeat domain 6                       |             |
|                  |           | [Source:HGNC Symbol;Acc:HGNC:19739]                     | 0.002268239 |
| ENSG00000154478  | GPR26     | G protein-coupled receptor 26                           |             |
|                  |           | [Source:HGNC Symbol;Acc:HGNC:4481]                      | 0.002268239 |
| ENSG00000174358  | SLC6A19   | solute carrier family 6 member 19                       |             |
|                  |           | [Source:HGNC Symbol;Acc:HGNC:27960]                     | 0.002268239 |
| ENSG00000235711  | ANKRD34C  | ankyrin repeat domain 34C                               |             |
|                  |           | [Source:HGNC Symbol;Acc:HGNC:33888]                     | 0.002268239 |
| ENSG00000170381  | SEMA3E    | semaphorin 3E                                           |             |
|                  |           | [Source:HGNC Symbol;Acc:HGNC:10727]                     | 0.002327494 |
| ENSG00000142611  | PRDM16    | PR/SET domain 16                                        |             |
|                  |           | [Source:HGNC Symbol;Acc:HGNC:14000]                     | 0.002350766 |
| ENSG00000205396  | LINC00661 | long intergenic non-protein coding RNA 661              |             |
|                  |           | [Source:HGNC Symbol;Acc:HGNC:27002]                     | 0.002366966 |
| ENSG00000253288  |           |                                                         | 0.00239082  |
| ENSG00000171435  | KSR2      | kinase suppressor of ras 2                              |             |
|                  |           | [Source:HGNC Symbol;Acc:HGNC:18610]                     | 0.002607962 |
| ENSG00000256616  |           |                                                         | 0.002639596 |
| ENSG00000171804  | WDR87     | WD repeat domain 87                                     |             |
|                  |           | [Source:HGNC Symbol;Acc:HGNC:29934]                     | 0.002806683 |
| ENSG00000237125  | HAND2-AS1 | HAND2 antisense RNA 1 (head to head)                    |             |
|                  |           | [Source:HGNC Symbol;Acc:HGNC:48872]                     | 0.00289999  |
| ENSG000002406 94 | PNMA2     | PNMA family member 2                                    |             |
|                  |           | [Source:HGNC Symbol;Acc:HGNC:9159]                      | 0.002940811 |
| ENSG00000102452  | NALCN     | sodium leak channel, non-selective                      |             |
|                  |           | [Source:HGNC Symbol;Acc:HGNC:19082]"                    | 0.003094645 |
| ENSG00000214929  | SPATA31D1 | SPATA31 subfamily D member 1                            |             |
|                  |           | [Source:HGNC Symbol;Acc:HGNC:37283]                     | 0.003264148 |
| ENSG00000115041  | KCNIP3    | potassium voltage-gated channel interacting protein 3   |             |

|                 |           |                                                                                                     |             |
|-----------------|-----------|-----------------------------------------------------------------------------------------------------|-------------|
| ENSG00000185038 | MROH2A    | [Source:HGNC Symbol;Acc:HGNC:15523]<br>maestro heat like repeat family member 2A                    | 0.00328034  |
| ENSG00000138892 | TTL8      | [Source:HGNC Symbol;Acc:HGNC:27936]<br>tubulin tyrosine ligase like 8                               | 0.003313878 |
| ENSG00000147573 | TRIM55    | [Source:HGNC Symbol;Acc:HGNC:34000]<br>tripartite motif containing 55                               | 0.003497603 |
| ENSG00000165323 | FAT3      | [Source:HGNC Symbol;Acc:HGNC:14215]<br>FAT atypical cadherin 3                                      | 0.003573936 |
| ENSG00000142623 | PADI1     | [Source:HGNC Symbol;Acc:HGNC:23112]<br>peptidyl arginine deiminase 1                                | 0.003629544 |
| ENSG00000146521 | LINC01558 | [Source:HGNC Symbol;Acc:HGNC:18367]<br>long intergenic non-protein coding RNA 1558                  | 0.003697796 |
| ENSG00000125255 | SLC10A2   | [Source:HGNC Symbol;Acc:HGNC:21235]<br>solute carrier family 10 member 2                            | 0.003779666 |
| ENSG00000103855 | CD276     | [Source:HGNC Symbol;Acc:HGNC:10906]<br>CD276 molecule                                               | 0.003857127 |
| ENSG00000168907 | PLA2G4F   | [Source:HGNC Symbol;Acc:HGNC:19137]<br>phospholipase A2 group IVF                                   | 0.004037668 |
| ENSG00000141668 | CBLN2     | [Source:HGNC Symbol;Acc:HGNC:27396]<br>cerebellin 2 precursor                                       | 0.00413675  |
| ENSG00000197991 |           | [Source:HGNC Symbol;Acc:HGNC:1544]<br>0.004252179                                                   | 0.004198501 |
| ENSG00000149633 | KIAA1755  | KIAA1755                                                                                            |             |
| ENSG00000157927 | RADIL     | [Source:HGNC Symbol;Acc:HGNC:29372]<br>Rap associating with DIL domain                              | 0.004331797 |
| ENSG00000138759 | FRAS1     | [Source:HGNC Symbol;Acc:HGNC:22226]<br>Fraser extracellular matrix complex subunit 1                | 0.004332718 |
| ENSG00000174963 | ZIC4      | [Source:HGNC Symbol;Acc:HGNC:19185]<br>Zic family member 4                                          | 0.004539725 |
| ENSG00000177551 | NHLH2     | [Source:HGNC Symbol;Acc:HGNC:20393]<br>nescient helix-loop-helix 2                                  | 0.004539725 |
| ENSG00000250230 |           | [Source:HGNC Symbol;Acc:HGNC:7818]<br>0.004576049                                                   | 0.004560802 |
| ENSG00000204929 |           | 0.00461274                                                                                          |             |
| ENSG00000163975 | MELTF     | melanotransferrin                                                                                   |             |
| ENSG00000095587 | TLL2      | [Source:HGNC Symbol;Acc:HGNC:7037]<br>tolloid like 2                                                | 0.004655716 |
| ENSG00000221826 | PSG3      | [Source:HGNC Symbol;Acc:HGNC:11844]<br>pregnancy specific beta-1-glycoprotein 3                     | 0.004686524 |
| ENSG00000105392 | CRX       | [Source:HGNC Symbol;Acc:HGNC:9520]<br>cone-rod homeobox                                             | 0.004686524 |
| ENSG00000188338 | SLC38A3   | [Source:HGNC Symbol;Acc:HGNC:2383]<br>solute carrier family 38 member 3                             | 0.004730282 |
| ENSG00000167654 | ATCAY     | [Source:HGNC Symbol;Acc:HGNC:18044]<br>"ATCAY, caytaxin"                                            | 0.004737254 |
| ENSG00000177511 | ST8SIA3   | [Source:HGNC Symbol;Acc:HGNC:779]<br>"ST8 alpha-N-acetyl-neuraminide alpha-2,8-sialyltransferase 3" | 0.004891089 |
| ENSG00000215895 |           | [Source:HGNC Symbol;Acc:HGNC:14269]<br>0.00498476                                                   | 0.00498476  |
| ENSG00000124466 | LYPD3     | LY6/PLAUR domain containing 3                                                                       | 0.005091461 |
| ENSG00000084636 | COL16A1   | [Source:HGNC Symbol;Acc:HGNC:24880]<br>collagen type XVI alpha 1 chain                              | 0.005118791 |
| ENSG00000104537 | ANXA13    | [Source:HGNC Symbol;Acc:HGNC:2193]<br>annexin A13                                                   | 0.00516436  |
| ENSG00000145526 | CDH18     | [Source:HGNC Symbol;Acc:HGNC:536]<br>cadherin 18                                                    | 0.005166641 |
| ENSG00000161103 |           | [Source:HGNC Symbol;Acc:HGNC:1757]<br>0.005294938                                                   | 0.005245896 |
| ENSG00000168484 | SFTPC     | surfactant protein C                                                                                |             |
| ENSG00000188886 | ASTL      | [Source:HGNC Symbol;Acc:HGNC:10802]<br>astacin like metalloendopeptidase                            | 0.005473496 |
| ENSG00000198765 | SYCP1     | [Source:HGNC Symbol;Acc:HGNC:31704]<br>synaptonemal complex protein 1                               | 0.005530506 |
| ENSG00000234177 | LINC01114 | [Source:HGNC Symbol;Acc:HGNC:11487]<br>long intergenic non-protein coding RNA 1114                  | 0.005554714 |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:49245]                                                                 | 0.005808942 |

|                 |           |                                                  |             |
|-----------------|-----------|--------------------------------------------------|-------------|
| ENSG00000091656 | ZFXH4     | zinc finger homeobox 4                           |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:30939]              | 0.005809417 |
| ENSG00000151572 | ANO4      | anoctamin 4                                      |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:23837]              | 0.005857886 |
| ENSG00000178965 | ERICH3    | glutamate rich 3                                 |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:25346]              | 0.005890875 |
| ENSG00000248587 | GDNF-AS1  | GDNF antisense RNA 1 (head to head)              |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:43592]              | 0.005890875 |
| ENSG00000144908 | ALDH1L1   | aldehyde dehydrogenase 1 family member L1        |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:3978]               | 0.006015103 |
| ENSG00000152822 | GRM1      | glutamate metabotropic receptor 1                |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:4593]               | 0.006033529 |
| ENSG00000138675 | FGF5      | fibroblast growth factor 5                       |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:3683]               | 0.006101348 |
| ENSG00000187772 | LIN28B    | lin-28 homolog B                                 |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:32207]              | 0.006111478 |
| ENSG00000227471 | AKR1B15   | aldo-keto reductase family 1 member B15          |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:37281]              | 0.006366933 |
| ENSG00000174502 | SLC26A9   | solute carrier family 26 member 9                |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:14469]              | 0.006716425 |
| ENSG00000078549 | ADCYAP1R1 | ADCYAP receptor type I                           |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:242]                | 0.006848491 |
| ENSG00000159650 | UROCI     | urocanate hydratase 1                            |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:26444]              | 0.006848491 |
| ENSG00000217094 | PPIAP31   | peptidylprolyl isomerase A pseudogene 31         |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:44962]              | 0.006866623 |
| ENSG00000006128 | TAC1      | tachykinin precursor 1                           |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:11517]              | 0.006929673 |
| ENSG00000158077 | NLRP14    | NLR family pyrin domain containing 14            |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:22939]              | 0.006952696 |
| ENSG00000223414 | LINC00473 | long intergenic non-protein coding RNA 473       |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:21160]              | 0.006952696 |
| ENSG00000144488 | ESPNL     | espin like                                       |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:27937]              | 0.007039881 |
| ENSG00000144730 | IL17RD    | interleukin 17 receptor D                        |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:17616]              | 0.007141116 |
| ENSG00000137819 | PAQR5     | progesterone and adipoQ receptor family member 5 |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:29645]              | 0.007179081 |
| ENSG00000162631 | NTNG1     | netrin G1                                        |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:23319]              | 0.007255358 |
| ENSG00000185974 | GRK1      | G protein-coupled receptor kinase 1              |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:10013]              | 0.007327997 |
| ENSG00000261275 |           |                                                  | 0.007327997 |
| ENSG00000249267 | LINC00939 | long intergenic non-protein coding RNA 939       |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:48631]              | 0.007349367 |
| ENSG00000227827 |           |                                                  | 0.007403828 |
| ENSG00000100065 | CARD10    | caspase recruitment domain family member 10      |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:16422]              | 0.007527421 |
| ENSG00000119125 | GDA       | guanine deaminase                                |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:4212]               | 0.007619923 |
| ENSG00000106304 | SPAM1     | sperm adhesion molecule 1                        |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:11217]              | 0.00781679  |
| ENSG00000250493 |           |                                                  | 0.007835589 |
| ENSG00000158258 | CLSTN2    | calsynenin 2                                     |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:17448]              | 0.008149414 |
| ENSG00000175329 | ISX       | intestine specific homeobox                      |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:28084]              | 0.008233566 |
| ENSG00000188488 | SERPINA5  | serpin family A member 5                         |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:8723]               | 0.008534971 |
| ENSG00000249584 | LINC02225 | long intergenic non-protein coding RNA 2225      |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:53094]              | 0.00866593  |
| ENSG00000147655 | RSPO2     | R-spondin 2                                      |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:28583]              | 0.008823914 |
| ENSG00000171587 | DSCAM     | DS cell adhesion molecule                        |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:3039]               | 0.008841283 |
| ENSG00000120738 | EGR1      | early growth response 1                          |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:3238]               | 0.008960131 |

