



(51) International Patent Classification:

C12Q 1/68 (2006.01) *G01N 33/15* (2006.01)
G06F 19/22 (2011.01)

(21) International Application Number:

PCT/US2012/053513

(22) International Filing Date:

31 August 2012 (31.08.2012)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

61/530,072 1 September 2011 (01.09.2011)

US

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(81) Designated States (unless otherwise indicated, for every

kind of national protection available): AE, AG, AL, AM,
AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY,
BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM,
DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT,
HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP,
KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD,
ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI,
NO, NZ, OM, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW,
SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM,
TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM,
ZW.

(84) Designated States (unless otherwise indicated, for every

kind of regional protection available): ARIPO (BW, GH,
GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ,
UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ,
TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV,
MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM,
TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW,
ML, MR, NE, SN, TD, TG).

Published:

— without international search report and to be republished
upon receipt of that report (Rule 48.2(g))

— with sequence listing part of description (Rule 5.2(a))

(54) Title: DIAGNOSIS AND TREATMENT OF ARTHRITIS USING EPIGENETICS

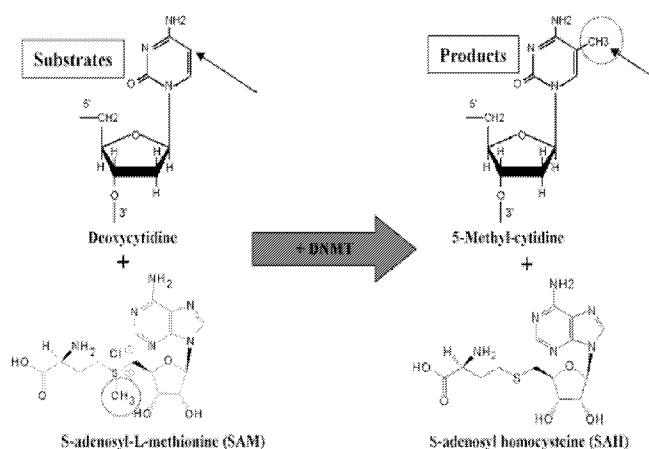


FIG. 1

(57) **Abstract:** Embodiments of the present invention include methods, compositions and kits for evaluating a diagnosis, prognosis, or response to treatment of a subject with a disorder such as rheumatoid arthritis or osteoarthritis. Some embodiments include identifying a therapeutic agent for treating a disorder such as rheumatoid arthritis or osteoarthritis.

DIAGNOSIS AND TREATMENT OF ARTHRITIS USING EPIGENETICS

RELATED APPLICATIONS

[0001] This application claims the benefit of U.S. Provisional Application No. 61/530,072 entitled “DIAGNOSIS AND TREATMENT OF ARTHRITIS USING EPIGENETICS” filed on September 1, 2011, which is incorporated herein by reference in its entirety.

REFERENCE TO SEQUENCE LISTING

[0002] The present application is being filed along with a Sequence Listing in electronic format. The Sequence Listing is provided as a file entitled UCSD055_001WO.TXT, created August 24, 2012, which is approximately 135,386 KB in size. The information in the electronic format of the Sequence Listing is incorporated herein by reference in its entirety.

FIELD OF THE INVENTION

[0003] Embodiments of the present invention include methods, compositions and kits for evaluating a diagnosis, prognosis, or response to treatment of a subject with a disorder such as rheumatoid arthritis or osteoarthritis. Some embodiments include identifying a therapeutic agent for treating a disorder such as rheumatoid arthritis or osteoarthritis.

BACKGROUND OF THE INVENTION

[0004] Rheumatoid arthritis is an immune-mediated disease marked by symmetric inflammation in diarthrodial joints and destruction of the extracellular matrix. Genomics has rapidly advanced our understanding of susceptibility and severity of RA, and many associated polymorphisms in key genes have been described. However, identical twins have a concordance rate of only 12-15% suggesting that other influences can affect either the onset or progression of disease, such as epigenetic regulation of gene expression. One of the most widely studied epigenetic mechanisms, especially in oncology, is DNA methylation, which plays a key role regulating and silencing gene expression and could potentially contribute to immune dysregulation.

[0005] The pathogenesis of Rheumatoid arthritis (RA) is complex and involves numerous cell types that contribute through adaptive and innate immune responses (Firestein GS. Evolving concepts of rheumatoid arthritis. *Nature*, 423:356-361, 2003). Fibroblast-like synoviocytes (FLS), which form the synovial intimal lining, play an integral role by producing key cytokines (*e.g.*, IL-6), small molecule mediators (*e.g.*, prostanoids), and proteases (*e.g.*,

metalloproteinases). While osteoclasts are the primary effectors of bone erosions in arthritis, FLS are responsible for cartilage damage by virtue of their ability to adhere to and invade cartilage extracellular matrix. This capacity requires homotypic aggregation mediated by the adhesion molecule cadherin-11, which directs intimal lining formation and supports an invasive phenotype (Kiener HP *et al.* Cadherin 11 promotes invasive behavior of fibroblast-like synoviocytes. *Arthritis Rheum.* 2009 May;60(5):1305-10). A well-defined relationship has long been recognized between synovial tissue histology and function and peripheral blood cell characteristics in diseases like RA, most likely because the circulating cells actively traffic between the synovium, lymph nodes, and peripheral blood (Malone DG *et al.* Immune function in severe, active rheumatoid arthritis. A relationship between peripheral blood mononuclear cell proliferation to soluble antigens and synovial tissue immunohistologic characteristics. *J Clin Invest.*, 74(4):1173–1185, 1984; Firestein, GS. Etiology and pathogenesis of rheumatoid arthritis, In: *Textbook of Rheumatology*, GS Firestein, *et al.* eds., Elsevier, Philadelphia, 8th edition, 2009, pp. 1035-86). Understanding the precise molecular mechanisms that regulate FLS and peripheral blood cell activation in inflammatory arthritis could provide insights into the pathogenesis of RA and lead to novel therapeutic strategies.

SUMMARY OF THE INVENTION

[0006] Some embodiments of the methods, compositions and kits provided herein include a method for diagnosing rheumatoid arthritis or osteoarthritis, determining a rheumatoid arthritis or osteoarthritis prognosis, or determining or predicting a response to treatment for rheumatoid arthritis or osteoarthritis in a subject comprising determining whether at least 2 nucleic acid loci or at least 2 genes in a sample from said subject have methylation states indicative of rheumatoid arthritis, osteoarthritis, a rheumatoid arthritis or osteoarthritis prognosis, or a response to treatment for rheumatoid arthritis or osteoarthritis.

[0007] Some embodiments also include comprising comparing the methylation states of the at least 2 loci or at least 2 genes in the sample from said subject with the methylation states of the loci or genes in normal tissue, tissue from a subject without said known rheumatoid arthritis or osteoarthritis prognosis, or tissue from a subject without said known response to treatment for rheumatoid arthritis or osteoarthritis.

[0008] In some embodiments, an increase or decrease in the extent of methylation of at least 2 loci or at least 2 genes compared to the extent of methylation of the loci or genes in normal tissue, tissue from a subject without said known rheumatoid arthritis or osteoarthritis prognosis, or tissue from a subject without said known response to treatment for rheumatoid

arthritis or osteoarthritis is indicative of the presence or absence of rheumatoid arthritis, osteoarthritis, a rheumatoid arthritis or osteoarthritis prognosis, or response to treatment for rheumatoid arthritis or osteoarthritis for the subject.

[0009] In some embodiments, the methylation states of said at least 2 loci or at least 2 genes are determined in fibroblasts from said subject. In some embodiments, the methylation state of said at least 2 loci or at least 2 genes is determined in synoviocytes from said subject. In some embodiments, the methylation states of said at least 2 loci or at least 2 genes are determined in fibroblast-like synoviocytes from said subject. In some embodiments, the methylation states of said at least 2 loci or at least 2 genes are determined in rheumatoid arthritis fibroblast-like synoviocytes from said subject. In some embodiments, the methylation states of said at least 2 loci or at least 2 genes are determined in osteoarthritis fibroblast-like synoviocytes from said subject.

[0010] In some embodiments, the methylation states of said at least 2 loci or at least 2 genes are determined in macrophage from said subject.

[0011] In some embodiments, the methylation states of said at least 2 loci or at least 2 genes are determined in peripheral blood cells from said subject. In some embodiments, the peripheral blood cell is selected from the group consisting of white blood cell, neutrophil, eosinophil, basophil, lymphocyte, B cell, plasma cell, T cell, natural killer cell, monocyte, and dendritic cell.

[0012] In some embodiments, the sample is selected from the group consisting of a tissue sample, a frozen tissue sample, a biopsy specimen, a surgical specimen, a cytological specimen, whole blood, bone marrow, cerebral spinal fluid, peritoneal fluid, lymph fluid, serum, plasma, urine, stool, and nipple aspirate.

[0013] In some embodiments, the at least 2 loci are selected from the group consisting of SEQ ID NO.s 1- 485512. In some embodiments, the at least 2 loci are selected from the group consisting of the loci listed in TABLE 6. In some embodiments, the at least 2 loci are selected from the group consisting of the loci listed in TABLE 7. In some embodiments, the at least 2 loci are selected from the group consisting of the loci listed in TABLE 8. In some embodiments, the at least 2 loci are selected from the group consisting of the loci listed in TABLE 3.

[0014] In some embodiments, the methylation states of at least 5 nucleic acid loci or at least 5 genes in said sample are determined. In some embodiments, the methylation states of at least 10 nucleic acid loci or at least 10 genes in said sample are determined. In some embodiments, the methylation states of at least 20 nucleic acid loci or at least 20 genes in said

sample are determined. In some embodiments, the methylation states of at least 50 nucleic acid loci or at least 50 genes in said sample are determined. In some embodiments, the methylation states of at least 100 nucleic acid loci or at least 100 genes are determined.

[0015] In some embodiments, the subject is a mammal. In some embodiments, the subject is a human.

[0016] In some embodiments, the nucleic acid loci are selected from the group consisting of the loci listed in TABLE 6. In some embodiments, the nucleic acid loci are selected from the group consisting of the loci listed in TABLE 7. In some embodiments, the nucleic acid loci are selected from the group consisting of the loci listed in TABLE 8.

[0017] Some embodiments of the methods, compositions and kits provided herein include a method for diagnosing rheumatoid arthritis or osteoarthritis, determining a rheumatoid arthritis or osteoarthritis prognosis, or determining or predicting a response to treatment for rheumatoid arthritis or osteoarthritis in a subject comprising determining the methylation states of a plurality of nucleic acid loci or the methylation states of a plurality of genes in a sample of said subject to obtain a methylation profile; and determining whether said methylation profile is indicative of rheumatoid arthritis, osteoarthritis, a rheumatoid arthritis or osteoarthritis prognosis, or a response to treatment for rheumatoid arthritis or osteoarthritis.

[0018] Some embodiments also include comparing the methylation state of the plurality of nucleic acid loci or the methylation state of the plurality of genes in the sample from said subject with the methylation state of the plurality of nucleic acid loci or the methylation state of the plurality of genes in normal tissue, tissue from a subject without said known rheumatoid arthritis or osteoarthritis prognosis, or tissue from a subject without said known response to treatment for rheumatoid arthritis or osteoarthritis.

[0019] In some embodiments, an increase or decrease in the extent of methylation of plurality of nucleic acid loci or of the methylation state of the plurality of genes compared to the extent of methylation of the plurality of nucleic acid loci or the extent of methylation of the plurality of genes in normal tissue, tissue from a subject without said known rheumatoid arthritis or osteoarthritis prognosis, or tissue from a subject without said known response to treatment for rheumatoid arthritis or osteoarthritis is indicative of the presence or absence of rheumatoid arthritis, osteoarthritis, a rheumatoid arthritis or osteoarthritis prognosis, or response to treatment for rheumatoid arthritis or osteoarthritis for the subject.

[0020] In some embodiments, the methylation state of said plurality of nucleic acid loci or said plurality of genes is determined in fibroblasts from said subject. In some embodiments, the methylation state of said plurality of nucleic acid loci or said plurality of genes

is determined in synoviocytes from said subject. In some embodiments, the methylation state of said plurality of nucleic acid loci or said plurality of genes is determined in fibroblast-like synoviocytes from said subject. In some embodiments, the methylation state of said plurality of nucleic acid loci or said plurality of genes is determined in rheumatoid arthritis fibroblast-like synoviocytes from said subject. In some embodiments, the methylation state of said plurality of nucleic acid loci or said plurality of genes is determined in osteoarthritis fibroblast-like synoviocytes from said subject.

[0021] In some embodiments, the methylation state of said plurality of nucleic acid loci or said plurality of genes is determined in macrophage from said subject.

[0022] In some embodiments, the methylation state of said plurality of nucleic acid loci or said plurality of genes is determined in peripheral blood cells from said subject. In some embodiments, the peripheral blood cell is selected from the group consisting of white blood cell, neutrophil, eosinophil, basophil, lymphocyte, B cell, plasma cell, T cell, natural killer cell, monocyte, and dendritic cell.

[0023] In some embodiments, the sample is selected from the group consisting of a tissue sample, a frozen tissue sample, a biopsy specimen, a surgical specimen, a cytological specimen, whole blood, bone marrow, cerebral spinal fluid, peritoneal fluid, lymph fluid, serum, plasma, urine, stool, and nipple aspirate.

[0024] In some embodiments, the plurality of nucleic acid loci is selected from the group consisting of SEQ ID NO.s 1- 485512. In some embodiments, the plurality of nucleic acid loci is selected from the group consisting of the loci listed in TABLE 6. In some embodiments, the plurality of nucleic acid loci is selected from the group consisting of the loci listed in TABLE 7. In some embodiments, the plurality of nucleic acid loci is selected from the group consisting of the loci listed in TABLE 8.

[0025] In some embodiments, the plurality genes is selected from the group consisting of the loci listed in TABLE 3.

[0026] In some embodiments, the methylation states of at least 5 nucleic acid loci or at least 5 genes in said sample are determined. In some embodiments, the methylation states of at least 10 nucleic acid loci or at least 10 genes in said sample are determined. In some embodiments, the methylation states of at least 20 nucleic acid loci or at least 20 genes in said sample are determined. In some embodiments, the methylation states of at least 50 nucleic acid loci or at least 50 genes in said sample are determined. In some embodiments, the methylation states of at least 100 nucleic acid loci or at least 100 genes are determined.

[0027] In some embodiments, the subject is a mammal. In some embodiments, the subject is a human.

[0028] Some embodiments of the methods, compositions and kits provided herein include a method of identifying a methylation profile indicative of rheumatoid arthritis, osteoarthritis, a rheumatoid arthritis or osteoarthritis prognosis, or a response to treatment for rheumatoid arthritis or osteoarthritis comprising determining the methylation states of a plurality of nucleic acid loci or the methylation states of a plurality of genes in a sample from a test subject with rheumatoid arthritis, osteoarthritis, a particular rheumatoid arthritis or osteoarthritis prognosis, or a particular response to treatment for rheumatoid arthritis or osteoarthritis; determining the methylation states of said plurality of nucleic acid loci or said plurality of genes in a sample from a control subject without rheumatoid arthritis, without osteoarthritis, without said rheumatoid arthritis or osteoarthritis prognosis or without said response to treatment for rheumatoid arthritis or osteoarthritis; and identifying loci or genes which are hypermethylated or hypomethylated in said sample from said test subject relative to said sample from said control subject to identify said methylation profile indicative of rheumatoid arthritis, osteoarthritis a rheumatoid arthritis or osteoarthritis prognosis, or a response to treatment for rheumatoid arthritis or osteoarthritis.

[0029] Some embodiments also include storing data representing said loci or said genes which are hypermethylated or hypomethylated in said sample from said test subject relative to said sample from said control subject on a non-transitory computer readable medium.

[0030] Some embodiments also include comparing the methylation states of a plurality of nucleic acid loci or the methylation states of a plurality of genes in a sample from a test subject with rheumatoid arthritis, osteoarthritis, a particular rheumatoid arthritis or osteoarthritis prognosis, or a particular response to treatment for rheumatoid arthritis or osteoarthritis with the methylation states of said plurality of nucleic acid loci or the methylation states of said plurality of genes in a sample from a control subject without rheumatoid arthritis, without osteoarthritis, without said rheumatoid arthritis or osteoarthritis prognosis or without said response to treatment for rheumatoid arthritis or osteoarthritis.

[0031] In some embodiments, the methylation state of said plurality of nucleic acid loci or said plurality of genes in a sample from said test subject or said control subject is determined in fibroblasts from said test subject or said control subject. In some embodiments, the methylation state of said plurality of nucleic acid loci or said plurality of genes in a sample from said test subject or said control subject is determined in synoviocytes from said test subject or said control subject. In some embodiments, the methylation state of said plurality of nucleic acid

loci or said plurality of genes in a sample from said test subject or control subject is determined in fibroblast-like synoviocytes from said test subject or said control subject. In some embodiments, the methylation state of said plurality of nucleic acid loci or said plurality of genes in a sample from said test subject or control subject is determined in rheumatoid arthritis fibroblast-like synoviocytes from said test subject or control subject. In some embodiments, the methylation state of said plurality of nucleic acid loci or said plurality of genes in a sample from said test subject or control subject is determined in osteoarthritis fibroblast-like synoviocytes from said test subject or control subject.

[0032] In some embodiments, the methylation state of said plurality of nucleic acid loci or said plurality of genes in a sample from said test subject or control subject is determined in macrophage from said test subject or control subject.

[0033] In some embodiments, the methylation state of said plurality of nucleic acid loci or said plurality of genes in a sample from said test subject or control subject is determined in peripheral blood cells from said test subject or control subject. In some embodiments, the peripheral blood cell is selected from the group consisting of white blood cell, neutrophil, eosinophil, basophil, lymphocyte, B cell, plasma cell, T cell, natural killer cell, monocyte, and dendritic cell.

[0034] In some embodiments, the sample is selected from the group consisting of a tissue sample, a frozen tissue sample, a biopsy specimen, a surgical specimen, a cytological specimen, whole blood, bone marrow, cerebral spinal fluid, peritoneal fluid, lymph fluid, serum, plasma, urine, stool, and nipple aspirate.

[0035] In some embodiments, the methylation states of at least 5 nucleic acid loci or at least 5 genes are determined. In some embodiments, the methylation states of at least 10 nucleic acid loci or at least 10 genes are determined. In some embodiments, the methylation states of at least 20 nucleic acid loci or at least 20 genes are determined. In some embodiments, the methylation states of at least 50 nucleic acid loci or at least 50 genes are determined. In some embodiments, the methylation states of at least 100 nucleic acid loci or at least 100 genes are determined.

[0036] In some embodiments, the subject is a mammal. In some embodiments, the subject is a human.

[0037] Some embodiments of the methods, compositions and kits provided herein include a method for diagnosing rheumatoid arthritis or osteoarthritis, determining a rheumatoid arthritis or osteoarthritis prognosis, or determining or predicting a response to treatment for rheumatoid arthritis or osteoarthritis in a subject comprising accessing first data representing the

methylation status of nucleic acid loci or the methylation status of at least one gene which are differentially methylated in individuals with rheumatoid arthritis, osteoarthritis a rheumatoid arthritis or osteoarthritis prognosis, or a response to treatment for rheumatoid arthritis or osteoarthritis wherein said data is stored on a non-transitory computer readable medium; instructing a computer to compare said first data to second data representing the methylation status of said nucleic acid loci or said at least one gene in a sample taken from said subject, wherein said data representing the methylation status of said nucleic acid loci or said at least one gene in a sample taken from said subject is stored on a non-transitory computer readable medium; and instructing said computer to provide an output indicating whether said comparison indicates that said subject has rheumatoid arthritis or osteoarthritis, has a positive or negative prognosis for rheumatoid arthritis or osteoarthritis prognosis, or indicates a positive or negative prediction for the subject's response to treatment for rheumatoid arthritis or osteoarthritis.

[0038] Some embodiments also include diagnosing rheumatoid arthritis or osteoarthritis, determining a rheumatoid arthritis or osteoarthritis prognosis, or determining or predicting a response to treatment for rheumatoid arthritis or osteoarthritis in said subject if said first data representing the methylation status of said nucleic acid loci or said at least one gene in a sample taken from said subject are significantly similar to said second data representing nucleic acid loci or genes which are differentially methylated in individuals with rheumatoid arthritis, osteoarthritis a rheumatoid arthritis or osteoarthritis prognosis, or a response to treatment for rheumatoid arthritis or osteoarthritis.

[0039] Some embodiments of the methods, compositions and kits provided herein include a method for diagnosing rheumatoid arthritis or osteoarthritis, determining a rheumatoid arthritis or osteoarthritis prognosis, or determining or predicting a response to treatment for rheumatoid arthritis or osteoarthritis in a subject comprising: determining the methylation states of at least 2 loci selected from the group consisting of SEQ ID NO.s 1-485512 in a sample obtained from the subject.

[0040] Some embodiments also include comparing the methylation states of the at least 2 loci in the sample with the methylation states of the loci in normal tissue, tissue from a subject with a known prognosis, or tissue from a subject with a known response to treatment.

[0041] In some embodiments, an increase or decrease in the extent of methylation of at least 2 loci compared to the extent of methylation of the loci in normal tissue, tissue from a subject with a known prognosis, or tissue from a subject with a known response to treatment is indicative of the presence or absence of rheumatoid arthritis, prognosis, or response to treatment for the subject.

[0042] In some embodiments, the methylation states of said at least 2 loci are determined in fibroblasts from said subject. In some embodiments, the methylation states of said at least 2 loci are determined in synoviocytes from said subject. In some embodiments, the methylation states of said at least 2 loci are determined in fibroblast-like synoviocytes from said subject. In some embodiments, the methylation states of said at least 2 loci are determined in rheumatoid arthritis fibroblast-like synoviocytes from said subject. In some embodiments, the methylation states of said at least 2 loci are determined in osteoarthritis fibroblast-like synoviocytes from said subject.

[0043] In some embodiments, the methylation states of said at least 2 loci are determined in macrophage from said subject.

[0044] In some embodiments, the methylation states of said at least 2 loci are determined in peripheral blood cells from said subject. In some embodiments, the peripheral blood cell is selected from the group consisting of white blood cell, neutrophil, eosinophil, basophil, lymphocyte, B cell, plasma cell, T cell, natural killer cell, monocyte, and dendritic cell.

[0045] In some embodiments, the sample is selected from the group consisting of a tissue sample, a frozen tissue sample, a biopsy specimen, a surgical specimen, a cytological specimen, whole blood, bone marrow, cerebral spinal fluid, peritoneal fluid, lymph fluid, serum, plasma, urine, stool, and nipple aspirate.

[0046] In some embodiments, the at least 2 loci are selected from the group consisting of the loci listed in TABLE 6. In some embodiments, the at least 2 loci are selected from the group consisting of the loci listed in TABLE 7. In some embodiments, the at least 2 loci are selected from the group consisting of the loci listed in TABLE 8. In some embodiments, the methylation states of at least 5 loci selected from the group consisting of the loci listed in TABLE 6, TABLE 7, and TABLE 8 are determined. In some embodiments, the methylation states of at least 10 loci selected from the group consisting of the loci listed in TABLE 6, TABLE 7, and TABLE 8 are determined. In some embodiments, the methylation states of at least 20 loci selected from the group consisting of the loci listed in TABLE 6, TABLE 7, and TABLE 8 are determined. In some embodiments, the methylation states of at least 50 loci selected from the group consisting of the loci listed in TABLE 6, TABLE 7, and TABLE 8 are determined. In some embodiments, the methylation states of at least 100 loci selected from the group consisting of the loci listed in TABLE 6, TABLE 7, and TABLE 8 are determined.

[0047] In some embodiments, the subject is a mammal. In some embodiments, the subject is a human.

[0048] Some embodiments of the methods, compositions and kits provided herein include a method for identifying a therapeutic agent for treating rheumatoid arthritis or osteoarthritis comprising contacting a cell with a test agent; and determining the methylation states in the contacted cell of at least 2 loci which have differential extents of methylation in individuals with rheumatoid arthritis or osteoarthritis relative to individuals without rheumatoid arthritis or osteoarthritis.

[0049] Some embodiments also include comparing the methylation states of the at least 2 loci in the contacted cell with the methylation states of the loci in a cell which was not contacted with the test agent; and selecting a test agent that increases or decreases the extent of methylation of the at least 2 loci in the cell contacted with the test agent compared to the extent of methylation of the at least 2 loci in a cell which was not contacted with the test agent such that the extent of methylation of the at least 2 loci in the cell contacted with the test agent is a methylation states associated with the absence of rheumatoid arthritis or osteoarthritis or with a reduction in the symptoms associated with rheumatoid arthritis osteoarthritis.

[0050] In some embodiments, the at least 2 loci are selected from the group consisting of SEQ ID NO.s 1-485512. In some embodiments, the at least 2 loci are selected from the group consisting of the loci listed in TABLE 6. In some embodiments, the at least 2 loci are selected from the group consisting of the loci listed in TABLE 7. In some embodiments, the at least 2 loci are selected from the group consisting of the loci listed in TABLE 8.

[0051] In some embodiments, the methylation states of at least 5 loci selected from the group consisting of the loci listed in TABLE 6, TABLE 7, and TABLE 8 are determined. In some embodiments, the methylation states of at least 10 loci selected from the group consisting of the loci listed in TABLE 6, TABLE 7, and TABLE 8 are determined. In some embodiments, the methylation states of at least 20 loci selected from the group consisting of the loci listed in TABLE 6, TABLE 7, and TABLE 8 are determined. In some embodiments, the methylation states of at least 50 loci selected from the group consisting of the loci listed in TABLE 6, TABLE 7, and TABLE 8 are determined. In some embodiments, the methylation states of at least 100 loci selected from the group consisting of the loci listed in TABLE 6, TABLE 7, and TABLE 8 are determined.

[0052] In some embodiments, the cell comprises a fibroblast. In some embodiments, the cell comprises a synoviocyte. In some embodiments, the cell comprises a fibroblast-like synoviocyte. In some embodiments, the cell comprises a rheumatoid arthritis fibroblast-like synoviocyte. In some embodiments, the cell comprises an osteoarthritis fibroblast-like synoviocyte.

[0053] In some embodiments, the cell comprises a macrophage.

[0054] In some embodiments, the cell comprises a peripheral blood cell. In some embodiments, the peripheral blood cell is selected from the group consisting of white blood cell, neutrophil, eosinophil, basophil, lymphocyte, B cell, plasma cell, T cell, natural killer cell, monocyte, and dendritic cell.

[0055] In some embodiments, the cell is mammalian. In some embodiments, the cell is a human.

[0056] In some embodiments, a sample comprises the cell, the sample selected from the group consisting of a tissue sample, a frozen tissue sample, a biopsy specimen, a surgical specimen, a cytological specimen, whole blood, bone marrow, cerebral spinal fluid, peritoneal fluid, lymph fluid, serum, plasma, urine, stool, and nipple aspirate.

[0057] Some embodiments of the methods, compositions and kits provided herein include a kit for diagnosing rheumatoid arthritis or osteoarthritis, determining a rheumatoid arthritis or osteoarthritis prognosis, or determining or predicting a response to treatment for rheumatoid arthritis or osteoarthritis in a subject comprising: a reagent for determining the methylation states of at least 2 loci which have differential extents of methylation in individuals with rheumatoid arthritis or osteoarthritis relative to individuals without rheumatoid arthritis or osteoarthritis.

[0058] In some embodiments, the at least 2 loci are selected from the group consisting of SEQ ID NO.s 1 – 485512. In some embodiments, the at least 2 loci are selected from the group consisting of the loci listed in TABLE 6, TABLE 7, and TABLE 8.

[0059] Some embodiments also include at least one polynucleotide primer comprising a sequence hybridizing to at least a portion of the at least 2 loci selected from the group consisting of the loci listed in TABLE 6, TABLE 7, and TABLE 8.

[0060] In some embodiments, the reagent comprises a restriction enzyme.

[0061] In some embodiments, the at least 2 loci are selected from the group consisting of the loci listed in TABLE 6. In some embodiments, the at least 2 loci are selected from the group consisting of the loci listed in TABLE 7. In some embodiments, the at least 2 loci are selected from the group consisting of the loci listed in TABLE 7. In some embodiments, the reagent can determine the methylation states of at least 5 loci selected from the group consisting of SEQ ID NO.s 1-485512. In some embodiments, the reagent can determine the methylation states of at least 5 loci selected from the group consisting of the loci listed in TABLE 6, TABLE 7, and TABLE 8. In some embodiments, the reagent can determine the methylation states of at least 10 loci selected from the group consisting of the loci listed in TABLE 6, TABLE 7, and

TABLE 8. In some embodiments, the reagent can determine the methylation states of at least 20 loci selected from the group consisting of the loci listed in TABLE 6, TABLE 7, and TABLE 8. In some embodiments, the reagent can determine the methylation states of at least 50 loci selected from the group consisting of the loci listed in TABLE 6, TABLE 7, and TABLE 8. In some embodiments, the reagent can determine the methylation states of at least 100 loci selected from the group consisting of the loci listed in TABLE 6, TABLE 7, and TABLE 8.

[0062] Some embodiments of the methods, compositions and kits provided herein include a method for determining whether an individual suffers from rheumatoid arthritis or osteoarthritis comprising determining the methylation states of at least 2 loci which have differential extents of methylation in individuals with rheumatoid arthritis or osteoarthritis relative to individuals without rheumatoid arthritis or osteoarthritis, wherein the individual is diagnosed with rheumatoid arthritis if the methylation state of said at least 2 loci are associated with rheumatoid arthritis and the individual is diagnosed with osteoarthritis if the methylation states of said at least 2 loci are associated with osteoarthritis.

[0063] In some embodiments, the at least 2 loci are selected from the group consisting of SEQ ID NO.s 1-485512. In some embodiments, the at least 2 loci are selected from the group consisting of the loci listed in TABLE 6. In some embodiments, the at least 2 loci are selected from the group consisting of the loci listed in TABLE 7. In some embodiments, the at least 2 loci are selected from the group consisting of the loci listed in TABLE 8.

[0064] In some embodiments, the methylation states of at least 5 loci selected from the group consisting of the loci listed in TABLE 6, TABLE 7, and TABLE 8 are determined. In some embodiments, the methylation states of at least 10 loci selected from the group consisting of the loci listed in TABLE 6, TABLE 7, and TABLE 8 are determined. In some embodiments, the methylation states of at least 20 loci selected from the group consisting of the loci listed in TABLE 6, TABLE 7, and TABLE 8 are determined. In some embodiments, the methylation states of at least 50 loci selected from the group consisting of the loci listed in TABLE 6, TABLE 7, and TABLE 8 are determined. In some embodiments, the methylation states of at least 100 loci selected from the group consisting of the loci listed in TABLE 6, TABLE 7, and TABLE 8 are determined.

[0065] Some embodiments of the methods, compositions and kits provided herein include a method for diagnosing rheumatoid arthritis or osteoarthritis, determining a rheumatoid arthritis or osteoarthritis prognosis, or determining or predicting a response to treatment for rheumatoid arthritis or osteoarthritis in a subject comprising: determining the methylation states

of at least 2 genes selected from the group consisting of the genes listed in TABLE 3 in a sample obtained from the subject.

[0066] Some embodiments also include comparing the methylation states of the at least 2 genes in the sample with the methylation states of the genes in normal tissue, tissue from a subject with a known prognosis, or tissue from a subject with a known response to treatment.

[0067] In some embodiments, an increase or decrease in the extent of methylation of at least 2 genes compared to the extent of methylation of the of the genes in normal tissue, tissue from a subject with a known prognosis, or tissue from a subject with a known response to treatment is indicative of the presence or absence of rheumatoid arthritis, prognosis, or response to treatment for the subject.

[0068] In some embodiments, the methylation states of said at least 2 loci are determined in fibroblasts from said subject. In some embodiments, the methylation states of said at least 2 loci are determined in synoviocytes from said subject. In some embodiments, the methylation states of said at least 2 loci are determined in fibroblast-like synoviocytes from said subject. In some embodiments, the methylation states of said at least 2 loci are determined in rheumatoid arthritis fibroblast-like synoviocytes from said subject. In some embodiments, the methylation states of said at least 2 loci are determined in osteoarthritis fibroblast-like synoviocytes from said subject.

[0069] In some embodiments, the methylation states of said at least 2 loci are determined in macrophage from said subject.

[0070] In some embodiments, the methylation states of said at least 2 loci are determined in peripheral blood cells from said subject. In some embodiments, the peripheral blood cell is selected from the group consisting of white blood cell, neutrophil, eosinophil, basophil, lymphocyte, B cell, plasma cell, T cell, natural killer cell, monocyte, and dendritic cell.

[0071] In some embodiments, the sample is selected from the group consisting of a tissue sample, a frozen tissue sample, a biopsy specimen, a surgical specimen, a cytological specimen, whole blood, bone marrow, cerebral spinal fluid, peritoneal fluid, lymph fluid, serum, plasma, urine, stool, and nipple aspirate.

[0072] In some embodiments, the methylation states of at least 5 genes selected from the group consisting of the genes listed in TABLE 3 are determined. In some embodiments, the methylation states of at least 10 genes selected from the group consisting of the genes listed in TABLE 3 are determined. In some embodiments, the methylation states of at least 20 genes selected from the group consisting of the genes listed in TABLE 3 are determined. In some

embodiments, the methylation states of at least 50 genes selected from the group consisting of the genes listed in TABLE 3 are determined.

[0073] In some embodiments, the subject is a mammal. In some embodiments, the subject is a human.

[0074] Some embodiments of the methods, compositions and kits provided herein include a method for identifying a therapeutic agent for treating rheumatoid arthritis or osteoarthritis comprising contacting a cell with a test agent; and determining the methylation states of at least 2 genes selected from the group consisting of the genes listed in TABLE 3 in the contacted cell.

[0075] Some embodiments also include comparing the methylation states of the at least 2 genes in the contacted cell with the methylation states of the genes in a cell which was not contacted with the test agent; and selecting a test agent that increases or decreases the extent of methylation of the at least 2 genes in the cell contacted with the test agent compared to the extent of methylation of the at least 2 genes in a cell which was not contacted with the test agent such that the extent of methylation of the at least 2 genes in the cell contacted with the test agent is a methylation states associated with the absence of rheumatoid arthritis or osteoarthritis or with a reduction in the symptoms associated with rheumatoid arthritis or osteoarthritis.

[0076] In some embodiments, the methylation states of at least 5 genes selected from the group consisting of the genes listed in TABLE 3 are determined. In some embodiments, the methylation states of at least 10 genes selected from the group consisting of the genes listed in TABLE 3 are determined. In some embodiments, the methylation states of at least 20 genes selected from the group consisting of the genes listed in TABLE 3 are determined. In some embodiments, the methylation states of at least 50 genes selected from the group consisting of the genes listed in TABLE 3 are determined.

[0077] In some embodiments, the cell comprises a fibroblast. In some embodiments, the cell comprises a synoviocyte. In some embodiments, the cell comprises a fibroblast-like synoviocyte. In some embodiments, the cell comprises a rheumatoid arthritis fibroblast-like synoviocyte. In some embodiments, the cell comprises an osteoarthritis fibroblast-like synoviocyte.

[0078] In some embodiments, the cell comprises a macrophage.

[0079] In some embodiments, the cell comprises a peripheral blood cell. In some embodiments, the peripheral blood cell is selected from the group consisting of white blood cell, neutrophil, eosinophil, basophil, lymphocyte, B cell, plasma cell, T cell, natural killer cell, monocyte, and dendritic cell.

[0080] In some embodiments, the cell is mammalian. In some embodiments, the cell is a human.

[0081] In some embodiments, a sample comprises the cell, the sample selected from the group consisting of a tissue sample, a frozen tissue sample, a biopsy specimen, a surgical specimen, a cytological specimen, whole blood, bone marrow, cerebral spinal fluid, peritoneal fluid, lymph fluid, serum, plasma, urine, stool, and nipple aspirate.

[0082] Some embodiments of the methods, compositions and kits provided herein include a kit for diagnosing rheumatoid arthritis or osteoarthritis, determining a rheumatoid arthritis or osteoarthritis prognosis, or determining or predicting a response to treatment for rheumatoid arthritis or osteoarthritis in a subject comprising: a reagent for determining the methylation states of at least 2 genes selected from the group consisting of the genes listed in TABLE 3.

[0083] Some embodiments also include at least one polynucleotide primer comprising a sequence hybridizing to at least a portion of the at least 2 genes selected from the group consisting of the genes listed in TABLE 3.

[0084] In some embodiments, the reagent comprises a restriction enzyme.

[0085] In some embodiments, the reagent can determine the methylation states of at least 5 genes selected from the group consisting of the genes listed in TABLE 3. In some embodiments, the reagent can determine the methylation states of at least 10 genes selected from the group consisting of the genes listed in TABLE 3. In some embodiments, the reagent can determine the methylation states of at least 20 genes selected from the group consisting of the genes listed in TABLE 3. In some embodiments, the reagent can determine the methylation states of at least 50 genes selected from the group consisting of the genes listed in TABLE 3.

[0086] Some embodiments of the methods, compositions and kits provided herein include a method for identifying a therapeutic agent for treating rheumatoid arthritis or osteoarthritis comprising contacting a cell with a test agent; and determining the methylation states of at least 2 genes selected from a gene encoding a protein that acts in a pathway that includes a protein encoded by a gene that is differentially methylated in a rheumatoid arthritis cell or that is differentially methylated in an osteoarthritis cell compared to a normal cell.