|                 |           |                                                               |             |
|-----------------|-----------|---------------------------------------------------------------|-------------|
| ENSG00000127129 | EDN2      | endothelin 2                                                  |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:3177]                            | 0.009244272 |
| ENSG00000157423 | HYDIN     | "HYDIN, axonemal central pair apparatus protein               |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:19368]"                          | 0.009244272 |
| ENSG00000196565 | HBG2      | hemoglobin subunit gamma 2                                    |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:4832]                            | 0.009327518 |
| ENSG00000235881 |           |                                                               | 0.009327518 |
| ENSG00000111262 | KCNA1     | potassium voltage-gated channel subfamily A member 1          |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:6218]                            | 0.009418575 |
| ENSG00000187527 | ATP13A5   | ATPase 13A5                                                   |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:31789]                           | 0.009514824 |
| ENSG00000188803 | SHISA6    | shisa family member 6                                         |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:34491]                           | 0.009514824 |
| ENSG00000175535 | PNLIP     | pancreatic lipase                                             |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:9155]                            | 0.009619326 |
| ENSG00000225953 | SATB2-AS1 | SATB2 antisense RNA 1                                         |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:26490]                           | 0.009647997 |
| ENSG00000136695 | IL36RN    | interleukin 36 receptor antagonist                            |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:15561]                           | 0.009810065 |
| ENSG00000259790 | ANP32BP1  | acidic nuclear phosphoprotein 32 family member B pseudogene 1 |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:24267]                           | 0.009820284 |
| ENSG00000225813 |           |                                                               | 0.009894409 |
| ENSG00000179008 | C14orf39  | chromosome 14 open reading frame 39                           |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:19849]                           | 0.009896903 |
| ENSG00000150893 | FREM2     | FRAS1 related extracellular matrix protein 2                  |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:25396]                           | 0.009945757 |
| ENSG00000197079 | KRT35     | keratin 35                                                    |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:6453]                            | 0.009945757 |
| ENSG00000231131 | LINC01468 | long intergenic non-protein coding RNA 1468                   |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:50913]                           | 0.010123625 |
| ENSG00000268388 | FENDRR    | FOXF1 adjacent non-coding developmental regulatory RNA        |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:43894]                           | 0.010151023 |
| ENSG00000159251 | ACTC1     | "actin, alpha, cardiac muscle 1                               |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:143]"                            | 0.010212535 |
| ENSG00000158125 | XDH       | xanthine dehydrogenase                                        |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:12805]                           | 0.010258334 |
| ENSG00000156222 | SLC28A1   | solute carrier family 28 member 1                             |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:11001]                           | 0.010392835 |
| ENSG00000260759 |           |                                                               | 0.010741484 |
| ENSG00000110975 | SYT10     | synaptotagmin 10                                              |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:19266]                           | 0.010787993 |
| ENSG00000186185 | KIF18B    | kinesin family member 18B                                     |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:27102]                           | 0.010844893 |
| ENSG00000110887 | DAO       | D-amino acid oxidase                                          |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:2671]                            | 0.011064297 |
| ENSG00000132297 | HHLA1     | HERV-H LTR-associating 1                                      |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:4904]                            | 0.011064297 |
| ENSG00000146839 | ZAN       | zonadhesin (gene/pseudogene)                                  |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:12857]                           | 0.011064297 |
| ENSG00000215864 | NBPF7     | NBPF member 7                                                 |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:31989]                           | 0.01113278  |
| ENSG00000233395 | LINC00841 | long intergenic non-protein coding RNA 841                    |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:27430]                           | 0.011213055 |
| ENSG00000177354 | C10orf71  | chromosome 10 open reading frame 71                           |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:26973]                           | 0.011268372 |
| ENSG00000148357 | HMCN2     | hemicentin 2                                                  |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:21293]                           | 0.01150342  |
| ENSG00000215405 | NA        | NA                                                            | 0.011599767 |
| ENSG00000203900 |           |                                                               | 0.011732314 |
| ENSG00000218672 |           |                                                               | 0.011732314 |
| ENSG00000261104 |           |                                                               | 0.011732314 |
| ENSG00000123243 | ITIH5     | inter-alpha-trypsin inhibitor heavy chain family member 5     |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:21449]                           | 0.011851589 |
| ENSG00000213467 | HMGB1P37  | high mobility group box 1 pseudogene 37                       |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:39184]                           | 0.011876979 |

|                 |           |                                                                  |             |
|-----------------|-----------|------------------------------------------------------------------|-------------|
| ENSG00000119283 | TRIM67    | tripartite motif containing 67                                   |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:31859]                              | 0.011900585 |
| ENSG00000166984 | TCP10L2   | t-complex 10 like 2                                              |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:21254]                              | 0.012009181 |
| ENSG00000204941 | PSG5      | pregnancy specific beta-1-glycoprotein 5                         |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:9522]                               | 0.012022323 |
| ENSG00000230552 |           |                                                                  | 0.012137266 |
| ENSG00000115155 | OTOF      | otoferlin                                                        |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:8515]                               | 0.012228668 |
| ENSG00000163395 | IGFN1     | immunoglobulin-like and fibronectin type III domain containing 1 |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:24607]                              | 0.012230791 |
| ENSG00000122778 | KIAA1549  | KIAA1549                                                         |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:22219]                              | 0.012393242 |
| ENSG00000169169 | CPT1C     | carnitine palmitoyltransferase 1C                                |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:18540]                              | 0.012437719 |
| ENSG00000160994 | CCDC105   | coiled-coil domain containing 105                                |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:26866]                              | 0.012486932 |
| ENSG00000237515 | SHISA9    | shisa family member 9                                            |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:37231]                              | 0.012486932 |
| ENSG00000105605 | CACNG7    | calcium voltage-gated channel auxiliary subunit gamma 7          |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:13626]                              | 0.012676606 |
| ENSG00000185739 | SRL       | sarcalumenin                                                     |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:11295]                              | 0.012676606 |
| ENSG00000101680 | LAMA1     | laminin subunit alpha 1                                          |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:6481]                               | 0.012767139 |
| ENSG00000240021 | TEX35     | testis expressed 35                                              |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:25366]                              | 0.012795538 |
| ENSG00000250423 | KIAA1210  | KIAA1210                                                         |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:29218]                              | 0.012935817 |
| ENSG00000198788 | MUC2      | "mucin 2, oligomeric mucus/gel-forming                           |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:7512]"                              | 0.012968601 |
| ENSG00000205312 | KRT17P4   | keratin 17 pseudogene 4                                          |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:50722]                              | 0.013016002 |
| ENSG00000214128 | TMEM213   | transmembrane protein 213                                        |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:27220]                              | 0.013016002 |
| ENSG00000178568 | ERBB4     | erb-b2 receptor tyrosine kinase 4                                |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:3432]                               | 0.013045986 |
| ENSG00000175084 | DES       | desmin                                                           |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:2770]                               | 0.013296119 |
| ENSG00000078295 | ADCY2     | adenylate cyclase 2                                              |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:233]                                | 0.013400191 |
| ENSG00000132639 | SNAP25    | synaptosome associated protein 25                                |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:11132]                              | 0.013440348 |
| ENSG00000187094 | CCK       | cholecystokinin                                                  |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:1569]                               | 0.013447765 |
| ENSG00000018625 | ATP1A2    | ATPase Na+/K+ transporting subunit alpha 2                       |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:800]                                | 0.013509365 |
| ENSG00000168542 | COL3A1    | collagen type III alpha 1 chain                                  |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:2201]                               | 0.013843652 |
| ENSG00000239921 | LINC01471 | long intergenic non-protein coding RNA 1471                      |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:51106]                              | 0.013848913 |
| ENSG00000233183 |           |                                                                  | 0.013964273 |
| ENSG00000167798 | C3P1      | complement component 3 precursor pseudogene                      |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:34414]                              | 0.013987555 |
| ENSG00000183778 | B3GALT5   | "beta-1,3-galactosyltransferase 5                                |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:920]"                               | 0.01405326  |
| ENSG00000168481 | LGI3      | leucine rich repeat LGI family member 3                          |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:18711]                              | 0.014132769 |
| ENSG00000227744 | LINC01940 | long intergenic non-protein coding RNA 1940                      |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:52763]                              | 0.014149077 |
| ENSG00000138162 | TACC2     | transforming acidic coiled-coil containing protein 2             |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:11523]                              | 0.014184675 |
| ENSG00000250049 |           |                                                                  | 0.014522615 |
| ENSG00000236445 | LINC00608 | long intergenic non-protein coding RNA 608                       |             |
|                 |           | Source:HGNC Symbol;Acc:HGNC:27179]                               | 0.014606813 |

|                 |           |                                                                                                  |             |
|-----------------|-----------|--------------------------------------------------------------------------------------------------|-------------|
| ENSG00000165966 | PDZRN4    | PDZ domain containing ring finger 4<br>[Source:HGNC Symbol;Acc:HGNC:30552]                       | 0.014718872 |
| ENSG00000169876 | MUC17     | "mucin 17, cell surface associated<br>[Source:HGNC Symbol;Acc:HGNC:16800]"                       | 0.014749092 |
| ENSG00000078898 | BPIFB2    | BPI fold containing family B member 2<br>[Source:HGNC Symbol;Acc:HGNC:16177]                     | 0.014831419 |
| ENSG00000130528 | HRC       | histidine rich calcium binding protein<br>[Source:HGNC Symbol;Acc:HGNC:5178]                     | 0.014902982 |
| ENSG00000111799 | COL12A1   | collagen type XII alpha 1 chain<br>[Source:HGNC Symbol;Acc:HGNC:2188]                            | 0.015069239 |
| ENSG00000185303 | SFTPA2    | surfactant protein A2<br>[Source:HGNC Symbol;Acc:HGNC:10799]                                     | 0.015347263 |
| ENSG00000146648 | EGFR      | epidermal growth factor receptor<br>[Source:HGNC Symbol;Acc:HGNC:3236]                           | 0.015466899 |
| ENSG00000205592 | MUC19     | "mucin 19, oligomeric<br>[Source:HGNC Symbol;Acc:HGNC:14362]"                                    | 0.015539471 |
| ENSG00000198597 | ZNF536    | zinc finger protein 536<br>[Source:HGNC Symbol;Acc:HGNC:29025]                                   | 0.015552452 |
| ENSG00000120332 | TNN       | tenascin N<br>[Source:HGNC Symbol;Acc:HGNC:22942]                                                | 0.015559411 |
| ENSG00000197406 | DIO3      | iodothyronine deiodinase 3<br>[Source:HGNC Symbol;Acc:HGNC:2885]                                 | 0.015755832 |
| ENSG00000204283 | LINC01973 | long intergenic non-protein coding RNA 1973<br>[Source:HGNC Symbol;Acc:HGNC:52800]               | 0.015755832 |
| ENSG00000151224 | MAT1A     | methionine adenosyltransferase 1A<br>[Source:HGNC Symbol;Acc:HGNC:6903]                          | 0.015829354 |
| ENSG00000257008 | GPR142    | G protein-coupled receptor 142<br>[Source:HGNC Symbol;Acc:HGNC:20088]                            | 0.015942034 |
| ENSG00000139220 | PPFIA2    | PTPRF interacting protein alpha 2<br>[Source:HGNC Symbol;Acc:HGNC:9246]                          | 0.015986308 |
| ENSG00000141946 | ZIM3      | zinc finger imprinted 3<br>[Source:HGNC Symbol;Acc:HGNC:16366]                                   | 0.015986308 |
| ENSG00000178171 | AMER3     | APC membrane recruitment protein 3<br>[Source:HGNC Symbol;Acc:HGNC:26771]                        | 0.015986308 |
| ENSG00000232756 |           |                                                                                                  | 0.015986308 |
| ENSG00000130477 | UNC13A    | unc-13 homolog A<br>[Source:HGNC Symbol;Acc:HGNC:23150]                                          | 0.016007101 |
| ENSG00000070886 | EPHA8     | EPH receptor A8<br>[Source:HGNC Symbol;Acc:HGNC:3391]                                            | 0.016008143 |
| ENSG00000253301 | LINC01606 | long intergenic non-protein coding RNA 1606<br>[Source:HGNC Symbol;Acc:HGNC:51656]               | 0.016008143 |
| ENSG00000006788 | MYH13     | myosin heavy chain 13<br>[Source:HGNC Symbol;Acc:HGNC:7571]                                      | 0.01606756  |
| ENSG00000183287 | CCBE1     | collagen and calcium binding EGF domains 1<br>[Source:HGNC Symbol;Acc:HGNC:29426]                | 0.016243979 |
| ENSG00000262691 |           |                                                                                                  | 0.016243979 |
| ENSG00000125740 | FOSB      | "FosB proto-oncogene, AP-1 transcription factor subunit<br>[Source:HGNC Symbol;Acc:HGNC:3797]"   | 0.016263717 |
| ENSG00000133083 | DCLK1     | doublecortin like kinase 1<br>[Source:HGNC Symbol;Acc:HGNC:2700]                                 | 0.01630694  |
| ENSG00000144820 | ADGRG7    | adhesion G protein-coupled receptor G7<br>[Source:HGNC Symbol;Acc:HGNC:19241]                    | 0.01630694  |
| ENSG00000178031 | ADAMTSL1  | ADAMTS like 1<br>[Source:HGNC Symbol;Acc:HGNC:14632]                                             | 0.016324743 |
| ENSG00000187905 | LRRC74B   | leucine rich repeat containing 74B<br>[Source:HGNC Symbol;Acc:HGNC:34301]                        | 0.016416472 |
| ENSG00000221878 | PSG7      | pregnancy specific beta-1-glycoprotein 7 (gene/pseudogene)<br>[Source:HGNC Symbol;Acc:HGNC:9524] | 0.016416472 |
| ENSG00000254101 | LINC02055 | long intergenic non-protein coding RNA 2055<br>[Source:HGNC Symbol;Acc:HGNC:52895]               | 0.016416472 |
| ENSG00000120251 | GRIA2     | glutamate ionotropic receptor AMPA type subunit 2<br>[Source:HGNC Symbol;Acc:HGNC:4572]          | 0.016488676 |
| ENSG00000233991 | NA        | NA                                                                                               | 0.016488676 |
| ENSG00000214402 | LCNL1     | lipocalin like 1<br>[Source:HGNC Symbol;Acc:HGNC:34436]                                          | 0.016554945 |
| ENSG00000224271 |           |                                                                                                  | 0.016611527 |
| ENSG00000257576 | HSPD1P4   | heat shock protein family D (Hsp60) member 1 pseudogene 4                                        |             |

|                 |           |                                                        |                                      |
|-----------------|-----------|--------------------------------------------------------|--------------------------------------|
| ENSG00000228549 |           | [Source:HGNC Symbol;Acc:HGNC:35146]                    | 0.016611527                          |
| ENSG00000178645 | C10orf53  | chromosome 10 open reading frame 53                    | 0.016653065                          |
| ENSG00000100078 | PLA2G3    | [Source:HGNC Symbol;Acc:HGNC:27421]                    | 0.016654478                          |
| ENSG00000154099 | DNAAF1    | phospholipase A2 group III                             | [Source:HGNC Symbol;Acc:HGNC:17934]  |
| ENSG00000183242 | WT1-AS    | dynein axonemal assembly factor 1                      | 0.016825197                          |
| ENSG00000124253 | PCK1      | [Source:HGNC Symbol;Acc:HGNC:30539]                    | 0.016918546                          |
| ENSG00000183304 | FAM9A     | WT1 antisense RNA                                      | [Source:HGNC Symbol;Acc:HGNC:18135]  |
| ENSG00000210127 | MT-TA     | phosphoenolpyruvate carboxykinase 1                    | 0.016918546                          |
| ENSG00000258679 |           | [Source:HGNC Symbol;Acc:HGNC:8724]                     | 0.016968016                          |
| ENSG00000130287 | NCAN      | family with sequence similarity 9 member A             | [Source:HGNC Symbol;Acc:HGNC:18403]  |
| ENSG00000088340 | FER1L4    | mitochondrially encoded tRNA alanine                   | 0.016968016                          |
| ENSG00000196415 | PRTN3     | [Source:HGNC Symbol;Acc:HGNC:7475]                     | 0.016968016                          |
| ENSG00000135917 | SLC19A3   | neurocan                                               | 0.016968016                          |
| ENSG00000233539 |           | [Source:HGNC Symbol;Acc:HGNC:2465]                     | 0.016985672                          |
| ENSG00000176584 | DMBT1P1   | "fer-1 like family member 4, pseudogene                | [Source:HGNC Symbol;Acc:HGNC:15801]" |
| ENSG00000135097 | MSI1      | proteinase 3                                           | 0.017112355                          |
| ENSG00000091128 | LAMB4     | [Source:HGNC Symbol;Acc:HGNC:9495]                     | 0.017180036                          |
| ENSG00000168367 | LINC00917 | solute carrier family 19 member 3                      | [Source:HGNC Symbol;Acc:HGNC:16266]  |
| ENSG00000224668 | IPO8P1    | deleted in malignant brain tumors 1 pseudogene 1       | 0.017342649                          |
| ENSG00000165757 | JCAD      | [Source:HGNC Symbol;Acc:HGNC:49497]                    | 0.017392388                          |
| ENSG00000166558 | SLC38A8   | musashi RNA binding protein 1                          | [Source:HGNC Symbol;Acc:HGNC:7330]   |
| ENSG00000185467 | KPNA7     | laminin subunit beta 4                                 | 0.017394805                          |
| ENSG00000247699 |           | [Source:HGNC Symbol;Acc:HGNC:6491]                     | 0.017415673                          |
| ENSG00000248975 | FAM216B   | long intergenic non-protein coding RNA 917             | [Source:HGNC Symbol;Acc:HGNC:48607]  |
| ENSG00000179813 | ZDHHC9    | importin 8 pseudogene 1                                | 0.017415673                          |
| ENSG00000188706 | FAIM2     | [Source:HGNC Symbol;Acc:HGNC:41955]                    | 0.017704945                          |
| ENSG00000135472 | NLRP13    | junctional cadherin 5 associated                       | [Source:HGNC Symbol;Acc:HGNC:29283]  |
| ENSG00000173572 | NLRP13    | [Source:HGNC Symbol;Acc:HGNC:29283]                    | 0.017712329                          |
| ENSG00000089199 | CHGB      | solute carrier family 38 member 8                      | [Source:HGNC Symbol;Acc:HGNC:32434]  |
| ENSG00000188112 | C6orf132  | [Source:HGNC Symbol;Acc:HGNC:32434]                    | 0.017722732                          |
| ENSG00000187068 | C3orf70   | karyopherin subunit alpha 7                            | [Source:HGNC Symbol;Acc:HGNC:21839]  |
| ENSG00000233973 | LINC01360 | 0.017767827                                            | 0.017813935                          |
| ENSG00000164265 | SCGB3A2   | family with sequence similarity 216 member B           | 0.017824111                          |
| ENSG00000176769 | TCERG1L   | [Source:HGNC Symbol;Acc:HGNC:26883]                    | 0.01797203                           |
| ENSG00000179709 | NLRP8     | zinc finger DHHC-type containing 9                     | [Source:HGNC Symbol;Acc:HGNC:18475]  |
| ENSG00000251557 | HNRNPKP3  | Fas apoptotic inhibitory molecule 2                    | [Source:HGNC Symbol;Acc:HGNC:17067]  |
|                 |           | NLR family pyrin domain containing 13                  | [Source:HGNC Symbol;Acc:HGNC:22937]  |
|                 |           | chromogranin B                                         | [Source:HGNC Symbol;Acc:HGNC:1930]   |
|                 |           | chromosome 6 open reading frame 132                    | [Source:HGNC Symbol;Acc:HGNC:21288]  |
|                 |           | chromosome 3 open reading frame 70                     | [Source:HGNC Symbol;Acc:HGNC:33731]  |
|                 |           | long intergenic non-protein coding RNA 1360            | [Source:HGNC Symbol;Acc:HGNC:50593]  |
|                 |           | secretoglobin family 3A member 2                       | [Source:HGNC Symbol;Acc:HGNC:18391]  |
|                 |           | transcription elongation regulator 1 like              | [Source:HGNC Symbol;Acc:HGNC:23533]  |
|                 |           | NLR family pyrin domain containing 8                   | [Source:HGNC Symbol;Acc:HGNC:22940]  |
|                 |           | heterogeneous nuclear ribonucleoprotein K pseudogene 3 |                                      |

|                 |           |                                                                                                                          |
|-----------------|-----------|--------------------------------------------------------------------------------------------------------------------------|
| ENSG00000149654 | CDH22     | [Source:HGNC Symbol;Acc:HGNC:42376] 0.018866754<br>cadherin 22                                                           |
| ENSG00000170426 | SDR9C7    | [Source:HGNC Symbol;Acc:HGNC:13251] 0.018978105<br>short chain dehydrogenase/reductase family 9C member 7                |
| ENSG00000225637 |           | [Source:HGNC Symbol;Acc:HGNC:29958] 0.018978105                                                                          |
| ENSG00000142408 | CACNG8    | 0.019088297<br>calcium voltage-gated channel auxiliary subunit gamma 8                                                   |
| ENSG00000230873 | STMND1    | [Source:HGNC Symbol;Acc:HGNC:13628] 0.019108077<br>stathmin domain containing 1                                          |
| ENSG00000236404 | VLDLR-AS1 | [Source:HGNC Symbol;Acc:HGNC:44668] 0.01920241<br>VLDLR antisense RNA 1                                                  |
| ENSG00000170927 | PKHD1     | [Source:HGNC Symbol;Acc:HGNC:49621] 0.01920241<br>"PKHD1, fibrocystin/polyductin                                         |
| ENSG00000237289 | CKMT1B    | [Source:HGNC Symbol;Acc:HGNC:9016]" 0.019345013<br>"creatine kinase, mitochondrial 1B                                    |
| ENSG00000229817 |           | [Source:HGNC Symbol;Acc:HGNC:1995]" 0.019345013                                                                          |
| ENSG00000259176 | NA        | 0.019542531<br>NA                                                                                                        |
| ENSG00000124092 | CTCFL     | 0.019829586<br>CCCTC-binding factor like                                                                                 |
| ENSG00000259156 | CHEK2P2   | [Source:HGNC Symbol;Acc:HGNC:16234] 0.019839425<br>checkpoint kinase 2 pseudogene 2                                      |
| ENSG00000203805 | PLPP4     | [Source:HGNC Symbol;Acc:HGNC:43578] 0.019859771<br>phospholipid phosphatase 4                                            |
| ENSG00000163914 | RHO       | [Source:HGNC Symbol;Acc:HGNC:23531] 0.019917239<br>rhodopsin                                                             |
| ENSG00000224435 | NF1P6     | [Source:HGNC Symbol;Acc:HGNC:10012] 0.019927103<br>neurofibromin 1 pseudogene 6                                          |
| ENSG00000240707 | LINC01168 | [Source:HGNC Symbol;Acc:HGNC:7771] 0.019927103<br>long intergenic non-protein coding RNA 1168                            |
| ENSG00000130045 | NXNL2     | [Source:HGNC Symbol;Acc:HGNC:49537] 0.019935944<br>nucleoredoxin like 2                                                  |
| ENSG00000162062 | TEDC2     | [Source:HGNC Symbol;Acc:HGNC:30482] 0.020063533<br>tubulin epsilon and delta complex 2                                   |
| ENSG00000172752 | COL6A5    | [Source:HGNC Symbol;Acc:HGNC:25849] 0.020213465<br>collagen type VI alpha 5 chain                                        |
| ENSG00000101871 | MID1      | [Source:HGNC Symbol;Acc:HGNC:26674] 0.020225168<br>midline 1                                                             |
| ENSG00000137648 | TMPRSS4   | [Source:HGNC Symbol;Acc:HGNC:7095] 0.020247513<br>transmembrane serine protease 4                                        |
| ENSG00000166473 | PKD1L2    | [Source:HGNC Symbol;Acc:HGNC:11878] 0.020387859<br>polycystin 1 like 2 (gene/pseudogene)                                 |
| ENSG00000257907 | EEF1A1P17 | [Source:HGNC Symbol;Acc:HGNC:21715] 0.020387859<br>eukaryotic translation elongation factor 1 alpha 1 pseudogene 17      |
| ENSG00000128917 | DLL4      | [Source:HGNC Symbol;Acc:HGNC:37890] 0.020486161<br>delta like canonical Notch ligand 4                                   |
| ENSG00000259380 |           | [Source:HGNC Symbol;Acc:HGNC:2910] 0.020505106                                                                           |
| ENSG00000179766 | ATP8B5P   | 0.020626924<br>"ATPase phospholipid transporting 8B5, pseudogene                                                         |
| ENSG00000204624 | DISP3     | [Source:HGNC Symbol;Acc:HGNC:27245]" 0.02065324<br>dispatched RND transporter family member 3                            |
| ENSG00000163689 | C3orf67   | [Source:HGNC Symbol;Acc:HGNC:29251] 0.02065324<br>chromosome 3 open reading frame 67                                     |
| ENSG00000132321 | IQCA1     | [Source:HGNC Symbol;Acc:HGNC:24763] 0.020743462<br>IQ motif containing with AAA domain 1                                 |
| ENSG00000249119 | MTND6P4   | [Source:HGNC Symbol;Acc:HGNC:26195] 0.020807093<br>mitochondrially encoded NADH:ubiquinone oxidoreductase core subunit 6 |
| ENSG00000019505 | SYT13     | [Source:HGNC Symbol;Acc:HGNC:39467] 0.020807093<br>pseudogene 4 [Source:HGNC Symbol;Acc:HGNC:39467] synaptotagmin 13     |
| ENSG00000143469 | SYT14     | [Source:HGNC Symbol;Acc:HGNC:14962] 0.020829887<br>synaptotagmin 14                                                      |
| ENSG00000196136 | SERPINA3  | [Source:HGNC Symbol;Acc:HGNC:23143] 0.020885035<br>serpin family A member 3                                              |
| ENSG00000165816 | VWA2      | [Source:HGNC Symbol;Acc:HGNC:16] 0.02099734<br>von Willebrand factor A domain containing 2                               |
| ENSG00000183317 | EPHA10    | [Source:HGNC Symbol;Acc:HGNC:24709] 0.021329095<br>EPH receptor A10                                                      |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:19987] 0.021329095                                                                          |

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| ENSG00000072041 | SLC6A15  | solute carrier family 6 member 15<br>[Source:HGNC Symbol;Acc:HGNC:13621]                          | 0.021369466 |
| ENSG00000009709 | PAX7     | paired box 7<br>[Source:HGNC Symbol;Acc:HGNC:8621]                                                | 0.021525887 |
| ENSG00000172350 | ABCG4    | ATP binding cassette subfamily G member 4<br>[Source:HGNC Symbol;Acc:HGNC:13884]                  | 0.021525887 |
| ENSG00000183876 | ARSI     | arylsulfatase family member I<br>[Source:HGNC Symbol;Acc:HGNC:32521]                              | 0.021711339 |
| ENSG00000213934 | HBG1     | hemoglobin subunit gamma 1<br>[Source:HGNC Symbol;Acc:HGNC:4831]                                  | 0.02185053  |
| ENSG00000186526 | CYP4F8   | cytochrome P450 family 4 subfamily F member 8<br>[Source:HGNC Symbol;Acc:HGNC:2648]               | 0.021913633 |
| ENSG00000161940 | BCL6B    | B cell CLL/lymphoma 6B<br>[Source:HGNC Symbol;Acc:HGNC:1002]                                      | 0.021959359 |
| ENSG00000164093 | PITX2    | paired like homeodomain 2<br>[Source:HGNC Symbol;Acc:HGNC:9005]                                   | 0.02227554  |
| ENSG00000110786 | PTPN5    | "protein tyrosine phosphatase, non-receptor type 5<br>[Source:HGNC Symbol;Acc:HGNC:9657]"         | 0.022304898 |
| ENSG00000145642 | SHISAL2B | shisa like 2B<br>[Source:HGNC Symbol;Acc:HGNC:34236]                                              | 0.022689972 |
| ENSG00000260411 | NA       | NA                                                                                                | 0.022689972 |
| ENSG00000135409 | AMHR2    | anti-Mullerian hormone receptor type 2<br>[Source:HGNC Symbol;Acc:HGNC:465]                       | 0.022721606 |
| ENSG00000259458 |          |                                                                                                   | 0.022776502 |
| ENSG00000068078 | FGFR3    | fibroblast growth factor receptor 3<br>[Source:HGNC Symbol;Acc:HGNC:3690]                         | 0.022896021 |
| ENSG00000161243 | FBXO27   | F-box protein 27<br>[Source:HGNC Symbol;Acc:HGNC:18753]                                           | 0.023440646 |
| ENSG00000101004 | NINL     | ninein like<br>[Source:HGNC Symbol;Acc:HGNC:29163]                                                | 0.023637109 |
| ENSG00000121207 | LRAT     | lecithin retinol acyltransferase<br>[Source:HGNC Symbol;Acc:HGNC:6685]                            | 0.023637109 |
| ENSG00000140527 | WDR93    | WD repeat domain 93<br>[Source:HGNC Symbol;Acc:HGNC:26924]                                        | 0.023652058 |
| ENSG00000236824 | BCYRN1   | brain cytoplasmic RNA 1<br>[Source:HGNC Symbol;Acc:HGNC:1022]                                     | 0.023652058 |
| ENSG00000101203 | COL20A1  | collagen type XX alpha 1 chain<br>[Source:HGNC Symbol;Acc:HGNC:14670]                             | 0.023671204 |
| ENSG00000233977 |          |                                                                                                   | 0.023671204 |
| ENSG00000148408 | CACNA1B  | calcium voltage-gated channel subunit alpha1 B<br>[Source:HGNC Symbol;Acc:HGNC:1389]              | 0.02389629  |
| ENSG00000134240 | HMGCS2   | 3-hydroxy-3-methylglutaryl-CoA synthase 2<br>[Source:HGNC Symbol;Acc:HGNC:5008]                   | 0.023926586 |
| ENSG00000112186 | CAP2     | cyclase associated actin cytoskeleton regulatory protein 2<br>[Source:HGNC Symbol;Acc:HGNC:20039] | 0.024121501 |
| ENSG00000182256 | GABRG3   | gamma-aminobutyric acid type A receptor gamma3 subunit<br>[Source:HGNC Symbol;Acc:HGNC:4088]      | 0.024155164 |
| ENSG00000166159 | LRTM2    | leucine rich repeats and transmembrane domains 2<br>[Source:HGNC Symbol;Acc:HGNC:32443]           | 0.024214399 |
| ENSG00000132972 | RNF17    | ring finger protein 17<br>[Source:HGNC Symbol;Acc:HGNC:10060]                                     | 0.024283188 |
| ENSG00000156076 | WIF1     | WNT inhibitory factor 1<br>[Source:HGNC Symbol;Acc:HGNC:18081]                                    | 0.024283188 |
| ENSG00000261649 | GOLGA6L7 | golgin A6 family like 7<br>[Source:HGNC Symbol;Acc:HGNC:37442]                                    | 0.024421599 |
| ENSG00000112238 | PRDM13   | PR/SET domain 13<br>[Source:HGNC Symbol;Acc:HGNC:13998]                                           | 0.02443315  |
| ENSG00000166391 | MOGAT2   | monoacylglycerol O-acyltransferase 2<br>[Source:HGNC Symbol;Acc:HGNC:23248]                       | 0.024463522 |
| ENSG00000166869 | CHP2     | calcineurin like EF-hand protein 2<br>[Source:HGNC Symbol;Acc:HGNC:24927]                         | 0.024463522 |
| ENSG00000218823 | PAPOLB   | poly(A) polymerase beta<br>[Source:HGNC Symbol;Acc:HGNC:15970]                                    | 0.024463522 |
| ENSG00000265041 |          |                                                                                                   | 0.024463522 |
| ENSG00000133124 | IRS4     | insulin receptor substrate 4<br>[Source:HGNC Symbol;Acc:HGNC:6128]                                | 0.024526611 |