[0087] Some embodiments also include comparing the methylation states of the at least 2 genes in the contacted cell with the methylation states of the genes in a cell which was not contacted with the test agent; and selecting a test agent that increases or decreases the extent of methylation of the at least 2 genes in the cell contacted with the test agent compared to the extent of methylation of the at least 2 genes in a cell which was not contacted with the test agent such

that the extent of methylation of the at least 2 genes in the cell contacted with the test agent are methylation states associated with the absence of rheumatoid arthritis or methylation states associated with the absence of osteoarthritis with a reduction in the symptoms associated with rheumatoid arthritis.

[0088] In some embodiments, the pathway is selected from the group consisting of the pathways listed in TABLE 5.

[0089] In some embodiments, the methylation states of at least 5 genes selected from genes encoding proteins that act in a pathway that includes a protein encoded by a gene that is differentially methylated in a rheumatoid arthritis cell compared to a normal cell or that is differentially methylated in an osteoarthritis cell compared to a normal cell. In some embodiments, the methylation states of at least 10 genes selected from genes encoding proteins that act in a pathway that includes a protein encoded by a gene that is differentially methylated in a rheumatoid arthritis cell compared to a normal cell or that is differentially methylated in an osteoarthritis cell compared to a normal cell.

[0090] In some embodiments, the cell comprises a fibroblast. In some embodiments, the cell comprises a synovial cell. In some embodiments, the cell comprises a fibroblast-like synovial cell. In some embodiments, the cell comprises a rheumatoid arthritis fibroblast-like synovial cell. In some embodiments, the cell comprises an osteoarthritis fibroblast-like synovial cell.

[0091] In some embodiments, the cell comprises a macrophage.

[0092] In some embodiments, the cell comprises a peripheral blood cell. In some embodiments, the peripheral blood cell is selected from the group consisting of white blood cell, neutrophil, eosinophil, basophil, lymphocyte, B cell, plasma cell, T cell, natural killer cell, monocyte, and dendritic cell.

[0093] In some embodiments, the cell is mammalian. In some embodiments, the cell is a human.

[0094] In some embodiments, a sample comprises the cell, the sample selected from the group consisting of a tissue sample, a frozen tissue sample, a biopsy specimen, a surgical specimen, a cytological specimen, whole blood, bone marrow, cerebral spinal fluid, peritoneal fluid, lymph fluid, serum, plasma, urine, stool, and nipple aspirate.

[0095] Some embodiments of the methods, compositions and kits provided herein include a method for identifying therapeutic agents for treating rheumatoid arthritis or osteoarthritis comprising contacting a cell with a test agent; and determining the activity of a

protein encoded by a gene differentially methylated in a rheumatoid arthritis cell or that is differentially methylated in an osteoarthritis cell compared to a normal cell.

[0096] Some embodiments also include comparing the activity of the protein in the contacted cell with the activity of the protein in a cell which was not contacted with the test agent; and selecting a test agent that increases or decreases the activity of protein in the cell contacted with the test agent compared to the activity of the protein in a cell which was not contacted with the test agent such that the activity of the protein in the cell contacted with the test agent is an activity associated with the absence of rheumatoid arthritis or an activity associated with the absence of osteoarthritis with a reduction in the symptoms associated with rheumatoid arthritis.

[0097] In some embodiments, the protein is encoded by a gene selected from the group consisting of the genes listed in TABLE 3.

[0098] In some embodiments, the cell comprises a fibroblast. In some embodiments, the cell comprises a synoviocyte. In some embodiments, the cell comprises a fibroblast-like synoviocyte. In some embodiments, the cell comprises a rheumatoid arthritis fibroblast-like synoviocyte. In some embodiments, the cell comprises an osteoarthritis fibroblast-like synoviocyte.

[0099] In some embodiments, the cell comprises a macrophage.

[0100] In some embodiments, the cell comprises a peripheral blood cell. In some embodiments, the peripheral blood cell is selected from the group consisting of white blood cell, including neutrophil, eosinophil, basophil, lymphocyte, B cell, plasma cell, T cell, natural killer cell, monocyte, and dendritic cell.

[0101] In some embodiments, the cell is mammalian. In some embodiments, the cell is a human.

[0102] Some embodiments of the methods, compositions and kits provided herein include a method of determining the methylation status of a plurality of human nucleic acid loci comprising contacting a nucleic acid sample from a human subject with a reagent capable of providing an indication of the methylation status of said loci, wherein said loci comprise at least 5 which have differential extents of methylation in individuals with rheumatoid arthritis or osteoarthritis relative to individuals without rheumatoid arthritis or osteoarthritis.

[0103] In some embodiments, said reagent is a restriction enzyme.

[0104] In some embodiments, said reagent is a primer.

[0105] In some embodiments, said reagent is a probe.

[0106] In some embodiments, said reagent comprises sodium bisulfite.

[0107] In some embodiments, the at least 5 loci are selected from the group consisting of SEQ ID NO.s 1- 485512. In some embodiments, the at least 5 loci are selected from the group consisting of the loci listed in TABLE 6, TABLE 7, and TABLE 8.

[0108] Some embodiments of the methods, compositions and kits provided herein include a nucleic acid array consisting essentially of nucleic acids useful for diagnosing rheumatoid arthritis or osteoarthritis, determining a prognosis of rheumatoid arthritis or osteoarthritis, or determining or predicting a response to treatment of a subject being evaluated for or suffering from rheumatoid arthritis or osteoarthritis, wherein said nucleic acids comprise at least 5 loci which have differential extents of methylation in individuals with rheumatoid arthritis or osteoarthritis relative to individuals without rheumatoid arthritis or osteoarthritis.

[0109] In some embodiments, said nucleic acids comprise at least 5 loci selected from the group consisting of SEQ ID NO.s 1-485512. In some embodiments, said nucleic acids comprise at least 5 loci selected from the group consisting of the loci listed in TABLE 6, TABLE 7, and TABLE 8. In some embodiments, said nucleic acids comprise at least 10 loci selected from the group consisting of the loci listed in TABLE 6, TABLE 7, and TABLE 8. In some embodiments, said nucleic acids comprise at least 20 loci selected from the group consisting of the loci listed in TABLE 6, TABLE 7, and TABLE 8. In some embodiments, said nucleic acids comprise at least 50 loci selected from the group consisting of the loci listed in TABLE 6, TABLE 7, and TABLE 8.

[0110] Some embodiments of the methods, compositions and kits provided herein include a method of ameliorating rheumatoid arthritis or osteoarthritis comprising evaluating the methylation status of a plurality of human nucleic acid loci in a nucleic acid sample from a human subject having symptoms of rheumatoid arthritis or osteoarthritis, wherein said loci comprise at least 5 loci which have differential extents of methylation in individuals with rheumatoid arthritis or osteoarthritis relative to individuals without rheumatoid arthritis or osteoarthritis; and administering a treatment for rheumatoid arthritis or osteoarthritis if said at least 5 loci have a methylation status indicative of rheumatoid arthritis or osteoarthritis.

[0111] In some embodiments, said nucleic acids comprise at least 5 loci selected from the group consisting of SEQ ID NO.s 1-485512. In some embodiments, said nucleic acids comprise at least 5 loci selected from the group consisting of the loci listed in TABLE 6, TABLE 7, and TABLE 8. In some embodiments, said nucleic acids comprise at least 10 loci selected from the group consisting of the loci listed in TABLE 6, TABLE 7, and TABLE 8. In some embodiments, said nucleic acids comprise at least 20 loci selected from the group consisting of the loci listed in TABLE 6, TABLE 7, and TABLE 8. In some embodiments, said nucleic acids

comprise at least 50 loci selected from the group consisting of the loci listed in TABLE 6, TABLE 7, and TABLE 8.

[0112] Some embodiments of the methods, compositions and kits provided herein include a mixture comprising a plurality of human nucleic acid loci from a human subject having symptoms indicative of potential rheumatoid arthritis or osteoarthritis and a reagent capable of providing an indication of the methylation status of said loci, wherein said loci comprise at least 5 loci which have differential extents of methylation in individuals with rheumatoid arthritis or osteoarthritis relative to individuals without rheumatoid arthritis or osteoarthritis.

[0113] In some embodiments, said nucleic acids comprise at least 5 loci selected from the group consisting of SEQ ID NO.s 1-485512. In some embodiments, said nucleic acids comprise at least 5 loci selected from the group consisting of the loci listed in TABLE 6, TABLE 7, and TABLE 8. In some embodiments, said nucleic acids comprise at least 10 loci selected from the group consisting of the loci listed in TABLE 6, TABLE 7, and TABLE 8. In some embodiments, said nucleic acids comprise at least 20 loci selected from the group consisting of the loci listed in TABLE 6, TABLE 7, and TABLE 8. In some embodiments, said nucleic acids comprise at least 50 loci selected from the group consisting of the loci listed in TABLE 6, TABLE 7, and TABLE 8.

BRIEF DESCRIPTION OF THE DRAWINGS

[0114] FIG. 1 depicts DNA methyltransferases (DNMTs) function. DNMTs transfer methyl groups from SAM to deoxycytidine. DNMT function can be affected by changes in methyl donors in the diet or by DNMT inhibitors, like 5-aza-2'-deoxycytidine (5-azaC). The analog 5-azacytidine is also incorporated into RNA and can interfere with many other cellular processes.

[0115] FIG. 2 depicts an ILLUMINA array analysis of DNA methylation in RA and OA FLS, and the hierarchical clustering and heatmap of differentially methylated loci. The methylation levels at the 1,859 significantly differentially methylated loci were used for hierarchical clustering. The clustering of the sample is shown by the dendrogram at the top and the clustering of the loci is shown by the dendrogram on the left. The methylation levels at the loci are shown in the heatmap.

[0116] FIG. 3 depicts hypomethylation of several genes in RA FLS basal expression compared to OA FLS. Gene expression was determined by PCR in 6 to 13 separate OA and RA FLS lines for 7 genes that were significantly hypomethylated (CHI3L1, COL1A1, MYEF2,

ITG4A, SYNJ2, STK24, MAP3K5). As a group, expression of hypomethylated genes in RA was significantly greater than OA ($P<0.01$); expression of genes that were normally methylated in RA was similar to OA, e.g., AXIN, IKKE, TBK1, NANOG, POU5F1, MAP2K6, IRF3.

[0117] FIG. 4 depicts an analysis of the focal adhesion pathway, with differentially methylated genes (ECM=extracellular matrix). Differentially methylated genes are present in key locations, most notably RTK, ITGA and ITGB.

[0118] FIG. 5 depicts a Cytoscape analysis to evaluate the networks affected by differential methylation and determine the most likely targets for subsequent analysis.

[0119] FIG. 6 depicts basal expression of DNMTs. DNMT expression was examined in resting cultured FLS. Synoviocytes were isolated from RA and OA synovium at the time of total joint replacement. 4th through 6th passage cells were evaluated by qPCR (graph shows relative expression units using the standard curve method).

[0120] FIG. 7 depicts decreased DNMT1 gene expression after IL-1 stimulation. FLS were stimulated with IL-1 for 24 hr and DNMT expression was determined by qPCR.

[0121] FIG. 8 depicts the decrease in DNMT function in FLS in response to IL-1. FLS were stimulated with 1 ng/ml of IL-1 for 14 days and extracts were assayed using the DNMT Activity/Inhibition Assay (Active Motif Co., Carlsbad, CA), which is an ELISA-based method that measures methylation of a CpG-enriched DNA substrate. A significant decline in total DNMT function ($p<0.05$) was observed.

DETAILED DESCRIPTION

[0122] Abnormalities in DNA methylation have been implicated in autoimmunity. The mechanism of the aggressive rheumatoid phenotype is uncertain, although several studies implicate abnormal tumor suppressor gene structure and function. Differential DNA methylation might lead to altered gene expression, synoviocyte function, and peripheral blood cell function. Global DNA methylation patterns in RA FLS were evaluated and compared to FLS derived from individuals with non-inflammatory joint disease. The data show that the RA FLS display a DNA methylome signature that distinguishes them from osteoarthritis (OA) FLS, with differentially methylated genes that are critical to cell trafficking, inflammation, and cell-extracellular matrix interactions. This signature could define risk factors for developing RA or represent imprinting due to the synovial milieu. A relationship exists between the immunopathologic status of the synovial milieu and peripheral blood mononuclear cell immune function (*See e.g.*, Malone, *et al.*, J Clin Invest., 74(4):1173-1185, 1984; Firestein, GS. Etiology and pathogenesis of rheumatoid arthritis, In: Textbook of Rheumatology, GS Firestein, et al. eds., Elsevier, Philadelphia, 8th

edition, 2009, pp. 1035-86). Peripheral blood mononuclear cells in patients with rheumatoid arthritis demonstrate global methylation abnormalities that parallel those found in cultured fibroblast-like synoviocytes, confirming that peripheral blood cells reflect synovial biology and synoviocyte function. Methylation of the IL-10 promoter has been studied in patients with RA (Fu L.H. *et al.*, Methylation status of the IL-10 gene promoter in the peripheral blood mononuclear cells of rheumatoid arthritis patients. *Yi Chuan*. 2007 Nov;29(11):1357-61). However, no previous data has identified patterns of specific combinations of loci or a distinctive methylome signature that can be used to diagnose RA or provide information on the potential response to therapy (Liu CC, *et al.* Global DNA methylation, DNMT1, and MBD2 in patients with rheumatoid arthritis. *Immunol Lett*. 2011;135:96-9; Karouzakis E, *et al.* DNA hypomethylation in rheumatoid arthritis synovial fibroblasts. *Arthritis Rheum*. 2009;60:3613-22).

[0123] Data implicating low DNA methylation in FLS is especially intriguing in the context of RA, where pathogenic FLS exhibit many features of partially transformed cells. DNMT regulation and the methylation status of FLS were examined in view of the association of DNA hypomethylation and an aggressive phenotype in cancer. As shown in this application, differences in basal RA vs. OA DNMT expression previously described were not confirmed. This may have been because conditions in the examples of this application were rigorously controlled by discontinuing methotrexate treatment up to a month before surgery. Furthermore, it was found that IL-1 significantly decreased DNMT1, DNMT3a, and DNMT3b gene expression within hours. The change in DNMT expression was accompanied by decreased DNMT function in nuclear extracts and global hypomethylation. More striking, as described in this application, an ILLUMINA methylation array study of RA and OA cells showed 100% concordance between DNA methylation patterns and the presence of RA, indicating that RA cells are imprinted with a distinctive methylation pattern that contributes to the pathogenesis of disease.

[0124] The unique pattern of DNA methylation in RA or OA, either taken *in toto* or when considered based on individual loci, genes, or pathways with differential methylation, has several implications. The pattern can be used for several applications, including: diagnosis of RA or OA; assessment of disease activity and prognosis of RA or OA; identification of novel therapeutic targets useful for the development of novel therapies for RA or OA; and the development of novel therapies that increase or decrease DNA methylation and alter the pattern, such as through DNMT inhibitors or activators.

[0125] Embodiments of the present invention include methods, compositions and kits for evaluating a diagnosis, prognosis, or response to treatment of a subject with a disorder such

as rheumatoid arthritis or osteoarthritis. Some embodiments include identifying a therapeutic agent for treating a disorder such as rheumatoid arthritis or osteoarthritis.

[0126] Like peripheral blood mononuclear cells, rheumatoid FLS exhibit an abnormal phenotype that contributes to disease pathogenesis (Firestein, GS. Invasive fibroblast-like synoviocytes in rheumatoid arthritis: Passive responders or transformed aggressors? *Arthritis Rheum* 39:1781-1790, 1996). Functional studies suggest that RA FLS are imprinted *in situ* and maintain these features after many passages in tissue culture. For example, RA FLS, unlike OA or normal synoviocytes, adhere to and invade cartilage explants in SCID mice (Müller-Ladner U *et al.* Synovial fibroblasts of patients with rheumatoid arthritis attach to and invade normal human cartilage when engrafted into SCID mice. *Am J Pathol.* 1996 Nov;149(5):1607-15). RA FLS can grow under anchorage-independent conditions and are less susceptible to contact inhibition. Apoptosis of RA synoviocytes *in situ* appears to be defective, which contributes to intimal lining hyperplasia (Baier A *et al.* Apoptosis in rheumatoid arthritis. *Curr Opin Rheumatol.* 2003 May;15(3):274-9). Data in a SCID mouse model show that RA synoviocytes can migrate from one site to another, thereby serving as a mechanism to spread the RA phenotype and cartilage damage to distant joints (Lefèvre S *et al.* Synovial fibroblasts spread rheumatoid arthritis to unaffected joints. *Nat Med.* 2009 Dec;15(12):1414-20). Despite these findings, RA FLS are not truly transformed, as they senesce in culture after 10 to 15 passages.

[0127] Several mechanisms have been implicated in the rheumatoid phenotype. For instance, resistance to apoptosis can be due, in part, to defective expression of Phosphatase and tensin homolog (PTEN) expression, high levels of sentrin, or preferential shunting of stressed cells to DNA repair rather than programmed cell death (Pap T *et al.* Activation of synovial fibroblasts in rheumatoid arthritis: lack of Expression of the tumour suppressor PTEN at sites of invasive growth and destruction. *Arthritis Res.* 2000;2(1):59-64; Franz JK *et al.* Expression of sentrin, a novel antiapoptotic molecule, at sites of synovial invasion in rheumatoid arthritis. *Arthritis Rheum.* 2000 Mar;43(3):599-607; and You X *et al.* PUMA-mediated apoptosis in fibroblast-like synoviocytes does not require p53. *Arthritis Res Ther.* 2006;8(6):R157). Somatic mutations of regulatory genes have been identified in cultured FLS, including the p53 tumor suppressor gene (Firestein GS *et al.* Somatic mutations in the p53 tumor suppressor gene in rheumatoid arthritis synovium. *Proc Natl Acad Sci USA,* 94: 10895-10900, 1997; Igarashi H *et al.* TP53 mutations coincide with the ectopic expression of activation-induced cytidine deaminase in the fibroblast-like synoviocytes derived from a fraction of patients with rheumatoid arthritis. *Clin Exp Immunol.* 2010 Jul 1;161(1):71-80; Inazuka M *et al.* Analysis of p53 tumour suppressor gene somatic mutations in rheumatoid arthritis synovium. *Rheumatology (Oxford).*

2000 Mar;39(3):262-6; and Rème T *et al.* Mutations of the p53 tumour suppressor gene in erosive rheumatoid synovial tissue. Clin Exp Immunol. 1998 Feb;111(2):353-8). Similar somatic mutations have also been described in peripheral blood mononuclear cells and synovial cells, confirming that these cell populations share many structural DNA characteristics that are either caused by RA or a result of the toxic synovial microenvironment (Cannons JL, et al. HPRT-mutant T cells in the peripheral blood and synovial tissue of patients with rheumatoid arthritis. Arthritis Rheum. 1998;41:1772-82).

[0128] The abnormal cells are more invasive and produce increased amounts of cytokines and metalloproteinases. Microdissection of rheumatoid synovium shows islands of mutant cells residing in the intimal lining that produce prodigious amount of IL-6 (Yamanishi Y *et al.* p53 regulates apoptosis, synovitis and joint destruction in collagen-induced arthritis. Amer J Pathol, 160:123-30, 2002). Microsatellite instability has also been identified in RA synovium, in part due to decreased DNA repair function (Lee S-H *et al.* Microsatellite instability and suppressed DNA repair enzyme expression in rheumatoid arthritis. J Immunol, 170:2214-20, 2003). Somatic mutations in several other genes, including mitochondrial DNA and structural proteins like vimentin, have also been reported (Bang H *et al.* Mutation and citrullination modifies vimentin to a novel autoantigen for rheumatoid arthritis. Arthritis Rheum. 2007 Aug;56(8):2503-11; Da Sylva TR *et al.* Somatic mutations in the mitochondria of rheumatoid arthritis synoviocytes. Arthritis Res Ther. 2005;7(4):R844-51). Most of these and other aggressive features appear to be result of imprinting by rheumatoid synovial environment. Thus, they serve as amplifying mechanisms that alters the natural history of disease and enhance extracellular matrix destruction and cytokine production, leading to a signature in the systemic circulation due to cellular trafficking that can be detected in peripheral blood cells, for example.

[0129] While the focus on gene sequences, mutations, and aggressive behavior has provided useful information, other mechanisms can change cell phenotype. Epigenetics, for instance, can profoundly influence cell activation and gene expression and include DNA methylation, histone modification, and microRNAs. Histone acetylation by histone acetyltransferases (HATs) can remodel chromatin and enhance gene expression while deacetylation by histone deacetylases (HDACs) has the opposite effect. The histone deacetylase HDAC1 is overexpressed in RA FLS and HDAC inhibitors decrease synoviocyte proliferation in culture and joint damage in collagen-induced arthritis (Horiuchi M *et al.* Expression and function of histone deacetylases in rheumatoid arthritis synovial fibroblasts. J Rheumatol. 2009 Aug;36(8):1580-9; Saouaf SJ *et al.* Deacetylase inhibition increases regulatory T cell function and decreases incidence and severity of collagen-induced arthritis. Exp Mol Pathol.

2009;87(2):99-104). MicroRNAs are another epigenetic mechanism that contribute to DNA accessibility and chromatin remodeling by directly targeting individual genes. Expression of some individual microRNAs like microRNA-124a, are decreased in RA compared with OA cells, leading to enhanced chemokine expression (Nakamachi Y *et al.* MicroRNA-124a is a key regulator of proliferation and monocyte chemoattractant protein 1 secretion in fibroblast-like synoviocytes from patients with rheumatoid arthritis. *Arthritis Rheum* 60:1294, 2009; Stanczyk J *et al.* Altered expression of microRNA-203 in rheumatoid arthritis synovial fibroblasts and its role in fibroblast activation. *Arthritis Rheum*. 2011 Feb;63(2):373-81).

[0130] DNA methylation is especially relevant to RA in terms of epigenetic mechanisms by virtue of its role in neoplasia as well as embryonic growth and development. Normal ontogeny relies on a carefully orchestrated sequence of DNA methylation to repress regulatory genes by methylating cytosine in CpG islands after they have completed their programmed role in early development (Christophersen NS and Helin K. Epigenetic control of embryonic stem cell fate. *J Exp Med*. 2010 Oct 25;207(11):2287-95). Methylation abnormalities have been associated with a variety of diseases, most notably cancer where hypomethylation and renewed expression of embryonic genes can allow cells to de-differentiate and escape from normal homeostatic controls (Kulis M and Esteller M. DNA methylation and cancer. *Adv Genet*. 2010;70:27-56). Hypermethylation has also been associated with certain malignancies (Ren J *et al.* DNA hypermethylation as a chemotherapy target. *Cell Signal*. 2011 Feb 21).

[0131] DNA methyltransferases (DNMTs) are responsible for initiating and maintaining CpG methylation in the human genome by converting cytosine to methylcytosine (FIG. 1) (Turek-Plewa J and Jagodzinski PP. The role of mammalian DNA methyltransferases in the regulation of gene expression. *Cell Mol Biol Lett*. 2005;10(4):631-47). In mammalian cells, DNMT1, DNMT3a, and DNMT3b are the primary enzymes responsible for CpG methylation. DNMT3a and DNMT3b mainly regulate *de novo* methylation while DNMT1 maintains methylation, especially during cell division. Thus, DNMT1 plays a greater role perpetuating methylation patterns in proliferating cells. Decreased DNMT expression is associated with global hypomethylation as well as suppressed methylation of individual genes that participate in malignant transformation (Shukla V *et al.* BRCA1 affects global DNA methylation through regulation of DNMT1. *Cell Res*. 2010 Nov;20(11):1201-15). DNMT expression and DNA methylation is not fixed but can be influenced by the environment and modify gene expression throughout life. The DNMTs can also maintain the methylation pattern during cell division, thereby allowing daughter cells to reflect the environmental influences of the parent cells.

[0132] DNMTs can also permit vertical transmission of parental DNA methylation (Ko YG *et al.* Stage-by-stage change in DNA methylation status of Dnmt1 locus during mouse early development. *J Biol Chem.* 2005 Mar 11;280(10):9627-34). This process allows relatively rapid responses to environmental stress that can persist over many cell divisions and even across generations (Rosenfeld. Animal models to study environmental epigenetics. *Biol Reprod.* 2010, 82:473-88; Kaati G *et al.* Transgenerational response to nutrition, early life circumstances and longevity. *Eur J Hum Genet.* 2007 Jul;15(7):784-90). For instance, pregnant mice fed a diet rich in methyl donors like folate have increased levels of DNA methylation for at least 2 subsequent generations. Methylation of the Runx3 gene, in particular, is increased by the high methyl donor diet and leads to enhanced Th2 lymphocyte differentiation and increased airway reactivity in murine asthma (Hollingsworth JW *et al.* In utero supplementation with methyl donors enhances allergic airway disease in mice. *J Clin Invest.* 2008 Oct;118(10):3462-9). Increased disease severity and airway remodeling can even be observed in F2 progeny and demonstrates how the environment can have multigenerational effects (Miller RL. Prenatal maternal diet affects asthma risk in offspring. *J Clin Invest.* 2008. 118:3265-8).

[0133] Abnormalities in DNA methylation have been implicated in autoimmunity. In addition to the murine model of airway disease, T cells can be affected by DNA methylation and influence Th2 differentiation (Gamper CJ *et al.* Identification of DNA methyltransferase 3a as a T cell receptor-induced regulator of Th1 and Th2 differentiation. *J Immunol.* 2009 Aug 15;183(4):2267-76). The DNMT inhibitor 5'-aza-2'-deoxycytidine (5-azaC) (Fandy TE. Development of DNA methyltransferase inhibitors for the treatment of neoplastic diseases. *Curr Med Chem.* 2009;16(17):2075-85) affects expression of many T cell genes, including IFN α , IL-4, CD70, and LFA-1. 5-azaC enhances autoreactivity and induces robust responses to normally sub-threshold stimulation (Richardson B. DNA methylation and autoimmune disease. *Clin Immunol.* 2003 Oct;109(1):72-9). T and B cell interactions are also affected, in part due to altered expression of surface receptors like CD70 (Oelke K *et al.* Overexpression of CD70 and overstimulation of IgG synthesis by lupus T cells and T cells treated with DNA methylation inhibitors. *Arthritis Rheum.* 2004 Jun;50(6):1850-60). Decreased DNA methylation in Th1 and Th2 cell genomic DNA is also associated with production of anti-dsDNA antibodies in vivo (Richardson B *et al.* Murine models of lupus induced by hypomethylated T cells. *Methods Mol Med.* 2004;102:285-94). Hypomethylation has been described in peripheral blood mononuclear cells in patients with RA (Liu CC *et al.* Global DNA methylation, DNMT1, and MBD2 in patients with rheumatoid arthritis. *Immunol Lett.* 2011 Mar 30;135(1-2):96-9. Epub 2010 Oct

16). Despite some evidence of abnormal global methylation, there is no information on specific loci, patterns of loci, genes, or pathways that are abnormally methylated in rheumatoid arthritis.

[0134] Evidence of hypomethylation is not restricted to adaptive immunity in rheumatic disease. Like peripheral blood cells, global genomic hypomethylation was recently reported in RA cultured fibroblast-like synoviocytes (FLS) compared with Osteoarthritis (OA) FLS (Karouzakis E *et al.* DNA hypomethylation in rheumatoid arthritis synovial fibroblasts. *Arthritis Rheum.* 2009 Dec;60(12):3613-22). This observation was associated with relatively low levels of DNMT1 gene expression that were unaffected by *in vitro* stimulation with IL-1 or TNF. DNMT3a or DNMT3b were not examined, and no studies were performed to determine whether DNMT function was abnormal. Culturing FLS in the presence of 5-azaC for 3 months to block DNA methylation increased expression of several genes implicated in RA. However, it is not certain which genes were hypomethylated and which ones were affected secondary to decreased methylation of other regulatory genes.

[0135] DNMT regulation and the methylation status of FLS were examined in view of the association of DNA hypomethylation and an aggressive phenotype in cancer. As shown in this application, it was found that IL-1 significantly decreased DNMT1, DNMT3a, and DNMT3b gene expression within hours. The change in DNMT expression was accompanied by decreased DNMT function in nuclear extracts and global hypomethylation. More striking, an ILLUMINA methylation array study of RA and OA cells showed 100% concordance between DNA methylation patterns and the presence of RA.

[0136] The unique patterns of DNA methylation in RA or OA have several implications. The patterns can be used for several applications, including: diagnosis of RA or OA; assessment of disease activity and prognosis of RA or OA; identification of novel therapeutic targets useful for the development of novel therapies for RA or OA; and the development of novel therapies that increase or decrease DNA methylation and alter the pattern, such as though DNMT inhibitors or activators.

Definitions

[0137] As used herein, "methylation" refers to cytosine methylation at positions C5 or N4 of cytosine, the N6 position of adenine or other types of nucleic acid methylation. In particular embodiments, "methylation" refers to cytosine methylation at positions C5 of cytosine, namely, 5-methyl cytosine. *In vitro* amplified DNA is unmethylated because *in vitro* DNA amplification methods do not retain the methylation pattern of the amplification template.

However, "unmethylated DNA" or "methylated DNA" can also refer to amplified DNA whose original template was unmethylated or methylated, respectively.

[0138] A "methylation profile" refers to a set of data representing the methylation states of two or more loci within a molecule of DNA from e.g., the genome of an individual or cells or tissues from an individual. The profile can indicate the methylation state of every cytosine base in an individual, can comprise information regarding a subset of the base pairs (e.g., the methylation state of specific restriction enzyme recognition sequence) in a genome, or can comprise information regarding regional methylation density of each locus.

[0139] As used herein, "methylation status" refers to the presence, absence and/or quantity of methylation at a particular nucleotide, or nucleotides within a portion of DNA. Determination of the methylation status of a particular DNA sequence (e.g., a locus, a DNA biomarker or DNA region as described herein) can involve determination of the methylation state of every cytosine in the sequence or can involve determination of the methylation state of a subset of the cytosines (such as the methylation state of cytosines in one or more specific restriction enzyme recognition sequences) within the sequence, or can involve determining regional methylation density within the sequence without providing precise information of where in the sequence the methylation occurs. The methylation status can optionally be represented or indicated by a "methylation value." A methylation value can be generated, for example, by quantifying the amount of intact DNA present following restriction digestion with a methylation dependent restriction enzyme. In this example, if a particular sequence in the DNA is quantified using quantitative PCR, an amount of template DNA approximately equal to a mock treated control indicates the sequence is not highly methylated whereas an amount of template substantially less than occurs in the mock treated sample indicates the presence of methylated DNA at the sequence. Accordingly, a value, i.e., a methylation value, for example from the above described example, represents the methylation status and can thus be used as a quantitative indicator of methylation status. This is of particular use when it is desirable to compare the methylation status of a sequence in a sample to a threshold value.

[0140] As used herein, "methylation-dependent restriction enzyme" refers to a restriction enzyme that cleaves or digests DNA at or in proximity to a methylated recognition sequence, but does not cleave DNA at or near the same sequence when the recognition sequence is not methylated. Methylation-dependent restriction enzymes include those that cut at a methylated recognition sequence (e.g., DpnI) and enzymes that cut at a sequence near but not at the recognition sequence (e.g., McrBC). For example, McrBC's recognition sequence is 5' RmC (N40-3000) RmC 3' where "R" is a purine and "mC" is a methylated cytosine and "N40-3000"

indicates the distance between the two RmC half sites for which a restriction event has been observed. McrBC generally cuts close to one half-site or the other, but cleavage positions are typically distributed over several base pairs, approximately 30 base pairs from the methylated base. McrBC sometimes cuts 3' of both half sites, sometimes 5' of both half sites, and sometimes between the two sites. Exemplary methylation-dependent restriction enzymes include, e.g., McrBC (see, e.g., U.S. Pat. No. 5,405,760), McrA, MrrA, BslI, GlaI and DpnI. One of skill in the art will appreciate that any methylation-dependent restriction enzyme, including homologs and orthologs of the restriction enzymes described herein, is also suitable for use in the present embodiments.

[0141] As used herein, "methylation-sensitive restriction enzyme" refers to a restriction enzyme that cleaves DNA at or in proximity to an unmethylated recognition sequence but does not cleave at or in proximity to the same sequence when the recognition sequence is methylated. Exemplary methylation-sensitive restriction enzymes are described in, e.g., McClelland et al., *Nucleic Acids Res.* 22(17):3640-59 (1994) and <http://rebase.neb.com>. Suitable methylation-sensitive restriction enzymes that do not cleave DNA at or near their recognition sequence when a cytosine within the recognition sequence is methylated at position C5 include, e.g., Aat II, Aci I, Acl I, Age I, Alu I, Asc I, Ase I, AsiS I, Bbe I, BsaA I, BsaH I, BsiE I, BsiW I, BsrF I, BssH II, BssK I, BstB I, BstN I, BstU I, Cla I, Eae I, Eag I, Fau I, Fse I, Hha I, HinP1 I, HinC II, Hpa II, Hpy99 I, HpyCH4 IV, Kas I, Mbo I, Mlu I, MapA1 I, Msp I, Nae I, Nar I, Not I, Pml I, Pst I, Pvu I, Rsr II, Sac II, Sap I, Sau3A I, Sfi I, Sfo I, SgrA I, Sma I, SnaB I, Tsc I, Xma I, and Zra I. Suitable methylation-sensitive restriction enzymes that do not cleave DNA at or near their recognition sequence when an adenosine within the recognition sequence is methylated at position N6 include, e.g., Mbo I. One of skill in the art will appreciate that any methylation-sensitive restriction enzyme, including homologs and orthologs of the restriction enzymes described herein, is also suitable for use in the present invention. One of skill in the art will further appreciate that a methylation-sensitive restriction enzyme that fails to cut in the presence of methylation of a cytosine at or near its recognition sequence may be insensitive to the presence of methylation of an adenosine at or near its recognition sequence. Likewise, a methylation-sensitive restriction enzyme that fails to cut in the presence of methylation of an adenosine at or near its recognition sequence may be insensitive to the presence of methylation of a cytosine at or near its recognition sequence. For example, Sau3AI is sensitive (i.e., fails to cut) to the presence of a methylated cytosine at or near its recognition sequence, but is insensitive (i.e., cuts) to the presence of a methylated adenosine at or near its recognition sequence. One of skill in the art will also appreciate that some methylation-sensitive restriction enzymes are blocked

by methylation of bases on one or both strands of DNA encompassing of their recognition sequence, while other methylation-sensitive restriction enzymes are blocked only by methylation on both strands, but can cut if a recognition site is hemi-methylated.

Evaluating a diagnosis, prognosis, or response to treatment

[0142] Some embodiments provided herein relate to methods for diagnosing, determining a prognosis, or determining or predicting a response to treatment. As used herein, diagnosing can include determining whether a methylation status of 1 or more loci is indicative of a disorder, such as rheumatoid arthritis. As used herein, determining a prognosis can include determining whether methylation status of 1 or more loci is indicative of a likelihood of improvement in symptoms of a disorder, such as rheumatoid arthritis. As used herein, determining or predicting a response to treatment can include determining whether methylation status of 1 or more loci after treatment is more similar to a normal status before treatment or earlier in the treatment regimen. In some embodiments of the methods and compositions provided herein, the 1 or more locus or 1 or more gene is a locus or gene with no known association with RA.

[0143] In some such embodiments, the methylation state of at least 1 locus or at least one gene selected from a locus or gene described herein in a sample obtained from a subject is determined. Examples of loci for which the methylation state may be evaluated include the loci listed in TABLE 6, TABLE 7, and TABLE 8. In some embodiments, loci for which the methylation state may be evaluated include SEQ ID NO.s:1 - 485512. In each sequence provided in SEQ ID NO.s 1 – 485512, the “C” which is potentially methylated is at position 61. Examples of genes for which the methylation state may be evaluated include the loci listed in TABLE 3. The nucleic acid sequences of the loci listed in TABLE 6, TABLE 7, and TABLE 8 and the genes listed in TABLE 3 are incorporated herein by reference. In some embodiments, additional loci and genes useful for the methods and compositions provided herein can be further identified using the methods described herein. In some embodiments, additional loci and genes useful for the methods and compositions provided herein are identified by conducting methylation analyses in additional samples, thereby providing an increased number of data points which could assist in the identification of further genes or loci having statistically significant differences in their methylation states. The sample can comprise an *in vivo* sample, an *in vitro* sample, or an *ex vivo* sample. It will be understood, that in some embodiments of the compositions or methods provided herein, a sample or cell can be *in vivo*. In some embodiments of the compositions or methods provided herein, a sample or cell can be *ex vivo*. Methods to determine the methylation

state of at least one locus or at least one gene are well known in the art and examples are provided herein. In some embodiments, the subject is a mammal, such as a human. In some embodiments, the methylation states of at least about 1, 2, 3, 4, 5, 10, 20, 30, 40, 50, 60, 70, 80, 90, 100, 200, 300, 400, 500 loci or more than 500 loci are determined. Some embodiments also include comparing the methylation state of the at least 1 locus in the sample with the methylation state of the locus in a normal cell, cell from a subject with a known prognosis, or cell from a subject with a known response to treatment. In some embodiments, the methylation states of at least about 1, 2, 3, 4, 5, 10, 20, 30, 40, 50, 60, 70, 80, 90, 100, 200, 300, 400, 500 genes or more than 500 genes are determined. Some embodiments also include comparing the methylation state of the at least 1 gene in the sample with the methylation state of the gene in a normal cell, cell from a subject with a known prognosis, or cell from a subject with a known response to treatment.