|                 |            |                                                            |             |
|-----------------|------------|------------------------------------------------------------|-------------|
| ENSG00000118733 | OLFM3      | olfactomedin 3                                             |             |
|                 |            | [Source:HGNC Symbol;Acc:HGNC:17990]                        | 0.024577949 |
| ENSG00000196091 | MYBPC1     | "myosin binding protein C, slow type                       |             |
|                 |            | [Source:HGNC Symbol;Acc:HGNC:7549]"                        | 0.024577949 |
| ENSG00000105357 | MYH14      | myosin heavy chain 14                                      |             |
|                 |            | [Source:HGNC Symbol;Acc:HGNC:23212]                        | 0.025148395 |
| ENSG00000167757 | KLK11      | kallikrein related peptidase 11                            |             |
|                 |            | [Source:HGNC Symbol;Acc:HGNC:6359]                         | 0.025148395 |
| ENSG00000226068 | HNRNPA3P4  | heterogeneous nuclear ribonucleoprotein A3 pseudogene 4    |             |
|                 |            | [Source:HGNC Symbol;Acc:HGNC:39773]                        | 0.025148395 |
| ENSG00000260072 |            |                                                            | 0.025148395 |
| ENSG00000130226 | DPP6       | dipeptidyl peptidase like 6                                |             |
|                 |            | [Source:HGNC Symbol;Acc:HGNC:3010]                         | 0.02515224  |
| ENSG00000144648 | ACKR2      | atypical chemokine receptor 2                              |             |
|                 |            | [Source:HGNC Symbol;Acc:HGNC:1565]                         | 0.02527518  |
| ENSG00000169862 | CTNND2     | catenin delta 2                                            |             |
|                 |            | [Source:HGNC Symbol;Acc:HGNC:2516]                         | 0.025318552 |
| ENSG00000137766 | UNC13C     | unc-13 homolog C                                           |             |
|                 |            | [Source:HGNC Symbol;Acc:HGNC:23149]                        | 0.025345898 |
| ENSG00000261177 |            |                                                            | 0.025565995 |
| ENSG00000060656 | PTPRU      | "protein tyrosine phosphatase, receptor type U             |             |
|                 |            | [Source:HGNC Symbol;Acc:HGNC:9683]"                        | 0.025652607 |
| ENSG00000260305 | NTRK3-AS1  | NTRK3 antisense RNA 1                                      |             |
|                 |            | [Source:HGNC Symbol;Acc:HGNC:27532]                        | 0.02580767  |
| ENSG00000187955 | COL14A1    | collagen type XIV alpha 1 chain                            |             |
|                 |            | [Source:HGNC Symbol;Acc:HGNC:2191]                         | 0.025820696 |
| ENSG00000089225 | TBX5       | T-box 5                                                    |             |
|                 |            | [Source:HGNC Symbol;Acc:HGNC:11604]                        | 0.025834296 |
| ENSG00000224209 | LINC00466  | long intergenic non-protein coding RNA 466                 |             |
|                 |            | [Source:HGNC Symbol;Acc:HGNC:27294]                        | 0.025987072 |
| ENSG00000151474 | FRMD4A     | FERM domain containing 4A                                  |             |
|                 |            | [Source:HGNC Symbol;Acc:HGNC:25491]                        | 0.026041989 |
| ENSG00000039987 | BEST2      | bestrophin 2                                               |             |
|                 |            | [Source:HGNC Symbol;Acc:HGNC:17107]                        | 0.026152714 |
| ENSG00000266795 | NA         | NA                                                         | 0.026198035 |
| ENSG00000181143 | MUC16      | "mucin 16, cell surface associated                         |             |
|                 |            | [Source:HGNC Symbol;Acc:HGNC:15582]"                       | 0.026247081 |
| ENSG00000069431 | ABCC9      | ATP binding cassette subfamily C member 9                  |             |
|                 |            | [Source:HGNC Symbol;Acc:HGNC:60]                           | 0.026486685 |
| ENSG00000100312 | ACR        | acrosin                                                    |             |
|                 |            | [Source:HGNC Symbol;Acc:HGNC:126]                          | 0.02666392  |
| ENSG00000254042 |            |                                                            | 0.026721536 |
| ENSG00000180251 | SLC9A4     | solute carrier family 9 member A4                          |             |
|                 |            | [Source:HGNC Symbol;Acc:HGNC:11077]                        | 0.026759131 |
| ENSG00000237390 |            |                                                            | 0.026759131 |
| ENSG00000246695 | RASSF8-AS1 | RASSF8 antisense RNA 1                                     |             |
|                 |            | [Source:HGNC Symbol;Acc:HGNC:48637]                        | 0.026759131 |
| ENSG00000256612 | CYP2B7P    | "cytochrome P450 family 2 subfamily B member 7, pseudogene |             |
|                 |            | [Source:HGNC Symbol;Acc:HGNC:2616]"                        | 0.026759131 |
| ENSG00000165973 | NELL1      | neural EGFL like 1                                         |             |
|                 |            | [Source:HGNC Symbol;Acc:HGNC:7750]                         | 0.026774963 |
| ENSG00000172900 |            |                                                            | 0.02698221  |
| ENSG00000149926 | FAM57B     | family with sequence similarity 57 member B                |             |
|                 |            | [Source:HGNC Symbol;Acc:HGNC:25295]                        | 0.02707614  |
| ENSG00000107295 | SH3GL2     | "SH3 domain containing GRB2 like 2, endophilin A1          |             |
|                 |            | [Source:HGNC Symbol;Acc:HGNC:10831]"                       | 0.027164347 |
| ENSG00000173227 | SYT12      | synaptotagmin 12                                           |             |
|                 |            | [Source:HGNC Symbol;Acc:HGNC:18381]                        | 0.027164347 |
| ENSG00000173013 | CCDC96     | coiled-coil domain containing 96                           |             |
|                 |            | [Source:HGNC Symbol;Acc:HGNC:26900]                        | 0.027208218 |
| ENSG00000268460 |            |                                                            | 0.02723306  |
| ENSG00000234512 | TLR12P     | "toll like receptor 12, pseudogene                         |             |
|                 |            | [Source:HGNC Symbol;Acc:HGNC:31754]"                       | 0.027406947 |
| ENSG00000135931 | ARMC9      | armadillo repeat containing 9                              |             |
|                 |            | [Source:HGNC Symbol;Acc:HGNC:20730]                        | 0.02759323  |
| ENSG00000148702 | HABP2      | hyaluronan binding protein 2                               |             |
|                 |            | [Source:HGNC Symbol;Acc:HGNC:4798]                         | 0.027601758 |

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| ENSG00000136535 | TBR1      | "T-box, brain 1<br>[Source:HGNC Symbol;Acc:HGNC:11590]"                                                                                                           | 0.028071412 |
| ENSG00000122121 | XPNPEP2   | X-prolyl aminopeptidase 2<br>[Source:HGNC Symbol;Acc:HGNC:12823]                                                                                                  | 0.028133383 |
| ENSG00000170442 | KRT86     | keratin 86<br>[Source:HGNC Symbol;Acc:HGNC:6463]                                                                                                                  | 0.028133383 |
| ENSG00000197408 | CYP2B6    | cytochrome P450 family 2 subfamily B member 6<br>[Source:HGNC Symbol;Acc:HGNC:2615]                                                                               | 0.028133383 |
| ENSG00000107807 | TLX1      | T cell leukemia homeobox 1<br>[Source:HGNC Symbol;Acc:HGNC:5056]                                                                                                  | 0.028207054 |
| ENSG00000164694 | FNDC1     | fibronectin type III domain containing 1<br>[Source:HGNC Symbol;Acc:HGNC:21184]                                                                                   | 0.028207054 |
| ENSG00000185313 | SCN10A    | sodium voltage-gated channel alpha subunit 10<br>[Source:HGNC Symbol;Acc:HGNC:10582]                                                                              | 0.028207054 |
| ENSG00000164107 | HAND2     | heart and neural crest derivatives expressed 2<br>[Source:HGNC Symbol;Acc:HGNC:4808]                                                                              | 0.028335907 |
| ENSG00000133454 | MYO18B    | myosin XVIIIIB<br>[Source:HGNC Symbol;Acc:HGNC:18150]                                                                                                             | 0.028417113 |
| ENSG00000167723 | TRPV3     | transient receptor potential cation channel subfamily V member 3<br>[Source:HGNC Symbol;Acc:HGNC:18084]                                                           | 0.028422765 |
| ENSG00000184012 | TMPRSS2   | transmembrane serine protease 2<br>[Source:HGNC Symbol;Acc:HGNC:11876]                                                                                            | 0.028422765 |
| ENSG00000233485 |           |                                                                                                                                                                   | 0.028645846 |
| ENSG00000261466 |           |                                                                                                                                                                   | 0.028645846 |
| ENSG00000119547 | ONECUT2   | one cut homeobox 2<br>[Source:HGNC Symbol;Acc:HGNC:8139]                                                                                                          | 0.028669408 |
| ENSG00000237222 | LINC01968 | long intergenic non-protein coding RNA 1968<br>[Source:HGNC Symbol;Acc:HGNC:52794]                                                                                | 0.028800664 |
| ENSG00000137573 | SULF1     | sulfatase 1<br>[Source:HGNC Symbol;Acc:HGNC:20391]                                                                                                                | 0.028919683 |
| ENSG00000161609 | CCDC155   | coiled-coil domain containing 155<br>[Source:HGNC Symbol;Acc:HGNC:26520]                                                                                          | 0.028967146 |
| ENSG00000250546 |           |                                                                                                                                                                   | 0.028987628 |
| ENSG00000226057 | PHF2P2    | PHD finger protein 2 pseudogene 2<br>[Source:HGNC Symbol;Acc:HGNC:38808]                                                                                          | 0.029139308 |
| ENSG00000177045 | SIX5      | SIX homeobox 5<br>[Source:HGNC Symbol;Acc:HGNC:10891]                                                                                                             | 0.029298722 |
| ENSG00000124440 | HIF3A     | hypoxia inducible factor 3 alpha subunit<br>[Source:HGNC Symbol;Acc:HGNC:15825]                                                                                   | 0.029322985 |
| ENSG00000234828 | IQCM      | IQ motif containing M<br>[Source:HGNC Symbol;Acc:HGNC:53443]                                                                                                      | 0.029461236 |
| ENSG00000116721 | PRAMEF1   | PRAME family member 1<br>[Source:HGNC Symbol;Acc:HGNC:28840]                                                                                                      | 0.029473652 |
| ENSG00000238116 |           |                                                                                                                                                                   | 0.029473652 |
| ENSG00000106689 | LHX2      | LIM homeobox 2<br>[Source:HGNC Symbol;Acc:HGNC:6594]                                                                                                              | 0.029512187 |
| ENSG00000169344 | UMOD      | uromodulin<br>[Source:HGNC Symbol;Acc:HGNC:12559]                                                                                                                 | 0.02959944  |
| ENSG00000174279 | EVX2      | even-skipped homeobox 2<br>[Source:HGNC Symbol;Acc:HGNC:3507]                                                                                                     | 0.029661965 |
| ENSG00000128573 | FOXP2     | forkhead box P2<br>[Source:HGNC Symbol;Acc:HGNC:13875]                                                                                                            | 0.029779428 |
| ENSG00000251596 | HADHAP1   | "hydroxyacyl-CoA dehydrogenase/3-ketoacyl-CoA thiolase/enoyl-CoA hydratase (trifunctional protein), alpha subunit pseudogene 1[Source:HGNC Symbol;Acc:HGNC:4802]" | 0.029954508 |
| ENSG00000002746 | HECW1     | "HECT, C2 and WW domain containing E3 ubiquitin protein ligase 1<br>[Source:HGNC Symbol;Acc:HGNC:22195]"                                                          | 0.029980732 |
| ENSG00000081248 | CACNA1S   | calcium voltage-gated channel subunit alpha1 S<br>[Source:HGNC Symbol;Acc:HGNC:1397]                                                                              | 0.029997906 |
| ENSG00000166596 | CFAP52    | cilia and flagella associated protein 52<br>[Source:HGNC Symbol;Acc:HGNC:16053]                                                                                   | 0.030027148 |
| ENSG00000205176 | REXO1L1P  | "REXO1 like 1, pseudogene<br>[Source:HGNC Symbol;Acc:HGNC:24660]"                                                                                                 | 0.030066221 |
| ENSG00000152910 | CNTNAP4   | contactin associated protein like 4<br>[Source:HGNC Symbol;Acc:HGNC:18747]                                                                                        | 0.030144659 |

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| ENSG00000106078 | COBL      | cordon-bleu WH2 repeat protein<br>[Source:HGNC Symbol;Acc:HGNC:22199]                                   | 0.030263618 |
| ENSG00000177103 | DSCAML1   | DS cell adhesion molecule like 1<br>[Source:HGNC Symbol;Acc:HGNC:14656]                                 | 0.030299369 |
| ENSG00000131044 | TTLL9     | tubulin tyrosine ligase like 9<br>[Source:HGNC Symbol;Acc:HGNC:16118]                                   | 0.030317293 |
| ENSG00000170703 | TTLL6     | tubulin tyrosine ligase like 6<br>[Source:HGNC Symbol;Acc:HGNC:26664]                                   | 0.030472844 |
| ENSG00000165379 | LRFN5     | leucine rich repeat and fibronectin type III domain containing 5<br>[Source:HGNC Symbol;Acc:HGNC:20360] | 0.030532839 |
| ENSG00000198929 | NOS1AP    | nitric oxide synthase 1 adaptor protein<br>[Source:HGNC Symbol;Acc:HGNC:16859]                          | 0.030532839 |
| ENSG00000236253 | SLC25A3P1 | solute carrier family 25 member 3 pseudogene 1<br>[Source:HGNC Symbol;Acc:HGNC:26869]                   | 0.030574302 |
| ENSG00000205667 | ARSH      | arylsulfatase family member H<br>[Source:HGNC Symbol;Acc:HGNC:32488]                                    | 0.030639161 |
| ENSG00000226440 |           |                                                                                                         | 0.030639161 |
| ENSG00000131183 | SLC34A1   | solute carrier family 34 member 1<br>[Source:HGNC Symbol;Acc:HGNC:11019]                                | 0.030803937 |
| ENSG00000225649 |           |                                                                                                         | 0.030847037 |
| ENSG00000006283 | CACNA1G   | calcium voltage-gated channel subunit alpha1 G<br>[Source:HGNC Symbol;Acc:HGNC:1394]                    | 0.030936635 |
| ENSG00000230392 |           |                                                                                                         | 0.030977697 |
| ENSG00000234130 |           |                                                                                                         | 0.031067495 |
| ENSG00000095637 | SORBS1    | sorbin and SH3 domain containing 1<br>[Source:HGNC Symbol;Acc:HGNC:14565]                               | 0.031086939 |
| ENSG00000198010 | DLGAP2    | DLG associated protein 2<br>[Source:HGNC Symbol;Acc:HGNC:2906]                                          | 0.031235492 |
| ENSG00000102290 | PCDH11X   | protocadherin 11 X-linked<br>[Source:HGNC Symbol;Acc:HGNC:8656]                                         | 0.031415941 |
| ENSG00000260027 | HOXB7     | homeobox B7<br>[Source:HGNC Symbol;Acc:HGNC:5118]                                                       | 0.031452441 |
| ENSG00000105664 | COMP      | cartilage oligomeric matrix protein<br>[Source:HGNC Symbol;Acc:HGNC:2227]                               | 0.031516506 |
| ENSG00000006071 | ABCC8     | ATP binding cassette subfamily C member 8<br>[Source:HGNC Symbol;Acc:HGNC:59]                           | 0.031578145 |
| ENSG00000077522 | ACTN2     | actinin alpha 2<br>[Source:HGNC Symbol;Acc:HGNC:164]                                                    | 0.031657927 |
| ENSG00000248966 | BCLAF1P1  | BCL2 associated transcription factor 1 pseudogene 1<br>[Source:HGNC Symbol;Acc:HGNC:51329]              | 0.031733491 |
| ENSG00000124749 | COL21A1   | collagen type XXI alpha 1 chain<br>[Source:HGNC Symbol;Acc:HGNC:17025]                                  | 0.031814031 |
| ENSG00000142675 | CNKSR1    | connector enhancer of kinase suppressor of Ras 1<br>[Source:HGNC Symbol;Acc:HGNC:19700]                 | 0.031815396 |
| ENSG00000116748 | AMPD1     | adenosine monophosphate deaminase 1<br>[Source:HGNC Symbol;Acc:HGNC:468]                                | 0.031850457 |
| ENSG00000181355 | OFCC1     | orofacial cleft 1 candidate 1<br>[Source:HGNC Symbol;Acc:HGNC:21017]                                    | 0.03221007  |
| ENSG00000162510 | MATN1     | "matrilin 1, cartilage matrix protein<br>[Source:HGNC Symbol;Acc:HGNC:6907]"                            | 0.032424937 |
| ENSG00000232392 |           |                                                                                                         | 0.032424937 |
| ENSG00000123572 | NRK       | Nik related kinase<br>[Source:HGNC Symbol;Acc:HGNC:25391]                                               | 0.032537919 |
| ENSG00000267324 |           |                                                                                                         | 0.032537919 |
| ENSG00000196361 | ELAVL3    | ELAV like RNA binding protein 3<br>[Source:HGNC Symbol;Acc:HGNC:3314]                                   | 0.032579843 |
| ENSG00000204661 | C5orf60   | chromosome 5 open reading frame 60<br>[Source:HGNC Symbol;Acc:HGNC:27753]                               | 0.032697662 |
| ENSG00000224059 | HSPA8P16  | heat shock protein family A (Hsp70) member 8 pseudogene 16<br>[Source:HGNC Symbol;Acc:HGNC:44931]       | 0.03275969  |
| ENSG00000114019 | AMOTL2    | angiominin like 2<br>[Source:HGNC Symbol;Acc:HGNC:17812]                                                | 0.033101928 |
| ENSG00000134871 | COL4A2    | collagen type IV alpha 2 chain<br>[Source:HGNC Symbol;Acc:HGNC:2203]                                    | 0.033101928 |
| ENSG00000162706 | CADM3     | cell adhesion molecule 3<br>[Source:HGNC Symbol;Acc:HGNC:17601]                                         | 0.033101928 |

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| ENSG00000188782 | CATSPER4    | cation channel sperm associated 4<br>[Source:HGNC Symbol;Acc:HGNC:23220]                    | 0.033196706                |
| ENSG00000147689 | FAM83A      | family with sequence similarity 83 member A<br>[Source:HGNC Symbol;Acc:HGNC:28210]          | 0.033349502                |
| ENSG00000079841 | RIMS1       | regulating synaptic membrane exocytosis 1<br>[Source:HGNC Symbol;Acc:HGNC:17282]            | 0.033394348                |
| ENSG00000103647 | CORO2B      | coronin 2B<br>[Source:HGNC Symbol;Acc:HGNC:2256]                                            | 0.033419797                |
| ENSG00000112499 | SLC22A2     | solute carrier family 22 member 2<br>[Source:HGNC Symbol;Acc:HGNC:10966]                    | 0.033434322                |
| ENSG00000183856 | IQGAP3      | IQ motif containing GTPase activating protein 3<br>[Source:HGNC Symbol;Acc:HGNC:20669]      | 0.033434322                |
| ENSG00000165300 | SLITRK5     | SLIT and NTRK like family member 5<br>[Source:HGNC Symbol;Acc:HGNC:20295]                   | 0.033483825                |
| ENSG00000229972 | IQCF3       | IQ motif containing F3<br>[Source:HGNC Symbol;Acc:HGNC:31816]                               | 0.033483825                |
| ENSG00000261949 | GFY         | golgi associated olfactory signaling regulator<br>[Source:HGNC Symbol;Acc:HGNC:44663]       | 0.033483825                |
| ENSG00000171487 | NLRP5       | NLR family pyrin domain containing 5<br>[Source:HGNC Symbol;Acc:HGNC:21269]                 | 0.033631095                |
| ENSG00000129946 | SHC2        | SHC adaptor protein 2<br>[Source:HGNC Symbol;Acc:HGNC:29869]                                | 0.033699292                |
| ENSG00000117501 | MROH9       | maestro heat like repeat family member 9<br>[Source:HGNC Symbol;Acc:HGNC:26287]             | 0.03391477                 |
| ENSG00000136574 | GATA4       | GATA binding protein 4<br>[Source:HGNC Symbol;Acc:HGNC:4173]                                | 0.034539616                |
| ENSG00000106648 | GALNTL5     | polypeptide N-acetylgalactosaminyltransferase like 5<br>[Source:HGNC Symbol;Acc:HGNC:21725] | 0.034620414                |
| ENSG00000188086 | PRSS45      | serine protease 45<br>[Source:HGNC Symbol;Acc:HGNC:30717]                                   | 0.034840251<br>0.034858474 |
| ENSG00000234537 |             |                                                                                             |                            |
| ENSG00000226741 | LINC02554   | long intergenic non-protein coding RNA 2554<br>[Source:HGNC Symbol;Acc:HGNC:53594]          | 0.034969314                |
| ENSG00000004948 | CALCR       | calcitonin receptor<br>[Source:HGNC Symbol;Acc:HGNC:1440]                                   | 0.034980702                |
| ENSG00000142549 | IGLON5      | IgLO family member 5<br>[Source:HGNC Symbol;Acc:HGNC:34550]                                 | 0.034980702<br>0.034980702 |
| ENSG00000250519 |             |                                                                                             |                            |
| ENSG00000183908 | LRRC55      | leucine rich repeat containing 55<br>[Source:HGNC Symbol;Acc:HGNC:32324]                    | 0.035005257                |
| ENSG00000253974 | NRG1-IT1    | NRG1 intronic transcript 1<br>[Source:HGNC Symbol;Acc:HGNC:43633]                           | 0.035154264                |
| ENSG00000162738 | VANGL2      | VANGL planar cell polarity protein 2<br>[Source:HGNC Symbol;Acc:HGNC:15511]                 | 0.035338561                |
| ENSG00000115648 | MLPH        | melanophilin<br>[Source:HGNC Symbol;Acc:HGNC:29643]                                         | 0.03575577                 |
| ENSG00000187997 | C17orf99    | chromosome 17 open reading frame 99<br>[Source:HGNC Symbol;Acc:HGNC:34490]                  | 0.03575577                 |
| ENSG00000140279 | DUOX2       | dual oxidase 2<br>[Source:HGNC Symbol;Acc:HGNC:13273]                                       | 0.035790036                |
| ENSG00000168077 | SCARA3      | scavenger receptor class A member 3<br>[Source:HGNC Symbol;Acc:HGNC:19000]                  | 0.035804565                |
| ENSG00000159337 | PLA2G4D     | phospholipase A2 group IVD<br>[Source:HGNC Symbol;Acc:HGNC:30038]                           | 0.035823277                |
| ENSG00000183580 | FBXL7       | F-box and leucine rich repeat protein 7<br>[Source:HGNC Symbol;Acc:HGNC:13604]              | 0.035823277<br>0.035823277 |
| ENSG00000218586 |             |                                                                                             |                            |
| ENSG00000184809 | B3GALT5-AS1 | B3GALT5 antisense RNA 1<br>[Source:HGNC Symbol;Acc:HGNC:16424]                              | 0.035845893                |
| ENSG00000132975 | GPR12       | G protein-coupled receptor 12<br>[Source:HGNC Symbol;Acc:HGNC:4466]                         | 0.035938935                |
| ENSG00000142910 | TINAGL1     | tubulointerstitial nephritis antigen like 1<br>[Source:HGNC Symbol;Acc:HGNC:19168]          | 0.035938935                |
| ENSG00000075891 | PAX2        | paired box 2<br>[Source:HGNC Symbol;Acc:HGNC:8616]                                          | 0.035996581                |
| ENSG00000186393 | KRT26       | keratin 26<br>[Source:HGNC Symbol;Acc:HGNC:30840]                                           | 0.036025366                |

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| ENSG00000167779 | IGFBP6      | insulin like growth factor binding protein 6<br>[Source:HGNC Symbol;Acc:HGNC:5475]                            | 0.036065767 |
| ENSG00000232667 |             |                                                                                                               | 0.036065767 |
| ENSG00000263711 |             |                                                                                                               | 0.036105875 |
| ENSG00000205054 | LINC01121   | long intergenic non-protein coding RNA 1121<br>[Source:HGNC Symbol;Acc:HGNC:49266]                            | 0.036340531 |
| ENSG00000146950 | SHROOM2     | shroom family member 2<br>[Source:HGNC Symbol;Acc:HGNC:630]                                                   | 0.036393162 |
| ENSG00000143867 | OSR1        | odd-skipped related transcription factor 1<br>[Source:HGNC Symbol;Acc:HGNC:8111]                              | 0.036631586 |
| ENSG00000205976 |             |                                                                                                               | 0.037140956 |
| ENSG00000196862 | RGPD4       | RANBP2-like and GRIP domain containing 4<br>[Source:HGNC Symbol;Acc:HGNC:32417]                               | 0.037154755 |
| ENSG00000148513 | ANKRD30A    | ankyrin repeat domain 30A<br>[Source:HGNC Symbol;Acc:HGNC:17234]                                              | 0.037278195 |
| ENSG00000101057 | MYBL2       | MYB proto-oncogene like 2<br>[Source:HGNC Symbol;Acc:HGNC:7548]                                               | 0.037361359 |
| ENSG00000139144 | PIK3C2G     | phosphatidylinositol-4-phosphate 3-kinase catalytic subunit type 2<br>Gamma[Source:HGNC Symbol;Acc:HGNC:8973] | 0.037546969 |
| ENSG00000247213 | LINC01498   | long intergenic non-protein coding RNA 1498<br>[Source:HGNC Symbol;Acc:HGNC:51164]                            | 0.037546969 |
| ENSG00000145242 | EPHA5       | EPH receptor A5<br>[Source:HGNC Symbol;Acc:HGNC:3389]                                                         | 0.037630556 |
| ENSG00000249215 | NCOA4P4     | nuclear receptor coactivator 4 pseudogene 4<br>[Source:HGNC Symbol;Acc:HGNC:52405]                            | 0.037740576 |
| ENSG00000079112 | CDH17       | cadherin 17<br>[Source:HGNC Symbol;Acc:HGNC:1756]                                                             | 0.037745905 |
| ENSG00000166118 | SPATA19     | spermatogenesis associated 19<br>[Source:HGNC Symbol;Acc:HGNC:30614]                                          | 0.037802718 |
| ENSG00000162006 | MSLN        | mesothelin-like<br>[Source:HGNC Symbol;Acc:HGNC:14170]                                                        | 0.037970738 |
| ENSG00000187123 | LYPD6       | LY6/PLAUR domain containing 6<br>[Source:HGNC Symbol;Acc:HGNC:28751]                                          | 0.037980544 |
| ENSG00000104313 | EYA1        | EYA transcriptional coactivator and phosphatase 1<br>[Source:HGNC Symbol;Acc:HGNC:3519]                       | 0.038059131 |
| ENSG00000237250 |             |                                                                                                               | 0.038171217 |
| ENSG00000105290 | APLP1       | amyloid beta precursor like protein 1<br>[Source:HGNC Symbol;Acc:HGNC:597]                                    | 0.038576481 |
| ENSG00000138650 | PCDH10      | protocadherin 10<br>[Source:HGNC Symbol;Acc:HGNC:13404]                                                       | 0.038631087 |
| ENSG00000198914 | POU3F3      | POU class 3 homeobox 3<br>[Source:HGNC Symbol;Acc:HGNC:9216]                                                  | 0.03865691  |
| ENSG00000117114 | ADGRL2      | adhesion G protein-coupled receptor L2<br>[Source:HGNC Symbol;Acc:HGNC:18582]                                 | 0.039101789 |
| ENSG00000185737 | NRG3        | neuregulin 3<br>[Source:HGNC Symbol;Acc:HGNC:7999]                                                            | 0.039101789 |
| ENSG00000197085 | NPSR1-AS1   | NPSR1 antisense RNA 1<br>[Source:HGNC Symbol;Acc:HGNC:22128]                                                  | 0.039361047 |
| ENSG00000230102 | LINC02028   | long intergenic non-protein coding RNA 2028<br>[Source:HGNC Symbol;Acc:HGNC:27718]                            | 0.039602594 |
| ENSG00000241158 | ADAMTS9-AS1 | ADAMTS9 antisense RNA 1<br>[Source:HGNC Symbol;Acc:HGNC:40625]                                                | 0.039646513 |
| ENSG00000146005 | PSD2        | pleckstrin and Sec7 domain containing 2<br>[Source:HGNC Symbol;Acc:HGNC:19092]                                | 0.039852243 |
| ENSG00000171533 | MAP6        | microtubule associated protein 6<br>[Source:HGNC Symbol;Acc:HGNC:6868]                                        | 0.040171006 |
| ENSG00000164294 | GPX8        | glutathione peroxidase 8 (putative)<br>[Source:HGNC Symbol;Acc:HGNC:33100]                                    | 0.040207131 |
| ENSG00000054356 | PTPRN       | "protein tyrosine phosphatase, receptor type N<br>[Source:HGNC Symbol;Acc:HGNC:9676]"                         | 0.040248543 |
| ENSG00000077080 | ACTL6B      | actin like 6B<br>[Source:HGNC Symbol;Acc:HGNC:160]                                                            | 0.040248543 |
| ENSG00000141434 | MEP1B       | meprin A subunit beta<br>[Source:HGNC Symbol;Acc:HGNC:7020]                                                   | 0.040590193 |
| ENSG00000183067 | IGSF5       | immunoglobulin superfamily member 5<br>[Source:HGNC Symbol;Acc:HGNC:5952]                                     | 0.040590193 |
| ENSG00000112337 | SLC17A2     | solute carrier family 17 member 2                                                                             |             |