[0144] In some embodiments, an increase or decrease in the methylation state of the at least 1 locus compared to the methylation state of the locus in normal cell, cell from a subject with a known prognosis, or cell from a subject with a known response to treatment is indicative of the diagnosis, prognosis, or response to treatment for the subject. In some embodiments, an increase or decrease in the methylation state of a locus selected from the group consisting of the loci listed in TABLE 6 is indicative of the diagnosis, prognosis, or response to treatment for the subject. In some embodiments, an increase or decrease in the methylation state of a locus selected from the group consisting of the loci listed in TABLE 7 is indicative of the diagnosis, prognosis, or response to treatment for the subject. In some embodiments, an increase or decrease in the methylation state of a locus selected from the group consisting of the loci listed in TABLE 8 is indicative of the diagnosis, prognosis, or response to treatment for the subject. In some embodiments, an increase or decrease in the methylation state of the at least 1 gene compared to the methylation state of the gene in a normal cell, cell from a subject with a known prognosis, or tissue from a subject with a known response to treatment is indicative of the diagnosis, prognosis, or response to treatment for the subject. In some embodiments, an increase or decrease in the methylation state of a gene selected from the group consisting of the genes listed in TABLE 3 is indicative of the diagnosis, prognosis, or response to treatment for the subject. In some embodiments, the increase or decrease in methylation occurs in a cell, such as a synoviocyte, such as a fibroblast-like synoviocyte, for example, a rheumatoid arthritis fibroblast-like synoviocyte or an osteoarthritis fibroblast-like synoviocyte. In some embodiments, the cell comprises macrophage. In some embodiments, the cell comprises a peripheral blood cell. As used herein, 'peripheral blood cell' can include a cellular component of blood which contains

DNA. Examples of peripheral blood cells include white blood cells, including neutrophils, eosinophils, basophils, lymphocytes, B cell, plasma cells, T cells, natural killer cells, monocytes, and dendritic cells. In some embodiments, the cell is mammalian, e.g., human. In some embodiments, the loci and genes which are differentially methylated in fibroblast-like synoviocytes from individuals with rheumatoid arthritis or osteoarthritis and the loci and genes which are differentially methylated in individuals with rheumatoid or osteoarthritis in cell types other than fibroblast-like synoviocytes may partially overlap. However, it is likely that there will be loci and genes which exhibit differential methylation in individuals with rheumatoid arthritis or osteoarthritis in one cell type which are not differentially methylated in other cell types from individuals with rheumatoid arthritis or osteoarthritis. Such differences in differential methylation may be a reflection of the fact that methylation patterns vary among different cell lineages. For example, differentially methylated loci and genes identified in T cells and in B cells types from individuals with rheumatoid arthritis or osteoarthritis can include loci and genes that are different in each cell type. Differentially methylated loci and genes in different cell types from individuals with rheumatoid arthritis or osteoarthritis can be identified using the methods described herein.

[0145] Some embodiments include methods of ameliorating rheumatoid arthritis or osteoarthritis in a subject. Some such embodiments include evaluating the methylation status of a plurality of human nucleic acid loci in a nucleic acid sample from a human subject having symptoms of rheumatoid arthritis or osteoarthritis. In some embodiments, the loci comprise at least about 5 loci, at least about 10 loci, at least about 15 loci, at least about 20 loci, at least about 25 loci, at least about 50 loci, and at least about 100 loci. In some embodiments the loci are selected from the group consisting of the loci listed in TABLE 6, TABLE 7, or TABLE 8. In some embodiments, the loci may be selected from SEQ ID NO.s:1 – 485512. Some embodiments also include administering a treatment for rheumatoid arthritis or osteoarthritis if the loci have a methylation status indicative of rheumatoid arthritis or osteoarthritis.

[0146] Some embodiments include a mixture comprising a plurality of human nucleic acid loci from a human subject having symptoms indicative of potential rheumatoid arthritis or osteoarthritis and a reagent capable of providing an indication of the methylation status of said loci. In some embodiments, the loci comprise at least about 5 loci, at least about 10 loci, at least about 15 loci, at least about 20 loci, at least about 25 loci, at least about 50 loci, and at least about 100 loci. In some embodiments the loci are selected from the group consisting of the loci listed in TABLE 6, TABLE 7, or TABLE 8. In some embodiments, the loci are selected from SEQ ID NO.s:1 - 485512

Methods to determine methylation state of a locus

[0147] In some embodiments, the methylation state of more than one DNA region, e.g., gene, locus or portion thereof is determined. In some embodiments, the methylation status of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97 or more than 97 of the DNA regions is determined.

[0148] In some embodiments, the methylation state of a DNA region or portion thereof is determined and then normalized (e.g., compared) to the methylation state of a control locus. Typically the control locus will have a known, relatively constant, methylation status. For example, the control sequence can be previously determined to have no, some or a high amount of methylation, thereby providing a relative constant value to control for error in detection methods, etc., unrelated to the presence or absence of a disorder. In some embodiments, the control locus is endogenous, i.e., is part of the genome of the individual sampled. For example, in mammalian cells, the testes-specific histone 2B gene (hTH2B in human) gene is known to be methylated in all somatic tissues except testes. Alternatively, the control locus can be an exogenous locus, i.e., a DNA sequence spiked into the sample in a known quantity and having a known methylation status.

[0149] A DNA region comprises a nucleic acid including one or more methylation sites of interest (e.g., a cytosine, a "microarray feature," or an amplicon amplified from select primers) and flanking nucleic acid sequences (i.e., "wingspan") of up to 4 kilobases (kb) in either or both of the 3' or 5' direction from the amplicon. This range corresponds to the lengths of DNA fragments obtained by randomly fragmenting the DNA before screening for differential methylation between DNA in two or more samples (e.g., carrying out methods used to initially identify differentially methylated loci). In some embodiments, the wingspan of the one or more DNA regions is about 0.5 kb, 0.75 kb, 1.0 kb, 1.5 kb, 2.0 kb, 2.5 kb, 3.0 kb, 3.5 kb or 4.0 kb in both 3' and 5' directions relative to the sequence represented by the microarray feature. The DNA region of interest can comprise and/or be immediately adjacent to a locus selected from the group consisting of the loci listed in TABLE 6, TABLE 7, or TABLE 8, or a gene selected from a gene listed in TABLE 3. In some embodiments, the locus may be selected from SEQ ID NO.s:1 – 485512. The nucleic acid sequences of the loci listed in TABLE 6, TABLE 7, and TABLE 8 are available, for example, in the Illumina CpG database, and included in SEQ ID NO.s:1 – 485512.

[0150] The methylation sites in a DNA region can reside in non-coding transcriptional control sequences (e.g., promoters, enhancers, etc.) or in coding sequences, including introns and exons of the loci listed in TABLE 6, TABLE 7, or TABLE 8, and genes listed in TABLE 3. In some embodiments, the methods comprise detecting the methylation status in the promoter regions (e.g., comprising the nucleic acid sequence that is about 1.0 kb, 1.5 kb, 2.0 kb, 2.5 kb, 3.0 kb, 3.5 kb or 4.0 kb 5' from the transcriptional start site through to the translational start site) of one or more of the locus identified in TABLE 6, TABLE 7, TABLE 8, or TABLE 3. In some embodiments, the locus may be selected from SEQ ID NO.s:1 – 485512.

[0151] Any method for detecting DNA methylation can be used in the methods provided herein. In some embodiments, an array can be used to determine the methylation state of at least one locus, such as the ILLUMINA HumanMethylation 450 BeadChip. DNA is treated with bisulfite to convert unmethylated cytosines to uracil, methylated cytosines are protected and remain cytosine. After the conversion step, a determination step is performed to identify whether a base at a particular locus was converted. Methylation status of the interrogated site is calculated as the ratio of the signal from a methylated probe relative to the sum of both methylated and unmethylated probes. This value, known as β , ranges continuously from 0 (unmethylated) to 1 (fully methylated). Arrays, such as the ILLUMINA HumanMethylation 450 BeadChip, include genes and CpG islands and other sequences.

[0152] In some embodiments, methods for detecting methylation include randomly shearing or randomly fragmenting the genomic DNA, cutting the DNA with a methylation-dependent or methylation-sensitive restriction enzyme and subsequently selectively identifying and/or analyzing the cut or uncut DNA. Selective identification can include, for example, separating cut and uncut DNA (e.g., by size) and quantifying a sequence of interest that was cut or, alternatively, that was not cut. *See, e.g.*, U.S. Pat. No. 7,186,512. Alternatively, the method can encompass amplifying intact DNA after restriction enzyme digestion, thereby only amplifying DNA that was not cleaved by the restriction enzyme in the area amplified. *See, e.g.*, U.S. patent application Ser. Nos. 10/971,986; 11/071,013; and 10/971,339. In some embodiments, amplification can be performed using primers that are gene specific. Alternatively, adaptors can be added to the ends of the randomly fragmented DNA, the DNA can be digested with a methylation-dependent or methylation-sensitive restriction enzyme, intact DNA can be amplified using primers that hybridize to the adaptor sequences. In this case, a second step can be performed to determine the presence, absence or quantity of a particular gene in an amplified pool of DNA. In some embodiments, the DNA is amplified using real-time, quantitative PCR.

[0153] In some embodiments, the methods comprise quantifying the average methylation density in a target sequence within a population of genomic DNA. In some embodiments, the method comprises contacting genomic DNA with a methylation-dependent restriction enzyme or methylation-sensitive restriction enzyme under conditions that allow for at least some copies of potential restriction enzyme cleavage sites in the locus to remain uncleaved; quantifying intact copies of the locus; and comparing the quantity of amplified product to a control value representing the quantity of methylation of control DNA, thereby quantifying the average methylation density in the locus compared to the methylation density of the control DNA.

[0154] The quantity of methylation of a locus of DNA can be determined by providing a sample of genomic DNA comprising the locus, cleaving the DNA with a restriction enzyme that is either methylation-sensitive or methylation-dependent, and then quantifying the amount of intact DNA or quantifying the amount of cut DNA at the DNA locus of interest. The amount of intact or cut DNA will depend on the initial amount of genomic DNA containing the locus, the amount of methylation in the locus, and the number (i.e., the fraction) of nucleotides in the locus that are methylated in the genomic DNA. The amount of methylation in a DNA locus can be determined by comparing the quantity of intact DNA or cut DNA to a control value representing the quantity of intact DNA or cut DNA in a similarly-treated DNA sample. The control value can represent a known or predicted number of methylated nucleotides. Alternatively, the control value can represent the quantity of intact or cut DNA from the same locus in another (e.g., normal, non-diseased) cell or a second locus.

[0155] By using at least one methylation-sensitive or methylation-dependent restriction enzyme under conditions that allow for at least some copies of potential restriction enzyme cleavage sites in the locus to remain uncleaved and subsequently quantifying the remaining intact copies and comparing the quantity to a control, average methylation density of a locus can be determined. As used herein, 'methylation density' can refer to the number of methylated C-residues within a region. If the methylation-sensitive restriction enzyme is contacted to copies of a DNA locus under conditions that allow for at least some copies of potential restriction enzyme cleavage sites in the locus to remain uncleaved, then the remaining intact DNA will be directly proportional to the methylation density, and thus may be compared to a control to determine the relative methylation density of the locus in the sample. Similarly, if a methylation-dependent restriction enzyme is contacted to copies of a DNA locus under conditions that allow for at least some copies of potential restriction enzyme cleavage sites in the locus to remain uncleaved, then the remaining intact DNA will be inversely proportional to the

methylation density, and thus may be compared to a control to determine the relative methylation density of the locus in the sample. Such assays are disclosed in, e.g., U.S. patent application Ser. No. 10/971,986.

[0156] Quantitative amplification methods (e.g., quantitative PCR or quantitative linear amplification) can be used to quantify the amount of intact DNA within a locus flanked by amplification primers following restriction digestion. Methods of quantitative amplification are disclosed in, e.g., U.S. Pat. Nos. 6,180,349; 6,033,854; and 5,972,602, as well as in, e.g., Gibson et al., *Genome Research* 6:995-1001 (1996); DeGraves, et al., *Biotechniques* 34(1):106-10, 112-5 (2003); Deiman B, et al., *Mol. Biotechnol.* 20(2):163-79 (2002). Amplifications may be monitored in "real time."

[0157] Additional methods for detecting DNA methylation can involve genomic sequencing before and after treatment of the DNA with bisulfite. See, e.g., Frommer et al., *Proc. Natl. Acad. Sci. USA* 89:1827-1831 (1992). When sodium bisulfite is contacted to DNA, unmethylated cytosine is converted to uracil, while methylated cytosine is not modified.

[0158] In some embodiments, restriction enzyme digestion of PCR products amplified from bisulfite-converted DNA is used to detect DNA methylation. See, e.g., Sadri & Hornsby, *Nucl. Acids Res.* 24:5058-5059 (1996); Xiong & Laird, *Nucleic Acids Res.* 25:2532-2534 (1997).

[0159] In some embodiments, a MethyLight assay is used alone or in combination with other methods to detect DNA methylation (see, Eads et al., *Cancer Res.* 59:2302-2306 (1999)). Briefly, in the MethyLight process genomic DNA is converted in a sodium bisulfite reaction (the bisulfite process converts unmethylated cytosine residues to uracil). Amplification of a DNA sequence of interest is then performed using PCR primers that hybridize to CpG dinucleotides. By using primers that hybridize only to sequences resulting from bisulfite conversion of unmethylated DNA, (or alternatively to methylated sequences that are not converted) amplification can indicate methylation status of sequences where the primers hybridize. Similarly, the amplification product can be detected with a probe that specifically binds to a sequence resulting from bisulfite treatment of a unmethylated (or methylated) DNA. If desired, both primers and probes can be used to detect methylation status. Thus, kits for use with MethyLight can include sodium bisulfite as well as primers or detectably-labeled probes (including but not limited to Taqman or molecular beacon probes) that distinguish between methylated and unmethylated DNA that have been treated with bisulfite. Other kit components can include, e.g., reagents necessary for amplification of DNA including but not limited to, PCR buffers, deoxynucleotides; and a thermostable polymerase.

[0160] In some embodiments, a Ms-SNuPE (Methylation-sensitive Single Nucleotide Primer Extension) reaction is used alone or in combination with other methods to detect DNA methylation (see, Gonzalgo & Jones, *Nucleic Acids Res.* 25:2529-2531 (1997)). The Ms-SNuPE technique is a quantitative method for assessing methylation differences at specific CpG sites based on bisulfite treatment of DNA, followed by single-nucleotide primer extension (Gonzalgo & Jones, *supra*). Briefly, genomic DNA is reacted with sodium bisulfite to convert unmethylated cytosine to uracil while leaving 5-methylcytosine unchanged. Amplification of the desired target sequence is then performed using PCR primers specific for bisulfite-converted DNA, and the resulting product is isolated and used as a template for methylation analysis at the CpG site(s) of interest.

[0161] Typical reagents (e.g., as might be found in a typical Ms-SNuPE-based kit) for Ms-SNuPE analysis can include, but are not limited to: PCR primers for specific gene (or methylation-altered DNA sequence or CpG island); optimized PCR buffers and deoxynucleotides; gel extraction kit; positive control primers; Ms-SNuPE primers for a specific gene; reaction buffer (for the Ms-SNuPE reaction); and detectably-labeled nucleotides. Additionally, bisulfite conversion reagents may include: DNA denaturation buffer; sulfonation buffer; DNA recovery reagents or kit (e.g., precipitation, ultrafiltration, affinity column); desulfonation buffer; and DNA recovery components.

[0162] In some embodiments, a methylation-specific PCR ("MSP") reaction is used alone or in combination with other methods to detect DNA methylation. An MSP assay entails initial modification of DNA by sodium bisulfite, converting all unmethylated, but not methylated, cytosines to uracil, and subsequent amplification with primers specific for methylated versus unmethylated DNA. See, Herman et al., *Proc. Natl. Acad. Sci. USA* 93:9821-9826, (1996); U.S. Pat. No. 5,786,146.

[0163] Additional methylation detection methods include, but are not limited to, methylated CpG island amplification (see, Toyota et al., *Cancer Res.* 59:2307-12 (1999)) and those described in, e.g., U.S. Patent Publication 2005/0069879; Rein, et al. *Nucleic Acids Res.* 26 (10): 2255-64 (1998); Olek, et al. *Nat. Genet.* 17(3): 275-6 (1997); and PCT Publication No. WO 00/70090.

[0164] Some embodiments provided herein include methods of determining the methylation status of a plurality of human nucleic acid loci. Some such embodiments include contacting a nucleic acid sample from a human subject with a reagent capable of providing an indication of the methylation status of said loci. In some embodiments, the loci comprise at least about 5 loci, at least about 10 loci, at least about 15 loci, at least about 20 loci, at least about 25

loci, at least about 50 loci, and at least about 100 loci. In some embodiments the loci are selected from the group consisting of the loci listed in TABLE 6, TABLE 7, or TABLE 8. In some embodiments, the reagent is a restriction enzyme. In some embodiments, the reagent is a primer. In some embodiments, the reagent is a probe. In some embodiments, the reagent comprises sodium bisulfite.

Identifying therapeutic agents

[0165] Some embodiments provided herein relate to methods for identifying therapeutic agents. Some such embodiments for identifying therapeutic agents which may be used to treat rheumatoid arthritis or osteoarthritis, can include contacting a cell with a test agent; and determining the methylation state of at least 1 locus selected from the loci listed in TABLE 6, TABLE 7, or TABLE 8 or at least one gene listed in Table 3 in the contacted cell. In some embodiments, the at least one locus may be selected from SEQ ID NO.s:1 – 485512. Some methods also include comparing the methylation state of the at least 1 locus, or at least 1 gene in the contacted cell with the methylation state of the locus or the gene in the cell not contacted with the test agent, and selecting a test agent that increases or decreases the methylation state of the at least 1 locus or the at least 1 gene in the cell contacted with the test agent compared to the methylation state of the locus or the gene in a cell not contacted with the test agent. For example, if a locus, a gene group of loci or group of genes are hypermethylated in individuals with RA, agents which reduce the level of methylation at the locus, the gene, group of loci or group of genes may be useful as therapeutic agents. Likewise, if a locus, a gene, group of loci or group of genes are hypomethylated in individuals with RA, agents which increase the level of methylation at the locus, the gene group of loci or group of genes may be useful as therapeutic agents. Likewise, agents which produce a methylation profile in cells contacted with the agent having a greater similarity to the methylation profile of individuals who do not suffer from RA relative to the methylation profile in cells which have not been contacted with the agent may be useful as therapeutic agents. Examples of test agents and potential therapeutic agents include small molecules (including but not limited to organic chemical compounds which have been obtained from natural sources or synthesized), nucleic acids (including but not limited to antisense nucleic acids, ribozymes, or siRNAs), peptides and proteins (including but not limited to cytokines TNF- α , and DMNTs).

[0166] In some embodiments, at least 1 locus is selected from the group consisting of the loci listed in TABLE 6. In some embodiments, at least 1 locus is selected from the group consisting of the loci listed in TABLE 7. In some embodiments, the at least one locus may be

selected from SEQ ID NO.s:1 – 485512. In some embodiments, at least 1 gene is selected from the group consisting of the gene listed in TABLE 3.

[0167] In some embodiments, the methylation states of at least about 5, 10, 20, 30, 40, 50, 60, 70, 80, 90, or 100 loci selected from the group consisting of the loci listed in TABLE 6, TABLE 7, or TABLE 8 are determined. In some embodiments, the methylation states of at least about 5, 10, 20, 30, 40, 50, 60, 70, 80, or 100 loci selected from the group consisting of the loci of SEQ ID NO.s:1 – 485512. In some embodiments, the methylation states of at least about 1, 5, 10, 20, 30, 40, 50 genes selected from the group consisting of the genes listed in TABLE 3 are determined

[0168] In some embodiments, the cell comprises a synoviocyte, such as a fibroblast-like synoviocyte, for example, a rheumatoid arthritis fibroblast-like synoviocyte or an osteoarthritis fibroblast-like synoviocyte. In some embodiments, the cell comprises a macrophage. In some embodiments, the cell comprises a peripheral blood cell. In some embodiments, the peripheral blood cell is selected from the group consisting of white blood cell, including neutrophil, eosinophil, basophil, lymphocyte, B cell, plasma cell, T cell, natural killer cell, monocyte, and dendritic cell. In some embodiments, the cell is mammalian, e.g., human.

[0169] More embodiments of methods for identifying therapeutic reagents include identifying agents that modulate methylation of genes encoding proteins that act in the same pathway as other proteins encoded by genes that are differentially methylated in rheumatoid arthritis or osteoarthritis or agents which modulate the activity of proteins in the same pathway as proteins encoded by genes which are differentially methylated in rheumatoid arthritis or osteoarthritis. Some methods for identifying a therapeutic agent for treating rheumatoid arthritis or osteoarthritis include contacting a cell with a test agent, and determining the methylation state of at least 1 gene selected from a gene encoding a protein that acts in a pathway that includes a protein encoded by a gene that is differentially methylated in a rheumatoid arthritis cell or osteoarthritis cell compared to a normal cell. Some methods also include comparing the methylation state of the at least 1 gene in the contacted cell with the methylation state of the gene in a cell which was not contacted with the test agent, selecting a test agent that increases or decreases the extent of methylation of the at least 1 gene in the cell contacted with the test agent compared to the extent of methylation of the at least 1 gene in a cell which was not contacted with the test agent such that the extent of methylation of the at least 1 gene in the cell contacted with the test agent is a methylation state associated with the absence of rheumatoid arthritis or osteoarthritis or with a reduction in the symptoms associated with rheumatoid arthritis or osteoarthritis. In some embodiments, the pathway is selected from focal adhesion,

glycosphingolipid biosynthesis - lacto and neolacto series, arrhythmogenic right ventricular cardiomyopathy (ARVC), ECM-receptor interaction, amoebiasis, leukocyte transendothelial migration, protein digestion and absorption, cell adhesion molecules (CAMs), nitrogen metabolism, ErbB signaling pathway, African trypanosomiasis, primary bile acid biosynthesis, Fc epsilon RI signaling pathway, mTOR signaling pathway, and adipocytokine signaling pathway.

Kits

[0170] Some embodiments provided herein relate to kits. Some such kits can be useful for diagnosing, determining a prognosis, or determining a response to treatment of a subject with a disorder, such as rheumatoid arthritis, comprising: a reagent for determining the methylation state of at least one locus selected from the group consisting of the loci listed in TABLE 6, TABLE 7, or TABLE 8. In some embodiments, the at least one locus may be selected from SEQ ID NO.s:1 – 485512. In some embodiments, the kit also includes at least one polynucleotide primer comprising a sequence hybridizing to at least a portion of the at least one locus selected from the group consisting of the loci listed in TABLE 6, TABLE 7, or TABLE 8. In some embodiments, the locus may be selected from SEQ ID NO.s:1 – 485512. In some embodiments, the kit can include one or more of methylation-dependent restriction enzymes, methylation-sensitive restriction enzymes, amplification (e.g., PCR) reagents, probes and/or primers. In some embodiments a reagent can determine the methylation states of at least about 1, 5, 10, 20, 30, 40, 50, 60, 70, 80, 90, 100 or more than 100 loci selected from the group consisting of the loci listed in TABLE 6, TABLE 7, or TABLE 8. In some embodiments, the at least about 1, 5, 10, 20, 30, 40, 50, 60, 70, 80, 90, 100 or more than 100 loci may be selected from SEQ ID NO.s:1 – 485512.

[0171] Some embodiments include kits for diagnosing, determining a prognosis, or determining or predicting a response to treatment of a subject with rheumatoid arthritis or osteoarthritis, comprising a reagent for determining the methylation state of at least one gene selected from the group consisting of the genes listed in TABLE 3. Some kits also include at least one polynucleotide primer comprising a sequence hybridizing to at least a portion of the at least one gene selected from the group consisting of the genes listed in TABLE 3. In some embodiments, the reagent comprises a restriction enzyme. In some embodiments a reagent can determine the methylation states of at least about 1, 5, 10, 20, 30, 40, 50, or more genes selected from the group consisting of the genes listed in TABLE 3.

[0172] Some embodiments include a nucleic acid array consisting essentially of nucleic acids useful for diagnosing rheumatoid arthritis or osteoarthritis, determining a prognosis of rheumatoid arthritis or osteoarthritis, or determining or predicting a response to treatment of a

subject being evaluated for or suffering from rheumatoid arthritis or osteoarthritis. In some such embodiments, the nucleic acids comprise at least about 5 loci, at least about 10 loci, at least about 15 loci, at least about 20 loci, at least about 25 loci, at least about 50 loci, and at least about 100 loci. In some embodiments the loci are selected from the group consisting of the loci listed in TABLE 6, TABLE 7, or TABLE 8. In some embodiments, the loci may be selected from SEQ ID NO.s:1 – 485512.

Computer-Based Methods

[0173] The calculations for the methods described herein can involve computer-based calculations and tools. For example, a methylation value for a DNA region or portion thereof can be compared by a computer to a threshold value, as described herein. The tools are advantageously provided in the form of computer programs that are executable by a general purpose computer system (referred to herein as a "host computer") of conventional design. The host computer may be configured with many different hardware components and can be made in many dimensions and styles (e.g., desktop PC, laptop, tablet PC, handheld computer, server, workstation, mainframe). Standard components, such as monitors, keyboards, disk drives, CD and/or DVD drives, and the like, may be included. Where the host computer is attached to a network, the connections may be provided via any suitable transport media (e.g., wired, optical, and/or wireless media) and any suitable communication protocol (e.g., TCP/IP); the host computer may include suitable networking hardware (e.g., modem, Ethernet card, WiFi card). The host computer may implement any of a variety of operating systems, including UNIX, Linux, Microsoft Windows, MacOS, or any other operating system.

[0174] Computer code for implementing aspects of the present invention may be written in a variety of languages, including PERL, C, C++, Java, JavaScript, VBScript, AWK, or any other scripting or programming language that can be executed on the host computer or that can be compiled to execute on the host computer. Code may also be written or distributed in low level languages such as assembler languages or machine languages.

[0175] The host computer system advantageously provides an interface via which the user controls operation of the tools. In the examples described herein, software tools are implemented as scripts (e.g., using PERL), execution of which can be initiated by a user from a standard command line interface of an operating system such as Linux or UNIX. Those skilled in the art will appreciate that commands can be adapted to the operating system as appropriate. In other embodiments, a graphical user interface may be provided, allowing the user to control operations using a pointing device. Thus, the present invention is not limited to any particular user interface.

[0176] Scripts or programs incorporating various features of the present invention may be encoded on various computer readable media for storage and/or transmission. Examples of suitable media include magnetic disk or tape, optical storage media such as compact disk (CD) or DVD (digital versatile disk), flash memory, and carrier signals adapted for transmission via wired, optical, and/or wireless networks conforming to a variety of protocols, including the Internet.

[0177] Some embodiments include methods for diagnosing rheumatoid arthritis or osteoarthritis, determining a rheumatoid arthritis or osteoarthritis prognosis, or determining or predicting a response to treatment for rheumatoid arthritis or osteoarthritis in a subject comprising accessing first data representing nucleic acid loci which are differentially methylated in individuals with rheumatoid arthritis, osteoarthritis a rheumatoid arthritis or osteoarthritis prognosis, or a response to treatment for rheumatoid arthritis or osteoarthritis wherein said data is stored on a non-transitory computer readable medium. Some embodiments also include instructing a computer to compare said first data to second data representing the methylation status of said nucleic acid loci in a sample taken from said subject, wherein said data representing the methylation status of said nucleic acid loci in a sample taken from said subject is stored on a non-transitory computer readable medium. Some embodiments also include diagnosing rheumatoid arthritis or osteoarthritis, determining a rheumatoid arthritis or osteoarthritis prognosis, or determining or predicting a response to treatment for rheumatoid arthritis or osteoarthritis in said subject if said first data representing the methylation status of said nucleic acid loci in a sample taken from said subject are significantly similar to said second data representing nucleic acid loci which are differentially methylated in individuals with rheumatoid arthritis, osteoarthritis a rheumatoid arthritis or osteoarthritis prognosis, or a response to treatment for rheumatoid arthritis or osteoarthritis.

[0178] While the present invention has been described in some detail for purposes of clarity and understanding, one skilled in the art will appreciate that various changes in form and detail can be made without departing from the true scope of the invention.

EXAMPLES

Example 1—Methylation of loci in RA and OA patients

Methods: Fibroblast-like synoviocytes

[0179] FLS were isolated from synovial tissues obtained from RA and OA patients at the time of joint replacement as described previously. The diagnosis of RA conformed to the American College of Rheumatology 1987 revised criteria. The protocol was approved by the

UCSD Human Subjects Research Protection Program. Synovial tissues were minced and incubated with 0.5 mg/ml collagenase VIII (Sigma) in serum-free RPMI (Mediatech, VA) for 1.5 h at 37°C, filtered through a 0.22 µm cell strainer, extensively washed, and cultured in DMEM supplemented with 10% FCS (endotoxin content <0.006 ng/ml; Gemini Biosciences, CA), penicillin, streptomycin, gentamicin and L-glutamine in a humidified 5% CO₂ incubator. After overnight culture, nonadherent cells were removed, and adherent cells were trypsinized, split at a 1:3 ratio, and cultured. Synoviocytes were used from passage 4 through 9, when FLS were a homogeneous population with <1% CD11b, <1% phagocytic, and <1% FcR II positive cells.

Patient phenotype

[0180] Synovial tissues were obtained at the time of clinically indicated total knee or hip joint replacement surgery except for one patient with RA who had wrist surgery. The mean ages of RA and OA patients were 53±9 and 68±16, respectively. Additional information on four patients (2 RA and 2 OA) was limited because the samples were de-identified. The erythrocyte sedimentation rates for the remaining RA and OA patients were 38±15 and 19±10, respectively. Of the 4 RA patients with clinical information, 3 were seropositive for serum rheumatoid factor or anti-CCP antibody and all were treated with low dose prednisone, 2 with methotrexate, 2 with a TNF blocker, and 1 with leflunomide. OA was mainly treated with acetaminophen and narcotics for pain.

Isolation of genomic DNA and qPCR analysis

[0181] RA and OA FLS were grown to 80% confluence and harvested. Genomic DNA of 10⁶ FLS was isolated using the MagMAX™ DNA Multi-Sample Kit (Applied Biosystems). DNA quality and quantity was assessed with a NanoDrop ND-2000 spectrometer (NanoDrop Technologies, Wilmington, DE, USA). mRNA from cultured FLS was isolated using RNA-STAT (Tel-Stat, TX) and cDNA was prepared, according to manufacturer's instructions using GeneAmp 2400 (Applied Biosystems). Quantitative real-time PCR was performed using Assays On Demand (Applied Biosystems) to determine relative mRNA levels using the GeneAmp 5700 Sequence Detection System (Applied Biosystems) as described previously. Standard curves for human MMP1 and GAPDH were generated. Sample Ct values were used to calculate the number of cell equivalents in the test samples. The data were then normalized to GAPDH expression to obtain relative cell equivalents.

Infinium HumanMethylation450 chip analysis

[0182] Genomic DNA was isolated from female RA and OA FLS as described. The Infinium HumanMethylation450 chip was processed as described by the manufacturer (Illumina, San Diego, CA). This chip covers 96% of RefSeq genes and provides comprehensive gene region

coverage, targeting multiple sites with promoter, 5' UTR, 1st exon, gene body and 3' UTR. Initial analysis was performed with the GenomeStudio methylation module, and then further analysed as described herein. The methylation level of a loci is measured as:

$$\beta = M / (U + M + 100)$$

[0183] M is the fluorescence level of the methylation probe and U is the methylation level of the unmethylated probe. A constant value of 100 is added to prevent division by a small number (or 0) when background subtraction was used. The β values varied from 0 (completely unmethylated) to 1 (completely methylated). To measure the difference in methylation at a loci between OA and RA the average β levels were compared.

Method for determining enrichment of multiple methylated loci

[0184] To avoid taking a single *P*-value cut-off when identifying genes that are enriched with differentially methylated (differentially methylated) loci, a variable cut-off scheme was used. Loci were ranked by their differentially methylated *P*-values. Then a *P*-value cut-off was taken. Those loci with *P*-value beneath the cut-off were taken to be differentially methylated and the rest were taken as not being differentially methylated. While doing this all *P*-value cut-offs beneath 0.05 were tried. Then for each gene, with loci beneath the *P*-value cut-off, the level which its loci were enriched beneath the cut-off was calculated as its enrichment factor (*EF*).

[0185] $EF = (\text{number of loci from gene A beneath cut-off} / \text{total loci from gene A}) / (\text{total number of loci beneath cut-off} / \text{total number of loci})$

[0186] If *EF* is greater than 1 then it means the genes loci are enriched with differentially methylated loci. For those genes with an *EF* greater than 1, a *P*-value for the level of enrichment was calculated using the hypergeometric distribution. The resulting *P*-values were corrected with the Benjamini-Hochberg correction. Genes with enrichment *P*-values beneath < 0.05 were recorded. If a gene was found to be enriched at multiple loci differentially methylated levels then only the level with the lower enrichment *P*-value was reported.

Pathway and gene ontology analyses

[0187] Pathway enrichment was carried out using the KEGG human pathways and modules (www.genome.jp/kegg/download). The enrichment analysis of 1859 loci was performed by mapping pathway to loci via the loci gene annotations, the *EF* of loci being enriched in KEGG pathway as calculated. If *EF* was greater than 1 then *P*-value for the level of enrichment was calculated using the hypergeometric distribution. The resulting *P*-values were corrected with the Benjamini-Hochberg correction. As the KEGG pathways represent groups of related bimolecular pathways a *P*-value cut-off of <0.1 was used as it would allow enrichment within individual bimolecular pathways to be identified. A *P*-value cut-off of <0.1 has been used previously during

KEGG pathway analysis (Xu et al. 2010 - Revealing parasite influence in metabolic pathways in Apicomplexa infected patients, *BMC Bioinformatics* 2010, 11(Suppl 11):S13; Shen et al. 2006 - Sepsis Plasma Protein Profiling with Immunodepletion, Three-Dimensional Liquid Chromatography Tandem Mass Spectrometry, and Spectrum Counting, *J. Proteome Res.*, 2006, 5 (11), pp 3154–3160, each incorporated by reference in their entireties). Gene ontology (GO) analysis was carried using human GO term associations (www.geneontology.org). GO term enrichment analysis was carried out using model-based gene set analysis which uses probabilistic inference to identify the active GO terms (Bauer, et al. 2010 GOing Bayesian: model-based gene set analysis of genome-scale data. *Nucleic Acids Res.* 2010;38:3523-32, incorporated by reference in its entirety). This approach naturally deals with overlapping GO categories and avoids the need for multiple testing correction. Marginal probability values >0.50 were considered significantly enriched.

Initial probe and data filtering

[0188] The DNA methylome in RA and control (OA) FLS was evaluated. The Infinium HumanMethylation450 chip (Illumina, Inc.) was used to determine the methylation status of 485,512 loci from FLS isolated from 11 female patients at the time of total joint replacement surgery (6 RA; 5 OA). Loci were removed from subsequent analysis if any of the probes for a locus could not be distinguished from background with a P -value < 0.01 or if enough beads present upon the chip for accurate measurement of their methylation level. After filtering, 476,331 loci were available for further analysis.

Global methylation status

[0189] To assess global methylation status of RA and OA FLS, the methylation scores over all filtered loci within a sample were summed. The difference between the two samples was assessed using Student's t -test. Initial analysis included all loci and was then repeated for only loci located in promoters. There were no significant differences between RA and OA (P -values 0.528 and 0.627, respectively). Therefore, globally hypo- or hypermethylation is not associated with RA when compared to OA. These results were confirmed using an antibody-based method to determine methylcytosine levels (Active Motif, Inc., Carlsbad, CA) where global methylation were similar for RA and OA (RA=0.85 $\pm$ 0.32; OA=1.00 $\pm$ 0.24; $n=10$ RA and 9 OA lines; $P>0.05$).

Analysis of differentially methylated individual loci

[0190] Although global methylation are not different for RA and OA, there were differentially methylated (differentially methylated) loci that cluster to the two diseases. To identify the autosomal loci that are differentially methylated between OA and RA two filters were

used: (i) an average difference in methylation level was greater than 0.1; and (ii) a P -value < 0.05 that calculated using the Student's t -test and corrected for multiple testing with the Benjamini-Hochberg adjustment. 1,859 loci in 1206 different genes were identified as significantly differentially methylated in RA FLS. TABLE 1 shows example numbers of hypermethylated and hypomethylated sites.

TABLE 1

	No. of loci hypomethylated in RA	No. of loci hypermethylated in RA
differentially methylated loci*	732	1127
differentially methylated genes**	63	144
differentially methylated KEGG pathways	10	6
differentially methylated GO terms	138	242
*differentially methylated = Differentially methylated; Difference between OA and RA > 0.1 , with $P < 0$ after Benjamini-Hochberg adjustment.		
**6 additional genes had both hypo- and hypermethylated loci (ADAMTS2, C7orf50, DIP2C, FRMD SH3PXD2A)		

[0191] Examples of genes identified with statistically significant differences between RA and OA at an individual locus using the ILLUMINA dataset are shown in TABLE 2. A mean value of OA methylation minus RA methylation; A P -value cut-off of < 0.05 was used for determining significance. Where the RA minus OA value was positive the locus in RA was hypermethylated; where the RA minus OA value was negative, the locus in RA was hypomethylated.

TABLE 2

	RA minus OA	Gene	Description
Hyper-methylated*	-0.34417	PHLPP1	PH domain and leucine rich repeat protein phosphatase 1
	-0.34108	RXRA	retinoid X receptor, alpha
	-0.30861	CYFIP1	cytoplasmic FMR1 interacting protein 1
	-0.30363	ADAMTS2	ADAM metalloproteinase with thrombospondin type 1 motif, 2
	-0.2964	CD55	CD55 molecule, decay accelerating factor for complement
	-0.27459	CABLES1	Cdk5 and Abl enzyme substrate 1
	-0.26569	HAS1	hyaluronan synthase 1
	-0.25362	ITGB8	integrin, beta 8
	-0.25333	HBEGF	heparin-binding EGF-like growth factor
	-0.23299	PTPN14	protein tyrosine phosphatase, non-receptor type 14
	-0.23228	COL4A2	collagen, type IV, alpha 2
	-0.23122	COL4A1	collagen, type IV, alpha 1

	RA minus OA	Gene	Description
	-0.21314	TGFBR2	transforming growth factor, beta receptor II (70/80kDa)
	-0.20915	EGF	epidermal growth factor
	-0.20692	ITGBL1	integrin, beta-like 1 (with EGF-like repeat domains)
	-0.20006	TIMP2	TIMP metalloproteinase inhibitor 2
	-0.19768	MAP3K1	mitogen-activated protein kinase kinase kinase 1
	-0.19005	FOXO1	forkhead box O1
Hypo-methylated	0.365	CHI3L1	chitinase 3-like 1 (cartilage glycoprotein-39)
	0.337	WISP3;WIS P3	WNT1 inducible signaling pathway protein 3
	0.333	STK24	serine/threonine kinase 24
	0.329	MMP20	matrix metalloproteinase 20
	0.322	EGFLAM	EGF-like, fibronectin type III and laminin G domain
	0.318	PTGIS	prostaglandin I2 (prostacyclin) synthase
	0.301	DCBLD1	discoidin, CUB and LCCL domain containing 1
	0.299	MAP3K5	mitogen-activated protein kinase kinase kinase 5 (ASK1)
	0.297	MGMT	O-6-methylguanine-DNA methyltransferase
	0.282	CDK14	cyclin-dependent kinase 14
	0.272	STAT3	signal transducer and activator of transcription 3
	0.270	ADAM32	ADAM metalloproteinase domain 32
	0.264	RASGRF2	Ras protein-specific guanine nucleotide-releasing factor 2
	0.253	CASP1	caspase 1, apoptosis-related cysteine peptidase
	0.225	P2RX6	purinergic receptor P2X, ligand-gated ion channel, 6
	0.195	TRAF2	TNF receptor-associated factor 2
	0.185	MEFV	Mediterranean fever

[0192] CpG methylation was significantly different in a number of genes implicated in RA. Several genes implicated in inflammation and immune responses are differentially methylated in RA.

[0193] A list of 1,859 loci is shown in TABLE 6 and TABLE 7. TABLE 6 and TABLE 7 list loci which are differentially methylated in RA compared to OA; a positive OA –RA value represents a loci which is hypomethylated in RA FLS (TABLE 6), a negative OA –RA value represents a loci which is hypermethylated in RA FLS (TABLE 7).

[0194] Permutation analysis was carried out to assess the significance of loci identified as differentially methylated. The 11 samples were randomly assigned to OA and RA while maintaining the same number of OA and RA labels, i.e., 5 OA and 6 RA. The permutation analysis was repeated 1,000 times. The average number of significant loci during the permutation

analysis was 4.9, compared to 1,859 for the correct disease identification. The permutation analysis strongly supports these loci as truly differentially methylated and not as a result of random chance.

[0195] To assess the ability of the 1,859 loci to distinguish OA from RA, the methylation patterns of the loci across the 11 samples were hierarchically clustered (FIG. 2). The clustering of the samples distinguishes OA from RA, which clearly segregate according to disease type. The clustering of the loci also shows that groups of loci have similar patterns of differentially methylated across the samples.

Analysis of genes with multiple differentially methylated loci

[0196] To examine genes that were significantly differentially methylated between OA and RA, genes that were enriched with multiple differentially methylated loci were identified (see Methods). This analysis was carried using all 1,859 differentially methylated loci identified in differentially methylated loci section. The data demonstrated that many genes have multiple CpGs that are hyper- or hypo- methylated. For example, *COL1A1* has 41 loci, and 4 are hypomethylated in RA ($P < 10^{-6}$) giving a “relative enrichment” of 79-fold compared to OA. Relative enrichment for *MEFV* (pyrin) hypomethylation is nearly 200-fold. Of interest, 4 of 16 loci in the TNF promoter are hypermethylated in RA (relative enrichment=451; $P < 10^{-9}$), suggesting that TNF regulation might be under the control of DNMTs in some patients. 207 genes were either enriched for multiple hyper- or hypomethylated loci (TABLE 1). Representative examples of hypomethylated- (hypo-) and hypermethylated- (hyper-) differentially methylated genes are shown in TABLE 3.

TABLE 3

Status in RA	Gene	No. of differentially methylated loci beneath cut-off	Total loci on array	P-value for enrichment	Enrichment factor
hypo	LOC146880	9	32	9.96E-18	245.34
hypo	SH3D20	6	15	5.58E-14	487.22
hypo	TACC2	7	70	4.60E-11	87.23
hypo	KCNJ9	4	15	1.95E-08	251.27
hypo	FUT4	4	20	4.90E-08	200.26
hypo	ARHGAP27	4	25	2.45E-07	130.45
hypo	OLFML3	3	9	2.97E-07	439.51
hypo	ACTN1	4	42	3.73E-07	116
hypo	TRIM15	4	82	3.79E-07	115.32
hypo	PDZRN3	4	50	9.44E-07	88.29

Status in RA	Gene	No. of differentially methylated loci beneath cut-off	Total loci on array	P-value for enrichment	Enrichment factor
hypo	COL1A1	4	41	1.26E-06	79.55
hypo	CD93	3	15	2.44E-06	200.26
hypo	ITGA4	3	18	4.52E-06	157.79
hypo	NFE2L3	3	19	7.74E-06	128.74
hypo	HRNBP3	5	189	8.88E-06	25.05
hypo	POMC	3	26	1.00E-05	115.53
hypo	SKAP1	3	27	1.09E-05	111.26
hypo	T	3	31	1.21E-05	106.8
hypo	RHOJ	2	9	2.16E-05	525.33
hypo	COL22A1	3	36	2.26E-05	83.44
hypo	BOC	3	35	2.32E-05	81.15
hypo	SCUBE1	2	23	6.91E-05	273.55
hypo	ROBO4	2	15	7.76E-05	252.46
hypo	HUNK	2	16	8.36E-05	236.68
hypo	AUTS2	3	114	8.36E-05	49.83
hypo	FPR2	2	11	9.00E-05	221.46
hypo	CASZ1	4	174	9.41E-05	21.76
hypo	MEFV	2	11	9.64E-05	200.66
hypo	MXRA8	2	18	9.64E-05	210.38
hypo	ARMC3	2	12	9.64E-05	203.01
hypo	STX1B	2	15	9.64E-05	199.51
hypo	USP54	2	9	9.64E-05	193.85
hypo	PLCH2	3	64	0.000112844	40.89
hypo	FXYP7	2	17	0.000112844	176.04
hypo	INSM1	2	13	0.000113996	169.79
hypo	MYEF2	2	13	0.000113996	169.79
hypo	P2RY6	2	21	0.000156705	142.51
hypo	CA4	2	15	0.000227225	116.31
hypo	AXIN2	2	37	0.000287729	102.35
hypo	SPSB1	2	46	0.000287729	102.78
hypo	KANK4	2	21	0.000316358	95.36
hypo	APCDD1	2	20	0.000419791	81.53
hypo	B3GNTL1	3	158	0.000474472	23.13

Status in RA	Gene	No. of differentially methylated loci beneath cut-off	Total loci on array	P-value for enrichment	Enrichment factor
hypo	ANGPT1	2	24	0.000585029	67.95
hypo	PRRX1	2	27	0.000625725	64.62
hypo	COL6A1	2	33	0.000696287	60.68
hypo	LRIG1	2	46	0.000726192	59.28
hypo	GLIS1	2	50	0.000828923	54.54
hypo	ST14	2	43	0.000921733	51.33
hypo	SYT7	2	54	0.001010062	48.83
hypo	PHC2	2	34	0.001014634	47.96
hypo	PLXNC1	2	34	0.001014634	47.96
hypo	PKNOX2	2	63	0.001243393	43.29
hypo	ODZ4	2	148	0.001280632	42.51
hypo	MYO7A	2	45	0.001280907	42.08
hypo	EBF2	2	47	0.001382296	40.29
hypo	NXN	3	193	0.002031781	12.67
hypo	PRKAR1B	3	224	0.002535422	11.68
hypo	SYNJ2	2	68	0.002651843	27.84
hypo	MAML2	2	70	0.002780925	27.05
hypo	GAS7	2	72	0.003896102	22.65
hypo	MYT1L	2	170	0.006150038	17.6
hypo	SMOC2	2	164	0.01010976	13.46
hyper	LOC90834	8	11	7.31E-18	375.88
hyper	BRD1	8	42	1.65E-12	98.45
hyper	C6orf25	5	42	1.90E-09	208.6
hyper	PCSK6	7	65	2.09E-09	55.66
hyper	LOC100292680	4	13	2.07E-08	291.99
hyper	PPM1L	5	37	6.18E-08	88.51
hyper	FERMT3	4	21	1.05E-07	180.76
hyper	TES	4	21	3.42E-07	132.58
hyper	PHYHD1	3	9	1.09E-06	316.32
hyper	IGSF6	3	6	1.21E-06	275.53
hyper	UACA	3	22	2.44E-06	238.95
hyper	TNF	4	27	2.66E-06	71.05
hyper	PRMT7	3	24	2.98E-06	219.03

Status in RA	Gene	No. of differentially methylated loci beneath cut-off	Total loci on array	P-value for enrichment	Enrichment factor
hyper	SEC14L3	3	9	3.07E-06	197
hyper	HSD3B7	3	17	3.07E-06	208.59
hyper	APP	2	19	3.30E-06	2002.59
hyper	MYPN	3	11	3.44E-06	189.82
hyper	HBEGF	3	10	3.74E-06	177.3
hyper	SLC22A1	3	13	3.74E-06	182.93
hyper	LOC100271831	3	9	5.20E-06	151.33
hyper	GPR1	3	14	6.06E-06	149.15
hyper	NINJ2	4	39	6.06E-06	53.01
hyper	GDPD3	3	10	6.90E-06	136.2
hyper	C21orf34	3	16	8.70E-06	130.5
hyper	KHDRBS3	3	17	1.24E-05	115.58
hyper	TRERF1	4	50	1.49E-05	41.35
hyper	COL4A2	5	139	1.53E-05	22.99
hyper	MIRLET7C	2	4	2.05E-05	591
hyper	SPATA18	3	27	3.95E-05	77.34
hyper	SEMA6D	3	22	5.67E-05	65.4
hyper	METTL9	3	25	5.67E-05	66.13
hyper	TIMP2	4	64	5.67E-05	28.37
hyper	KIAA1949	4	100	6.11E-05	27.84
hyper	NRM	2	43	8.35E-05	299.71
hyper	NSMCE2	3	32	0.000105867	51.66
hyper	SLC9A1	3	27	0.000109957	50.44
hyper	C17orf99	2	10	0.000113832	236.4
hyper	MIR1301	2	6	0.000143314	197
hyper	PLXNA2	3	45	0.00015859	43.66
hyper	GALNT12	2	9	0.00018091	176.15
hyper	STX2	3	38	0.000181317	40.8
hyper	CPT1A	3	59	0.000185452	40.31
hyper	EHD4	3	36	0.000185452	39.97
hyper	MYH15	2	14	0.000191884	168.86
hyper	FGL2	2	6	0.000226795	144.6
hyper	RPH3AL	4	154	0.000226795	18.08

Status in RA	Gene	No. of differentially methylated loci beneath cut-off	Total loci on array	P-value for enrichment	Enrichment factor
hyper	SCARA5	3	39	0.000253629	34.92
hyper	BTC	2	14	0.000270028	135.57
hyper	CETN1	2	11	0.00029116	126.55
hyper	NPL	2	8	0.000332725	113.5
hyper	LARP4	2	20	0.000332725	118.2
hyper	NADK	3	47	0.000334772	30.61
hyper	ITPK1	3	65	0.000345734	30.23
hyper	ZEB2	3	59	0.000346791	30.05
hyper	CCDC25	2	12	0.000360628	106.54
hyper	TMOD4	2	9	0.000360628	106.58
hyper	EGF	2	13	0.000360628	107.08
hyper	SLC1A2	2	32	0.000360628	109.52
hyper	ADCK5	2	22	0.000364838	107.45
hyper	RNF165	2	16	0.000413716	99.09
hyper	CSNK1G2	3	53	0.000425925	27.15
hyper	ERRFI1	2	20	0.000448119	94.9
hyper	ESCO2	2	14	0.000464905	91.32
hyper	CHST11	3	55	0.000464905	26.16
hyper	MUC6	3	56	0.00047946	25.69
hyper	ITGB8	2	13	0.00050411	84.78
hyper	ST5	3	71	0.00050411	24.97
hyper	FANCA	2	28	0.000525004	84.43
hyper	MYF6	2	11	0.00055928	78.87
hyper	SETD1A	2	30	0.000588655	78.8
hyper	RUFY3	2	17	0.000595625	77.05
hyper	MYOM1	2	12	0.000597351	75.67
hyper	ARL4D	2	15	0.000638325	73.47
hyper	NXPH2	2	21	0.000774146	66.29
hyper	MGAT3	2	18	0.000776579	65.67
hyper	AKT3	2	30	0.000841298	63.26
hyper	RELL1	2	23	0.000896152	60.52
hyper	CARS	2	23	0.000896152	60.52
hyper	TRAPPC9	4	215	0.000916221	11

Status in RA	Gene	No. of differentially methylated loci beneath cut-off	Total loci on array	P-value for enrichment	Enrichment factor
hyper	LZTS1	2	22	0.000916221	59.54
hyper	PPP2R5C	2	59	0.000924708	59.4
hyper	DLX3	2	16	0.000963235	56.75
hyper	AMBRA1	2	28	0.000986075	56.62
hyper	SDCBP2	2	24	0.001039634	54.58
hyper	LMBRD1	2	17	0.00105958	53.41
hyper	ARHGAP1	2	18	0.00106039	53.29
hyper	TBCD	5	352	0.001086318	7.34
hyper	ACSL1	2	30	0.001086318	52.85
hyper	PLCB3	2	26	0.001238237	49.17
hyper	MAP3K1	2	24	0.001394061	45.92
hyper	LRRFIP1	2	76	0.001408026	46.11
hyper	BAI2	2	36	0.001513586	44.04
hyper	ZNRF1	2	26	0.001594799	42.39
hyper	ITGBL1	2	23	0.001628294	41.71
hyper	SPPL2B	2	38	0.001642638	41.72
hyper	PIGV	2	23	0.001779686	39.48
hyper	KLF12	2	40	0.001784969	39.63
hyper	FOXO1	2	32	0.002026288	36.94
hyper	C1QTNF1	2	39	0.002125118	35.69
hyper	NCK2	2	53	0.002125118	35.81
hyper	CYTH1	2	37	0.002143776	35.4
hyper	APOLD1	2	34	0.002203548	34.76
hyper	HTRA1	2	38	0.002233352	34.47
hyper	CCDC146	2	28	0.002665635	30.98
hyper	CRYL1	2	42	0.002665635	31.19
hyper	COL4A1	2	71	0.003503044	26.73
hyper	GPR133	3	165	0.003819221	10.75
hyper	PHACTR2	2	40	0.004172106	23.98
hyper	ANK3	2	38	0.004173533	23.89
hyper	RPTOR	5	432	0.004520935	5.02
hyper	CACNA2D3	2	76	0.005405541	20.86
hyper	LHFPL2	2	44	0.005447591	20.64

Status in RA	Gene	No. of differentially methylated loci beneath cut-off	Total loci on array	P-value for enrichment	Enrichment factor
hyper	TG	2	47	0.00554287	20.41
hyper	KANK2	2	45	0.005602318	20.18
hyper	SRPK2	2	45	0.005602318	20.18
hyper	PITPNM2	2	48	0.005684708	19.98
hyper	ADAM12	2	52	0.005720838	19.88
hyper	MICAL3	2	47	0.005961209	19.32
hyper	FILIP1L	2	45	0.005961209	19.28
hyper	GALNS	2	73	0.006100028	19.07
hyper	ARHGAP26	2	61	0.006687473	18.07
hyper	ARHGEF7	2	74	0.006937548	17.7
hyper	WIPI2	2	64	0.007267014	17.22
hyper	PTPN14	2	59	0.00801136	16.26
hyper	CUX1	2	215	0.00801136	16.3
hyper	SORBS2	2	81	0.00806007	16.17
hyper	HPCAL1	2	60	0.008172002	15.99
hyper	DNMT3A	2	77	0.00881667	15.35
hyper	TNS3	2	79	0.009173569	14.96
hyper	SLC6A3	2	69	0.009173569	14.98
hyper	PTPRG	2	96	0.01090562	13.64
hyper	MIR548G	2	65	0.01127773	13.35
hyper	ASAP2	2	70	0.01183843	12.97
hyper	C3orf26	2	67	0.01183843	12.95
hyper	NAV1	2	68	0.01212126	12.76
hyper	CREB5	2	82	0.01424866	11.7
hyper	CTBP2	2	102	0.02110821	9.4
hyper	TCERG1L	2	105	0.02218092	9.14
hyper	SHANK2	3	262	0.02489354	4.97
hyper	CMIP	2	113	0.02508337	8.49
hyper	BAT2	2	161	0.02704674	8.14
hyper	EIF2C2	2	117	0.02919953	7.76
hyper	RPS6KA2	2	244	0.02919953	7.78
hyper	PRKCZ	2	263	0.03328032	7.22

Correlation of gene expression and methylation status

[0197] Functional analysis of the differentially methylated was performed by evaluating expression of several representative genes with hypo- and normally methylated loci in RA FLS by qPCR. FIG. 3 shows the results for several hypomethylated genes. These genes included ITGA4, COL1A1, MYEF2, SYNJ2, CHI3L1, STK24, and MAP3K5. As a group, expression of genes with hypomethylated loci was significantly greater in RA than OA FLS (n=7 genes; $P<0.01$). On the other hand, expression of normally methylated genes was similar in RA and OA FLS (n=7 genes; $P>0.10$).

[0198] Higher expression in RA was demonstrated for most hypomethylated genes, and the differences were significant when the genes were evaluated as a group ($P<0.01$ for RA vs. OA). Some genes, such as STK24, were not significantly different in RA and could reflect more than methylation *in vitro*. Nevertheless, these data demonstrated that methylation is reflected in gene expression patterns in RA and could contribute to production of inflammatory mediators in RA.

Pathway and gene ontology analyses

[0199] Biological pathways and gene ontologies that are enriched with differentially methylated loci were evaluated. Loci were mapped to pathways via their relationships to genes within pathways for KEGG pathways and for GO using all 1,859 differentially methylated loci identified (TABLE 1). Pathway analysis showed that interactions between cells and the matrix and cell recruitment were especially prominent in the differentially methylated group, including focal adhesion, mTOR signaling, cell adhesion molecules, leukocyte transendothelial interactions, and ECM-receptor interactions. FIG 4 depicts the pathway 'Focal adhesion', which was enriched with loci that are significantly less methylated in RA. A list of differential GO terms and an analysis of hypomethylated and hypermethylated terms in RA with marginal probability >0.5 is shown in TABLE 4.

TABLE 4

	ID	Marginal probability	Name
RA Hypomethylated	GO:0003713	0.99836	Transcription coactivator activity
	GO:0051117	0.98512	ATPase binding
	GO:0031519	0.95603	PcG protein complex
	GO:0045944	0.92189	Positive regulation of transcription from RNA polymerase II promoter
	GO:0019897	0.81989	Extrinsic to plasma membrane
	GO:0008134	0.81119	Transcription factor binding

	ID	Marginal probability	Name
	GO:0015467	0.78847	G-protein activated inward rectifier potassium channel activity
	GO:0017157	0.76244	Regulation of exocytosis
	GO:0007369	0.74990	Gastrulation
	GO:0035257	0.70985	Nuclear hormone receptor binding
	GO:0004221	0.59229	Ubiquitin thiolesterase activity
	GO:0004629	0.55446	Phospholipase C activity
	GO:0009897	0.53595	External side of plasma membrane
	GO:0015629	0.52284	Actin cytoskeleton
	GO:0022610	0.51076	Biological adhesion
RA Hypermethylated	GO:0005794	0.77055	Golgi apparatus
	GO:0007166	0.76581	Cell surface receptor linked signaling pathway
	GO:0005488	0.60305	Binding

[0200] Of interest, the number of GO terms associated with hypomethylated DNA in RA was greater than for hypermethylated DNA (15 vs. 3). Thus, hypomethylated terms clustered with hypomethylation in RA, especially related to membrane and transcription factor biology. This analysis can be used to identify novel therapeutic targets for RA. More examples of pathways useful to identify novel therapeutic targets for RA are shown in TABLE 5.

TABLE 5

Status in RA	Path group	Path name	Enrichment factor	DM loci in path	Total loci in path	P-value
hypo	Cell Communication	Focal adhesion	2.615457643	20	6226	0.007005624
hypo	Glycan Biosynthesis and Metabolism	Glycosphingolipid biosynthesis - lacto and neolacto series	9.88097044	5	412	0.007005624
hypo	Cardiovascular Diseases	Arrhythmogenic right ventricular cardiomyopathy (ARVC)	3.862390722	10	2108	0.007378046
hypo	Signaling Molecules and Interaction	ECM-receptor interaction	3.303009997	12	2958	0.007378046
hypo	Infectious Diseases	Amoebiasis	3.278225332	11	2732	0.01087908
hypo	Immune System	Leukocyte transendothelial migration	3.339589681	10	2438	0.01366817
hypo	Digestive System	Protein digestion and absorption	3.090564183	9	2371	0.03435163

Status in RA	Path group	Path name	Enrichment factor	DM loci in path	Total loci in path	P-value
hypo	Endocrine System	Adipocytokine signaling pathway	3.505131458	7	1626	0.04363638
hypo	Signaling Molecules and Interaction	Cell adhesion molecules (CAMs)	2.542760663	10	3202	0.06198887
hypo	Energy Metabolism	Nitrogen metabolism	6.691988748	3	365	0.08527128
hyper	Signal Transduction	ErbB signaling pathway	2.295320174	18	2272	0.0580967
hyper	Infectious Diseases	African trypanosomiasis	4.05913013	8	571	0.0580967
hyper	Lipid Metabolism	Primary bile acid biosynthesis	5.625639088	4	206	0.0950006
hyper	Immune System	Fc epsilon RI signaling pathway	2.345183916	13	1606	0.0950006
hyper	Signal Transduction	mTOR signaling pathway	2.295464506	14	1767	0.0950006
hyper	Endocrine System	Adipocytokine signaling pathway	2.316337866	13	1626	0.0950006

Network analysis

[0201] Cytoscape was used to evaluate networks affected by differential methylation and to determine likely targets for subsequent analysis. In a preliminary study, interactions between hypomethylated genes and their neighbors were evaluated. A portion of the Cytoscape analysis is shown in FIG. 5. Significant nodes included key hypomethylated loci (*e.g.*, *STAT3*, *MAP3K5*, *CHI3L1*, *STK24*) (circle size indicates degree of hypomethylation). FIG. 5 depicts how these loci interact with each other and with multiple additional pathways, and describes how the methylated genes might regulate inflammatory responses in RA. This map shows only a fraction of the interactions and provides an unbiased view of how methylation affects synovocyte function.

Basal expression of DNMTs

[0202] After discovering that RA FLS are differentially methylated, DNMT expression in resting cultured FLS was examined. Synovocytes were isolated from RA and OA synovium at the time of total joint replacement. 4th through 6th passage cells were evaluated by qPCR. FIG. 6 depicts graphs of relative expression of DNMT1, DNMT3a, and DNMT3b in OA FLS and RA FLS. Unexpectedly, expression levels of DNMTs in RA and OA were found to be similar. In view of these findings, changes in DNMT expression in FLS was examined, and the role of cytokines, *e.g.*, IL-1, in RA, that may contribute to a DNMT profile was examined.

Decreased DNMT1 gene expression after IL-1 stimulation

[0203] FLS were stimulated with IL-1 for 24 hr and DNMT expression was determined by qPCR. Unexpectedly, DNMT1 and DNMT3a gene expression significantly decreased after exposure to modest concentrations of IL-1 (FIG. 7). After noting that IL-1 decreased DNMT mRNA, time course experiments were performed to assess the kinetics of the effect. Cells were stimulated with 1 ng/ml of IL-1 for various time periods and qPCR was performed. DNMT mRNA levels begin to decrease within 2 to 8 hrs after exposure to the cytokine (data not shown).

IL-1 decreases DNMT function in FLS

[0204] A functional assay was performed to determine if IL-1 suppresses DNA methylation activity of the DNMTs. FLS were stimulated with 1 ng/ml of IL-1 for 14 days and extracts were assayed using the DNMT Activity/Inhibition Assay (Active Motif Co., Carlsbad, CA), which is an ELISA-based method that measures methylation of a CpG-enriched DNA substrate. As shown in FIG. 8, a significant decline in total DNMT function ($p < 0.05$) was observed.

Discussion

[0205] FLS form the synovial intimal lining and play an integral role in the pathogenesis of RA by producing key cytokines, small molecule mediators, and proteases. While osteoclasts are the primary effectors of bone erosions in arthritis, FLS are responsible for cartilage damage by virtue of their ability to adhere to and invade the cartilage extracellular matrix. This capacity requires homotypic aggregation mediated by the adhesion molecule cadherin-11, which directs intimal lining formation and supports an invasive phenotype. Understanding the molecular mechanisms that regulate FLS activation could provide insights into the pathogenesis of RA and lead to novel therapeutic strategies. In the present application, the epigenetic profile of RA was evaluated by exploring a newly discovered DNA methylation signature that could potentially affect adaptive and innate immune functions, through their effects on synoviocytes and immune cells in the blood and joint.

[0206] Rheumatoid FLS exhibit a unique aggressive phenotype that contributes to the cytokine milieu and joint destruction. Functional studies suggest that RA cells are imprinted in situ and maintain these features after many passages in tissue culture. For example, RA FLS, unlike OA or normal synoviocytes, adhere to and invade cartilage explants in SCID mice. RA FLS can grow under anchorage-independent conditions, are less susceptible to contact inhibition, resistant to apoptosis. RA synoviocytes can potentially “metastasize” and transfer the invasive phenotype from one joint to another.

[0207] Several mechanisms have been implicated in this persistently aggressive phenotype, including abnormal sentrin or PTEN expression, preferential shunting of stressed cells to DNA repair rather than programmed cell death., and somatic mutations of regulatory genes. Microsatellite instability has also been identified in RA synovium, in part due to decreased DNA repair. These genetic modifications potentially serve to amplify disease severity.

[0208] While the focus on gene sequences in FLS and in disease association studies has provided important insights, other mechanisms can change cell phenotype. Epigenetics, for instance, can profoundly influence cell activation and gene expression through a variety of mechanisms, including DNA methylation, histone modification, and microRNA production. DNA methylation could be especially relevant in RA, in light of role in neoplasia and embryonic growth. Normal ontogeny relies on a carefully orchestrated sequence of DNA methylation to repress regulatory genes by methylating cytosine in CpG loci, either in promoters or in genes themselves. Methylation abnormalities have been associated with many diseases, most notably cancer where renewed expression or inappropriate suppression of genes allows cells to escape normal homeostatic controls. Hypomethylation and hypermethylation are associated with many malignancies and can contribute to transformation.

[0209] DNA methyltransferases (DNMTs) are responsible for initiating and maintaining CpG methylation in the human genome by converting cytosine to methylcytosine. In mammalian cells, DNMT1, DNMT3a, and DNMT3b are the primary enzymes responsible for CpG methylation. DNMT3a and DNMT3b mainly regulate de novo methylation while DNMT1 maintains methylation, especially during cell division. DNMT expression and DNA methylation are not immutable but are influenced by the environment and modify gene expression throughout life and even in progeny. For instance, pregnant mice fed a diet rich in methyl donors give birth to pups with increased levels of DNA methylation and increased airway reactivity in murine asthma for at least two subsequent generations.

[0210] Global hypomethylation has been described in peripheral blood mononuclear cells of patients with RA, although the specific genes involved are not known. Modest global hypomethylation was also reported in cultured RA FLS when compared to OA cells. In contrast, our studies showed that global methylation levels are similar in OA and RA FLS using two different techniques (ELISA-based and chip based). Thus, RA FLS do not appear to be hypomethylated overall, but like neoplasia, display a pattern of hypermethylated and hypomethylated genes.

[0211] The ILLUMINA chip analysis identified distinct methylation profiles of OA and RA FLS involving 1859 loci located in 1206 genes. Cluster analysis showed that the two

types of FLS could be easily distinguished based solely on the methylation patterns. The results were confirmed using a variety of additional analyses that reduced the possibility of random chance as an explanation. Additional analysis identified 207 genes with multiple hyper- or hypomethylated loci. Many of these genes play a key role in inflammation, matrix regulation, leukocyte recruitment and immune responses. Gene expression levels correlated with methylation status, with high expression in hypomethylated genes in RA FLS and normal expression in genes that were not differentially methylated. Given the number of influences that can potentially alter gene expression *in vitro*, the general concordance between methylation and mRNA levels was striking.

[0212] The data described herein provide evidence that epigenetic changes are present in RA synoviocytes and that they persist in culture. Imprinting could potentially occur before clinical disease and contribute to susceptibility. Alternatively, and perhaps more likely, the changes can be induced after initiation of synovitis. In the latter situation, the inflammatory milieu could potentially imprint synoviocytes and affect their function for many passages. Thus, local inflammation could potentially alter expression of enzymes responsible for initiating and maintaining DNA methylation. This process imprints synoviocytes, peripheral blood cells that are present in synovium for a short period of time, and immune cells, alters their behaviour, and ultimately changes the natural history of disease.

[0213] The ability to distinguish RA and control cells based solely on the DNA methylome could provide major insights into how the epigenetic profile of various tissues contribute to the pathogenesis of RA. In addition to identifying novel targets among the differentially methylated genes, it could also lead to interesting diagnostic or personalized medicine applications after sufficient data are available to correlate the methylome to phenotype.

Example 2—Methylation of loci in peripheral blood cells

Isolation of genomic DNA from peripheral blood cells

[0214] Approximately 6-8 ml of blood was drawn into a DB CPT tube (BD cat# 362760) and inverted 10 times. Four tubes per patient were drawn. The tubes were stored at room temperature until processed. Processing was performed in less than four hours after being drawn. The tubes were spun 30 minutes at 3000 rpm. The mononuclear cell layer was carefully removed and washed in at least 10 volumes of cold PBS with 0.1% BSA (Buffer 1: PBS Invitrogen cat# 14190, BSA Gemini cat# 700-100P). Mononuclear cells were then spun at 1600 rpm for 10 minutes. Cells were then resuspended in 3 ml of cold PBS supplemented with 0.1% BSA and 2 mM EDTA (Buffer 2: Buffer 1 plus EDTA Invitrogen cat# 15575020). Cells were

then counted and divided into 2 ml eppendorf tubes as follows: 0.5 ml for T-cell isolation, 1.5 ml for B-cell isolation, 0.75 ml for monocyte isolation, and 0.25 ml for whole PBMCs. These were spun again at 1600 rpm for 10 minutes and supernatants were discarded. The whole PBMC fraction was frozen while the others continued the specific cell type separation.

Separation of PBMCs into specific cell types

[0215] Cells in the PBMC preparation above were separated into B cell preparations, T cell preparations and monocyte preparations as follows. Dynabeads magnetic beads (CD19 pan B Invitrogen cat# 111-43D, CD2 pan T Invitrogen cat# 111-59D, CD14 monocyte Invitrogen cat# 111-49D) were used for the specific cell-type isolation. The magnetic bead mixtures were added to 1 ml of cold Buffer 2 according to the number of cells (50 μ l T-cell bead isolation mixture per 10^7 cells, 25 μ l B-cell bead isolation mixture per 2.5×10^7 cells, and 25 μ l monocyte isolation bead mixture per 10^7 cells), mixed well and applied to the magnet for 3 minutes to wash the beads. Supernatants were discarded. Mononuclear cell pellets were then gently resuspended in 1.5 ml of cold buffer 2 and added to their appropriate bead isolation mixture. The bead/cell mixture was incubated at 4°C while turning end-over-end for 20 minutes. The bead/cell mixture was then applied to the magnet for 3 minutes and supernatants were discarded. The bead/cell mixture was then washed 3 times by removing from the magnet, adding 1 ml cold Buffer 2, gently mixing, reapplying to the magnet, and discarding the supernatant. The cell/bead mixture was then frozen until DNA Isolation was performed. The DNA isolation was performed with DNeasy Blood and tissue Kit (Qiagen cat# 69504). The protocol for cultured cells was followed and included the recommendation of RNase A (Qiagen cat# 19101) treatment. DNA eluents were then concentrated using Amicon ultra 30K filers (Millipore cat# UFC503096). Concentrated DNA was then quantified using Quant-it Picogreen reagent (Invitrogen cat# P7589). Concentrations were then standardized to 100 ng/ μ l.

[0216] PBMC preparations may also be separated into other cell types, such as white blood cells, neutrophils, eosinophils, basophils, lymphocytes, plasma cells, natural killer cells, and dendritic cells using procedures such as those described above or other methods familiar to those skilled in the art. Macrophages may be separated from other cell types using methods well known in the art. In some embodiments, particular cell types can be enriched and/or isolated using a variety of methods, such methods are well known in the art and include immunological methods, fluorescent activated cell sorting (FACS) methods, and affinity chromatography methods. For example, cells such as eosinophils can be enriched/isolated using antibodies specific to specific receptors on the cell surface such as L-selectin, and VLA-4 (Sriramarao P., et al., (1994) J. Immunol. 153:4238-46, incorporated by reference in its entirety) Neutrophils may be

isolated using density gradients or using antibodies specific to other cell surface receptors (Firestein G.S., et al., (1995) J. Immunol. 154:326-34, incorporated by reference in its entirety).

Analysis of methylation states of loci in PBMCs or specific cell types separated from PBMC preparations in individuals with RA or OA

[0217] Samples of genomic DNA are obtained from peripheral blood mononuclear cells or specific cell types separated from PBMC preparations as described above. The samples are obtained from individuals with RA, individuals with OA, individuals with a known prognosis for rheumatoid arthritis or osteoarthritis, individuals with a known response to treatment for rheumatoid arthritis or osteoarthritis and control subjects without rheumatoid arthritis, without osteoarthritis, without the known prognosis for rheumatoid arthritis or osteoarthritis, or without the known response to treatment for rheumatoid arthritis or osteoarthritis using methods described herein. The methylation states of loci for each set of genomic DNA is determined as described herein for genomic DNA from FLS cells.

[0218] Hypomethylated and hypermethylated loci in individuals with RA, individuals with OA, individuals with a known prognosis for rheumatoid arthritis or osteoarthritis, individuals with a known response to treatment for rheumatoid arthritis or osteoarthritis are identified by comparing the methylation states of the loci to the methylation states of the loci in control subjects without rheumatoid arthritis, without osteoarthritis, without the known prognosis for rheumatoid arthritis or osteoarthritis, or without the known response to treatment for rheumatoid arthritis or osteoarthritis respectively using the methods described herein for FLS cells.

[0219] In some embodiments, hypomethylated and hypermethylated loci in RA genomic DNA relative to the methylation state of loci in OA genomic DNA are identified. In other embodiments hypomethylated and hypermethylated loci in RA genomic DNA relative to the methylation state of loci in genomic DNA from control subjects without RA are identified. In some embodiments, hypomethylated and hypermethylated loci in OA genomic DNA relative to the methylation state of loci in genomic DNA are identified from control subjects without OA are identified.

[0220] Genes with multiple differentially methylated loci are analyzed as described herein for genomic DNA from FLS cells, Gene expression and methylation status are analyzed as described herein for genomic DNA from FLS cells, Pathway analyses and gene ontology analyses are performed as described herein for genomic DNA from FLS cells. Network and DNMT analyses as described herein for genomic DNA from FLS cells.

Example 3—Evaluation of a subject for RA, OA, individuals with RA, a particular prognosis for rheumatoid arthritis or osteoarthritis, or a particular response to treatment for rheumatoid arthritis or osteoarthritis

[0221] Genomic DNA is obtained from a subject and the methylation states of one or more loci having differential methylation in individuals with individuals with RA, individuals with OA, individuals with a particular prognosis for rheumatoid arthritis or osteoarthritis, or individuals with a particular response to treatment for rheumatoid arthritis or osteoarthritis is determined.

[0222] In some embodiments, the methylation state of the one or more differentially methylated loci in the genomic DNA from the subject is compared with the methylation state of the one or more differentially methylated loci in normal tissue, tissue from a subject with a known prognosis, or tissue from a subject with a known response to treatment. In other embodiments, the methylation state of the one or more differentially methylated loci in the genomic DNA from the subject is compared with a methylation state of the one or more differentially methylated loci known to be indicative of RA or a lack thereof, OA or a lack thereof, a particular prognosis for rheumatoid arthritis or osteoarthritis or a lack thereof, or a particular response to treatment for rheumatoid arthritis or osteoarthritis or a lack thereof.

[0223] The genomic DNA may be obtained from any desired cell type, including the cell types listed herein. For example, the genomic DNA may be obtained from FLS cells, a peripheral blood sample or a specific cell type separated from a PBMC sample obtained from a subject. If the methylation state of the one or more differentially methylated loci is a methylation state known to be indicative of RA, a particular prognosis for rheumatoid arthritis or osteoarthritis, or a particular response to treatment for rheumatoid arthritis or osteoarthritis the subject is determined to have RA, the particular prognosis for rheumatoid arthritis or osteoarthritis, or the particular response to treatment for rheumatoid arthritis or osteoarthritis. A treatment regimen consistent with this determination may then be administered..