|                 |           |                                                                                             |             |
|-----------------|-----------|---------------------------------------------------------------------------------------------|-------------|
| ENSG00000161682 | FAM171A2  | [Source:HGNC Symbol;Acc:HGNC:10930]<br>family with sequence similarity 171 member A2        | 0.040803316 |
| ENSG00000116833 | NR5A2     | [Source:HGNC Symbol;Acc:HGNC:30480]<br>nuclear receptor subfamily 5 group A member 2        | 0.040923418 |
| ENSG00000143355 | LHX9      | [Source:HGNC Symbol;Acc:HGNC:7984]<br>LIM homeobox 9                                        | 0.040938395 |
| ENSG00000139767 | SRRM4     | [Source:HGNC Symbol;Acc:HGNC:14222]<br>serine/arginine repetitive matrix 4                  | 0.041155655 |
| ENSG00000227036 | LINC00511 | [Source:HGNC Symbol;Acc:HGNC:29389]<br>long intergenic non-protein coding RNA 511           | 0.041207854 |
| ENSG00000105549 | THEG      | [Source:HGNC Symbol;Acc:HGNC:43564]<br>theg spermatid protein                               | 0.041207854 |
| ENSG00000104967 | NOVA2     | [Source:HGNC Symbol;Acc:HGNC:13706]<br>NOVA alternative splicing regulator 2                | 0.041581527 |
| ENSG00000183206 | POTEC     | [Source:HGNC Symbol;Acc:HGNC:7887]<br>POTE ankyrin domain family member C                   | 0.041600384 |
| ENSG00000184302 | SIX6      | [Source:HGNC Symbol;Acc:HGNC:33894]<br>SIX homeobox 6                                       | 0.041620804 |
| ENSG00000245651 |           | [Source:HGNC Symbol;Acc:HGNC:10892]<br>transmembrane protein 125                            | 0.041631474 |
| ENSG00000179178 | TMEM125   |                                                                                             | 0.041631474 |
| ENSG00000231422 | LINC01516 | [Source:HGNC Symbol;Acc:HGNC:28275]<br>long intergenic non-protein coding RNA 1516          | 0.041791867 |
| ENSG00000104435 | STMN2     | [Source:HGNC Symbol;Acc:HGNC:51211]<br>stathmin 2                                           | 0.041868067 |
| ENSG00000185069 | KRT76     | [Source:HGNC Symbol;Acc:HGNC:10577]<br>keratin 76                                           | 0.041944166 |
| ENSG00000060709 | RIMBP2    | [Source:HGNC Symbol;Acc:HGNC:24430]<br>RIMS binding protein 2                               | 0.042071807 |
| ENSG00000261115 | TMEM178B  | [Source:HGNC Symbol;Acc:HGNC:30339]<br>transmembrane protein 178B                           | 0.042101327 |
| ENSG00000261623 | LINC02179 | [Source:HGNC Symbol;Acc:HGNC:44112]<br>long intergenic non-protein coding RNA 2179          | 0.042193233 |
| ENSG00000153165 | RGPD3     | [Source:HGNC Symbol;Acc:HGNC:53041]<br>RANBP2-like and GRIP domain containing 3             | 0.042224694 |
| ENSG00000253230 | LINC00599 | [Source:HGNC Symbol;Acc:HGNC:32416]<br>long intergenic non-protein coding RNA 599           | 0.042347063 |
| ENSG00000236078 | LINC01447 | [Source:HGNC Symbol;Acc:HGNC:27231]<br>long intergenic non-protein coding RNA 1447          | 0.042450091 |
| ENSG00000230133 | LINC01721 | [Source:HGNC Symbol;Acc:HGNC:50783]<br>long intergenic non-protein coding RNA 1721          | 0.042463159 |
| ENSG00000237636 | ANKRD26P3 | [Source:HGNC Symbol;Acc:HGNC:52508]<br>ankyrin repeat domain 26 pseudogene 3                | 0.042512831 |
| ENSG00000264954 | PRR29-AS1 | [Source:HGNC Symbol;Acc:HGNC:39689]<br>PRR29 antisense RNA 1                                | 0.042582368 |
| ENSG00000166689 | PLEKHA7   | [Source:HGNC Symbol;Acc:HGNC:51822]<br>pleckstrin homology domain containing A7             | 0.042699245 |
| ENSG00000173826 | KCNH6     | [Source:HGNC Symbol;Acc:HGNC:27049]<br>potassium voltage-gated channel subfamily H member 6 | 0.04272194  |
| ENSG00000253864 | NA        | [Source:HGNC Symbol;Acc:HGNC:18862]<br>NA                                                   | 0.042801591 |
| ENSG00000166292 | TMEM100   |                                                                                             | 0.042900836 |
| ENSG00000137203 | TFAP2A    | [Source:HGNC Symbol;Acc:HGNC:25607]<br>transcription factor AP-2 alpha                      | 0.043052047 |
| ENSG00000165970 | SLC6A5    | [Source:HGNC Symbol;Acc:HGNC:11742]<br>solute carrier family 6 member 5                     | 0.043105155 |
| ENSG00000184908 | CLCNKB    | [Source:HGNC Symbol;Acc:HGNC:11051]<br>chloride voltage-gated channel Kb                    | 0.043105155 |
| ENSG00000197893 | NRAP      | [Source:HGNC Symbol;Acc:HGNC:2027]<br>nebulin related anchoring protein                     | 0.043516345 |
| ENSG00000169126 | ARMC4     | [Source:HGNC Symbol;Acc:HGNC:7988]<br>armadillo repeat containing 4                         | 0.043567821 |
| ENSG00000245248 | USP2-AS1  | [Source:HGNC Symbol;Acc:HGNC:25583]<br>USP2 antisense RNA 1 (head to head)                  | 0.043632647 |
| ENSG00000242866 | STRC      | [Source:HGNC Symbol;Acc:HGNC:48673]<br>stereocilin                                          | 0.043635087 |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:16035]<br>stereocilin                                          | 0.043658722 |

|                 |           |                                                   |             |
|-----------------|-----------|---------------------------------------------------|-------------|
| ENSG00000164393 | ADGRF2    | adhesion G protein-coupled receptor F2            |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:18991]               | 0.044026611 |
| ENSG00000100033 | PRODH     | proline dehydrogenase 1                           |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:9453]                | 0.044045719 |
| ENSG00000136352 | NKX2-1    | NK2 homeobox 1                                    |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:11825]               | 0.044046233 |
| ENSG00000165566 | AMER2     | APC membrane recruitment protein 2                |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:26360]               | 0.044155809 |
| ENSG00000163995 | ABLIM2    | actin binding LIM protein family member 2         |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:19195]               | 0.044231879 |
| ENSG00000165495 | PKNOX2    | PBX/knotted 1 homeobox 2                          |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:16714]               | 0.044261202 |
| ENSG00000144115 | THNSL2    | threonine synthase like 2                         |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:25602]               | 0.044590058 |
| ENSG00000157214 | STEAP2    | STEAP2 metalloredutase                            |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:17885]               | 0.044717969 |
| ENSG00000229240 | LINC00710 | long intergenic non-protein coding RNA 710        |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:27386]               | 0.044849493 |
| ENSG00000168356 | SCN11A    | sodium voltage-gated channel alpha subunit 11     |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:10583]               | 0.044881812 |
| ENSG00000130508 | PXDN      | peroxidasin                                       |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:14966]               | 0.044899327 |
| ENSG00000166444 | ST5       | suppression of tumorigenicity 5                   |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:11350]               | 0.044899327 |
| ENSG00000140600 | SH3GL3    | "SH3 domain containing GRB2 like 3, endophilin A3 |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:10832]"              | 0.045237232 |
| ENSG00000214181 | NA        | NA                                                | 0.045237232 |
| ENSG00000144681 | STAC      | SH3 and cysteine rich domain                      |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:11353]               | 0.045389235 |
| ENSG00000166863 | TAC3      | tachykinin 3                                      |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:11521]               | 0.045474144 |
| ENSG00000169436 | COL22A1   | collagen type XXII alpha 1 chain                  |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:22989]               | 0.045474144 |
| ENSG00000172137 | CALB2     | calbindin 2                                       |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:1435]                | 0.045474144 |
| ENSG00000223566 | TNRC18P2  | trinucleotide repeat containing 18 pseudogene 2   |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:34014]               | 0.045474144 |
| ENSG00000175267 | VWA3A     | von Willebrand factor A domain containing 3A      |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:27088]               | 0.045495146 |
| ENSG00000175267 | VWA3A     | von Willebrand factor A domain containing 3A      |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:27088]               | 0.045495146 |
| ENSG00000183780 | SLC35F3   | solute carrier family 35 member F3                |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:23616]               | 0.045495146 |
| ENSG00000228983 | SLC47A1P1 | solute carrier family 47 member 1 pseudogene 1    |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:51849]               | 0.045495146 |
| ENSG00000269332 | GOLGA2P9  | golgin A2 pseudogene 9                            |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:49921]               | 0.045495146 |
| ENSG00000081800 | SLC13A1   | solute carrier family 13 member 1                 |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:10916]               | 0.045528908 |
| ENSG00000155816 | FMN2      | formin 2                                          |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:14074]               | 0.045528908 |
| ENSG00000091137 | SLC26A4   | solute carrier family 26 member 4                 |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:8818]                | 0.045601783 |
| ENSG00000129990 | SYT5      | synaptotagmin 5                                   |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:11513]               | 0.045601783 |
| ENSG00000173702 | MUC13     | "mucin 13, cell surface associated                |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:7511]"               | 0.045601783 |
| ENSG00000116176 | TPSG1     | tryptase gamma 1                                  |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:14134]               | 0.045645845 |
| ENSG00000250420 | AACSP1    | acetoacetyl-CoA synthetase pseudogene 1           |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:18226]               | 0.045645845 |
| ENSG00000104055 | TGM5      | transglutaminase 5                                |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:11781]               | 0.045691236 |
| ENSG00000109101 | FOXN1     | forkhead box N1                                   |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:12765]               | 0.045781    |
| ENSG00000131386 | GALNT15   | polypeptide N-acetylgalactosaminyltransferase 15  |             |
|                 |           | [Source:HGNC Symbol;Acc:HGNC:21531]               | 0.045798489 |