Example 4—Evaluation of a methylation state of loci in control subjects compared to methylation state of loci in RA FLS and OA FLS

[0224] Genomic DNA is obtained from a subject without RA and a subject without OA and the methylation states of one or more loci having differential methylation in RA FLS and OA FLS cells, respectively, is determined.

[0225] In some embodiments, the methylation state of the one or more differentially methylated loci in RA FLS and OA FLS cells is compared to a methylation state of the one or

more differentially methylated loci in the genomic DNA from a subject without RA and in the genomic DNA from a subject without OA, respectively. In some embodiments, the methylation state of loci indicative of the absence of RA or OA in a subject are determined.

[0226] The genomic DNA may be obtained from any desired cell type, including the cell types listed herein. For example, the genomic DNA may be obtained from FLS cells, a peripheral blood sample or a specific cell type separated from a PBMC sample obtained from a subject. If the methylation state of the one or more differentially methylated loci is a methylation state known to be indicative of RA, a particular prognosis for rheumatoid arthritis or osteoarthritis, or a particular response to treatment for rheumatoid arthritis or osteoarthritis the subject is determined to have RA, the particular prognosis for rheumatoid arthritis or osteoarthritis, or the particular response to treatment for rheumatoid arthritis or osteoarthritis. A treatment regimen consistent with this determination may then be administered.

Example 5—Evaluation of methylation state of loci in peripheral blood mononuclear cells (PBMCs)

[0227] The methylation states of loci in PBMCs were determined with methods substantially similar to those described herein using the ILLUMINA HumanMethylation 450 BeadChip. Differentially methylated loci (DML) were identified with average methylation differences between OA and RA of >0.10 . RA/OA differential methylation was conducted using a t-test. P-values were converted to q-values to account for multiple hypothesis testing, and DML with q-values <0.25 were considered to be potential PBMC biomarkers. TABLE 8 lists about 2544 RA/OA PBMC DML with associated data including the OA-RA average methylation difference, CG identifier associated with the Illumina 450K beadchip (Locus), associated genes, and the genomic location of the potentially methylated C of the CpG (+ strand) determined using the UCSC hg19 reference genome. The CpG* column of Table 8 lists values for “chromosome : chromosome co-ordinate.”

TABLE 6

OA - RA	Locus	Associated gene	SEQ ID No.
0.39071	cg20114732	T	361932
0.37096	cg03044684	HUNK	62005
0.36569	cg20824939		372791
0.36469	cg19081101	CHI3L1	345293
0.36368	cg13225830		243918
0.36153	cg27244773	ARHGAP27;ARHGAP27;ARHGAP27	475250
0.34388	cg02792136	DIP2C	56847
0.33702	cg12557114	WISP3;WISP3	233566
0.33333	cg06043820	ZNF592	119061
0.33296	cg07804470	STK24	151872
0.33037	cg12578486	UBAC2;UBAC2;UBAC2	233879
0.32914	cg18886274		342488
0.32889	cg12651286	MMP20	235219
0.32591	cg10035831	RPTOR;RPTOR	191245
0.32183	cg12476044	EGFLAM;EGFLAM;EGFLAM;EGFLAM	232241
0.32154	cg16214653		298250
0.32018	cg06550177		127813
0.31828	cg06357305	PTGIS	124318

OA - RA	Locus	Associated gene	SEQ ID No.
0.31549	cg27250435		475334
0.31524	cg24203758	SH3D20	425444
0.31391	cg18675043	SH3PXD2A	338965
0.30767	cg11173579	HUNK	210693
0.30665	cg21514164		383094
0.30602	cg21670717		385687
0.30248	cg09182085		176526
0.30113	cg09230154	MACF1;MACF1	177251
0.30097	cg27642470	DCBLD1	482028
0.2993	cg23413809	SIX2	412582
0.29885	cg07474842	MAP3K5	1415804
0.29665	cg23004031	MGMT	405673
0.29622	cg02727484	KCNMA1;KCNMA1;KCNMA1;KCNMA1	55565
0.29494	cg07227049	VRK2;VRK2;VRK2;VRK2;VRK2;VRK2	141396
0.28978	cg06223539	SHANK2	122219
0.28958	cg19674091	IDH2	354510
0.28897	cg06966660	TACC2;TACC2;TACC2;TA CC2	136119
0.28527	cg22778178		401834
0.28511	cg12427162	SFT2D2	231416

OA - RA	Locus	Associated gene	SEQ ID No.
0.28455	cg16854917	NCRNA00085	309652
0.28177	cg03834767	CDK14	77306
0.28129	cg17820022	PLCH2	324801
0.27987	cg05040219	GLIS1	100492
0.27931	cg00807684	RBMS3;RBMS3;RBMS3	17055
0.27912	cg10536999	NFE2L3	200194
0.27826	cg22458832		396980
0.2773	cg09257635	GJC2	177820
0.27706	cg24576026	SEPT9;SEPT9	431206
0.27474	cg01999051	BRP44L	40997
0.27386	cg10820084	COL1A1	204937
0.27361	cg07696516	LIMCH1;LIMCH1;LIMCH1;L IMCH1;LIMCH1;LIMCH1;LI MCH1	149907
0.27349	cg10937408	HNRNP3	206779
0.2732	cg07021447	ACTN1;ACTN1;ACTN1	137188
0.27261	cg13644549	C7orf50;C7orf50;C7orf50	252081
0.27247	cg26787787		467264
0.27222	cg10881749		205937
0.27192	cg24718015	STAT3;STAT3;STAT3	433677
0.27022	cg03780701	ADAM32	76382

OA - RA	Locus	Associated gene	SEQ ID No.
0.26961	cg13735018	SYNJ2	254007
0.26932	cg19391924	HRNBP3	349887
0.26888	cg13551141	PSMB7	250097
0.2674	cg14370520	FAM188B	267054
0.26591	cg01660999	ANGPT1	34240
0.26415	cg13626830	RASGRF2	251743
0.26352	cg20441502	FXVD7;FXVD1;FXVD1	366782
0.26348	cg01833196	SH3PXD2A	37634
0.26334	cg00369056		7795
0.26334	cg13683667		252916
0.26327	cg19576241		352883
0.26302	cg21983607		390212
0.26214	cg03666350		74131
0.26137	cg05166871	SKAP1;SKAP1	102879
0.2612	cg15366684	ADAMTS2;ADAMTS2	284322
0.26116	cg25885684		451999
0.26059	cg17290488	C5orf45;C5orf45	316572
0.25763	cg19954341	T	359498
0.25735	cg20668662	SH3PXD2A	370194
0.25696	cg24657523	MYEF2	432522

OA - RA	Locus	Associated gene	SEQ ID No.
0.24859	cg23489226		413717
0.24854	cg15745401	P2RY6;P2RY6	290636
0.24785	cg24752267		434286
0.24696	cg09527270	POMC;POMC	182597
0.24687	cg00145961	NTRK3;NTRK3;NTRK3	3269
0.24685	cg15323840	SYNJ2	283724
0.24679	cg11261412	B3GNTL1	212263
0.24671	cg04723534	C2CD2	94311
0.2467	cg03771840	TRIM15	76209
0.24643	cg03472954	PRKAR1B;PRKAR1B;PRKAR1B;PRKAR1B;PRKAR1B	70250
0.24643	cg235333513	MYO7A;MYO7A;MYO7A	414506
0.24628	cg19010441	MED12L;GPR171	344302
0.24604	cg06186245	TMEM45A	121509
0.24529	cg23834919		419111
0.24525	cg00037856		943
0.24513	cg27338607		476928
0.24455	cg05287372	C3orf64	105151
0.24329	cg14905634	TRHDE	277082
0.24298	cg11692307	PLCH2	219166

OA - RA	Locus	Associated gene	SEQ ID No.
0.25675	cg03537386	COL16A1	71519
0.25598	cg25616600		448034
0.25566	cg20201270		363196
0.25559	cg01229787		25802
0.25515	cg08145723	ST14	158133
0.25468	cg07878514	INSM1;INSM1	153203
0.25399	cg06189394	LRIG1	121568
0.25382	cg08830502		170348
0.25298	cg05979619	MERTK	117911
0.25278	cg16402635	CASP1;CARD16;CASP1;CASP1;CASP1;CASP1;CAR D16	301579
0.25223	cg17007374		311924
0.25189	cg26681770	PMEPA1;PMEPA1;PMEPA1;PMEPA1	465572
0.25166	cg04649852		92984
0.25103	cg16282024	DERL1;DERL1	299433
0.25043	cg01392518	T	28927
0.24945	cg05590156	TRIO	110699
0.24922	cg24174557	TMEM49	425007
0.24886	cg00225902	LRIG1	4852
0.24875	cg03401875	ADAMTS2;ADAMTS2	68835

OA - RA	Locus	Associated gene	SEQ ID No.
0.23548	cg08718098		168443
0.23462	cg17896243		326150
0.23435	cg09385667	PDZRN3	180096
0.2343	cg09529093	ANGPT1	182630
0.23254	cg10960920	PGCP	207207
0.23124	cg07107756	CARD14;CARD14	138866
0.23111	cg07480647	GPR153	145935
0.23044	cg11218619		211494
0.23008	cg05721365	LOC146880;LOC146880	113082
0.22965	cg21531685	PDZRN3	383375
0.22946	cg12854371	LOC146880;LOC146880	238254
0.22905	cg04028695		81035
0.22873	cg05665651	ANKRD11	112125
0.22861	cg09259235		177859
0.2273	cg15341866		283990
0.22729	cg03019360		61484
0.22691	cg19409546		350194
0.22689	cg26098164	BMP7	455309
0.22559	cg23965931	STOX2	421288
0.22486	cg27292547		475989

OA - RA	Locus	Associated gene	SEQ ID No.
0.24275	cg04677410	MAML2	93491
0.24251	cg16561266	LOC146880;LOC146880	304457
0.24244	cg09461792		181455
0.24119	cg00548708		11644
0.24101	cg11120154		209834
0.24078	cg14587335	HRNBP3	271586
0.23936	cg09650180	GMEB2	184694
0.23799	cg09379935	P2RY6;P2RY6	180013
0.23797	cg21680719	FHL3	385790
0.23791	cg24917131		437034
0.23723	cg12097883	LOC146880;LOC146880	226317
0.23698	cg03558269		71975
0.2367	cg08870914		171157
0.23667	cg14501219	LOC146880;LOC146880	269672
0.2365	cg09180564	OLFM3	176500
0.23608	cg02477603		50448
0.23603	cg14260695		264921
0.23574	cg08613122	PRKAR1B;PRKAR1B;PRKAR1B;PRKAR1B;PRKAR1B	166544
0.23559	cg25577130	CA4	447341

OA - RA	Locus	Associated gene	SEQ ID No.
0.21765	cg26303870	ACTN1;ACTN1;ACTN1	458957
0.21683	cg01095004		23112
0.21596	cg13369952	JAKMIP2	246290
0.21555	cg26159368		456463
0.21526	cg10328583	PLEKHG5;PLEKHG5;PLEK HG5;PLEKHG5	196553
0.21524	cg22041190	PKNOX2	391040
0.21505	cg13717446	LOC146880;LOC146880	253646
0.215	cg20134287	AUTS2;AUTS2	362245
0.21488	cg16755214		308115
0.21465	cg00599219	MEFV	12810
0.21458	cg13470462	BOC	248426
0.21391	cg13027183	JARID2	240842
0.21382	cg14467181		268995
0.21371	cg04674201		93425
0.2137	cg16936561	RAB11FIP5	310943
0.21339	cg13393580	MXRA8	246755
0.21294	cg00813162	ACTN1;ACTN1;ACTN1	17174
0.21281	cg21687563	TTC28	385895
0.21199	cg07076816		138253
0.21196	cg10195336	ARHGEF10	194213

OA - RA	Locus	Associated gene	SEQ ID No.
0.22459	cg10094238	ARHGAP27;ARHGAP27;AR HGAP27	192273
0.22433	cg26938118	NEDD4L;NEDD4L;NEDD4L; NEDD4L;NEDD4L;NEDD4L; NEDD4L;NEDD4L;NEDD4L	470085
0.22395	cg12741645	AEN	236560
0.22392	cg11189268	ARHGAP27;ARHGAP27	210952
0.22268	cg10481134	C2orf58	199061
0.22247	cg25213720	MXD3;MXD3	441707
0.22232	cg07357716		143726
0.22207	cg10975897	JARID2	207446
0.22204	cg10177197	DHCR24	193879
0.22183	cg26215428	PKD2	457374
0.2215	cg01451808		30240
0.22132	cg24186459		425188
0.2211	cg14910684		277182
0.21926	cg01040786		21929
0.21871	cg07146912	PDZRN3	139702
0.21843	cg01359469	TRIP4	28275
0.2181	cg07459478	VOPP1	145466
0.21793	cg06012804		118540
0.21771	cg25335841		443510

OA - RA	Locus	Associated gene	SEQ ID No.
0.2085	cg01322214	C7orf31	27599
0.20824	cg22972806	LYPD6B	405136
0.20805	cg12531838	DIP2C	233187
0.20773	cg06946797		135711
0.20742	cg11394820		214445
0.2069	cg06132400		120606
0.20684	cg13505393	LRRC32;LRRC32	249183
0.20661	cg02931762		59687
0.20651	cg23367392	GLI3	411874
0.20651	cg21699330	NFE2L3	386040
0.20618	cg09532095	THUMP2;THUMP2	182672
0.20597	cg029555287		60173
0.20575	cg07980854		155098
0.20548	cg21838924	CLDN4	388015
0.20493	cg09703910		185605
0.20481	cg03179435	FRMD4A	64565
0.20458	cg25946605	CYS1	452893
0.20455	cg12473775	RHOD	232200
0.20401	cg05467716	LOC146880	108495
0.20331	cg18476176	CNTF;ZFP91-CNTF	335848

OA - RA	Locus	Associated gene	SEQ ID No.
0.21167	cg26588688		463998
0.21129	cg14524975	ITGB7	270223
0.21125	cg05373161	TMEM231;TMEM231;TME M231	106877
0.21109	cg10283505	FUT4;FUT4	195763
0.2109	cg27190145	DAAM2	474406
0.21048	cg23403980	SMG6;SMG6	412406
0.21047	cg10734665	ATP10A	203498
0.2102	cg01071185		22591
0.20996	cg13313047	CABLES1;CABLES1;CABL ES1	245295
0.20986	cg18325315	GTF2IRD1;GTF2IRD1	333329
0.2097	cg24478420		429606
0.20967	cg20489026	KCNJ9	367521
0.20958	cg09119854	AXIN2	175345
0.2095	cg02186748	COL1A1	44750
0.20938	cg08223717	EEPD1	159595
0.20902	cg17265829	FAT4	316130
0.20884	cg04158862	KIAA0247	83588
0.2087	cg01521220	MIR1203;SKAP1;SKAP1	31528
0.20851	cg20472384	DIP2C	367281

OA - RA	Locus	Associated gene	SEQ ID No.
0.19821	cg27638057	C18orf45	481936
0.19814	cg19764489	KCNQ1;KCNQ1	356206
0.19799	cg05501859	C11orf17;C11orf17	109151
0.19792	cg02108623	PRDM1	43306
0.19791	cg18229049	NXN	331759
0.1975	cg15557036		287330
0.19749	cg03284879		66524
0.19681	cg23899450		420132
0.19665	cg16896313		310257
0.19654	cg11738198		219981
0.19638	cg25104234		439983
0.19612	cg08863777	FUT4	171018
0.19591	cg03143849	CDKN1C;CDKN1C;CDKN1C	63866
0.19551	cg27608563	CMIP	481430
0.19548	cg15601264		288057
0.19518	cg25712088	DIP2C	449437
0.19493	cg14003265	TRAF2	259423
0.19481	cg16926213		310774
0.19467	cg15339026		283944
0.19466	cg16429975	ACOT7;ACOT7	302121

OA - RA	Locus	Associated gene	SEQ ID No.
0.20322	cg18362448	SSBP4;SSBP4	333911
0.20314	cg19245980		347655
0.20291	cg27342781		476987
0.20279	cg08011255	B3GNTL1	155601
0.2027	cg25252585	FXRD7	442281
0.20218	cg08170227	ACTN1;ACTN1;ACTN1	158605
0.20196	cg01700462	C20orf123	34874
0.20185	cg08920174		172096
0.20181	cg06180729	LDLRAD3	121411
0.20165	cg03144232	STX1B	63872
0.20053	cg05302100	COL1A1	105438
0.20037	cg01572653		32559
0.20024	cg00509485		10852
0.20012	cg02077068	GPRC5B	42649
0.19965	cg08797704		169751
0.19946	cg25674613		448920
0.19907	cg14236519	C7orf50;C7orf50;C7orf50	264409
0.19873	cg09371059		179858
0.19866	cg07250758	VWCE	141804
0.19825	cg14463068	MYT1L	268912

OA - RA	Locus	Associated gene	SEQ ID No.
0.19047	cg03179447		64567
0.18988	cg15457718		285805
0.18981	cg27169559		474039
0.1897	cg00660305	PRKAR1B;PRKAR1B;PRKAR1B; R1B;PRKAR1B;PRKAR1B; PRKAR1B	13970
0.1891	cg20142501	NXN	362369
0.18892	cg15298286	C17orf72	283380
0.18871	cg25954269		453043
0.18845	cg25418528	P2RX6;P2RX6	444919
0.18829	cg27132535		473446
0.18828	cg15449664	THY1	285660
0.18804	cg09109656		175197
0.18788	cg04070601	FMNL3;FMNL3	81748
0.18776	cg20882260	CACNA1C;	373464
0.18756	cg18267489	CD93	332434
0.1875	cg20463302	SH3D20	367133
0.18746	cg22020227	OLFML3	390677
0.18628	cg11419575		214920
0.18581	cg23369564	PLEKHO1	411901
0.18537	cg04768998	WIPF1;WIPF1	95158

OA - RA	Locus	Associated gene	SEQ ID No.
0.19451	cg19780308	MAML3	356489
0.19435	cg01741688	SH3RF3	35665
0.19412	cg15465501		285947
0.19412	cg08639948		167048
0.19403	cg12453623		231887
0.19394	cg19093370	PLD6	345512
0.19388	cg10331829	SLC1A2	196611
0.19382	cg01806382		37024
0.1935	cg20953052	MIR548F2;ERBB4;ERBB4	374498
0.19341	cg20917077	CPA5;CPA5;CPA5	373937
0.19321	cg16434331	SLC39A11;SLC39A11	302207
0.19286	cg06581409		128362
0.1925	cg13229078		243978
0.19228	cg07044938		137615
0.19221	cg22853713	CASZ1;CASZ1	403146
0.19142	cg23878906		419768
0.19138	cg10469520		198872
0.19133	cg24229188	HMG20B	425784
0.19107	cg27185501		474347
0.19077	cg03556869	UST	71956

OA - RA	Locus	Associated gene	SEQ ID No.
0.18147	cg14054883	SYK;SYK;SYK;SYK	260571
0.1814	cg05147262	ENAM	102478
0.1812	cg21242079	ADAMTS7	379397
0.18059	cg26523175	PDZK1IP1	462775
0.18031	cg04778236	SPSB1	95348
0.18026	cg01820962	NT5DC1	37371
0.18025	cg12315995		229820
0.17993	cg17250262	LBH	315917
0.17965	cg14227785		264238
0.17877	cg10882304	TACC2;TACC2;TACC2;TA CC2	205944
0.17828	cg07047570	INSM1;INSM1	137657
0.17808	cg07286123	CD93	142424
0.17794	cg14089493		261291
0.17787	cg07997634	SLC25A13;SLC25A13;SLC 25A13	155378
0.1776	cg18628732		338265
0.17747	cg12239557	TACC2;TACC2	228662
0.17737	cg06376402	INPP5A	124706
0.17726	cg09642857		184563
0.17704	cg17099048	COL22A1	313414

OA - RA	Locus	Associated gene	SEQ ID No.
0.18526	cg06605053		128746
0.18519	cg05008070	DACT1;DACT1	99885
0.18519	cg16030113		295289
0.18514	cg00472879	SORBS1;SORBS1;SORBS 1;SORBS1;SORBS1;SORB S1;SORBS1	10022
0.18466	cg14832378		275849
0.18464	cg27438889	TACC2;TACC2;TACC2;TA CC2	478571
0.18403	cg04098052		82284
0.184	cg26275647	MDFIC;MDFIC	458453
0.18384	cg05757757		113669
0.18333	cg01198994	MXRA8	25206
0.1833	cg16104139		296436
0.18322	cg09866374		188450
0.18317	cg17797591	AXIN2	324404
0.18247	cg00250409		5354
0.18239	cg09976669	SWAP70	190212
0.18236	cg22231400	SLC17A7	393823
0.18227	cg02351674		48045
0.18188	cg11676636	ARHGAP22	218912
0.18152	cg00831127	EPHB2;EPHB2	17525

OA - RA	Locus	Associated gene	SEQ ID No.
0.17206	cg14251267	ZBTB46	264704
0.1718	cg20052079	JARID2	360990
0.17144	cg19161251	LMO4	346462
0.17138	cg01364478	PRRX1;PRRX1	28365
0.17129	cg14255700	IPPK	264808
0.17113	cg07067577	SH3D20	138069
0.17078	cg27345989	NXN	477039
0.17062	cg21029769	ST14	375731
0.17054	cg26821721	KLHL29	467947
0.17025	cg13890428		257013
0.17003	cg15134506	USP54	280991
0.17002	cg21142398	GLIS1	377429
0.16954	cg08533336	USP2;USP2	165172
0.16947	cg18006637	FAM13A;FAM13A	327818
0.16924	cg23692500		417116
0.16901	cg01093786	MAML2	23085
0.169	cg00285394	SQLE	6012
0.16825	cg20673819	C6orf176;C6orf176	370286
0.16804	cg03676578		74324
0.168	cg21946195	ATOH8	389751

OA - RA	Locus	Associated gene	SEQ ID No.
0.17689	cg10819733		204928
0.17667	cg26477792		462022
0.17575	cg00373436	TAGLN3;TAGLN3;TAGLN3	7897
0.17567	cg15029402		279170
0.17558	cg19080233		345285
0.17527	cg00157016	PFN4	3525
0.17525	cg02278646	ANO6;ANO6;PLEKHA9;ANO6	46492
0.17489	cg14684457	NFE2L3	273413
0.17474	cg09125999	DSCAML1	175477
0.17462	cg04940251		98587
0.17444	cg07135032	LMX1A	139425
0.17437	cg03491895		70579
0.17348	cg07459019		145455
0.17324	cg03762242	GAS7;GAS7;GAS7	76010
0.17305	cg23585686		415170
0.17287	cg00400827		8476
0.17285	cg02284273	FRMD4A	46611
0.17232	cg03560973	POMC;POMC	72034
0.17213	cg22304543		394846
0.17212	cg24147392	LOC440461	424521

OA - RA	Locus	Associated gene	SEQ ID No.
0.16411	cg14103872	OLFML2A	261610
0.16404	cg19996406		360145
0.16364	cg16568084		304587
0.16364	cg13165983		242911
0.16332	cg00409696		8667
0.16319	cg11733958	MPRIP;MPRIP	219898
0.16308	cg08458711	BSND	163781
0.16261	cg18861112	WDFY2	342032
0.16254	cg21293455		380108
0.16247	cg06526620	FUT4	127302
0.16242	cg12303623	USP54	229638
0.16225	cg06501835		126864
0.16225	cg05243389	MYEF2	104339
0.1619	cg15372959	TACC2;TACC2;TACC2;TA CC2	284406
0.16187	cg08879365		171347
0.16183	cg00802386		16940
0.16175	cg16224163	LPP	298398
0.16119	cg02276070	ARSI	46431
0.16116	cg00702126	VWA1;VWA1	14846
0.1611	cg04674421		93433

OA - RA	Locus	Associated gene	SEQ ID No.
0.16791	cg10346364	LOC100130987;CLCF1;CL CF1	196856
0.16785	cg08935841		172361
0.16779	cg02216727	GJD3;GJD3	45257
0.16775	cg13088556		241806
0.16685	cg20860726	MYT1L	373230
0.16671	cg11927233	NPM1;NPM1;NPM1	223346
0.16655	cg17842189	TBC1D22A	325238
0.16649	cg23508201		414035
0.16631	cg18772205	KLHL6	340567
0.16625	cg18402987		334557
0.16616	cg10350880	EPHB4	196929
0.16606	cg03943115	SPRR2D	79303
0.16531	cg03967266		79784
0.16529	cg09099242	MMRN2	175043
0.16453	cg08302650	LRRC24;LRRC14	161144
0.1644	cg08049717	AMOTL2	156270
0.16429	cg03764092	TBXAS1;TBXAS1;TBXAS1; TBXAS1;TBXAS1;TBXAS1	76037
0.16421	cg07275179	ATXN7;ATXN7	142217
0.16413	cg05529123		109677

OA - RA	Locus	Associated gene	SEQ ID No.
0.15736	cg08005872		155513
0.1573	cg00094585		2207
0.15729	cg04944536		98671
0.15686	cg04658243	RPTOR;RPTOR	93139
0.15641	cg11454459		215415
0.15627	cg11084571	KANK4	209299
0.15582	cg26227310	TLX1NB	457602
0.15574	cg05541311		109868
0.15565	cg00095431		2233
0.15534	cg08548284		165445
0.15493	cg03919650	MEFV	78874
0.15488	cg05786009		114191
0.15461	cg04024827	FLJ12825	80948
0.15448	cg15653254		289035
0.1544	cg04649598	ODZ4	92979
0.15426	cg08615354		166583
0.15398	cg05909702		116481
0.15394	cg08785724		169563
0.15382	cg00990769	MATN2;MATN2	20836
0.15381	cg08734931	FRMD4A	168749

OA - RA	Locus	Associated gene	SEQ ID No.
0.16107	cg08333931	SH3D20	161705
0.16089	cg27177158		474183
0.16083	cg04948016		98755
0.1607	cg19144071		346231
0.1607	cg10628617	SCUBE1	201790
0.16063	cg19542987	ARMC3	352374
0.16049	cg27265404		475561
0.16007	cg03756522		75895
0.15976	cg19856845	RIN3	357783
0.15961	cg09492169	ARHGAP27;ARHGAP27	181962
0.15953	cg27458177		478888
0.1592	cg03303857	GRIK4	66884
0.15887	cg11845549		221989
0.15871	cg15246712	EBF2	282686
0.15867	cg08009487	KRT4;KRT4	155576
0.15857	cg21429516		381785
0.15832	cg13552867	KCNJ9	250134
0.15799	cg22044408		391096
0.1579	cg13440947	GFRA1;GFRA1	247730
0.15763	cg14363469		266959

OA - RA	Locus	Associated gene	SEQ ID No.
0.1482	cg24537942	KANK4	430673
0.14803	cg22958076		404890
0.14799	cg02079741	POMC;POMC	42708
0.14778	cg12055422		225496
0.14773	cg13947999		258288
0.1477	cg13121428	TGFB3	242270
0.14752	cg25651608		448592
0.14738	cg03573945	EBF2	72279
0.14713	cg07922154	ARG2	154039
0.14713	cg06516502		127100
0.14685	cg26719062		466225
0.14673	cg00020474		497
0.14661	cg07015554		137042
0.1466	cg02095937	TRIM59	43034
0.14648	cg22111167	PTPRJ;PTPRJ	392026
0.14639	cg16892553	PRR15L;PRR15L	310202
0.14634	cg00512602	SH3D20	10920
0.14595	cg27359636		477238
0.14577	cg23325335		411144
0.14539	cg15671996	TRIM15	289301

OA - RA	Locus	Associated gene	SEQ ID No.
0.15277	cg05277096	PDZRN3	104972
0.15274	cg25169706	ST5;ST5;ST5	A441040
0.15273	cg24572745	BOC	431168
0.15262	cg21176130	HLA-E	378075
0.15251	cg00514353	PCDH1	10956
0.15225	cg25515269	ITGA4	446437
0.15211	cg25653204	FPR2	448621
0.15196	cg25349820		443748
0.15173	cg11401293	COL6A1	214569
0.15074	cg14036069	NEK6;NEK6;NEK6	260162
0.15059	cg14110685		261719
0.15038	cg11673092	ARMC3	218848
0.15033	cg24098326	TACC2;TACC2;TACC2;TA CC2	423638
0.15015	cg17783086	LOC146880;LOC146880	324191
0.14948	cg17332379	LOC146880;LOC146880	317320
0.14904	cg266697605		465886
0.1489	cg16637224		305900
0.14883	cg19793499	AUTS2;AUTS2	356717
0.14862	cg13698865	COL5A1	253254
0.14823	cg14955976		277886

OA - RA	Locus	Associated gene	SEQ ID No.
0.14257	cg26950531	DPF1;DPF1;DPF1	470304
0.14252	cg23270841	PARD3B;PARD3B;PARD3B	410288
0.1418	cg00542975	CLASP1;CLASP1;CLASP1	11524
0.14168	cg06644998		129612
0.14118	cg04567302	SLC44A4	91475
0.14106	cg26002568		453787
0.14087	cg04289208	LGR6;LGR6	86168
0.14072	cg13085980	PLXNC1	241773
0.14055	cg18124852		329967
0.14042	cg13214162		243716
0.14037	cg07103748		138784
0.14016	cg04756252	SLA;SLA;TG;SLA	94952
0.13944	cg17253459	OLFML3	315956
0.1392	cg04601228	AUTS2;AUTS2	92149
0.13894	cg10005270	C10orf90	190712
0.13871	cg13948956		258313
0.1387	cg01211852		25460
0.13832	cg01654566		34124
0.13826	cg09528501		182620
0.13793	cg21688152	B3GNTL1	385901

OA - RA	Locus	Associated gene	SEQ ID No.
0.14536	cg14725580	C6orf106;C6orf106	274100
0.14511	cg13724550	FGF1;FGF1;FGF1;FGF1;F GF1;FGF1;FGF1	253793
0.14497	cg19399514	RFTN1	349989
0.14495	cg11790417		220854
0.14482	cg15152115		281271
0.1445	cg11474182	CNTNAP3	215691
0.14435	cg05123976		101999
0.1441	cg03009240	FZR1	61309
0.14404	cg09359810	FRMD6	179634
0.14388	cg23931919		420690
0.14388	cg10321236	MYO7A;MYO7A;MYO7A	196418
0.1436	cg11222217	CASZ1;CASZ1	211555
0.14337	cg21487363	FOXP1;FOXP1	382660
0.14296	cg23522194	PLA2G4C;PLA2G4C;PLA2 G4C	414285
0.14295	cg26871180		468843
0.14284	cg16139517	CNTN4	297000
0.14275	cg15371815	CRIM1	284394
0.14258	cg24118856	PPAN-P2RY11;P2RY11	423968
0.14258	cg15400997	PLXNC1	284893

OA - RA	Locus	Associated gene	SEQ ID No.
0.13472	cg25599473	SMOC2;SMOC2	447739
0.13467	cg23200466 ₁	FBXW11;FBXW11;FBXW1 ₁	408900
0.13452	cg09868780	LVRN	188458
0.13444	cg05246303	ITGA4	104393
0.13439	cg03213259	TRADD	65187
0.13426	cg07067982	SLC43A3;SLC43A3;SLC43A3;SLC43A3	138080
0.13383	cg24960118	PKHD1;PKHD1	437734
0.13373	cg06942124		135615
0.13373	cg06443678		125849
0.13342	cg18674487		338954
0.13337	cg11268280		212378
0.13318	cg08681473	COL1A1	167753
0.13306	cg03143046		63849
0.13304	cg06842253		133582
0.13286	cg26363935	NWD1	460109
0.13282	cg24250588	CLDN19;CLDN19	426051
0.13272	cg01579600		32722
0.13255	cg20567368		368674
0.13204	cg20054157	SFTA1P	361020

OA - RA	Locus	Associated gene	SEQ ID No.
0.13778	cg25472296	DOCK1	445774
0.13777	cg21951457	TACC2;TACC2;TACC2;TA CC2	389827
0.13769	cg08102611	GAS7	157232
0.13766	cg13008631	IRS1	240565
0.13745	cg20535425		368163
0.13721	cg04689880		93734
0.13713	cg04768479		95139
0.13705	cg20438277	CD93	366734
0.13663	cg10301879	C6orf105;C6orf105	196052
0.13653	cg19582200	SCUBE1	352974
0.13647	cg25967170		453238
0.13638	cg06620993	SH3PXD2A	129075
0.13588	cg12812165	NIN;NIN;NIN	237654
0.13581	cg13053992		241251
0.13547	cg14598213	NGFR	271799
0.13528	cg19193956		346894
0.13503	cg06021990	FLT1	118695
0.13498	cg01715025	RNF115	35160
0.13498	cg05787209	STX1B	114223
0.13486	cg14206273	CASZ1;CASZ1	263709

OA - RA	Locus	Associated gene	SEQ ID No.
0.12794	cg05376469		106960
0.1279	cg10331500	TGFA;TGFA	196606
0.12762	cg06983052	LRRC8D;LRRC8D	136433
0.12762	cg12019475		224847
0.12739	cg16900264		310326
0.12733	cg01055696		22251
0.12706	cg00652846	BOC	13828
0.12699	cg17265419	ITGA4	316124
0.12692	cg07570498	PHC2;PHC2	147621
0.12659	cg17504145	CRYBB2	320177
0.12646	cg00872354		18374
0.12628	cg08504407	HRNBP3	164658
0.12625	cg19072083		345194
0.12581	cg22660447	C16orf7	399970
0.12507	cg18169095	LAD1	330752
0.12494	cg24167667		424904
0.12488	cg02281167	TRIM15	46550
0.12477	cg18771659	SPRR1B	340554
0.12456	cg13197521	SPSB1	243430
0.12441	cg23733123	MARVELD1;MARVELD1	417794

OA - RA	Locus	Associated gene	SEQ ID No.
0.13169	cg16052198	FPR2	295658
0.13115	cg12888521		238770
0.13102	cg21322248	PSTPIP1	380448
0.13082	cg23418965	PKNX2	412666
0.13073	cg10193441	HRNBP3	194174
0.13072	cg25566312	TGFB1	447171
0.13053	cg00334821	LIMK1	7073
0.13046	cg18132405	LEPREL1;LEPREL1	330109
0.13036	cg13893782	PDE7B	257077
0.13034	cg12575928	GAS2	233842
0.13018	cg03669949	DDX43;DDX43	74206
0.13012	cg19528338	BMP2	352128
0.13001	cg15878619	TUBB	292734
0.1298	cg07187808	KCNJ9	140601
0.1297	cg06641357		129537
0.12946	cg06618298	MYO10	129012
0.12929	cg04332927		87001
0.12922	cg11041060	SMOC2;SMOC2	208580
0.12875	cg19264571	APCDD1	347991
0.12861	cg00832547	RAGE	17556

OA - RA	Locus	Associated gene	SEQ ID No.
0.12439	cg19681793	THBS2	354639
0.12435	cg22373687		395848
0.12435	cg01838728		37759
0.12422	cg03083517	COL22A1	62783
0.12417	cg01149239	MF12;MF12	24207
0.12417	cg05593669		110779
0.12379	cg00348891		7377
0.12362	cg19125999	C1orf172	345998
0.12359	cg26221801	C20orf195	457494
0.12334	cg01325188	BANP;BANP	27654
0.12301	cg08066024	NRXN1;NRXN1	156540
0.12289	cg04344730	DAB1	87247
0.12282	cg03467555		70136
0.12254	cg22124564	AMZ1	392246
0.12211	cg09882901		188677
0.1218	cg26472922		461941
0.12177	cg22810790	CA4	402441
0.1217	cg20396299		366115
0.1215	cg01399485	CASZ1;CASZ1	29081
0.12144	cg27423739		478314

OA - RA	Locus	Associated gene	SEQ ID No.
0.12144	cg11857093		222224
0.12129	cg04004513	SKAP1;SKAP1	80529
0.12105	cg16731157	RCAN3	307717
0.12064	cg04757806	FUT4	94983
0.12052	cg10930901		206696
0.12044	cg09728333		185957
0.12032	cg22159835	NRXN2;NRXN2;NRXN2	392801
0.12007	cg10168635	C2orf88;C2orf88;C2orf88;C2orf88	193705
0.1198	cg12891678		238813
0.11957	cg06382546	LRP1B	124829
0.11923	cg16118803	MOG;MOG;MOG;MOG;MOG; G;MOG;MOG;MOG;MOG; MOG;MOG	296688
0.11879	cg24642523	HSPA2	432315
0.11842	cg05280131	FAM128A;LOC150776	105029
0.11823	cg23693749		417137
0.11821	cg25255713	EVPLL	442316
0.11814	cg23257225	ADORA1;ADORA1	410054
0.11813	cg12536891	CLPB	233264
0.11771	cg08922201	SYT7	172124
0.11744	cg16274954	DPCR1	299319

OA - RA	Locus	Associated gene	SEQ ID No.
0.11242	cg03779072		76349
0.11235	cg00795584		16819
0.11176	cg06938705		135549
0.11144	cg04263215	NDUFS2;ADAMTS4	85649
0.11144	cg09296742		178512
0.11107	cg18804920	CNTNAP2	341118
0.11103	cg12835313	CACNA2D3	237974
0.11083	cg07157030	RHOJ;RHOJ	139948
0.11062	cg19725553	BLVRA	355438
0.11045	cg13777287	CNKSR3	254763
0.11016	cg26048630	PRRX1;PRRX1	454529
0.10972	cg02666837		54361
0.10966	cg11073796		209086
0.10936	cg04554928	TRIM15	91220
0.10888	cg17963461		327141
0.1087	cg15580417	KCNJ9	287721
0.10863	cg21602520	BCL2;BCL2	384588
0.10849	cg21817750	MRPS27	387694
0.10849	cg21306949		380293
0.10796	cg09126995	PHC2;PHC2	175501

OA - RA	Locus	Associated gene	SEQ ID No.
0.11728	cg04011829	SLCO4A1	80684
0.11703	cg16143578	ROBO4;ROBO4	297069
0.11698	cg09966895	ODZ4	190045
0.11691	cg24113950		423878
0.11646	cg19119609		345922
0.11612	cg05663064	COL6A1	112083
0.1161	cg19388972		349838
0.11582	cg05979400	LOC100128731	117903
0.11568	cg01311341	KIAA1671	27416
0.11546	cg06825512	APCDD1	133201
0.11466	cg26292150	ZDHHC19	458748
0.1146	cg06282247		123104
0.11404	cg17438457		319053
0.11398	cg06427611	PARVB	125571
0.11372	cg11386098	SYT7	214308
0.11358	cg13188382		243299
0.11315	cg03409151	ALDH7A1	68983
0.11311	cg18771300	RHOJ	340543
0.11298	cg15320349		283665
0.11293	cg03840259	GRAP2	77400

OA - RA	Locus	Associated gene	SEQ ID No.
0.10783	cg23931734	CA12;CA12	420686
0.10741	cg036679504	LRRC2;LRRC2;TDGF1	74369
0.10704	cg05272790	TMPRSS13	104903
0.10702	cg10512203	COL9A2	199691
0.10677	cg17848515	SMPD4;SMPD4;SMPD4;S MPD4;SMPD4;SMPD4;SM PD4;FAM128B	325326
0.10643	cg06824523	PLCH2	133178
0.10623	cg24833464	KRTAP3-1	435563
0.1062	cg01619846	UHRF1;UHRF1	33506
0.10589	cg00089821		2084
0.1058	cg02506908	HPD	51094
0.10525	cg24248680	FAM24B	426016
0.10495	cg22261895	PLBD1	394295
0.10453	cg25638443	ST8SIA1	448399
0.10437	cg08770647	ROBO4	169334
0.10378	cg10663897		202375
0.10325	cg09075327	PSD3	174665
0.10321	cg11505113	VASH2;VASH2;VASH2	216106
0.10291	cg24251135	USP38	426061
0.1029	cg26824174	OLFML3	467994

OA - RA	Locus	Associated gene	SEQ ID No.
0.10284	cg11912513		223148
0.10264	cg03887520		78268
0.1024	cg21674153	B4GALT6	385733
0.10236	cg17147466		314205
0.10181	cg21931864	SH3D20	389527
0.10134	cg09469870		181594
0.10132	cg06294384		123314
0.10127	cg22693493		400543
0.10127	cg05492433	COL22A1	108970
0.10066	cg06915112		135102
0.10002	cg14320626		266136

TABLE 7

OA - RA	Locus	Associated gene	SEQ ID No.
-0.10022	cg00490976		10388
-0.10038	cg000082140		1884
-0.10076	cg04080530		81955
-0.10083	cg25035059	CHD7	438996
-0.10092	cg09944434		189753
-0.10117	cg14538532	PBX2	270543
-0.10144	cg27165033		473953
-0.10204	cg03110300	CPLX4	63236
-0.10239	cg14729148	CUGBP2;CUGBP2;CUGB P2;CUGBP2	274152
-0.10249	cg15730121	DLGAP4;DLGAP4;DLGA P4	290375
-0.10256	cg24037389	SCARA5	422606
-0.10268	cg20933239		374167
-0.10274	cg10627737	COL4A2	201776
-0.1028	cg19006947	PLCB3	344239
-0.10299	cg08613239		166546
-0.10305	cg15645757	UBE2Q1	288883
-0.10316	cg19056664	CLPTM1L	345033
-0.10356	cg03741475		75606

OA - RA	Locus	Associated gene	SEQ ID No.
-0.10398	cg26332797	CTTNBP2	459481
-0.10398	cg07447015	ANKRD11	145230
-0.10414	cg06823060	CMIP;CMIP	133147
-0.10436	cg05150973	EHD1	102541
-0.10453	cg05587232	C7orf50;C7orf50;C7orf50	110657
-0.10463	cg26949393	AGAP3	470288
-0.10493	cg07266910	ZMAT3;ZMAT3	142085
-0.10509	cg01993576	SLC29A1;SLC29A1	40885
-0.10514	cg22907277	C7orf50;C7orf50;C7orf50	404094
-0.10515	cg12544243	GRIN3B	233359
-0.10541	cg23078123	GPR177	407010
-0.10541	cg09545918	COL8A1;MIR548G;COL8 A1	182887
-0.1056	cg15067032		279802
-0.10586	cg24781973	FMN1	434762
-0.1059	cg07576033	C16orf11	147740
-0.10596	cg02256384		46036
-0.10602	cg08371643	CA4	162329
-0.10751	cg10985158	NAV1	207637
-0.10791	cg06531624		127430
-0.10813	cg25570929	COLEC12	447236

OA - RA	Locus	Associated gene	SEQ ID No.
-0.11193	cg01821635		37390
-0.11205	cg03131767	ABCB9;ABCB9;ABCB9	63648
-0.11209	cg26576937	EBF4	463815
-0.11214	cg15142477	RNF165	281126
-0.1125	cg13893427		257066
-0.11262	cg17527422	C12orf68;C12orf68	320633
-0.1128	cg08642731	C10orf71;C10orf71	167107
-0.11281	cg15006627	GPRC5A	278771
-0.11292	cg12626411	PRG4;PRG4;PRG4;MIR548F1;PRG4	234784
-0.1131	cg22851557	PRDM16;PRDM16	403103
-0.11319	cg26803803	DNMT3A;DNMT3A;MIR1301;DNMT3A	467585
-0.11355	cg18746826	SCARA5	340084
-0.11368	cg26186331	DAB2	456925
-0.11378	cg15696968	KIAA1949;NRM9;KIAA1949	289755
-0.11389	cg11014810	SH3PXD2A	208137
-0.11393	cg14190889	HLA-H	263376
-0.11407	cg17655346	CACNA2D3	322379
-0.11414	cg24777564	ADAMTS12	434703
-0.11439	cg04156383	PDE4DIP;PDE4DIP;PDE4DIP	83534

OA - RA	Locus	Associated gene	SEQ ID No.
-0.1085	cg00997264		20997
-0.10866	cg18494399	SLC1A2	336159
-0.10876	cg21406461	IFI16	381503
-0.10879	cg24395452	SPATA18	428258
-0.109	cg10903916	ASAP2;ASAP2	206293
-0.1093	cg06330375	TSC2;TSC2;TSC2	123883
-0.10957	cg00779797	CAPN2;CAPN2	16482
-0.11024	cg18145505	GREM1	330327
-0.11042	cg26883033		469090
-0.11044	cg25334834	VGLL4;VGLL4;VGLL4;VGLL4	443491
-0.11048	cg18565130	C7orf50;C7orf50;C7orf50	337296
-0.11085	cg06067955	MYPN	119469
-0.11124	cg11147154	FLNC;FLNC	210249
-0.11125	cg14473823		269143
-0.11142	cg18324583		333319
-0.11152	cg24917359	C1QTNF1;C1QTNF1;C1QTNF1	437035
-0.11155	cg22346073	CLASP1;CLASP1;CLASP1	395428
-0.1116	cg04958191	ASPH;ASPH;ASPH;ASPH	98926
-0.11187	cg12160741	BRF1	227383

OA - RA	Locus	Associated gene	SEQ ID No.
-0.11621	cg10239022	GPR133	195020
-0.1167	cg17753942		323769
-0.11676	cg21540399	PTPRG	383531
-0.11688	cg16538359		304039
-0.11692	cg01320211	SEMA6D;SEMA6D;SEMA6D;SEMA6D	27561
-0.11693	cg02020821	PPP2R5C;PPP2R5C;PPP2R5C	41450
-0.11698	cg06873401	LHFPL2	134232
-0.11705	cg15671083	UCN3	289292
-0.1173	cg00102093		2393
-0.11732	cg21356710	MFSD2B	380867
-0.11738	cg21205282		378649
-0.11761	cg07723948	OSGIN1;OSGIN1;OSGIN1	150463
-0.1177	cg16500916		303286
-0.11772	cg24634422	SLC1A2	432160
-0.11788	cg06755262		131696
-0.11803	cg24698488	MMP14	433309
-0.11805	cg01675953	MCF2L;MCF2L	34463
-0.11814	cg15547672	RPTOR;RPTOR	287142

OA - RA	Locus	Associated gene	SEQ ID No.
-0.11448	cg02296376	MIR1286;RTN4R	46872
-0.11454	cg00145875		3263
-0.11464	cg21862126		388401
-0.11468	cg12181407		227738
-0.11476	cg21733013	RAPGEF5	386423
-0.11485	cg25379549	ADARB2	444296
-0.11508	cg07815521	MIR641;AKT2	152123
-0.11512	cg03037030	TNF	61825
-0.11515	cg14930864	YWHAQ	277519
-0.11516	cg23980760	ACCSL;ACCSL	421559
-0.11517	cg26858414	CDSN;PSORS1C1	468630
-0.11524	cg10831642	SH3PXD2A	205142
-0.11537	cg03901836	C2orf57	78575
-0.11539	cg16705287	POLR2E	307214
-0.11541	cg05557262	FAM180A	110128
-0.11544	cg03860038		77780
-0.11546	cg20989591	C7orf50;C7orf50;C7orf50	375141
-0.1157	cg03627771	GRAMD1B	73371
-0.1158	cg02145701	BANP;BANP	43968
-0.11616	cg13093380	ALK	241873

OA - RA	Locus	Associated gene	SEQ ID No.
-0.12013	cg19678029	KCNQ1OT1;KCNQ1;KCNQ1	354576
-0.12018	cg09915421		189251
-0.12024	cg15827092		291857
-0.12026	cg25827666	SH2D2A;SH2D2A;NTRK1;NTRK1;SH2D2A;SH2D2A;SH2D2A	451242
-0.12033	cg14166209		262818
-0.12033	cg06647382	PKD2	129663
-0.12099	cg13543096	LOC100271831;GDPD3	249930
-0.12099	cg06679262		130241
-0.12103	cg05514932	RETSAT	109417
-0.12105	cg22624391		399439
-0.12109	cg19480385		351330
-0.12113	cg08325842	ZFP91;ZFP91-CNTF	161555
-0.12122	cg15368872	KLRK1	284353
-0.12175	cg27313492	WFIKKN1	476470
-0.12203	cg05182583	BAT2	103165
-0.12205	cg22193013	CHRNA7	393284
-0.12211	cg16209444	ACOX2	298173
-0.12214	cg20577102		368824
-0.12217	cg06326425	GPC6	123816

OA - RA	Locus	Associated gene	SEQ ID No.
-0.11827	cg23850174		419365
-0.1184	cg05429527		107954
-0.11845	cg27437823	MAP3K14	478553
-0.11865	cg15470365	SORBS2;SORBS2;SORBS2;SORBS2	286032
-0.1187	cg24577455	PRKCZ;PRKCZ;PRKCZ	431245
-0.11873	cg18458739	BCAS3;BCAS3	335553
-0.11874	cg11335264	CAPZB	213463
-0.11901	cg00961940	TIMP2	20220
-0.11901	cg04712892	NRAP;NRAP	94119
-0.11917	cg27582168	FANCA	481016
-0.11931	cg17294136	CACNA2D1	316631
-0.11937	cg13932122		257954
-0.11937	cg10637688		201971
-0.11938	cg05384139	PITPNM2	107123
-0.11954	cg04554240	ESYT3	91205
-0.11954	cg22429169	ZNF335	396572
-0.11965	cg03917297		78835
-0.11967	cg19408740	IGSF8	350178
-0.11986	cg09745791	CTRB1	186257
-0.12011	cg06521562	JRK;JRK	127195

OA - RA	Locus	Associated gene	SEQ ID No.
		3;TATDN3;TATDN3	
-0.12442	cg14771877	C17orf99	274788
-0.12455	cg02866149	C20orf117	58258
-0.12464	cg02667577	WIPI2;WIPI2;WIPI2;WIPI2	54375
-0.12507	cg19973338	C17orf99	359782
-0.12517	cg13709561	SCARA5	253479
-0.12585	cg14118850	HPCAL1;HPCAL1	261879
-0.1259	cg03728674		75338
-0.12611	cg25340361	COMMD1	443580
-0.12613	cg07347019		143506
-0.12631	cg16000393	TNK2;TNK2	294736
-0.12649	cg02898239		58930
-0.12655	cg16323245	ZBTB20;ZBTB20	300173
-0.12655	cg00907661	ZDHC20	19059
-0.12665	cg23986495		421674
-0.12691	cg13720395	YWHAG	253710
-0.12696	cg00643876	TBC1D24	13650
-0.12697	cg14781826	BPTF;BPTF	275014
-0.12748	cg01476807	FBXO30	30709
-0.1277	cg19659642	CD9	354321

OA - RA	Locus	Associated gene	SEQ ID No.
-0.1226	cg24353272	RRP15	427604
-0.12271	cg06306791		123517
-0.12281	cg11253913	CALD1;CALD1;CALD1;C	212154
-0.12285	cg08352422		161993
-0.12293	cg16044109	HEG1	295491
-0.12298	cg23198815		408873
-0.12305	cg23922753		420530
-0.12305	cg15442583	CDGAP	285507
-0.12317	cg02248749	TNXB	45883
-0.12323	cg13455257	TMOD4	248067
-0.12337	cg00740389	ITGB7	15652
-0.12369	cg08448751	SEMA3G	163578
-0.1237	cg20663448	FILIP1	370104
-0.12374	cg00819141		17296
-0.12375	cg00161791		3633
-0.12376	cg01569083	TNF	32491
-0.12392	cg00254017	MAP3K1	5441
-0.12398	cg24885556	ITGA7	436558
-0.12399	cg21082141	PRDM8	376504
-0.12415	cg01785514	TATDN3;TATDN3;TATDN	36554

OA - RA	Locus	Associated gene	SEQ ID No.
-0.13031	cg09664445	KIAA0664	184948
-0.13045	cg06708731	DBH	130785
-0.13094	cg11585805		217365
-0.13101	cg10626556	KIAA0406	201746
-0.13101	cg09982224	ALDH3B1	190313
-0.13118	cg09437523		181003
-0.13123	cg06769258	MFSD7	132014
-0.13123	cg05299140		105372
-0.1315	cg25735648		449823
-0.13164	cg20865778	TCIRG1;TCIRG1	373291
-0.13179	cg12450872		231834
-0.13196	cg00154554	RECE;RECE	3460
-0.1321	cg10006897	PCBP3;PCBP3	190741
-0.13211	cg14602234		271884
-0.13235	cg08917489	EYA4;EYA4;EYA4	172050
-0.13261	cg24088438	FERMT3;FERMT3;FERMT3;FERMT3	423490
-0.13277	cg07325692		143137
-0.13288	cg08013109	ULK1	155629
-0.13289	cg09337391	ZMYND8;ZMYND8;ZMYND8	179281

OA - RA	Locus	Associated gene	SEQ ID No.
-0.12785	cg21455901	CRYL1	382161
-0.1279	cg01876531	PLXNA2	38448
-0.12817	cg03925072		78966
-0.12858	cg24267275		426255
-0.12861	cg10356210	KCNK3	197004
-0.1289	cg12145349	NAA40	227108
-0.12904	cg11820824	S100A16	221475
-0.12906	cg26989053	NTAN1	471015
-0.12914	cg09119494	E2F2	175337
-0.12918	cg18904855		342756
-0.12918	cg00572560		12164
-0.12919	cg25242423	RTBDN;RTBDN	442118
-0.12926	cg26745520	GRK5	466632
-0.12934	cg07044523	S100A5	137607
-0.12938	cg10048215	APOLD1;APOLD1	191451
-0.12949	cg10471743		198906
-0.12978	cg00767886	EHD4	16225
-0.12983	cg26562772	DUSP10;DUSP10;DUSP10	463554
-0.13012	cg00877958		18503
-0.13016	cg21230535	FTCD	379161

OA - RA	Locus	Associated gene	SEQ ID No.
-0.13574	cg16950726	NLGN2	311097
-0.13588	cg07466788	SLC16A3;SLC16A3;SLC16A3	145619
-0.13613	cg00767135	ODZ3	16210
-0.13616	cg01336162	TGFB3	27842
-0.13632	cg05007126	SDCBP2	99869
-0.13637	cg12045511	EHD4	225319
-0.13667	cg18028470	PIGV	328228
-0.13671	cg15773893	DOCK10	291034
-0.13693	cg05652528	DNMT3A;DNMT3A;DNMT3A;MIR1301	111855
-0.13703	cg19931529	UGP2;UGP2	359121
-0.1372	cg22488568	SLC9A1	397378
-0.13723	cg14904034	HPCAL1;HPCAL1	277047
-0.13747	cg27027230	ARID5B	471633
-0.1377	cg06607384	C14orf159;C14orf159;C14orf159;C14orf159	128776
-0.13773	cg09766355	NPL	186590
-0.13778	cg17015522	C1QTNF1;C1QTNF1;C1QTNF1	312055
-0.13789	cg19494960	RPTOR;RPTOR	351529
-0.13793	cg07366462	ADCY5	143859

OA - RA	Locus	Associated gene	SEQ ID No.
-0.13298	cg12430302	SPSB1	231458
-0.13311	cg22912818	TMCO3	404171
-0.13319	cg08338281	WIBG	161768
-0.13321	cg10097651		192354
-0.13345	cg08122070	NADK	157631
-0.13393	cg10723746	SPPL2B;SPPL2B	203334
-0.13398	cg21656522		385493
-0.134	cg24598094	SLC30A1	431596
-0.13423	cg03466066		70093
-0.13424	cg19503826	EPN1;EPN1;EPN1	351690
-0.13442	cg18330041	YWHAH	333416
-0.13456	cg25707745		449371
-0.13486	cg09018904	ANO10	173744
-0.13517	cg07908868	PLXNA2	153755
-0.13522	cg01364674		28371
-0.13527	cg24995976	PEAR1	438225
-0.13549	cg17802464	SEC14L3	324476
-0.13562	cg23941016	TBC1D2B;TBC1D2B	420855
-0.13568	cg14504636	AP2A2	269745
-0.13571	cg17846466	MCOLN2	325303

OA - RA	Locus	Associated gene	SEQ ID No.
-0.14014	cg03649589	CSGALNACT1;CSGALNACT1;CT1;CSGALNACT1	73790
-0.14031	cg07877964	USP7	153196
-0.14044	cg17499955		320108
-0.14047	cg17407629	PAM;PAM;PAM;PAM	318547
-0.14048	cg04305228	MICAL3	86473
-0.14066	cg24499411	TNS3	429956
-0.14066	cg17125990		313833
-0.14069	cg16608018		305379
-0.14074	cg15053322	SEC14L3	279556
-0.14077	cg11263420	FCGRT;FCGRT	212295
-0.14081	cg11437140	TIMP2	215182
-0.14083	cg07328796		143190
-0.14111	cg00528616	ZNRF1	11235
-0.14116	cg13619044	C7orf41	251590
-0.14119	cg03277153		66388
-0.14128	cg22321646	LZTS1	395060
-0.14131	cg11462252	SLIT3	215511
-0.14143	cg02711975	SNTG2	55231
-0.14153	cg18890417	RHOBTB2;RHOBTB2,RHOBTB2	342552

OA - RA	Locus	Associated gene	SEQ ID No.
-0.138	cg04075247	LGALS12;LGALS12;LGALS12;LGALS12	81844
-0.13801	cg01174811	PDE4D;PDE4D;PDE4D	24728
-0.13825	cg15536489	C7orf50;C7orf50;C7orf50	286952
-0.13832	cg00622170	C4orf10;NOP14	13248
-0.13853	cg08743794	KIAA1949;NRM;KIAA1949	168897
-0.13873	cg21370522	TNF	381016
-0.13878	cg06047674	FRMD4A	119120
-0.13896	cg12225794		228457
-0.13921	cg05905731		116408
-0.13924	cg03407594	MUC6	68950
-0.13938	cg26605914	SKI	464218
-0.1394	cg07359991	HSD3B7;HSD3B7;HSD3B7;SETD1A	143753
-0.13946	cg14780449		274978
-0.13949	cg16843799	FLJ39653;FLJ39653	309488
-0.13957	cg26805263	TNFRSF19;TNFRSF19	467622
-0.13961	cg13460740	MGC16703;P2RX6;P2RX6	248181
-0.13977	cg05488681		108898
-0.13998	cg17810878	ANO6;ANO6;ANO6	324639
-0.14009	cg12416561	C4orf22	231221

OA - RA	Locus	Associated gene	SEQ ID No.
-0.1432	cg17594351	MYF6	321588
-0.14328	cg12464631		232068
-0.14333	cg04244932		85279
-0.14351	cg04955877	ZHX2	98883
-0.14362	cg07618453	KCNQ1;KCNQ1	148575
-0.14384	cg27121309	ACER3	473247
-0.14384	cg14807945	ZEB2;ZEB2	275475
-0.14392	cg04142988	PCSK6;PCSK6;PCSK6;P CSK6;PCSK6;PCSK6;PC SK6;PCSK6	83265
-0.14429	cg00925950	PSKH1	19464
-0.14432	cg21933359	KHDRBS3	389559
-0.14433	cg11287400	MITF;MITF;MITF	212678
-0.14465	cg00926267	MKL1	19470
-0.14468	cg16098340	MIR548C;RASSF3	296333
-0.14478	cg08630040		166875
-0.14489	cg25880242		451900
-0.145	cg09706277	CD276;CD276	185655
-0.14524	cg07062388	LMBRD1	137963
-0.14533	cg02470874	PPM1L	50305
-0.14552	cg00997251	ARHGAP26;ARHGAP26	20995

OA - RA	Locus	Associated gene	SEQ ID No.
-0.14155	cg19704102		355015
-0.14158	cg01982724		40687
-0.14161	cg01506917	TRERF1	31222
-0.14162	cg13868106		256590
-0.14164	cg27121538	SV2B;SV2B	473253
-0.14179	cg18657389	EVPL	338738
-0.14191	cg07044115		137597
-0.14228	cg26775558	TCF7L2;TCF7L2;TCF7L2; TCF7L2;TCF7L2;TCF7L2	467042
-0.14233	cg01860954		38147
-0.14249	cg23951190	CPNE4	421020
-0.14255	cg20721467	MYST4	371233
-0.14265	cg12138483	CLPP	227002
-0.14272	cg11478024	ANKS1A	215738
-0.14274	cg16289449	FERMT3;FERMT3;FERM T3;FERMT3	299541
-0.14274	cg14050363		260484
-0.14285	cg03905247	NCOR2;NCOR2	78635
-0.14288	cg08993079	ADAM12;ADAM12	173319
-0.14309	cg16224727	FBRSL1	298403
-0.14309	cg06385449	FERMT3;FERMT3	124889

OA - RA	Locus	Associated gene	SEQ ID No.
-0.14869	cg02092181	DOT1L	42966
-0.1488	cg13798679		255238
-0.14883	cg17073306	MYL5;MYL5	312976
-0.1489	cg17015179	PPT1;PPT1	312048
-0.14935	cg01343936		27981
-0.14948	cg11258484		212233
-0.14951	cg13971140	LASS4	258695
-0.14961	cg07282201	TBC1D10C	142343
-0.14982	cg12424504	MACC1	231361
-0.14985	cg01312762	CCDC134	27446
-0.15027	cg09568355		183338
-0.15031	cg08800856	NRXN2;NRXN2	169806
-0.15034	cg23617530		415668
-0.15048	cg02076598	KIAA1671	42633
-0.15058	cg18375707	PLCB3	334103
-0.1507	cg15833565	ERI3	291986
-0.15079	cg04101009		82356
-0.15089	cg09302355	FERMT3;FERMT3	178600
-0.15093	cg06191091		121594
-0.1512	cg07812957		152057

OA - RA	Locus	Associated gene	SEQ ID No.
-0.1456	cg16996242	ZMYM4	311738
-0.14564	cg12316142	DPYSL3	229823
-0.14568	cg05624853	HSD3B7;HSD3B7;HSD3B7	111349
-0.14588	cg05433460	ARHGAP1;ZNF408	108004
-0.1463	cg01226417		25743
-0.14632	cg00063979		1516
-0.14661	cg00498804	ST5;ST5;ST5	10580
-0.14682	cg22132509	PPM1L	392374
-0.14711	cg22166248	NXPH2	392926
-0.14724	cg02563600	KIAA0182;KIAA0182	52166
-0.14756	cg12681001	TNF	235670
-0.14759	cg23590159	UBXN11;UBXN11;UBXN11	415243
-0.14761	cg21528927	SLC6A12;SLC6A12;SLC6A12	383331
-0.1477	cg02742775	C12orf34	55869
-0.14778	cg10273072	C21orf34	195585
-0.14801	cg22927076		404363
-0.14817	cg03070550	HTRA1	62547
-0.14858	cg18791929	MYH15	340884
-0.14861	cg05991539	C6orf25;C6orf25;C6orf25;C6orf25;C6orf25	118154

OA - RA	Locus	Associated gene	SEQ ID No.
-0.15364	cg06569229	FAT3	128143
-0.15382	cg26485376		462139
-0.15389	cg15513221		286669
-0.15389	cg08577912		165952
-0.15392	cg05778820	SLC9A1	114033
-0.15397	cg02222066	CYTH1;CYTH1	45356
-0.15413	cg02112681	C7orf50;C7orf50;C7orf50	43376
-0.15419	cg02913511	CNNM4	59256
-0.15421	cg25368116		444093
-0.15435	cg01357135	PPM1L	28229
-0.15439	cg26139338	KLF12	456089
-0.15451	cg19351617	SIGIRR;SIGIRR;SIGIRR	349235
-0.15453	cg22852065	SPATA18	403114
-0.15478	cg14455925		268761
-0.15478	cg00594561	DLX3	12719
-0.15482	cg26114961	C6orf25;C6orf25;C6orf25; C6orf25;C6orf25;C6orf25	455644
-0.15511	cg09996076	HSD3B7;HSD3B7;HSD3B7; 7;SETD1A	190546
-0.15544	cg07821417	ARVCF	152230
-0.1557	cg23991482	LSM7	421773

OA - RA	Locus	Associated gene	SEQ ID No.
-0.15121	cg11724147	HIBADH	219728
-0.15134	cg27402999	SLC9A9	477987
-0.15154	cg02814691	NPL	57253
-0.15199	cg03907570	PRKAR1B;PRKAR1B;PR KAR1B;PRKAR1B;PRKA R1B;PRKAR1B	78679
-0.15217	cg13166875	SEC14L3	242924
-0.15227	cg26048923	TRAPPC9;TRAPPC9	454532
-0.15243	cg12884495	WBP2;UNC13D	238717
-0.15272	cg23558764		414863
-0.15282	cg05648614	ARL8B	111782
-0.15283	cg07449758	C6orf25;C6orf25;C6orf25; C6orf25;C6orf25;C6orf25	145282
-0.15287	cg19642408		354063
-0.15303	cg14831085	PCSK6;PCSK6;PCSK6;P CSK6;PCSK6;PCSK6;PC SK6;PCSK6	275823
-0.15304	cg01882991		38611
-0.15305	cg20848130	GJC2	373060
-0.15327	cg16032111	PPP2R1B;PPP2R1B	295322
-0.15331	cg12268531	HSP90B3P	229089
-0.15337	cg08287887	OR7E37P	160856
-0.15355	cg14526997	EHMT1;EHMT1	270270

OA - RA	Locus	Associated gene	SEQ ID No.
-0.15611	cg00751386	CTNNA2;CTNNA2	15883
-0.15614	cg02316852	RPA1	47305
-0.15619	cg21350115	CALCRL;CALCRL	380795
-0.15672	cg12526091		233088
-0.1568	cg02481950	METTL9;IGSF6;METTL9	50548
-0.157	cg19019345	ST5	344432
-0.15712	cg13552337	NDOR1;NDOR1;NDOR1; NDOR1	250119
-0.15733	cg19321263	TRIM26	348840
-0.15767	cg07506749		146418
-0.15773	cg26197679		457116
-0.15792	cg03680790	STX2;STX2	74392
-0.15802	cg05744888	EIF2C2;EIF2C2	113460
-0.1583	cg00433709	ZNRF1	9174
-0.15835	cg22856279		403194
-0.15845	cg15256491	FOXK1	282829
-0.15854	cg20171297	MYF6;MYF6	362835
-0.15858	cg11244402	FOXO1	211986
-0.15879	cg14510322		269863
-0.15902	cg24236839	KDM4B	425869
-0.15907	cg01353907	GPR133	28172

OA - RA	Locus	Associated gene	SEQ ID No.
-0.15926	cg23935522	ZDHHC17	420759
-0.15938	cg01893068		38791
-0.15944	cg20432350	KCND3;KCND3	366636
-0.15948	cg07453773	ST5;ST5;ST5	145358
-0.15956	cg11370814		214057
-0.15957	cg07820423		152210
-0.15972	cg00550928	MGAT3;MGAT3	11698
-0.15977	cg16576811	NEDD4L;NEDD4L;NEDD4L; NEDD4L;NEDD4L;NEDD4L; NEDD4L;NEDD4L;NEDD4L; NEDD4L	304754
-0.15996	cg03285617	NT5E	66533
-0.1605	cg08145262	FRS2;FRS2	158124
-0.16083	cg07791897		151636
-0.16096	cg13127591	KRTAP9-9;KRTAP9-8	242341
-0.1612	cg00029979		743
-0.1613	cg18702278	PDE6B;PDE6B;PDE6B	339372
-0.16132	cg25683744	NINJ2	449043
-0.16135	cg13675051	RNF19A;RNF19A	252709
-0.16155	cg20364025	GALNS	365624
-0.16174	cg22649800	OGDH;OGDH	399813
-0.16179	cg07692929	OLFM1	149840

OA - RA	Locus	Associated gene	SEQ ID No.
-0.16437	cg16746362	C6orf25;C6orf25;C6orf25; C6orf25;C6orf25;C6orf25	307984
-0.16464	cg03273420	SMCR7;SMCR7;SMCR7	66322
-0.16496	cg04221461	AKT3;AKT3	84805
-0.16524	cg13573761	C4orf23	250625
-0.1653	cg17807913		324584
-0.16531	cg19506253	CYTIP	351732
-0.16538	cg00895231		18812
-0.16547	cg00671823	GTF3C1	14204
-0.16584	cg23632029	OR10A5	415943
-0.16593	cg04345118	PAX8;PAX8;LOC654433; PAX8;PAX8;PAX8;LOC44 0839	87257
-0.16595	cg09228831	GPRIN3	177227
-0.16609	cg05910124	TRAPPC9;TRAPPC9	116485
-0.16622	cg15124432	CDC34	280793
-0.16631	cg03199366		64930
-0.16651	cg21524538	SDCBP2	383268
-0.16652	cg22950982	MAPKAPK3	404771
-0.1666	cg26807536	LOC100271831;GDPD3	467662
-0.16661	cg16618389		305550
-0.16665	cg18347607		333691

OA - RA	Locus	Associated gene	SEQ ID No.
-0.16208	cg02903929		59057
-0.16229	cg10447977	ADAMTS9	198519
-0.1623	cg05383524	MGRN1;MGRN1;MGRN1; MGRN1	107108
-0.16237	cg25902666	CSNK1G2	452187
-0.16237	cg07662964	BRD1;LOC90834	149327
-0.16243	cg14299931	ARHGEF7;ARHGEF7;AR HGEF7;ARHGEF7;ARHG EF7;ARHGEF7	265726
-0.16257	cg02017814	NSMCE2	41390
-0.16265	cg01703196		34921
-0.16293	cg02119955	ITGBL1	43511
-0.16305	cg17987982		327555
-0.1631	cg02449461	ARRB1;ARRB1	49866
-0.16315	cg03928874	LY86	79027
-0.16339	cg07735586		150671
-0.1634	cg21089930	DTX4	376611
-0.16371	cg25105578		440013
-0.16389	cg04021454	TAF12;TAF12	80874
-0.16408	cg21126020	TRIM10;TRIM10	377162
-0.16417	cg27395226	SRPK2	477869
-0.16428	cg09141623	PRKG1;PRKG1	175757

OA - RA	Locus	Associated gene	SEQ ID No.
-0.16921	cg08462367		163870
-0.16922	cg07412186	ATXN1;ATXN1	144647
-0.16923	cg02988730	AMPD2;AMPD2;AMPD2	60882
-0.16929	cg20090290	AMBRA1	361565
-0.16937	cg25296103	ZEB2;ZEB2	442878
-0.1694	cg25124489	PRKCE	440332
-0.1695	cg07739478	C6orf25;C6orf25;C6orf25; C6orf25;C6orf25;C6orf25	150742
-0.16956	cg10090414		192177
-0.16978	cg08937102	NADK	172382
-0.16999	cg10785394		204327
-0.17008	cg05425699	TNS3	107909
-0.1701	cg12987138		240257
-0.17028	cg04558553	UGT2B7	91298
-0.17028	cg21764632	WIPI2;WIPI2;WIPI2;WIPI 2;WIPI2	386908
-0.17032	cg01306151	C16orf7	27295
-0.17039	cg22718891		400997
-0.17042	cg21346154	TGFA;TGFA	380741
-0.17048	cg21241151		379374
-0.17049	cg25091527	COL4A1	439775

OA - RA	Locus	Associated gene	SEQ ID No.
-0.16674	cg24828746	ZBTB7A	435490
-0.16708	cg01386735	LMBRD1	28819
-0.16723	cg12214366	ANTXR2;ANTXR2	228267
-0.16727	cg04132452	PPM1L	83027
-0.1674	cg17923377	BRD1;LOC90834	326503
-0.1675	cg00659931	PCSK6;PCSK6;PCSK6;P CSK6;PCSK6;PCSK6;PC SK6;PCSK6	13955
-0.16751	cg01412400	RPTOR;RPTOR	29361
-0.16763	cg18507146	ZNF236	336390
-0.16773	cg17001765	PGBD2;PGBD2	311841
-0.16781	cg23683146		416923
-0.16815	cg22688687	C19orf42	400457
-0.16825	cg10969245	DAGLA	207350
-0.16826	cg15637527	ARHGAP1	288736
-0.16829	cg11903920	TCERG1L	223003
-0.1685	cg15268191		283001
-0.16862	cg03204322	SAMD13;SAMD13;SAMD 13	65015
-0.16866	cg09906928	LHFPL2	189108
-0.1688	cg23808165		418718
-0.16903	cg15594550	ZNF696	287945

OA - RA	Locus	Associated gene	SEQ ID No.
		G;FILIP1L;FILIP1L	
-0.17247	cg08791347	FRMD4A	169648
-0.17248	cg08656333		167353
-0.17277	cg14121740		261943
-0.17277	cg05514531	GBE1	109409
-0.17287	cg00045902	PWWP2B;PWWP2B	1131
-0.17294	cg20584712	BAT2	368914
-0.17333	cg09305096	GULP1	178661
-0.17333	cg09156542		176059
-0.17338	cg05660874	SPPL2B;SPPL2B	112045
-0.17344	cg01397912	C19orf51;TNNI3	29052
-0.17357	cg19164997	CAPN5	346507
-0.17408	cg26110562	AGAP1;AGAP1	455549
-0.17424	cg19583934	RASA3	352999
-0.17429	cg20319604	PPM1B;PPM1B;PPM1B;P PM1B;PPM1B	364994
-0.17454	cg02955940	CORIN	60186
-0.17456	cg05426956	HTRA1	107922
-0.17468	cg00128100	KIAA1949;NRM;KIAA194 9	2929
-0.17519	cg01786151		36566

OA - RA	Locus	Associated gene	SEQ ID No.
-0.17072	cg26581714	SPATA18	463898
-0.17077	cg04771838	COL4A2	95213
-0.17083	cg04988694	TBCD	99510
-0.17083	cg05697734		112662
-0.17096	cg25221919		441857
-0.17096	cg18071202	LOC100292680	328953
-0.17113	cg19184688		346756
-0.17114	cg13740185	C10orf105;CDH23	254087
-0.17123	cg05801329		114496
-0.17126	cg26576576	PTPN14	463811
-0.17157	cg14692453	ANKRD23	273553
-0.17158	cg10143416		193223
-0.17163	cg05856321		115416
-0.17167	cg00230120	LOC100292680	4919
-0.17176	cg24152251		424608
-0.17178	cg18030453	LARS2	328261
-0.17206	cg25749107		450067
-0.17211	cg26457569	KANK2;KANK2	461638
-0.17223	cg08890627	SEC14L1;SEC14L1;SEC1 4L1;SEC14L1;SEC14L1	171586
-0.17237	cg22481643	C3orf26;FILIP1L;MIR548	397283

OA - RA	Locus	Associated gene	SEQ ID No.
-0.17783	cg21548131	NLGN1	383703
-0.178	cg02971328	RAC1;RAC1	60519
-0.17804	cg04857881	ITFG1	96921
-0.17826	cg16653138	PRKCZ;PRKCZ;PRKCZ	306192
-0.17831	cg22146612		392580
-0.17849	cg17627813	PRDM10;PRDM10;PRDM10	322003
-0.17863	cg24522085	LASS6	430348
-0.17898	cg02374207	MACROD1	48511
-0.17927	cg01286133	APP;APP;APP;APP;APP	26850
-0.17931	cg04644504	SEN8;MYO9A	92888
-0.17974	cg01923312	SLC22A3	39391
-0.1805	cg25541708		446789
-0.1806	cg15852553		292348
-0.18062	cg18722504	HBEGF	339716
-0.18072	cg20440552		366770
-0.18085	cg12979590	CUGBP1	240142
-0.18112	cg18664915	C7orf50;C7orf50;C7orf50	338829
-0.18131	cg18080303	LAMA4;LAMA4;LAMA4;LAMA4;LAMA4	329086
-0.18135	cg12496975	RAPGEF3;RAPGEF3;RA PGEF3	232622