|                 |           |                                                                                                      |                            |
|-----------------|-----------|------------------------------------------------------------------------------------------------------|----------------------------|
| ENSG00000183016 | NA        | NA                                                                                                   | 0.045937358                |
| ENSG00000248746 | ACTN3     | actinin alpha 3 (gene/pseudogene)<br>[Source:HGNC Symbol;Acc:HGNC:165]                               | 0.045937358<br>0.04595318  |
| ENSG00000259010 | UNC5D     | unc-5 netrin receptor D<br>[Source:HGNC Symbol;Acc:HGNC:18634]                                       | 0.046099925                |
| ENSG00000156687 | EEF1B2P2  | eukaryotic translation elongation factor 1 beta 2 pseudogene 2<br>[Source:HGNC Symbol;Acc:HGNC:3209] | 0.046129239                |
| ENSG00000143107 | FNDC7     | fibronectin type III domain containing 7<br>[Source:HGNC Symbol;Acc:HGNC:26668]                      | 0.046229298<br>0.046269835 |
| ENSG00000230615 | ACOT1     | acyl-CoA thioesterase 1<br>[Source:HGNC Symbol;Acc:HGNC:33128]                                       | 0.046363122                |
| ENSG00000118194 | TNNT2     | "troponin T2, cardiac type<br>[Source:HGNC Symbol;Acc:HGNC:11949]"                                   | 0.046453265                |
| ENSG00000172995 | ARPP21    | cAMP regulated phosphoprotein 21<br>[Source:HGNC Symbol;Acc:HGNC:16968]                              | 0.046453265                |
| ENSG00000156103 | MMP16     | matrix metalloproteinase 16<br>[Source:HGNC Symbol;Acc:HGNC:7162]                                    | 0.04649564                 |
| ENSG00000164904 | ALDH7A1   | aldehyde dehydrogenase 7 family member A1<br>[Source:HGNC Symbol;Acc:HGNC:877]                       | 0.04649564                 |
| ENSG00000224743 | TEX26-AS1 | TEX26 antisense RNA 1<br>[Source:HGNC Symbol;Acc:HGNC:42784]                                         | 0.04649564                 |
| ENSG00000185823 | NPAP1     | nuclear pore associated protein 1<br>[Source:HGNC Symbol;Acc:HGNC:1190]                              | 0.04652545                 |
| ENSG00000018607 | ZNF806    | zinc finger protein 806<br>[Source:HGNC Symbol;Acc:HGNC:33228]                                       | 0.046600673                |
| ENSG00000179270 | C2orf71   | chromosome 2 open reading frame 71<br>[Source:HGNC Symbol;Acc:HGNC:34383]                            | 0.046600673                |
| ENSG00000186862 | PDZD7     | PDZ domain containing 7<br>[Source:HGNC Symbol;Acc:HGNC:26257]                                       | 0.046710668                |
| ENSG00000227525 | RPL7P6    | ribosomal protein L7 pseudogene 6<br>[Source:HGNC Symbol;Acc:HGNC:32430]                             | 0.046989116                |
| ENSG00000236229 | VEZF1P1   | vascular endothelial zinc finger 1 pseudogene 1<br>[Source:HGNC Symbol;Acc:HGNC:32320]               | 0.047105132                |
| ENSG00000171564 | FGB       | fibrinogen beta chain<br>[Source:HGNC Symbol;Acc:HGNC:3662]                                          | 0.047251427<br>0.047316621 |
| ENSG00000257175 | LOC285556 | "Homo sapiens uncharacterized mRNA.<br>[Source:RefSeq mRNA;Acc:NM_001354435]"                        | 0.047420932                |
| ENSG00000102287 | GABRE     | gamma-aminobutyric acid type A receptor epsilon subunit<br>[Source:HGNC Symbol;Acc:HGNC:4085]        | 0.047603565<br>0.0476766   |
| ENSG00000150086 | NA        | NA                                                                                                   | 0.0476766                  |
| ENSG00000168959 | GRM5      | glutamate metabotropic receptor 5<br>[Source:HGNC Symbol;Acc:HGNC:4597]                              | 0.0476766                  |
| ENSG00000184304 | PRKD1     | protein kinase D1<br>[Source:HGNC Symbol;Acc:HGNC:9407]                                              | 0.0476766<br>0.047795615   |
| ENSG00000204055 | ASB5      | ankyrin repeat and SOCS box containing 5<br>[Source:HGNC Symbol;Acc:HGNC:17180]                      | 0.047913021                |
| ENSG00000123977 | DAW1      | dynein assembly factor with WD repeats 1<br>[Source:HGNC Symbol;Acc:HGNC:26383]                      | 0.047973                   |
| ENSG00000156413 | FUT6      | fucosyltransferase 6<br>[Source:HGNC Symbol;Acc:HGNC:4017]                                           | 0.047988989                |
| ENSG00000101276 | SLC52A3   | solute carrier family 52 member 3<br>[Source:HGNC Symbol;Acc:HGNC:16187]                             | 0.048129781                |
| ENSG00000168079 | SCARA5    | scavenger receptor class A member 5<br>[Source:HGNC Symbol;Acc:HGNC:28701]                           | 0.048129781<br>0.048129781 |
| ENSG00000254561 | ROR1-AS1  | ROR1 antisense RNA 1<br>[Source:HGNC Symbol;Acc:HGNC:40508]                                          | 0.048194625                |
| ENSG00000223949 | SP5       | Sp5 transcription factor<br>[Source:HGNC Symbol;Acc:HGNC:14529]                                      | 0.048312303<br>0.04840783  |
| ENSG00000204241 | CBARP     | CACN beta subunit associated regulatory protein<br>[Source:HGNC Symbol;Acc:HGNC:28617]               | 0.048411296                |
| ENSG00000099625 | OAZ3      | ornithine decarboxylase antizyme 3                                                                   |                            |
| ENSG00000143450 |           |                                                                                                      |                            |

|                  |          |                                                                                         |             |
|------------------|----------|-----------------------------------------------------------------------------------------|-------------|
| ENSG00000015520  | NPC1L1   | [Source:HGNC Symbol;Acc:HGNC:8097]<br>NPC1 like intracellular cholesterol transporter 1 | 0.048617065 |
| ENSG000000188162 | OTOG     | [Source:HGNC Symbol;Acc:HGNC:7898]<br>otogelin                                          | 0.048746819 |
| ENSG000000125492 | BARHL1   | [Source:HGNC Symbol;Acc:HGNC:8516]<br>BarH like homeobox 1                              | 0.048746819 |
| ENSG000000145832 | SLC25A48 | [Source:HGNC Symbol;Acc:HGNC:953]<br>solute carrier family 25 member 48                 | 0.048820483 |
| ENSG000000185686 | PRAME    | [Source:HGNC Symbol;Acc:HGNC:30451]<br>preferentially expressed antigen in melanoma     | 0.048934402 |
| ENSG000000229147 | SMPD4P2  | [Source:HGNC Symbol;Acc:HGNC:9336]<br>sphingomyelin phosphodiesterase 4 pseudogene 2    | 0.048934402 |
|                  |          | [Source:HGNC Symbol;Acc:HGNC:39674]                                                     | 0.049012128 |

**[000181]** A listing of selected and preferred AC3 RNA markers of impending flare, based on their scores and relevance to sublining fibroblast cells is provided below in Table 9. These markers are particularly selected for determining and predicting impending RA flares. The markers are selected from COL1A2, COL5A1, COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1 and ZFH4.

**[000182]** The markers include several genes for collagen alpha chain subunits, including COL1A2, COL5A1, COL16A1, COL14A1 and COL4A2, as follows: COL1A2 Collagen alpha-2(I) chain. This gene encodes the alpha 2 (pro-a2(1)) chain component of type I collagen, the fibrillary collagen found in most connective tissues; COL5A1 Collagen Type V Alpha 1 Chain a component of type V collagen, which is a low abundance fibrillar collagen; COL16A1 Collagen alpha-1(XVI) chain. This gene encodes the alpha chain of type XVI collagen, a member of the FACIT collagen family (fibril-associated collagens with interrupted helices). Collagen type XVI is a fibril-forming collagen that maintains the integrity of the extracellular matrix; COL14A1 Collagen alpha-1(XIV) chain is a protein that in humans is encoded by the *COL14A1* gene. It likely plays a role in collagen binding and cell-cell adhesion; COL4A2 The COL4A2 gene encodes the alpha-2 chain of type IV collagen. Type IV collagen is associated with laminin, entactin, and heparan sulfate proteoglycans to form the sheetlike basement membranes that separate epithelium from connective tissue.

**[000183]** Additional markers are PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1 and ZFH4. PXDN (peroxidase) is a heme-containing peroxidase that is secreted into the extracellular matrix and is involved in extracellular matrix formation. ST5 (Suppression Of Tumorigenicity 5 protein), also called DENN Domain Containing 2B. This gene was identified by its ability to suppress the tumorigenicity of HeLa cells in nude mice. The protein encoded by this gene contains a C-terminal region that shares similarity with the Rab 3 family of small GTP binding proteins. This protein preferentially binds to the SH3 domain of c-Abl kinase, and acts as a regulator of MAPK1/ERK2 kinase, which may contribute to its ability to reduce the tumorigenic phenotype in cells. May be involved in cytoskeletal organization and tumorigenicity. DCLK1 (Doublecortin Like Kinase 1) is a microtubule-associated protein kinase - a serine/threonine-protein kinase. Doublecortin Like Kinase 1 has been identified as a tuft cell marker in the small intestine and has been reported to mark tumor stem cells in the intestine and pancreas. SCARA5 (Scavenger receptor class A, member 5) is involved

in lineage commitment and differentiation of mesenchymal stem cells to adipocytes. EGFR corresponds to epidermal growth factor receptor and is a cell membrane spanning protein induces cell differentiation and proliferation. Alteration and overexpression associated with various cancers. Numerous EGFR antibodies, including specific neutralizing antibodies, have been developed and are in clinical development or clinical practice for applications in cancer. EGR1 (Early growth response protein 1) - also known as ZNF268 (zinc finger protein 268) or NGFI-A (nerve growth factor-induced protein A). *EGR-1* is a mammalian transcription factor. *EGR-1* is a mechano-sensitive transcriptional factor that stimulates IGF-1R transcription, resulting in vascular remodeling of vein grafts. Early growth response protein 1 is a transcription factor that is rapidly induced by growth factors, cytokines, and stress signals such as radiation, injury, or mechanical stress. ZFHX4 (Zinc Finger Homeobox 4) Predicted to have RNA polymerase II proximal promoter sequence-specific DNA binding activity. RNA polymerase II specific DNA-binding transcription factor activity.

**[000184]** Notably all of the markers provided in Table 9 are also listed in Table 5 above, which provided transcripts common to synovial sublining fibroblasts and AC3. Table 5 also included the  $\alpha$  collagen chain gene COL3A1, COMP, FNDC1, GALNT15, SULF1, GPX8 and IGFBP6. COL3A2 corresponds to collagen Type III alpha 1 chain. COMP (cartilage oligomeric matrix protein) Can mediate the interaction of chondrocytes with the cartilage extracellular matrix and may play a role in the structural integrity of cartilage via its interaction with other extracellular matrix proteins such as the collagens and fibronectin. FNDC1 (fibronectin Type III domain containing 1) has alternative names Activation-associated cDNA protein and expressed in synovial lining protein and is an activator of G-protein signaling. GALNT15 (Polypeptide N-Acetylgalactosaminyltransferase 15) is a membrane-bound polypeptide N-acetylgalactosaminyltransferases that catalyzes the first step in mucin-type O-glycosylation of peptides in the Golgi apparatus. SULF1 (Sulfatase 1) is an extracellular heparan sulfate endosulfatase. The enzyme is secreted through the Golgi and is subsequently localized to the cell surface and selectively removes 6-O-sulfate groups from heparan sulfate chains of heparan sulfate proteoglycans. GPX8 (Glutathione Peroxidase 8) is a protein disulfide isomerase and is involved in cellular response to oxidative stress, reducing H<sub>2</sub>O<sub>2</sub> content and oxidative stress in the ER. IGFBP6 (Insulin-like growth factor-binding protein 6) binds insulin-like growth factor and fibronectin and has been shown to modulate the growth promoting effects of the IGFs on cell culture.

TABLE 9  
RNA Markers of Impending Flare

| SYMBOL  | Column 1 | geneset                                   | ENSG            | Gene               | AUC         | PCT non-zero | pct.nonzero.other | baseMean_prime |
|---------|----------|-------------------------------------------|-----------------|--------------------|-------------|--------------|-------------------|----------------|
| COL1A2  | SC-F1    | Fibroblast-CD34+<br>sublining (SC-F1)     | ENSG00000164692 | ENSG00000164692.13 | 0.84468179  | 1            | 0.532809984       | 51.509861398   |
| COL1A2  | SC-F2    | Fibroblast-HLA-DRAhi<br>sublining (SC-F2) | ENSG00000164692 | ENSG00000164692.13 | 0.921394835 | 1            | 0.509613353       | 51.509861398   |
| COL1A2  | SC-F3    | Fibroblast-DKK3+<br>sublining (SC-F3)     | ENSG00000164692 | ENSG00000164692.13 | 0.906702534 | 1            | 0.555704441       | 51.509861398   |
| PXDN    | SC-F2    | Fibroblast-HLA-DRAhi<br>sublining (SC-F2) | ENSG00000130508 | ENSG00000130508.6  | 0.843306415 | 0.831710709  | 0.16670188        | 24.409015138   |
| PXDN    | SC-F3    | Fibroblast-DKK3+<br>sublining (SC-F3)     | ENSG00000130508 | ENSG00000130508.6  | 0.836927155 | 0.881578947  | 0.227029096       | 24.409015138   |
| COL5A1  | SC-F1    | Fibroblast-CD34+<br>sublining (SC-F1)     | ENSG00000130635 | ENSG00000130635.11 | 0.769189965 | 0.809917355  | 0.263486312       | 24.050387975   |
| COL5A1  | SC-F2    | Fibroblast-HLA-DRAhi<br>sublining (SC-F2) | ENSG00000130635 | ENSG00000130635.11 | 0.884892773 | 0.95132128   | 0.214874287       | 24.050387975   |
| COL5A1  | SC-F3    | Fibroblast-DKK3+<br>sublining (SC-F3)     | ENSG00000130635 | ENSG00000130635.11 | 0.917280819 | 0.98245614   | 0.282733538       | 24.050387975   |
| ZFH4    | SC-F1    | Fibroblast-CD34+<br>sublining (SC-F1)     | ENSG00000091656 | ENSG00000091656.11 | 0.778380395 | 0.714876033  | 0.207125604       | 23.828346616   |
| ZFH4    | SC-F3    | Fibroblast-DKK3+<br>sublining (SC-F3)     | ENSG00000091656 | ENSG00000091656.11 | 0.789767117 | 0.802631579  | 0.228177642       | 23.828346616   |
| COL16A1 | SC-F2    | Fibroblast-HLA-DRAhi<br>sublining (SC-F2) | ENSG00000084636 | ENSG00000084636.12 | 0.87323477  | 0.835883171  | 0.105852525       | 23.789446496   |
| ST5     | SC-F2    | Fibroblast-HLA-DRAhi<br>sublining (SC-F2) | ENSG00000166444 | ENSG00000166444.13 | 0.833490889 | 0.816411683  | 0.158673146       | 23.39530374    |
| DCL1    | SC-F1    | Fibroblast-CD34+<br>sublining (SC-F1)     | ENSG00000133083 | ENSG00000133083.10 | 0.786731154 | 0.700413223  | 0.168075684       | 23.123692573   |
| DCL1    | SC-F2    | Fibroblast-HLA-DRAhi<br>sublining (SC-F2) | ENSG00000133083 | ENSG00000133083.10 | 0.831312828 | 0.799721836  | 0.126558208       | 23.123692573   |
| EGR1    | SC-F1    | Fibroblast-CD34+<br>sublining (SC-F1)     | ENSG00000120738 | ENSG00000120738.7  | 0.753816991 | 0.950413223  | 0.650764895       | 21.499587093   |
| EGR1    | SC-F2    | Fibroblast-HLA-DRAhi<br>sublining (SC-F2) | ENSG00000120738 | ENSG00000120738.7  | 0.805075452 | 0.993045897  | 0.629410522       | 21.499587093   |
| COL14A1 | SC-F1    | Fibroblast-CD34+<br>sublining (SC-F1)     | ENSG00000187955 | ENSG00000187955.7  | 0.886990583 | 0.983471074  | 0.305354267       | 21.350721991   |
| COL14A1 | SC-F2    | Fibroblast-HLA-DRAhi<br>sublining (SC-F2) | ENSG00000187955 | ENSG00000187955.7  | 0.917607177 | 0.991655076  | 0.27044158        | 21.350721991   |

|         |       |                                           |                  |                     |             |             |             |              |
|---------|-------|-------------------------------------------|------------------|---------------------|-------------|-------------|-------------|--------------|
| COL14A1 | SC-F3 | Fibroblast-DKK3+<br>sublining (SC-F3)     | ENSG000000187955 | ENSG000000187955.7  | 0.852312874 | 0.969298246 | 0.339203675 | 21.350721991 |
| SCARA5  | SC-F1 | Fibroblast-CD34+<br>sublining (SC-F1)     | ENSG000000168079 | ENSG000000168079.12 | 0.749160744 | 0.785123967 | 0.289653784 | 20.554709341 |
| SCARA5  | SC-F3 | Fibroblast-DKK3+<br>sublining (SC-F3)     | ENSG000000168079 | ENSG000000168079.12 | 0.819901316 | 0.890350877 | 0.309341501 | 20.554709341 |
| COL4A2  | SC-F2 | Fibroblast-HLA-DRAhi<br>sublining (SC-F2) | ENSG000000134871 | ENSG000000134871.13 | 0.841252655 | 0.866481224 | 0.187618846 | 12.249482672 |
| EGFR    | SC-F1 | Fibroblast-CD34+<br>sublining (SC-F1)     | ENSG000000146648 | ENSG000000146648.11 | 0.763756222 | 0.729338843 | 0.230072464 | 10.692550335 |
| EGFR    | SC-F2 | Fibroblast-HLA-DRAhi<br>sublining (SC-F2) | ENSG000000146648 | ENSG000000146648.11 | 0.803273527 | 0.820584145 | 0.191421931 | 10.692550335 |