OA - RA	Locus	Associated gene	SEQ ID No.
-0.17536	cg20788482		372245
-0.17539	cg04724873	KIAA1751	94344
-0.17547	cg11473240	KRT31	215681
-0.17547	cg10539122	NAV1;MIR1231;NAV1	200240
-0.17549	cg02123534	ADAP1	43564
-0.17597	cg05776861	ARHGEF7;ARHGEF7;ARHGEF7;ARHGEF7;ARHGEF7	113995
-0.17599	cg01104590	CARS;CARS;CARS;CAR S	23322
-0.17623	cg24888581	AGAP1;AGAP1	436607
-0.17625	cg18805457	TCERG1;TCERG1	341130
-0.17669	cg08189139		158940
-0.17672	cg17644903	ZDBF2	322224
-0.17677	cg20725334		371301
-0.1769	cg00851627		17937
-0.177	cg05891054	STAT5B	116105
-0.17702	cg13609694		251374
-0.17731	cg19482843	EIF2C2;EIF2C2	351362
-0.17753	cg19975759	B3GNTL1	359813
-0.17754	cg24864413	SLC22A1;SLC22A1	436118
-0.1776	cg10592521	MEX3D	201161

OA - RA	Locus	Associated gene	SEQ ID No.
-0.18457	cg00646241	SHANK2	13697
-0.18467	cg24290996		426537
-0.18474	cg13690679		253081
-0.18479	cg18926409		343073
-0.18495	cg19589494		353114
-0.18496	cg12806353	PLA1A	237540
-0.1853	cg00237010	NINJ2	5072
-0.18559	cg04144521	MFS6	83296
-0.18565	cg07833951		152463
-0.18583	cg04056576	PPM1L	81465
-0.18583	cg14837896	THBS4	275954
-0.18588	cg22330533	BRD1;LOC90834	395190
-0.18592	cg03659680	LYN;LYN	73997
-0.18618	cg06795960	ARL4D	132561
-0.1862	cg14679230	LIPE	273341
-0.18622	cg00873517	KHDRBS3	18398
-0.18626	cg13613044		251444
-0.18636	cg20021790	RPH3AL	360547
-0.1866	cg08279097	DCLRE1B	160695
-0.18672	cg13613439	PHYHD1;PHYHD1;PHYH D1;PHYHD1;PHYHD1	251453

OA - RA	Locus	Associated gene	SEQ ID No.
-0.18167	cg25677376		448951
-0.18198	cg06476926	TBCD	126410
-0.18258	cg16161418	KIAA1949;KIAA1949	297331
-0.18265	cg14661139	UBE2J2;UBE2J2;LOC100 128842;UBE2J2;UBE2J2	273045
-0.18273	cg07930874	SLAIN1;SLAIN1	154214
-0.18302	cg13912858	SORT1	257507
-0.18327	cg06059810	RUFY3;RUFY3;RUFY3;R UFY3;RUFY3	119317
-0.18359	cg01822532	LRP5	37414
-0.18366	cg05059607	PITPNC1;PITPNC1	100893
-0.18367	cg07547798	NSMCE2	147165
-0.18371	cg04761972		95031
-0.18382	cg15932980	STX2;STX2	293635
-0.18394	cg17425351		318837
-0.18398	cg09777237	ELN;ELN;ELN;ELN;ELN	186754
-0.18403	cg04068914	MTHFSD;MTHFSD;MTHF SD;MTHFSD;MTHFSD;M THFSD;MTHFSD;FLJ306 79	81718
-0.18411	cg07224918	ARHGEF10L;ARHGEF10 L	141354
-0.1845	cg24269082	TBCD	426275

OA - RA	Locus	Associated gene	SEQ ID No.
-0.18904	cg064445944	PIK3R1;PIK3R1;PIK3R1	125887
-0.18909	cg19623595		353718
-0.18909	cg05145297	HIP1	102438
-0.18938	cg11626175	JARID2	218013
-0.18939	cg05310046	THSD4	105621
-0.18981	cg26005086	JAG1	453833
-0.18991	cg09990852	RUFY3;RUFY3;RUFY3;RUFY3;RUFY3	190465
-0.19005	cg23413567	FOXO1	412578
-0.19014	cg11815008	CETN1	221367
-0.19024	cg14883993	NFIC;NFIC	276772
-0.1905	cg27302175	ZSWIM6	476195
-0.19064	cg05647929	CFC1B;CFC1	111770
-0.19077	cg00859622	VSTM2L	18096
-0.19081	cg25940447	GNPDA1	452774
-0.19085	cg00213052		4580
-0.19087	cg03057216	VPS72;TMOD4	62283
-0.19087	cg01932663	C3orf26;FILIP1L;FILIP1L	39583
-0.19118	cg25026329	APLP2;APLP2;APLP2;APLP2;APLP2	438829
-0.1912	cg06758827	TRIO	131795

OA - RA	Locus	Associated gene	SEQ ID No.
-0.18676	cg25331919	LIPG	443459
-0.18684	cg16046833	SNX7;SNX7	295544
-0.18685	cg02535674		51638
-0.18728	cg27554156	GSG1;GSG1;GSG1;GSG1	480508
-0.18728	cg24940885		437453
-0.1873	cg02360002		48201
-0.18738	cg04912273	SLC9A1	98039
-0.18751	cg18321354	CARD11	333265
-0.18756	cg10453419	PCSK6;PCSK6;PCSK6;P CSK6;PCSK6;PCSK6;PC SK6;PCSK6	198614
-0.18757	cg04833731	GDPD3;GDPD3;LOC1002 71831	96391
-0.18789	cg16872841	COL4A2	309904
-0.18796	cg08176694	PITPNM2	158725
-0.1881	cg08426898		163219
-0.18822	cg02813863	APOLD1;APOLD1	57236
-0.1885	cg02959282	NCK1	60268
-0.1885	cg11458974	HMOX1	215460
-0.18885	cg01156373	ERBB4;ERBB4	24354
-0.18902	cg08405910	NCK2;NCK2;NCK2	162877

OA - RA	Locus	Associated gene	SEQ ID No.
-0.19464	cg04081835		81973
-0.1948	cg05297666	ETS1	105349
-0.19506	cg19252218	ARL4D	347770
-0.19508	cg11668573	FNIP2	218773
-0.19509	cg07879785	CRYL1	153222
-0.19518	cg04005958		80561
-0.19522	cg01617074	SLC45A4;SLC45A4	33454
-0.19532	cg12560421		233610
-0.19534	cg00498089		10560
-0.19543	cg17622952		321946
-0.1955	cg05541460		109873
-0.19558	cg02073224	MEGF6	42570
-0.19569	cg07983363	PCSK6;PCSK6;PCSK6;P CSK6;PCSK6;PCSK6;PC SK6;PCSK6	155143
-0.19582	cg00989315	CDCA7L;CDCA7L;CDCA7 L	20808
-0.19585	cg11634496		218142
-0.19592	cg14887955		276836
-0.19603	cg10345724	C7orf50;C7orf50;C7orf50	196843
-0.1963	cg14002578	GALNT12	259402
-0.19635	cg02670123	ITGA6;ITGA6	54419

OA - RA	Locus	Associated gene	SEQ ID No.
-0.19133	cg09353563	UACA;UACA;UACA	179511
-0.19136	cg20629021	CPT1A;CPT1A	369542
-0.19145	cg07823562	CYTH1;CYTH1	152263
-0.19146	cg23429240	CORO1C	412803
-0.19147	cg03320743		67233
-0.19215	cg10407488	ARHGEF12	197843
-0.19222	cg19876649	MYOM1;MYOM1	358154
-0.19233	cg13148151	LIMD1	242630
-0.19234	cg24073770		423219
-0.19257	cg08010094	NXPH2	155586
-0.19262	cg01742357	RAPGEF4;RAPGEF4	35676
-0.19263	cg05957190	CHST11	117447
-0.19286	cg07394266	C9orf71	144374
-0.19326	cg00689612	TIMP2	14559
-0.19327	cg12131324	RPTOR;RPTOR	226898
-0.19329	cg07155381	RPH3AL	139908
-0.1934	cg13189271	JARID2	243319
-0.19379	cg03447908	CLEC3B	69735
-0.1938	cg19185706	LDB3;LDB3;LDB3	346776
-0.19452	cg12744888	MYH15	236621

OA - RA	Locus	Associated gene	SEQ ID No.
-0.19972	cg24536145	SORBS2	430636
-0.19978	cg16875057	STK39	309942
-0.20006	cg01698392	TIMP2	34835
-0.2003	cg12251803	LRRFIP1;LRRFIP1;LRRFIP1	228847
-0.20035	cg21007971	PLA2G6;BAIAP2L2;PLA2G6	375427
-0.20045	cg04142824	ATP11A;ATP11A	83262
-0.20048	cg00435616	C7orf50;C7orf50;C7orf50	9208
-0.20064	cg04094923		82221
-0.20076	cg13496793	ZBTB34	249014
-0.20101	cg23659250	BRD1;LOC90834	416462
-0.20138	cg15690822	RFFL;RFFL	289648
-0.2019	cg02019508	ATF7;ATF7;ATF7	41425
-0.20196	cg08577298		165938
-0.20213	cg25238480	GALNTL4	442087
-0.20221	cg12294678	NOS3	229476
-0.20232	cg21881338	AACS	388735
-0.2025	cg24901662	PARD3	436800
-0.20251	cg11407540	EGF	214668
-0.20269	cg07069839		138124

OA - RA	Locus	Associated gene	SEQ ID No.
-0.19673	cg12056017	ANKRD44	225506
-0.19679	cg03462604	C2orf18	70013
-0.1968	cg02800733	CD320;CD320	57003
-0.19696	cg18835549	TRIM40	341642
-0.19701	cg08079387	LOC90834;BRD1	156793
-0.19706	cg22251117	RPH3AL	394137
-0.19709	cg02382878		48672
-0.1974	cg14710529	ASAP2;ASAP2	273872
-0.19767	cg01891925	BTC	38772
-0.19768	cg20439101	MAP3K1	366753
-0.19769	cg06709178	INPP5B	130792
-0.19814	cg07573020	ANKH	147681
-0.19821	cg08373573	MUC6	162363
-0.19832	cg27396760	CMIP;CMIP	477898
-0.19891	cg05796178	LZTS1	114384
-0.19909	cg25345520		443680
-0.19912	cg21562035	KANK2;KANK2	383932
-0.19945	cg06136573		120675
-0.19954	cg18756557	LOC100292680	340244
-0.19966	cg06049177	GSR	119151

OA - RA	Locus	Associated gene	SEQ ID No.
-0.20638	cg25266816		442457
-0.20669	cg15984712		294427
-0.2068	cg08124461	CGNL1	157691
-0.20692	cg12555652	ITGBL1	233545
-0.20701	cg06707286	PCSK6;PCSK6;PCSK6;P CSK6;PCSK6;PCSK6;PC SK6;PCSK6	130749
-0.20713	cg12758625	RNF24;RNF24;RNF24	236809
-0.20719	cg16241878	FRMD5	298677
-0.20733	cg06389019	SLC9A3R1	124935
-0.20737	cg02803847	BUB3;BUB3	57065
-0.20737	cg07376547		144035
-0.20746	cg20625588	MUC6	369496
-0.20756	cg05415840	ARC;ARC	107735
-0.2077	cg00311751	TRERF1	6568
-0.20775	cg02465887	DCHS2	50200
-0.20799	cg02392737	ADCY9	48895
-0.20804	cg13043815	C21orf63	241083
-0.20812	cg06232466	CACNA1H;CACNA1H	122343
-0.20827	cg08490246		164404
-0.20838	cg05964487		117593

OA - RA	Locus	Associated gene	SEQ ID No.
-0.20308	cg21931263		389515
-0.20316	cg11561301	C4orf6	216983
-0.20337	cg07795513	ATF6	151706
-0.20362	cg04589673		91937
-0.20374	cg06418113	RNF165	125411
-0.20385	cg01471802	TRIM6- TRIM34;TRIM6;TRIM6	30616
-0.20416	cg15884713	NINJ2	292821
-0.2046	cg22043118	TMED7- TICAM2;TICAM2;TMED7- TICAM2	391069
-0.20502	cg07593326	PCCA;PCCA	148106
-0.20504	cg12800012	SH3PXD2A	237419
-0.20507	cg04667640	ZFHX3;ZFHX3	93314
-0.20511	cg00527307		11212
-0.2055	cg13300630	ROBO1;ROBO1;ROBO1; ROBO1	245107
-0.20558	cg25888386		452027
-0.2057	cg03571277	ACCN1	72232
-0.20574	cg19660729	KIF26A	354335
-0.206	cg13689563	ZNF136	253055
-0.20627	cg27585074	CSNK1G2	481080

OA - RA	Locus	Associated gene	SEQ ID No.
-0.21292	cg26295272	FLNB;FLNB;FLNB;FLNB	458803
-0.21314	cg05450916	TGFBR2;TGFBR2	108229
-0.21317	cg04893454		97666
-0.21341	cg22219255		393632
-0.21349	cg23198558	ARHGAP26;ARHGAP26	408866
-0.21367	cg19353947	ZEB2;ZEB2;ZEB2	349264
-0.21373	cg04208996		84534
-0.2138	cg02534659		51624
-0.21385	cg04266607	JAZF1	85718
-0.21392	cg07042532	CREB5;CREB5;CREB5	137576
-0.21393	cg09130535	ADRBK1	175551
-0.21397	cg24919468		437059
-0.21428	cg00058644		1391
-0.2144	cg06127541	RRAS2;RRAS2	120526
-0.21446	cg16497661	CKB	303238
-0.21492	cg02712587	EIF2AK4	55252
-0.21494	cg00232092	FBXL18	4975
-0.21509	cg13679772	FOXN3	252820
-0.21555	cg01915822	ADCK5	39234
-0.21558	cg11460562	TNPO1;TNPO1	215482

OA - RA	Locus	Associated gene	SEQ ID No.
-0.20854	cg15891850	KLF12	292938
-0.20874	cg20218678	FAM10A4	363445
-0.20882	cg01569709		32505
-0.20902	cg15044010	SRPK2;SRPK2	279419
-0.20915	cg10269431	EGF	195527
-0.20964	cg01064758	TG;SLA;SLA	22444
-0.21022	cg12597325	STX2;STX2	234249
-0.21045	cg20263733	ATP2C1;ATP2C1;ATP2C1;ATP2C1	364115
-0.21084	cg02872914	CTBP2;CTBP2;CTBP2	58381
-0.21116	cg14153069	PHYHD1;PHYHD1;PHYHD1;PHYHD1	262529
-0.21127	cg21617357	HTATIP2;HTATIP2;HTATIP2;HTATIP2	384851
-0.2114	cg23723013	KCNAB1;KCNAB1;KCNAB1	417619
-0.21172	cg02497428	METTL9;GSF6;METTL9	50892
-0.2118	cg12018521	TES	224833
-0.21202	cg02773403	ANK3	56524
-0.21204	cg00765737	COL4A2	16178
-0.21216	cg06432487		125644
-0.21225	cg13447820		247908
-0.21276	cg04470324	FSTL4	89614

OA - RA	Locus	Associated gene	SEQ ID No.
-0.21999	cg18129282		330053
-0.22012	cg26325949	SYNPO2;SYNPO2;SYNP O2	459352
-0.22027	cg07091154	SHANK2	138518
-0.22031	cg27584112		481064
-0.22034	cg20203400	TMEM182	363230
-0.22065	cg14125542	FAM49A	262013
-0.22071	cg00380924	RPS6KA2;RPS6KA2	8060
-0.22081	cg18887296	PPFIA3	342507
-0.22107	cg17858500	C20orf27	325500
-0.22142	cg04974647		99207
-0.22165	cg20334115	PYCR2	365215
-0.22175	cg16523645	ITPK1;ITPK1;ITPK1	303721
-0.22212	cg12525096		233069
-0.22213	cg20131219	PHLDB2;PHLDB2;PHLDB 2;PHLDB2	362199
-0.22244	cg21750426	MIRLET7C;C21orf34;C21 orf34;MIR99A	386667
-0.22263	cg17918796		326430
-0.22269	cg14165772		262803
-0.22294	cg14081251	ST6GALNAC4;ST6GALN AC4	261114
-0.22318	cg01824625	EPHA3;EPHA3	37465

OA - RA	Locus	Associated gene	SEQ ID No.
-0.21561	cg14375985	CTBP2;CTBP2;CTBP2	267187
-0.21562	cg04267284	PYGB	85734
-0.21585	cg19093405	CACNA2D3	345515
-0.21621	cg02668218		54387
-0.21671	cg25286715		442752
-0.21697	cg14772660	SLC5A7	274806
-0.21707	cg01495332	GRB10;GRB10;GRB10	31016
-0.21758	cg00446697	HCCA2	9405
-0.21821	cg03844838	DIP2C	77475
-0.21834	cg25799348	FOXK1	450816
-0.21849	cg08702689	PRRX1;PRRX1	168159
-0.21863	cg13495373	CREB5;CREB5;CREB5	248982
-0.21887	cg11165960		210588
-0.21906	cg24721647	ACSL1	433758
-0.21922	cg15380511		284521
-0.21944	cg07739826	OSBP	150749
-0.21962	cg18780243	EEF1DP3	340687
-0.21966	cg13289202	ABTB2	244906
-0.21972	cg00684423	GPER;C7orf50;C7orf50;G PER;C7orf50	14439
-0.21994	cg06013113	RAB40C	118547

OA - RA	Locus	Associated gene	SEQ ID No.
		REM;CREM;CREM;CREM;CREM	
-0.22674	cg15853771		292370
-0.22677	cg05242915		104329
-0.22727	cg09264140	FMNL1	177950
-0.22741	cg24977338	RGPD8;RGPD5	437964
-0.22749	cg27469810	CETN1	479043
-0.22788	cg00653025		13831
-0.22788	cg05285759	TBCK;TBCK;TBCK;TBCK	105125
-0.22818	cg12642431	UACA;UACA	235055
-0.22826	cg09169413	P11	176276
-0.22856	cg23079012		407020
-0.2289	cg23904501	PTPRS;PTPRS;PTPRS;PTPRS	420216
-0.22901	cg07631435	ZBTB16;ZBTB16	148813
-0.22976	cg13752933	DAPK1	254331
-0.22984	cg19173502	MIRLET7C;C21orf34;C21orf34	346603
-0.22995	cg21502482	SPATA7;SPATA7	382912
-0.22997	cg03144446		63874
-0.23001	cg01164141		24508
-0.23003	cg27314273	PTPRG	476489

OA - RA	Locus	Associated gene	SEQ ID No.
-0.22327	cg20080845	BRD1;LOC90834	361454
-0.2235	cg15016481	LRRFIP1;LRRFIP1;LRRFP1 P1;LRRFIP1;LRRFIP1	278955
-0.22429	cg04112058	SHCBP1	82595
-0.22434	cg17879450	MACF1	325874
-0.2244	cg12399224	ZBTB46	230928
-0.22443	cg22909677	ARMC2	404123
-0.22448	cg25874123	MYOM1;MYOM1	451828
-0.22451	cg18720326	ADAMTS2;ADAMTS2	339675
-0.2246	cg16230121	APBB1;APBB1	298473
-0.22463	cg21848191	RAD51L1;RAD51L1;RAD 51L1	388170
-0.22463	cg19026231	GALK1	344545
-0.22483	cg07080231		138324
-0.22528	cg17531430	BIN1;BIN1;BIN1;BIN1;BIN 1;BIN1;BIN1;BIN1;BIN1;B IN1	320696
-0.22531	cg07807373		151942
-0.22568	cg09038971	CHST11	174071
-0.22576	cg16624521		305662
-0.22583	cg10031769	CREM;CREM;CREM;CRE M;CREM;CREM;CREM;C REM;CREM;CREM;CRE M;CREM;CREM;CREM;C	191189

OA - RA	Locus	Associated gene	SEQ ID No.
-0.23315	cg26983411		470886
-0.23331	cg01417625	LAMC2;LAMC2	29483
-0.23345	cg06112923	STEAP2;STEAP2;STEAP2	120290
-0.23386	cg22416916	SLC22A1;SLC22A1	396454
-0.23403	cg10492417	FANCA	199244
-0.23409	cg02540833	SHANK2	51760
-0.2342	cg09329079	TMEM184A	179139
-0.23446	cg08135718	CUX1;CUX1;CUX1	157939
-0.23468	cg20724690	CAB39;CAB39;CAB39	371287
-0.23494	cg20192387	RPS6KA2;RPS6KA2	363087
-0.23519	cg09169739	GFPT2	176289
-0.23558	cg22396663	MAD1L1;MAD1L1;MAD1L1	396208
-0.23597	cg02923628		59493
-0.23632	cg03109660	RELL1;RELL1	63223
-0.23648	cg06562964	RELL1;RELL1	128035
-0.23857	cg17133045	AKT3;AKT3	313972
-0.23937	cg03606098	NADK	72963
-0.23938	cg18771195	RPH3AL	340542
-0.23963	cg10013121	TRERF1	190859

OA - RA	Locus	Associated gene	SEQ ID No.
-0.23018	cg13879937	EHD4	256817
-0.23035	cg11168687	ACSL1	210627
-0.23037	cg22905866		404070
-0.23047	cg19788250	APP;APP;APP;APP;APP	356630
-0.23055	cg19478371	PPP2R5C;PPP2R5C;PPP2R5C;PPP2R5C	351294
-0.23081	cg08153404		158265
-0.23098	cg11945474		223676
-0.23103	cg07470830		145712
-0.23116	cg09537792	ANKRD11	182760
-0.23122	cg17880118	COL4A1	325886
-0.2315	cg07468585		145653
-0.23177	cg00108038	LOC100292680	2509
-0.23183	cg23560676	NSMCE2	414881
-0.23213	cg11063877	LARP4;LARP4;LARP4;LARP4;LARP4;LARP4	208898
-0.23228	cg19735406	COL4A2	355626
-0.23258	cg09259797		177870
-0.23286	cg05314142	SLC22A1;SLC22A1	105694
-0.23299	cg06519061	PTPN14	127144

OA - RA	Locus	Associated gene	SEQ ID No.
-0.24502	cg00026412	ANK3	645
-0.24505	cg25089903	NINJ2	439753
-0.24567	cg23708624	CCDC146;FGL2	417387
-0.24585	cg25838968	PLXNA2	451397
-0.24656	cg02724461	GALNS	55487
-0.24687	cg23669855	LYSMD4	416659
-0.24737	cg19547694	BRD1;LOC90834	352451
-0.24757	cg13962170		258544
-0.24861	cg17798857	UACA;UACA	324425
-0.24871	cg09741789	FBN1	186193
-0.24879	cg04721825	PRKCA	94264
-0.24908	cg01556677	SEMA3C	32186
-0.24945	cg19450056		350853
-0.24949	cg25141441	RORA;RORA;RORA;RORA A	440625
-0.24973	cg04265492	BAI2	85697
-0.25006	cg03870329		77949
-0.25077	cg25206802	SACS	441606
-0.25093	cg25483191	TRIM55;TRIM55;TRIM55; TRIM55	445943
-0.25124	cg08535361	NTN4	165209

OA - RA	Locus	Associated gene	SEQ ID No.
-0.23979	cg02781060		56673
-0.23996	cg22117968		392140
-0.2401	cg11520719	ARID1B;ARID1B;ARID1B	216320
-0.24011	cg04126956	TRAPPC9;TRAPPC9	82912
-0.24087	cg01312265	TCERG1L	27436
-0.24102	cg09873409	PLXNA4;PLXNA4	188543
-0.24159	cg00089451		2073
-0.24161	cg27446233	PFKM;PFKM;PFKM;PFK M;PFKM	478685
-0.24161	cg07251141	ADAM12;ADAM12	141811
-0.24173	cg02773698	FCHSD2	56533
-0.2419	cg11028872		208387
-0.24214	cg06865642	BRD1;LOC90834	134034
-0.24269	cg18000216	ERC2	327710
-0.24279	cg14558716	ATF1	270966
-0.24303	cg06165742	FOXP2;FOXP2;FOXP2	121155
-0.24317	cg07491828	MKL2	146139
-0.24321	cg05495611	EXT2;EXT2	109044
-0.24432	cg00264129	HBEGF	5659
-0.24487	cg20539449		368227
-0.24494	cg07877629		153192

OA - RA	Locus	Associated gene	SEQ ID No.
-0.2568	cg14457429		268785
-0.25731	cg16834726	DCTN2	309390
-0.25741	cg14523881	VASH2;VASH2;VASH2	270202
-0.25788	cg05208056	NCK2;NCK2;NCK2	103597
-0.25817	cg07525751	SLC6A3	146753
-0.25823	cg03855388	CPT1A;CPT1A	77697
-0.25832	cg22308453	DPYSL2	394900
-0.25865	cg07911905	CHST11	153817
-0.25865	cg05196076	FBXO31;FBXO31	103393
-0.25949	cg18371976	TRERF1	334048
-0.25957	cg16878214	PLEKHF2	309991
-0.25958	cg20655877		369984
-0.26099	cg21197233	ARHGAP20	378484
-0.26155	cg15568998	AGMAT	287517
-0.26178	cg27511861		479747
-0.26219	cg12564175	ESCO2;CCDC25	233667
-0.26237	cg16090790		296212
-0.2632	cg12552626	CCDC146;FGL2	233502
-0.26416	cg11072779	ANXA4	209068
-0.26569	cg22352504	HAS1	395515

OA - RA	Locus	Associated gene	SEQ ID No.
-0.25143	cg04425710	ESCO2;CCDC25	88827
-0.25168	cg08464954		163934
-0.25182	cg13661832		252443
-0.25199	cg10259111	GNG2	195382
-0.25214	cg24331722		427189
-0.25249	cg26529437	ITGB8	462893
-0.25283	cg25706447	PIGV	449350
-0.25296	cg26131670	SLC4A4;SLC4A4	455944
-0.25313	cg11274148	RPTOR;RPTOR	212468
-0.25324	cg14571004	GALNT12	271226
-0.25333	cg26306638	HBEGF	459010
-0.25362	cg08412699	ITGB8	162975
-0.25409	cg12208381	CSNK1G2	228165
-0.25453	cg11611676		217803
-0.25457	cg13665060		252509
-0.25472	cg16784943	ITPK1;ITPK1;ITPK1	308597
-0.25501	cg24534767		430608
-0.25576	cg03778207	ME3;ME3;ME3	76334
-0.25579	cg09088836		174888
-0.25665	cg26543192		463160

OA - RA	Locus	Associated gene	SEQ ID No.
-0.27391	cg12619262		234658
-0.27459	cg26551026	CABLES1;CABLES1	463331
-0.27512	cg03078520	MICAL3;MICAL3;MICAL3	62698
-0.27559	cg19295451	PCSK6;PCSK6;PCSK6;P CSK6;PCSK6;PCSK6;PC SK6;PCSK6	348451
-0.2759	cg01359165		28268
-0.27611	cg03389789	FBXW8;FBXW8	68597
-0.27642	cg27199697	DLX3	474550
-0.27828	cg19995595	ITPK1;ITPK1;ITPK1	360131
-0.2796	cg19600494		353349
-0.28011	cg22801134	PRICKLE2	402255
-0.28065	cg20140333		362329
-0.28088	cg00101350	MGAT3;MGAT3	2375
-0.28176	cg10784341	PHACTR2;PHACTR2	204295
-0.28206	cg233338380	CUX1;CUX1;CUX1	411370
-0.28216	cg22122925	ERRF1	392216
-0.28241	cg06235645	SEMA6D;SEMA6D;SEMA 6D;SEMA6D;SEMA6D;SE MA6D	122412
-0.28268	cg16474725	CLIC5;CLIC5	302879
-0.28421	cg14054582		260566

OA - RA	Locus	Associated gene	SEQ ID No.
-0.26608	cg07263759		142020
-0.26615	cg18022344	METTL9;IGSF6;METTL9	328111
-0.2662	cg24033633		422524
-0.26675	cg05310185	TACC2;TACC2;TACC2;T ACC2	105623
-0.26683	cg02606505	NKTR	53079
-0.26684	cg05899338	ZNF239;ZNF239;ZNF239	116275
-0.26725	cg06385757	PRKAR1B;PRKAR1B;PR KAR1B;PRKAR1B;PRKA R1B;PRKAR1B	124893
-0.26763	cg14178899	ERRF1	263095
-0.2679	cg03372385	LRRC16A	68299
-0.26797	cg25072766	CARS;CARS;CARS;CAR S	439518
-0.26865	cg20608783	BAI2	369275
-0.26917	cg07776993	ADCK5	151365
-0.27071	cg01295631		27066
-0.27154	cg06836480	DHRS9;DHRS9;DHRS9	133449
-0.27159	cg01957599	FAM13AOS	40119
-0.2728	cg17478992	SLC12A8	319759
-0.27286	cg12884466	MRPL3	238716
-0.27379	cg13200640		243476

OA - RA	Locus	Associated gene	SEQ ID No.
-0.29814	cg14334389	SPARCL1;SPARCL1	266428
-0.29818	cg04304338	ANKRD33B	86451
-0.29932	cg02847703	BTC	57849
-0.30181	cg23155767	GPR1;GPR1	408172
-0.30344	cg09819635	KHDRBS3	187501
-0.30363	cg25131079	ADAMTS2;ADAMTS2	440427
-0.30642	cg12754854	PHYHD1;PHYHD1	236759
-0.30675	cg08943696	GPR133	172510
-0.30689	cg03983715	PRMT7	80095
-0.30824	cg09287328		178354
-0.30861	cg03713317	CYFIP1;CYFIP1	74995
-0.31349	cg23666829	TBCD	416590
-0.31884	cg26253868		458047
-0.32034	cg03700279	PREPL;PREPL;PREPL;P REPL;PREPL;PREPL;PR EPL	74742
-0.32126	cg12894142		238844
-0.32278	cg16689609	UTRN	306875
-0.32343	cg12359895	LOC100216001;LOC3385 88	230357
-0.32409	cg19244380	AMBRA1;AMBRA1	347620
-0.32631	cg01928411	LARP4;LARP4;LARP4;LA	39500

OA - RA	Locus	Associated gene	SEQ ID No.
-0.2851	cg19926144	DIP2C	359006
-0.28525	cg26214026	ATXN2	457353
-0.28725	cg18030133	PHACTR2;PHACTR2;PH ACTR2;PHACTR2	328254
-0.28771	cg22716599	DNM3;DNM3	400952
-0.28822	cg00745735	MYPN	15768
-0.28884	cg02071553	MIR216B	42524
-0.28893	cg01756899		35949
-0.28929	cg05928904		116850
-0.28962	cg01598421	TG	33081
-0.28997	cg02131142	TBC1D9B;TBC1D9B	43723
-0.29156	cg03412557	RUNDC2A	69042
-0.29166	cg17947992		326928
-0.29212	cg00855685	SEMA5A	18020
-0.29231	cg08672203	PPAP2A;PPAP2A	167602
-0.29315	cg17613911	STK32A	321844
-0.29506	cg23666374	AUTS2;AUTS2;AUTS2	416583
-0.29533	cg16666745	GALNT10	306478
-0.2964	cg26826631	CD55;CD55	468043
-0.29748	cg17919396	ALDH1A3	326446
-0.29758	cg01574912		32628

OA - RA	Locus	Associated gene	SEQ ID No.
-0.41512	cg20071744	TRAPPC9;TRAPPC9	361314
-0.43386	cg15853299	TBCD	292363

OA - RA	Locus	Associated gene	SEQ ID No.
		RP4;LARP4;LARP4;LARP4	
-0.32706	cg25254949		442307
-0.32836	cg23159678	NOVA1;NOVA1;NOVA1	408237
-0.33031	cg11520439	LOC286367	216313
-0.33087	cg11937508	GPR1;GPR1	223523
-0.33212	cg12205433	TES;TES	228120
-0.33433	cg18901940	MYPN;MYPN	342719
-0.34043	cg10362527	GPR1;GPR1	197111
-0.34108	cg14570632	RXRA	271222
-0.34414	cg03361973	SEMA6D;SEMA6D;SEMA6D;SEMA6D;SEMA6D	68105
-0.34417	cg05073720	PHLPP1	101171
-0.34459	cg16087541	TES;TES	296173
-0.34847	cg09835421	PRMT7	187811
-0.34934	cg21161187	SLC6A3	377787
-0.35195	cg02666566		54356
-0.35418	cg18262591	CPT1A;CPT1A	332336
-0.37588	cg16808481	TES;TES	309027
-0.38211	cg14604584		271938
-0.40768	cg05110241	PRMT7	101782

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
-0.435	PDHA2	4:96760945	cg10590622	201120
-0.433	CNTNAP5	2:124971544	cg01013522	21327
-0.432	COLEC11	2:3675155	cg10724632	203346
-0.432	RD3	1:211667751	cg22481673	397284
-0.424	RBM28	7:127950724	cg03119308	63402
-0.423		13:21896301	cg13730219	253914
-0.423		8:142283564	cg04123498	82844
-0.421	MYOCD	17:12562530	cg14192979	263428
-0.421	SLFN12	17:33734664	cg20086657	361521
-0.417		2:150845309	cg15958422	293993
-0.409	IFT43;TGFB3	14:76443578	cg21193926	378403
-0.405	FAM101A;NCOR2;ZNF664-FAM101A	12:124810173	cg13127920	242348
-0.403	SLC2A9	4:10009916	cg21795255	387383
-0.403	ATXN7L1	7:105306555	cg11957130	223895
-0.403	TRIM64C	11:49073835	cg06445586	125882
-0.400	HLA-A	6:29906977	cg26739327	466540
-0.394	SCN4B	11:118022607	cg22251955	394153
-0.392	LINC00254	16:1939295	cg10051493	191486

TABLE 8

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
-0.603	LIMS1	2:109251064	cg10879348	205889
-0.603		15:97311928	cg04875706	97278
-0.572		17:35161825	cg11331837	213402
-0.563	ACOT11	1:55014160	cg01802772	36934
-0.552	GNAS	20:57463991	cg09885502	188727
-0.527		11:28642652	cg26387458	460494
-0.511	HDAC11	3:13555664	cg26845082	468403
-0.506		3:22422855	cg20979384	374956
-0.484		1:204556835	cg13232075	244024
-0.478	AP2A2	11:1001560	cg16999994	311801
-0.463	ALS2CR12	2:202163482	cg07227024	141394
-0.463		4:82273176	cg07454933	145378
-0.456	CPO	2:207803547	cg17600943	321671
-0.455	FAM19A5	22:48896579	cg11019791	208228
-0.452	FHIT	3:60420416	cg16140565	297019
-0.443		6:75775380	cg15706692	289960
-0.439	ATP11A	13:113539522	cg21463262	382273

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
-0.349	MAST2	1:46420220	cg22337626	395319
-0.346	KIAA1908;PSMG3	7:1616229	cg23403836	412403
-0.346	SUMO3;UBE2G2	21:46220161	cg00272795	5810
-0.337	OR10K1	1:158435277	cg01463139	30452
-0.337	SLCO2B1	11:74861433	cg20704148	370892
-0.329	SPATS2L	2:201289756	cg17174466	314712
-0.327	SFT2D3;WD R33	2:128453335	cg03738707	75556
-0.325	HLA-DRB1	6:32555411	cg00598125	12786
-0.323	CCHCR1;PSORS1C2	6:31107186	cg07414487	144678
-0.322	HLA-A	6:29913343	cg19585676	353041
-0.320	LOC100628307	14:80858152	cg07572984	147668
-0.318	PSORS1C3	6:31148606	cg01982166	40677
-0.313	PTGER3;ZRBANB2-AS1	1:71511514	cg11418303	214891
-0.313		10:131209556	cg02372404	48486
-0.310		7:158750985	cg00413089	8734
-0.307	HCG4B	6:29894152	cg25644740	448500
-0.305		2:5605864	cg23233416	409551

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
-0.391	MIR4457;TE RT	5:1300309	cg14597862	271789
-0.390		14:22279816	cg16423096	302000
-0.384	RPL27A;SNORA3;SNORA45;ST5	11:8714324	cg15828613	291887
-0.382	MXRA7	17:74679597	cg03810198	76895
-0.378	CD82	11:44649802	cg21974656	390131
-0.377	BPIFA2	20:31755943	cg05840533	115130
-0.377	CCDC109B	4:110524473	cg17082366	313142
-0.375	TRIM24	7:138229989	cg12743416	236587
-0.374	RPTOR	17:78935070	cg17906851	326284
-0.371	KDM2B	12:121893769	cg07741840	150784
-0.370	HCG4B	6:29895204	cg26121931	455779
-0.369	NSMCE4A	10:123731471	cg19360212	349382
-0.369	NMNAT3	3:139397901	cg15295200	283344
-0.366		12:25454990	cg25134647	440489
-0.365		6:55778951	cg11290949	212735
-0.361	MRPL23	11:1985287	cg06258939	122771
-0.351		4:8569129	cg06991380	136538
-0.350	CDH4;MIR1257	20:60520624	cg16423285	302003