**[000185]**      PRIME CELLS

**[000186]**      These unusual RNAs identified in blood as indicators of an RA flare, particularly those of AC3, identified a unique cell in blood samples denoted Pre-Inflammatory Mesenchymal Cells (PRIME cells). RNA sequencing of these cells confirmed that they were enriched with AC3 cluster genes, synovial fibroblast genes, and expressed classic synovial fibroblast genes such as FAP, DKK3, CDH11 as well as collagens and laminins. PRIME cells are activated just prior to flare and are then evident at flare in inflamed synovium as inflammatory sublining fibroblasts.

**[000187]**      Cell surface markers characteristic of the PRIME cells identified and described herein are PDPN+, CD45- and CD31-. PRIME cells can be sorted or characterized as CD45-,CD31-PDPN+ cells. Also, the cell surface receptor and marker IL17RD+ can additionally be utilized to differentiate, identify and characterize PRIME cells. IL17RD is an AC3 gene marker (see Table 3 above). CD45 and CD31 are often present on cells in blood, therefore a blood cell which lacks both of these specific markers would be unusual. CD45 is a pan-leukocyte protein with tyrosine phosphatase activity involved in the regulation of signal transduction in hematopoiesis. CD45 is also known as protein tyrosine phosphatase, receptor type, C (PTPRC). CD45 was originally designated leukocyte common antigen, reflecting its general expression on leukocytes. CD31 represents platelet endothelial cell adhesion molecule (PECAM-1). This molecule plays a key role in removing aged neutrophils from the body, and is found on the surface of platelets, monocytes, neutrophils and some types of T cells.

**[000188]**      In contrast, the presence of PDPN – and also of IL17RD – on the surface of a population of cells, particularly CD45- and CD31- cells in blood, is unusual. PDPN (Podoplanin) is a well conserved mucin-type transmembrane protein and is heavily O-glycosylated with diverse distribution in human tissues. Podoplanin binds to C-type lectin receptor-2 (CLEC-2) and is associated with malignant progression and tumor metastasis in several types of cancer. Anti-podoplanin antibody has been evaluated and shown effective in LPS-induced lung injury (Lax S et al (2017) *BMJ Open Respiratory Res* 4:e000257.doi:10.1136/bmjresp-2017-000257). Podoplanin antibodies have been investigated in pulmonary metastasis and in malignant mesothelioma (Kato Y (2015) *Oncotarget* 6(34):36003-36018; Abe S et al (2013) *J Immunol* 190(12):6239-6249).

**[000189]**      IL17RD (IL-17 Receptor D), a membrane protein of the IL-17 receptor family, is a feedback loop inhibitor of fibroblast growth factor mediated Ras-MAPK signaling and ERK activation. IL17RD binds IL-17A and mediates pro-inflammatory gene expression downstream of IL-17A.

**[000190]**      Antibodies targeting IL-17 cytokines and their receptors are being used in treatment of some autoimmune diseases. In RA, IL-17A acts locally on synoviocytes and osteoblasts contributing to synovitis and joint disruption, Although some positive results have been seen in psoriasis and psoriatic arthritis, results with biologics targeting IL-17 in RA have been mixed, underscoring the need to identify patients or clinical/biological scenarios where therapeutics such as

IL-17 biologics will be effective (Robert M and Miossec P (2019) Front Med 5:364; doi:10.3389/fmed.2018.00364; Fragoulis GE et al (2016) Ann Rev Med 67:337-353). Targeting IL-17 or IL17D based on RNA markers and/or PRIME cell analysis may be a more effective approach to treatment of RA, particularly if administration upon recognition of an imminent flare could be implemented.

**[000191]** This invention may be embodied in other forms or carried out in other ways without departing from the spirit or essential characteristics thereof. The present disclosure is therefore to be considered as in all aspects illustrated and not restrictive, the scope of the invention being indicated by the appended Claims, and all changes which come within the meaning and range of equivalency are intended to be embraced therein.

**[000192]** Various references are cited throughout this Specification, each of which is incorporated herein by reference in its entirety.

WHAT IS CLAIMED IS:

1. A method for monitoring and predicting a rheumatoid arthritis (RA) flare or increased RA disease activity in a patient comprising:
  - (a) isolating a blood sample from said patient;
  - (b) evaluating the blood sample for expression or quantitatively increased amounts of one or more sets of antecedent RNA markers, protein markers or cell markers selected from:
    - (i) markers or proteins selected from COL1A2, COL5A1, COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1, ZFHX4, COL3A1, COMP, FNDC1, GALNT15, SULF1, GPX8 and IGFBP6 as set out in Table 5;
    - (ii) markers or proteins selected from COL1A2, COL5A1, COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1 and ZFHX4 as set out in Table 9;
    - (iii) AC2 markers or proteins as provided in Table 7;
    - (iv) AC3 markers or proteins as provided in Table 8; and
    - (v) cell markers CD45- CD31-PDPN+;
  - (c) wherein the expression or quantitatively increased amounts of the RNA markers or proteins or the presence of the cell markers predicts an impending RA flare.
2. The method of claim 1, wherein the expression or quantitatively increased amounts of the AC2 RNA markers or proteins predicts an RA flare in about 2 weeks or about 12-14 days or up to 3 weeks.
3. The method of claim 1, wherein the expression or quantitatively increased amounts of the AC3 RNA markers or proteins predicts an RA flare in about 1 week or about 5-7 days or up to 2 weeks.
4. The method of claim 1, wherein a subset of at least 20 of the AC2 or AC3 markers are evaluated.
5. The method of claim 1, wherein a subset of at least 20 of the AC2 and at least 20 of the AC3 markers are evaluated.
6. The method of claim 1, wherein a subset of at least 10 of the AC2 or AC3 markers are evaluated.

7. The method of claim 1, wherein a subset of at least 10 of the AC2 and at least 10 of the AC3 markers are evaluated.
8. The method of claim 1, wherein sublining fibroblast markers selected from the AC3 markers or proteins are evaluated.
9. The method of claim 1, wherein AC3 markers or proteins expressed by CD34+, HLADR+ and DKK3+ cells are evaluated.
10. The method of claim 1, wherein the cell marker IL17RD is also evaluated.
11. The method of claim 1, wherein RNA expression is assessed by RT PCR.
12. The method of claim 1 wherein protein expression is assessed using specific antibodies.
13. The method of claim 1 wherein cell markers are evaluated using FACs analysis.
14. The method of claim 1 wherein the antecedent RNA markers or protein markers or selected from:
  - (a) markers or proteins selected from COL1A2, COL5A1, COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1, ZFHX4, COL3A1, COMP, FNDC1, GALNT15, SULF1, GPX8 and IGFBP6 as set out in Table 5;
  - (b) markers or proteins selected from COL1A2, COL5A1, COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1 and ZFHX4 as set out in Table 9; and
  - (c) AC3 markers or proteins as provided in Table 8;
 are reduced, significantly decreased, nearly absent, or absent in peripheral blood during an RA flare or once a patient exhibits symptoms of an RA flare.
15. A method for predicting an impending RA flare and treating a flare in a patient, the method comprising:
  - a) isolating a blood sample from the patient;
  - b) contacting the blood sample with reagents specific for markers selected from a panel of RNA or protein markers to assess expression of the RNA or protein markers, wherein the panel of RNA or protein markers is selected from:
    - (i) markers or proteins selected from COL1A2, COL5A1, COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1, ZFHX4, COL3A1, COMP, FNDC1, GALNT15, SULF1, GPX8 and IGFBP6 as set out in Table 5;

- (ii) markers or proteins selected from COL1A2, COL5A1, COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1 and ZFHX4 as set out in Table 9;
  - (iii) AC2 markers or proteins as provided in Table 7; and
  - (iv) AC3 markers or proteins as provided in Table 8;
- c) comparing expression of the markers selected from a panel of RNA or protein markers in the blood sample to expression of the markers in a control blood sample to determine if expression of the markers selected from a panel of RNA or protein markers in the blood sample is increased relative to expression in the control blood sample, wherein detection of increased expression serves to predict an impending RA flare in a patient;
- and treating the patient thereby diagnosed with an impending RA flare by administering a therapeutically effective amount of one or more disease modifying agent for treating RA.
16. The method of claim 15, wherein RNA expression is assessed by RT PCR.
17. The method of claim 15, wherein protein expression is assessed using specific antibodies.
18. The method of claim 15, wherein the expression or quantitatively increased amounts of the AC2 RNA markers or proteins predicts an RA flare in about 2 weeks or about 12-14 days or about 3 weeks.
19. The method of claim 15, wherein the expression or quantitatively increased amounts of RNA or protein markers selected from:
- (a) markers or proteins selected from COL1A2, COL5A1, COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1, ZFHX4, COL3A1, COMP, FNDC1, GALNT15, SULF1, GPX8 and IGFBP6;
  - (b) markers or proteins selected from COL1A2, COL5A1, COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1 and ZFHX4; and
  - (c) the AC3 RNA markers or proteins;
- predicts an RA flare in about 1 week or about 5-7 days or about 2 weeks.
20. The method of claim 15, wherein the disease modifying agent for treating RA is one or more agent selected from a nonsteroidal anti-inflammatory drug (NSAID), steroid, methotrexate, disease-modifying antirheumatic drug (DMARDs), biologic DMARD, and oral janus kinase (JAK) inhibitor.
21. The method of claim 20, wherein the DMARD is selected from methotrexate (Trexall, Otrexup), leflunomide (Arava), hydroxychloroquine (Plaquenil) and sulfasalazine (Azulfidine).

22. The method of claim 20, wherein the biologic DMARD is selected from abatacept (Orencia), adalimumab (Humira), anakinra (Kineret), baricitinib (Olmiant), certolizumab (Cimzia), etanercept (Enbrel), golimumab (Simponi), infliximab (Remicade), rituximab (Rituxan), sarilumab (Kevzara), tocilizumab (Actemra) and tofacitinib (Xeljanz).
23. The method of claim 20, wherein the biologic DMARD is a tumor necrosis factor (TNF) inhibitor.
24. The method of claim 20, wherein the biologic DMARD is combined with an NSAID and/or with methotrexate.
25. The method of claim 20, wherein the JAK inhibitor is selected from tofacitinib (Xeljanz and Xeljanz XR), baricitinib (Olmiant), and upadacitinib (Rinvoq).
26. The method of claim 15, wherein the disease modifying agent for treating RA is an IL-17 antibody or an IL17RD blocking antibody.
27. A circulating pre-inflammatory mesenchymal (PRIME) cell characterized as a CD45-CD31-PDPN+ cell, wherein the presence of the cell in peripheral blood is indicative or predictive of an impending RA flare.
28. The PRIME cell of claim 27, which additionally expresses IL17RD and is IL17RD+.
29. A method of predicting an impending RA flare comprising evaluating a blood sample from a patient for the presence of a PRIME cell characterized as a CD45-CD31-PDPN+ cell, wherein the presence of detectable PRIME cells in peripheral blood in a patient predicts an impending RA flare in the patient.
30. The method of claim 29, further evaluating for the presence of IL17RD on a CD45-CD31-PDPN+ cell.
31. A method for evaluating and treating an impending flare in an RA patient comprising evaluating the peripheral blood of a patient for the presence of a PRIME cell characterized as a CD45-CD31-PDPN+IL17RD+ cell and treating a patient that is positive for PRIME cells in their peripheral blood with a disease modifying agent for RA.
32. The method of claim 31, wherein the patient is treated with an IL-17 or IL-17RD antibody.

33. The method of claim 32, wherein the patient is further treated with an anti-inflammatory agent and/or an immune modulating agent.
34. A set of RNA or protein markers for evaluating and predicting an impending RA flare in a patient comprising the markers selected from:
- (i) markers selected from COL1A2, COL5A1, COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1, ZFHX4, COL3A1, COMP, FNDC1, GALNT15, SULF1, GPX8 and IGFBP6 as set out in Table 5;
  - (ii) markers selected from COL1A2, COL5A1, COL16A1, COL14A1, COL4A2, PXDN, ST5, DCLK1, SCARA5, EGFR, EGR1 and ZFHX4 as set out in Table 9;
  - (iii) a subset of at least 20 markers from the AC2 markers provided in Table 7; and
  - (iv) a subset of at least 20 markers from the AC3 markers provided in Table 8.
35. The marker set of claim 34, wherein the subset of AC2 markers comprises naïve B cell gene markers and markers of developmental pathways for naïve B cells and leukocytes.
36. The marker set of claim 34, wherein the subset of AC3 markers comprises markers of cartilage morphogenesis, endochondral bone growth, extracellular matrix organization and sublining fibroblasts.
37. A system or kit for predicting an impending RA flare comprising a set of markers of claim 34 or a set of probes and/or antibodies for evaluating a set of markers of claim 34.
38. The system or kit of claim 37, which further comprises a means for collection of the patient's blood by fingerstick.