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
-0.279		13:27077539	cg03531388	71371
-0.278	CASP7	10:115465924	cg01128042	23762
-0.278	HCG4B	6:29895260	cg24838316	435648
-0.278		2:69440951	cg024444957	49778
-0.277	OR51A2;OR51A4	11:4976263	cg25641451	448448
-0.274	FRMD4A	10:13972210	cg07629776	148782
-0.274		22:25571929	cg19707653	355076
-0.272	ATHL1;NLRP6	11:285037	cg22280068	394534
-0.269	SORBS2	4:186549051	cg09120722	175360
-0.267		11:5384517	cg26567385	463630
-0.265	MRPL44;WDY1	2:224813276	cg15176306	281664
-0.265		19:29218101	cg04546413	91043
-0.264		10:47964834	cg16435686	302231
-0.264		7:158750244	cg12954512	239779
-0.263		16:14380714	cg03940883	79274
-0.262	B4GALT6	18:29205358	cg11986743	224388
-0.261	FBRSL1	12:133078117	cg23836570	419138
-0.259	LOC440905	2:130795582	cg18480627	335932

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
-0.305	SLC47A2	17:19620263	cg08102564	157230
-0.302	SYS1;SYS1-DBNDD2;TP53TG5	20:44007674	cg17811452	324650
-0.301	COL4A2	13:111115558	cg07618759	148582
-0.300	CDC48;EPHA10	1:38180356	cg06437931	125736
-0.300	RPTOR	17:78809403	cg20502501	367732
-0.299	NDRG4	16:58534681	cg00758881	16033
-0.296	ITIH1;ITIH3	3:52828628	cg05393861	107345
-0.296	DPM2;FAM102A	9:130705120	cg01681863	34567
-0.295	TTC34	1:2710376	cg21783012	387180
-0.292	HCG4B	6:29895175	cg23681866	416899
-0.290	HCG4B	6:29895187	cg15411272	285048
-0.288	PSMD9;WDR66	12:122356390	cg21171335	377993
-0.286	BOC	3:112927486	cg27187580	474373
-0.286	MCF2L	13:113688132	cg15388766	284663
-0.285	B4GALNT4	11:364752	cg25497175	446150
-0.283		8:92570895	cg11420142	214927
-0.281		7:158751184	cg12744031	236605

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
-0.238	RNF213	17:78264297	cg11606607	217718
-0.237	TMEM39B	1:32535981	cg10312513	196231
-0.234	LPIN1	2:11888753	cg00523161	11124
-0.234	SGK110	19:56061334	cg18795732	340965
-0.232	LOC154822; VIPR2	7:158821175	cg25909532	452273
-0.231		7:158750384	cg11945929	223689
-0.229		1:161410551	cg22730047	401169
-0.228	PLEC	8:145003776	cg18000391	327713
-0.227		17:80849463	cg14195178	263473
-0.226	HOXA3;HOX A4;LOC1001 33311	7:27170394	cg19142026	346203
-0.225		6:16962712	cg19300401	348504
-0.225	FAM66A	8:12237626	cg10206627	194443
-0.223	HTATIP2	11:20384377	cg26155681	456393
-0.221	AP2A2	11:970389	cg12893697	238836
-0.220	COL4A2	13:1111111172	cg19218082	347212
-0.218	PAPLN	14:73712902	cg14834903	275901
-0.218	OSBPL5	11:3174092	cg06120313	120406
-0.217	C1orf86;PRK CZ	1:2120985	cg20300514	364680

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
-0.257	SLC27A1	19:17600122	cg02707854	55128
-0.257		5:54117761	cg25997988	453719
-0.257	ATOH1	4:94759825	cg05893845	116159
-0.256	LOC1002894 73	20:1757570	cg03299990	66803
-0.252	COL18A1	21:46921982	cg05638648	111601
-0.251		7:1923695	cg12169700	227539
-0.250	C1orf86;PRK CZ	1:2121039	cg26227225	457598
-0.248		5:31106255	cg12908908	239081
-0.247	FAM157B	9:141105974	cg04824555	96218
-0.247		7:1976457	cg03075889	62651
-0.246	SLC6A3	5:1420305	cg07664579	149363
-0.245	ADAMTS2	5:178565001	cg01387905	28837
-0.243		7:136832262	cg05364766	106693
-0.241		19:13276344	cg19225953	347327
-0.241	PSMD9;WDR 66	12:122356400	cg22618164	399325
-0.239		4:9479622	cg01394167	28957
-0.239		12:125411922	cg07877257	153188
-0.238		7:158750607	cg00815399	17228

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
-0.205		10:43522343	cg08461752	163848
-0.205	LASP1	17:37024042	cg20826740	372827
-0.204	NSUN4	1:46807113	cg17806798	324558
-0.204		1:149145082	cg16661522	306375
-0.204	PTP4A3	8:142427117	cg04687040	93680
-0.204		5:92414398	cg18783429	340738
-0.203	FLJ37453	1:16154831	cg21385522	381217
-0.203		12:132869069	cg05948955	117271
-0.202	RADIL	7:4854126	cg08799816	169789
-0.202		1:34615965	cg21440084	381930
-0.201	ARHGEF40;C 14orf176;ZNF 219	14:21567333	cg00968545	20358
-0.200		7:1948755	cg16178271	297641
-0.199	TNS1	2:218707806	cg17588704	321484
-0.198	HLA-C	6:31241294	cg05338672	106118
-0.197	SLC27A1	19:17599784	cg17132030	313955
-0.196		11:19699299	cg18593660	337773
-0.196		16:1797050	cg07869343	153029
-0.195	GAS2L2;RAS L10B	17:34067305	cg23633026	415965

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
-0.217		7:1367727	cg23896876	420086
-0.216	EGLN2;MIA- RAB4B;RAB4 B;RAB4B- EGLN2	19:41307778	cg21653913	385460
-0.216		13:80755568	cg00750481	15862
-0.216		5:176099987	cg11583351	217324
-0.215		5:125171542	cg12599971	234303
-0.215	MYO1D	17:31149877	cg01050010	22131
-0.213	DPYSL4;JAK MIP3	10:134001728	cg10144198	193247
-0.213		19:21863715	cg26562263	463546
-0.213	NDRG4	16:58533979	cg27113419	473118
-0.212	BMP4	14:54410717	cg16720578	307533
-0.210		5:134388224	cg03827835	77177
-0.209	C1orf86;PRK CZ	1:2121349	cg05337761	106096
-0.209	SFT2D3;WD R33	2:128453445	cg11059159	208817
-0.208	APOA1;APO C3;SIK3	11:116708413	cg09558982	183152
-0.207	SFT2D3;WD R33	2:128453484	cg25277809	442618
-0.206		7:158750417	cg10079374	191993

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
	55			
-0.185	SLC9A3	5:502291	cg14137381	262235
-0.184	CLDN22;CLD N24;WWC2	4:184250312	cg14241748	264522
-0.184	MMD2	7:5000111	cg02276823	46453
-0.184	COL5A1	9:137691430	cg13889467	257004
-0.184		6:30000187	cg01915885	39235
-0.184	SLC47A2	17:19627822	cg12434897	231546
-0.183	KRTAP4-7	17:39240789	cg23827950	418999
-0.182		19:29218302	cg12756686	236783
-0.182	GAB2	11:78052863	cg24769381	434565
-0.182		13:33854227	cg15405588	284964
-0.182		13:112978703	cg19891452	358388
-0.180	C11orf53	11:1111148753	cg27649396	482130
-0.179		19:29218774	cg03161606	64225
-0.178	ADAP1;COX1 ₉	7:1003645	cg08735705	168762
-0.178	MTG1;PAOX	10:135202877	cg06080948	119697
-0.177	NEUROG3	10:71339632	cg02330874	47587
-0.177	C10orf96	10:118084587	cg02721176	55417
-0.177	BAI1	8:143546858	cg02048922	41986

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
-0.195		7:158790006	cg09640425	184513
-0.195	LRR27	10:134150581	cg25076597	439582
-0.194	LOC440905	2:130795350	cg25180228	441163
-0.194	ZC3H12D	6:149785754	cg24131442	424218
-0.193	CES1	16:55867072	cg03744383	75666
-0.193	ACSF3	16:89152443	cg00324979	6844
-0.192		16:56000067	cg00991179	20841
-0.192	AP2A2	11:970664	cg06064525	119407
-0.192	CHTOP;S100 A1;S100A13	1:153599704	cg11343894	213623
-0.190	DBNL;PGAM 2;POLM	7:44104860	cg07075347	138233
-0.189	MYO10	5:16895511	cg02288345	46701
-0.189		19:29218262	cg14983838	278359
-0.189	EIF2D	1:206786180	cg21936179	389599
-0.189	FN3K;TBCD	17:80708632	cg02398342	49038
-0.188	TM7SF4	8:105342491	cg04554929	91221
-0.187	NXN	17:707141	cg20403644	366219
-0.187	NFATC1	18:77292443	cg06675417	130167
-0.186	KIAA1751	1:1886501	cg06090818	119880
-0.185	LOC1005070	12:133180238	cg26621607	464484

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
	N1L			
-0.170	ADAMTS7	15:79107452	cg23450377	413109
-0.170	PCSK6	15:101932559	cg27370471	477437
-0.170		19:1737123	cg08692111	167944
-0.170	C5orf38;IRX2	5:2743124	cg18803147	341088
-0.169	BAI1	8:143581481	cg26953288	470357
-0.169	STK32B	4:5374425	cg14422932	268145
-0.168		X:152584950	cg03201165	64963
-0.168	POU5F1;PS ORS1C3	6:31146845	cg20073472	361344
-0.168	NDRG4	16:58534708	cg04484415	89876
-0.168	FAM20C	7:194798	cg12042135	225245
-0.167	EDN1	6:12292676	cg27565517	480713
-0.167	C1QTNF8	16:1152511	cg06394109	125022
-0.167	KLK5;KLK6	19:51456308	cg00768359	16234
-0.166	ADAP1	7:961457	cg06589239	128495
-0.166		11:134892703	cg21757617	386803
-0.166	HOXA3;HOX A4;HOXA5;L OC10013331 1	7:27170892	cg14359292	266882

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
-0.176		8:119750651	cg26711508	466113
-0.176	GPR50	X:150351493	cg20071203	361302
-0.175	LARS2	3:45429626	cg13510812	249280
-0.175	TUBG2	17:40808068	cg24417155	428624
-0.175	OR12D2	6:29364799	cg25786333	450628
-0.174	RASA3	13:114872606	cg27086157	472626
-0.174	C21orf128;U MODL1	21:43529162	cg02489157	50718
-0.174	MYT1L	2:2119533	cg26383138	460416
-0.174		10:125751386	cg00502035	10662
-0.174		7:102134668	cg17207545	315260
-0.173	NRG1	8:32579253	cg20127899	362151
-0.173	CHTOP;S100 A1;S100A13	1:153599671	cg13946767	258256
-0.173	APOA1BP;IQ GAP3;TTC24	1:156551787	cg09319828	178942
-0.172	ATP11A	13:113413587	cg08484560	164316
-0.171	NKX2-3	10:101287609	cg10947831	206964
-0.171		5:171057282	cg10881242	205925
-0.171	ADAP1;COX1 9	7:1003710	cg12575883	233841
-0.171	CRAMP1L;H	16:1722957	cg04245870	85306

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
-0.160	ACAP1;KCTD11;TMEM95	17:7253720	cg02676175	54546
-0.160	HAAO	2:43023945	cg14631114	272427
-0.160	WWP2	16:69830414	cg03424554	69244
-0.160	PGRMC2	4:129212177	cg02096220	43042
-0.159	SHISA6	17:11142733	cg23474049	413465
-0.159		6:28447107	cg12584458	233995
-0.159	ZP2	16:21222939	cg18249108	332126
-0.159	CLCNKA;HS PB7	1:16349079	cg08231696	159747
-0.158	SPINK7	5:147699718	cg08859406	170938
-0.158	GNAS	20:57463503	cg11480267	215775
-0.158	STX2	12:131303247	cg11011512	208090
-0.158	ADCK4	19:41208803	cg07615236	148518
-0.158		6:148540308	cg21796170	387391
-0.158	NDRG4	16:58534157	cg05725404	113149
-0.157	ANXA9;CER S2	1:150954826	cg13320146	245435
-0.157	SAMD3	6:130504413	cg24048806	422810
-0.157	TCL6	14:96129574	cg05093429	101497
-0.157		6:55761410	cg17273096	316241

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
-0.165	LCP1	13:46757415	cg06477663	126420
-0.165	SPAG11A	8:7720259	cg23703303	417310
-0.165		19:21767566	cg19051117	344954
-0.165	OR10R2	1:158450237	cg04132017	83014
-0.165	LOC284661	1:4481995	cg20252997	363933
-0.164	FHOD3	18:34327498	cg21367586	380971
-0.164	PCDHB4	5:140501812	cg06048354	119137
-0.164	HLA-DQB2	6:32729174	cg04418355	88678
-0.164		6:28447087	cg26968378	470632
-0.163	BAI1	8:143580965	cg09544050	182856
-0.163	LOC440905	2:130794753	cg25239986	442097
-0.163	SPINK5	5:147473666	cg04829448	96297
-0.163	ZNF718	4:124342	cg12717203	236185
-0.163	TIAM2	6:155464712	cg24207161	425489
-0.162	PACS2	14:105830721	cg19499452	351610
-0.162	MCTS1	X:119738550	cg00357087	7563
-0.162	RASA3	13:114900021	cg06611532	128857
-0.161		4:187984958	cg19632603	353880
-0.160	ITGA11	15:68713677	cg02454536	49961

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
-0.154	MICA	6:31382027	cg20144487	362399
-0.153		6:156983263	cg052822260	105071
-0.153	MIR1283-1;MIR518B;MIR518F;MIR519B;MIR519C;MIR520A;MIR520B;MIR523;MIR525;MIR526A1;MIR526B	19:54199538	cg26325497	459342
-0.153	MKX	10:28030033	cg13806489	255420
-0.153		10:53639124	cg06976598	136324
-0.153	CHTOP;S100A1;S100A13	1:153600156	cg07898899	153567
-0.152		11:24346161	cg05202300	103488
-0.152	LOC728613	5:1641766	cg08769156	169313
-0.152	LOC100506388;RPH3AL	17:184106	cg15996459	294655
-0.151	PALMD	1:100111849	cg24603803	431699
-0.151	HCG4B	6:29895116	cg15671450	289296
-0.151		8:88760082	cg05893029	116145
-0.150	GPR158	10:25620462	cg01006048	21182
-0.150		14:95155784	cg16462006	302671

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
-0.156	B3GNTL1	17:81008971	cg17652174	322327
-0.156	RNF219	13:79234251	cg01819759	37343
-0.156	GGNBP2;MYO19;PIGW	17:34891843	cg02097479	43078
-0.156		7:79964738	cg22110839	392010
-0.156	HOXA3;HOXA4;LOC100133311	7:27170412	cg11410718	214730
-0.155		6:58777827	cg26951520	470325
-0.155	KIRREL3-AS3	11:126872863	cg17273911	316252
-0.155	NRXN1	2:51260399	cg00345522	7288
-0.155		14:106025958	cg27055313	472099
-0.155		4:60001000	cg11281224	212579
-0.154		4:9479947	cg12006118	224679
-0.154	IL12RB1	19:18170383	cg26642774	464790
-0.154		1:22599443	cg07371337	143948
-0.154	ZNF845	19:53828996	cg22256944	394221
-0.154		13:112705636	cg01896130	38843
-0.154	HOTAIR;HOXC12	12:54354590	cg05573844	110417
-0.154		13:61758710	cg15508935	286618

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
-0.147		7:93960063	cg01827933	37531
-0.147	LHX6	9:124983482	cg13832372	255929
-0.147	ISL1	5:50688913	cg26293019	458765
-0.147	DBNL;PGAM2;POLM	7:44105050	cg16627090	305718
-0.147		3:193587490	cg21197336	378486
-0.147		14:107095056	cg07958169	154668
-0.147	SNED1	2:241975140	cg09991306	190473
-0.147	HOXA3;HOXA4;HOXA5;LOC10013331	7:27170755	cg03724423	75252
-0.147	SEPT3;WBP2NL	22:42395067	cg22189786	393238
-0.147		2:208541770	cg03716125	75048
-0.146		5:66541588	cg11553311	216848
-0.146	KTN1;KTN1-AS1	14:56046098	cg16907514	310470
-0.146	FAM116B;PLXNB2	22:50753068	cg20435485	366698
-0.146	HOXA3;HOXA4;LOC10013331	7:27170388	cg07317062	142981
-0.145	HLA-A	6:29911295	cg09535358	182715

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
-0.150	PALM2;PALM2-AKAP2	9:112562314	cg13690280	253070
-0.150	LOC100507055;P2RX2	12:133185615	cg18833933	341613
-0.150	IGF2;IGF2-AS;INS-IGF2;MIR483	11:2154132	cg11717189	219595
-0.149	MYO16	13:109833854	cg10697882	202881
-0.149	SUMO3	21:46239952	cg22595657	398990
-0.149	EME2;MRPS34;NME3;SPSB3	16:1822124	cg09540102	182804
-0.149	TTL10	1:1118157	cg16366262	300931
-0.149		7:158269409	cg17429772	318912
-0.149		12:133003907	cg04741728	94673
-0.148	SHANK2	11:70493931	cg05794931	114366
-0.148	CRTAC1	10:99734513	cg19421526	350393
-0.148	PXDN	2:1734344	cg12760299	236833
-0.148		6:28447115	cg21903646	389050
-0.148	GGNBP1;LINC00336	6:33561099	cg04329454	86936
-0.148	CLGN	4:141317067	cg22901919	403995
-0.147	COL11A2;RXRB	6:33158020	cg16507569	303394

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
-0.143		13:99084682	cg03040740	61905
-0.143		6:284446840	cg01792601	36700
-0.142	LRRC15	3:194091167	cg07048348	137676
-0.142		1:37231474	cg21952052	389839
-0.142	DFNA5	7:24742552	cg25709790	449401
-0.142	PACS2	14:105830606	cg12425861	231390
-0.142	INPP5K;LOC100306951;PI TPNA	17:1412950	cg07185664	140562
-0.141	LOC100506388;RPH3AL	17:184131	cg24871089	436253
-0.141	DDX58	9:32525315	cg14286514	265460
-0.141		7:158789849	cg19418458	350346
-0.141	ARHGAP30;P VRL4	1:161042063	cg00862398	18157
-0.141	IKZF3;ZBPBP2	17:38024146	cg16810031	309049
-0.141		17:21416281	cg00007215	167
-0.141		8:23605601	cg03324961	67319
-0.141	PDE6B	4:645781	cg01132407	23844
-0.140	HHIPL1	14:100130465	cg18678107	339014
-0.140	MTG1;PAOX	10:135202906	cg24644436	432348
-0.140	CES1	16:55866757	cg03880033	78129

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
-0.145	ARNTL	11:13302098	cg13286116	244869
-0.145	MSH5;MSH5-SAPCD1;SAPCD1;VWA7	6:31731881	cg03392100	68641
-0.145	IL31;LRRC43	12:122651623	cg14874216	276626
-0.145	MSH5;MSH5-SAPCD1;SAPCD1;VWA7	6:31734192	cg13187827	243288
-0.144	SERPINB6	6:2972435	cg08155050	158293
-0.144	DLGAP2	8:1455764	cg10636144	201951
-0.144	SAMD11	1:869368	cg13692836	253138
-0.144	RPH3AL	17:146926	cg04172345	83843
-0.144		1:228743235	cg12437277	231594
-0.143		17:79455736	cg09841001	187897
-0.143	C11orf53;C11orf92	11:1111155021	cg03554573	71909
-0.143	ATXN1	6:16413624	cg11291305	212741
-0.143	FEM1A	19:4785374	cg14818248	275598
-0.143	HLA-A	6:29912713	cg18349863	333730
-0.143	TP73	1:3600879	cg17471939	319626
-0.143		1:2863815	cg25137787	440554
-0.143	ARNT2	15:80824318	cg19708986	355104

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
-0.137	PAX2	10:102592366	cg03286031	66537
-0.137	TEX2	17:62341028	cg18312782	333101
-0.137		2:226913713	cg05293897	105270
-0.136	TMEM72-AS1	10:45374906	cg20638675	369712
-0.136	HLA-DQB2	6:32729130	cg07180897	140474
-0.136	ALK	2:29751968	cg01412762	29371
-0.136		19:29218732	cg12667521	235503
-0.136	TOX2	20:42548586	cg20889774	373555
-0.136	RECK	9:36036514	cg13392078	246714
-0.136	MIR593	7:127720749	cg20426275	366531
-0.136	ODZ4	11:78948859	cg12642289	235052
-0.136	MTERF	7:91510405	cg16284459	299467
-0.136	RBFOX3	17:77302162	cg08223357	159591
-0.136		18:44770781	cg24371990	427906
-0.136	CACNA1C	12:2696048	cg08166587	158536
-0.136	DAB1	1:58089001	cg00026909	659
-0.135		6:156983304	cg08839808	170533
-0.135	MTG1;PAOX	10:135202839	cg17143376	314138
-0.135	PIP5K1A;VP S72	1:151170427	cg24720336	433732

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
-0.139	TLX1NB	10:102872719	cg17034508	312397
-0.139	PCDHB17;PC DHB6	5:140530410	cg23247945	409860
-0.139	TMEM100	17:53800484	cg18040354	328429
-0.139	PRKG2	4:82075193	cg22772235	401742
-0.139	SEL1L2	20:13830102	cg17971895	327285
-0.139		5:74908142	cg19683494	354666
-0.139		2:131010647	cg27624826	481683
-0.139	HIPK4;PRX	19:40904691	cg24923931	437130
-0.138	SCN7A	2:167350883	cg14771658	274784
-0.138		15:98196247	cg19459332	350984
-0.137	PMPCA;SDC CAG3;SNAP C4	9:139299357	cg14108380	261681
-0.137		16:62984521	cg02248103	45873
-0.137	CYB5D2;ZZE F1	17:4043867	cg04417708	88669
-0.137	CST11;CSTL 1	20:23433608	cg11657817	218579
-0.137	CTC1;LINC00 324	17:8124867	cg20250341	363887
-0.137	CNR2;FUCA1	1:24195143	cg24792360	434918
-0.137	PKNOX2	11:125170859	cg23418965	412666

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
	87			
-0.132	OCA2	15:28014040	cg15194100	281887
-0.132	NAV1	1:201644923	cg24253904	426103
-0.132	SLC24A6	12:113773298	cg12583184	233973
-0.131		3:42265641	cg18812386	341259
-0.131	GREB1;MIR4429	2:11680020	cg11534680	216555
-0.131	TXNRD1	12:104676774	cg15775217	291055
-0.131	CCBL2;RBMXL1	1:89459529	cg11309454	213030
-0.131	GPR12	13:27338713	cg14339397	266524
-0.131		9:34810228	cg13923371	257761
-0.131	IFI44;IFI44L	1:79114976	cg07107453	138862
-0.130		5:171057196	cg07871442	153079
-0.130	OVCH2	11:7709186	cg25833922	451333
-0.130	PSMD11	17:30770961	cg09309269	178739
-0.130	DEFA4;DEFA6	8:6783521	cg02932321	59694
-0.130	TEPP	16:58016655	cg01479664	30752
-0.130	IL28B	19:39737768	cg04722177	94275
-0.130	IL20RA	6:137366545	cg08823985	170226

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
-0.135	ANKS3;C16orf71;ZNF500	16:4793770	cg00605362	12928
-0.135		11:91950460	cg20506843	367791
-0.135	RTN4RL1	17:1835482	cg23676314	416771
-0.135		2:10984512	cg00442205	9317
-0.134	ZDHHC13	11:19138045	cg00161556	3630
-0.134	PAPLN	14:73712491	cg09636214	184437
-0.134	CTRB2	16:75242114	cg08467866	163985
-0.133	ZNF718	4:125112	cg10197305	194260
-0.133	IGF2;IGF2-AS;INS-IGF2;MIR483	11:2154113	cg13165070	242895
-0.133		2:38099030	cg02752932	56067
-0.133	TACC2	10:123873748	cg23828763	419014
-0.133		7:115116310	cg04544267	91006
-0.133	CES1	16:55866997	cg23196985	408839
-0.133	CCDC105	19:15121385	cg18739061	339959
-0.133		19:43203368	cg24333150	427217
-0.132	FXYD2;FXYD6-FXYD2	11:117696743	cg11820026	221463
-0.132	DAB2IP	9:124363848	cg21234082	379229
-0.132	LOC1002891	7:99195819	cg12290671	229416

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
-0.128	MITF	3:69915302	cg03831180	77231
-0.128	PTN	7:137029097	cg15284177	283213
-0.128		1:149155792	cg27554973	480528
-0.127	ENTPD1;LOC728558	10:97624891	cg09217157	177016
-0.127	ZFPM1	16:88536950	cg05183538	103174
-0.127	CCDC64B;H CFC1R1;THO C6;TNFRSF1 2A	16:3079953	cg07063883	137997
-0.127	APOA1BP;IQ GAP3;TTC24	1:156551873	cg01010328	21258
-0.127	NRG1	8:32076032	cg23964820	421269
-0.127	MTG1;PAOX	10:135203102	cg18563886	337268
-0.127		13:112984840	cg27260867	475484
-0.127	AKAP8;AKAP 8L	19:15488902	cg22765626	401667
-0.127		18:37379468	cg15612221	288285
-0.127		17:21416258	cg10674575	202559
-0.127		13:100583872	cg07223206	141319
-0.126	KLK1;KLK15	19:51334890	cg26325285	459337
-0.126	GALNT9;LOC 100130238	12:132859608	cg10173694	193804

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
-0.130	PA2G4;RPL4 1;ZC3H10	12:56509603	cg18500368	336269
-0.129		14:26338282	cg16725552	307629
-0.129	ATHL1;NLRP 6	11:281516	cg06432119	125636
-0.129	GIMAP4	7:150264767	cg08960815	172781
-0.129	KLHL29	2:23839710	cg01387450	28832
-0.129		12:114701413	cg10233830	194930
-0.129		2:62521325	cg22770637	401725
-0.129	ALK	2:30142677	cg00643897	13652
-0.129	SEMA5B	3:122712271	cg11160908	210504
-0.129	TTF2	1:117604726	cg19319037	348805
-0.129	C20orf54	20:741798	cg19037007	344707
-0.129		12:69725435	cg22375663	395880
-0.129		8:41585554	cg17182837	314877
-0.128		3:118144311	cg20207443	363278
-0.128	LINC00299	2:8444004	cg18854004	341911
-0.128		11:106239635	cg01152624	24270
-0.128	GNAS;GNAS -AS1	20:57431202	cg09437522	181002
-0.128		13:112978683	cg20923605	374019

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
-0.124		1:161409970	cg00975746	20506
-0.124	KCNK10	14:88791298	cg02883668	58609
-0.124		15:34788847	cg10767425	203961
-0.124		8:49044542	cg11491002	215895
-0.124	DLGAP4	20:35064637	cg01463540	30456
-0.124	HSP90B3P	1:92099858	cg04090794	82132
-0.124	NOSIP;PRR G2	19:50084626	cg21913888	389236
-0.124	ISL1	5:50692281	cg24549912	430883
-0.124	STC2	5:172751331	cg01984743	40717
-0.124		2:72079276	cg07258910	141932
-0.123	PKD1L2	16:81254169	cg03406106	68931
-0.123	ANO4	12:101187093	cg25027699	438862
-0.123	TRIM21	11:4415203	cg07244098	141703
-0.123	MRPL38;TRI M65	17:73892097	cg01453052	30258
-0.123	BTN3A3	6:26442290	cg12537337	233273
-0.123	LOC1001296 20;LPPR5	1:99469634	cg24373253	427922
-0.123	FYN	6:112165062	cg26846943	468428
-0.123	ASB1	2:239334832	cg08773314	169376

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
-0.126	ATG4C	1:63249199	cg24082680	423369
-0.126		7:102330635	cg06322601	123757
-0.126		3:73723546	cg02131018	43720
-0.126	HIPK4;PRX	19:40904851	cg00478479	10159
-0.126	GNAT1;SLC3 8A3	3:50242325	cg15335139	283889
-0.126	CYP4F30P	2:131451149	cg14204395	263669
-0.126		16:88804051	cg26748794	466680
-0.126	HUNK	21:33242495	cg15636421	288718
-0.125	KLHL29	2:23840282	cg17129809	313908
-0.125	MEIS1	2:66657913	cg10835286	205203
-0.125	NUP98;PGAP 2	11:3817849	cg19247588	347686
-0.125	MIR4287;SC ARA5	8:27735178	cg04214878	84655
-0.125	SPINK7	5:147699892	cg13022905	240779
-0.125	PTH1R	3:46936655	cg02527881	51488
-0.125	GIMAP4	7:150264987	cg00323915	6821
-0.125	PTHLH	12:28120054	cg20389635	366021
-0.125	EIF2D	1:206786174	cg16966520	311311
-0.124		7:27475596	cg10070328	191836

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
-0.121	DOK7	4:3487436	cg15652666	289019
-0.121	OR6B3;PRR2 ₁	2:240985618	cg10906826	206344
-0.121	FBLN7	2:112898400	cg09982942	190323
-0.120	CXCR7	2:237478664	cg03626672	73351
-0.120	MBTPS2	X:21858304	cg21195120	378430
-0.120	NLRP3;OR2B ₁₁	1:247616686	cg14830002	275801
-0.120	CTAGE11P	13:75814496	cg17109374	313605
-0.120		5:177395755	cg11264997	212321
-0.120	GAS7;RCVR _N	17:9805074	cg26853458	468546
-0.120	GAD2	10:26531942	cg23052437	406538
-0.120	LCE2A	1:152670843	cg13697387	253231
-0.120	SPDYC	11:64936920	cg23079866	407032
-0.119	SPTBN2	11:66487938	cg04883026	97440
-0.119	HOTTIP;HOX A11-AS1;HOXA13	7:27236674	cg01363170	28338
-0.119	SYS1;SYS1-DBNDD2	20:43991402	cg00385441	8134
-0.119	ZNF876P	4:204382	cg00569896	12104
-0.119	CCDC71;KLHDC8B	3:49203081	cg18590502	337716

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
-0.123	FAM163A	1:179713788	cg14748380	274436
-0.122	KIAA1143;KIF15	3:44802604	cg09333631	179217
-0.122	MAP3K7	6:91297516	cg18683523	339091
-0.122		4:9382953	cg02136252	43830
-0.122		5:141616065	cg24749559	434242
-0.122		15:101389733	cg07035436	137452
-0.122		5:72510846	cg26653990	465004
-0.122		17:789555599	cg11521079	216324
-0.122		2:227476235	cg08982961	173162
-0.122	LRRC27	10:134150542	cg22586726	398883
-0.122	EXOC7;GAL R2;SRP68;ZACN	17:74073876	cg07909178	153763
-0.121	TAF3	10:7859768	cg09994553	190530
-0.121	CDK12;MED1	17:37608096	cg15445000	285571
-0.121	HLA-DPA1;HLA-DPB1	6:33043849	cg22483030	397307
-0.121	NUBP1	16:10837135	cg09079882	174735
-0.121	TSLP	5:110407538	cg15739437	290539
-0.121	PSMD9;WDR66	12:122356598	cg21016266	375557

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
	D13;SEZ6L2			
-0.118	EIF2D	1:206786178	cg16639185	305935
-0.118	PXN	12:120688744	cg22564731	398621
-0.118	MIR4757;OSR1	2:19553950	cg00954878	20061
-0.118	PROX1	1:214152805	cg26054764	454613
-0.117	CDH3	16:68691561	cg09821218	187538
-0.117	LPP	3:188115336	cg23651889	416316
-0.117		5:72666838	cg11316517	213156
-0.117	DSCR3	21:38630506	cg18380783	334168
-0.117		7:136190456	cg03439301	69540
-0.117	TMEM100	17:53800554	cg03233426	65601
-0.117	PSMD11	17:30770932	cg20190559	363067
-0.117		5:171057078	cg11620716	217943
-0.117	FN3K;TBCD	17:80708513	cg00809820	17098
-0.117	SECTM1	17:80285515	cg05744064	113450
-0.117	NCOA1	2:24806444	cg23648923	416268
-0.117	LOC100128398;ZNF606	19:58515046	cg09577391	183474
-0.117	LOC100289187	7:99195788	cg24024660	422355

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
-0.119	GRAMD2	15:72448319	cg12252008	228855
-0.119		16:76228294	cg06827491	133242
-0.119	LOC116437	12:131645153	cg07374109	143989
-0.119	CACNG4	17:64973939	cg23968154	421320
-0.119	NAV1	1:201619295	cg04179952	83989
-0.119		12:58934471	cg01919941	39316
-0.119		13:21893289	cg21970626	390084
-0.119	ANXA9;FAM63A	1:150969592	cg21859421	388363
-0.119		1:10895517	cg17480077	319783
-0.118	LRR27	10:134150489	cg21370255	381012
-0.118	POTEA	8:43147397	cg26969150	470647
-0.118	HOXA3;HOXA4;LOC100133311	7:27170313	cg04317399	86720
-0.118	C1orf86;PRKCZ	1:2121449	cg08200543	159156
-0.118		8:81143546	cg16745033	307963
-0.118		7:136362483	cg11678250	218935
-0.118	SPIN2B	X:57147918	cg12074688	225883
-0.118		8:144152376	cg17001448	311828
-0.118	ASPHD1;KCTD	16:29912700	cg10093648	192261

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
-0.115	RGMA	15:93615146	cg21079003	376460
-0.115	PGM5P2	9:69148624	cg18861917	342052
-0.115	ZBED4	22:50250283	cg20618087	369398
-0.115	LARS2	3:45429742	cg04459086	89409
-0.115	TACC2	10:123886914	cg26111575	455575
-0.115	ST8SIA2	15:92939006	cg08289525	160900
-0.115	ANO7	2:242147702	cg00255732	5474
-0.115	LRRC34;LRR IQ4	3:169531864	cg10994914	207829
-0.115		14:88097221	cg26252794	458035
-0.115	DGKB	7:14415317	cg03229767	65553
-0.114	LRRC27	10:134150690	cg02535060	51631
-0.114	LOC100131138	12:111374169	cg09792970	187023
-0.114	CNNM2	10:104676907	cg15439196	285445
-0.114	CCNYL1	2:208572165	cg18757817	340266
-0.114	PRRX1	1:170631847	cg22693806	400548
-0.114		11:44489577	cg03708694	74912
-0.114	DKFZp434L192	7:56563820	cg21216010	378877
-0.114	NRP1	10:33612892	cg17425818	318845

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
-0.117		16:77535527	cg06794141	132525
-0.117		2:192792315	cg01836906	37718
-0.117	LELP1	1:153175842	cg00298977	6302
-0.117	ODF1	8:103556749	cg27000960	471198
-0.117	GCK	7:44229319	cg16476432	302901
-0.117		11:2211939	cg19586845	353065
-0.117	HCG4;LOC554223	6:29761905	cg25193571	441364
-0.117	CTNND2	5:11588971	cg01937840	39702
-0.116	MYOM2	8:1994478	cg20219329	363455
-0.116		15:30337018	cg14398295	267622
-0.116	RASAL1	12:113574368	cg16890739	310176
-0.116		15:36699121	cg02763009	56272
-0.116	BIRC7;FLJ16779;MIR3196;NKAIN4	20:61878032	cg12649455	235197
-0.116		7:1250246	cg07034004	137422
-0.116		5:170763642	cg23036405	406232
-0.116	NCR1	19:55417647	cg12952132	239747
-0.116		1:22591361	cg13048466	241145
-0.115	GLP1R	6:39015339	cg19772011	356340

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
-0.113	MTG1;PAOX	10:135202522	cg10902549	206273
-0.113	NR2F1	5:92927796	cg26067259	454804
-0.113		2:218048915	cg00549040	11649
-0.113	GRK4	4:3043527	cg01807241	37046
-0.113	TNXB	6:32066446	cg14011987	259623
-0.113	SNED1	2:241975756	cg26707709	466046
-0.113		6:28446794	cg03350138	67869
-0.113	C6orf48;HSP A1B;SNORD 48;SNORD52	6:31806478	cg17794996	324365
-0.113	CBX7	22:39545030	cg18708252	339475
-0.113	UPF2	10:12085641	cg00513208	339475
-0.113		17:80860250	cg04497611	90135
-0.112	DMD	X:31285129	cg06746884	131521
-0.112	FGF4	11:69587473	cg26765567	466900
-0.112		6:30419373	cg03507875	70857
-0.112		19:29217858	cg25267487	442467
-0.112		16:84953424	cg01765164	36115
-0.112	DGKG	3:185912486	cg18172135	330799
-0.112		13:111451972	cg22731513	401204

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
-0.114	TFCP2	12:51570174	cg21570277	384054
-0.114	LHX6	9:124982834	cg17930194	326612
-0.114	MMP17	12:132317128	cg01830463	37580
-0.114	LRR27	10:134150567	cg07119315	139090
-0.114		8:67317506	cg02934300	59732
-0.114	DBNL;PGAM 2;POLM	7:44105721	cg21088488	376592
-0.114		1:113425263	cg10541466	200276
-0.114	AGAP1	2:236774164	cg03785646	76466
-0.114		7:73424891	cg09076650	174691
-0.114		6:1449399	cg18182981	331002
-0.114	NDUFA12	12:95397704	cg22141781	392510
-0.114	HOXA3;HOX A4;HOXA5;L OC10013331 1	7:27170880	cg04321618	86813
-0.113	MIR4283-1;MIR4283-2	7:63085215	cg10945855	206928
-0.113	PPIL2	22:22020076	cg04983276	99379
-0.113		2:72079413	cg24516106	430249
-0.113		10:125222790	cg11653519	218499
-0.113		7:21209781	cg08701183	168131

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
-0.111	ITIH1;ITIH3	3:52824283	cg18404041	334584
-0.111	PDE6B	4:648752	cg17643796	322207
-0.111	TRIM7	5:180614858	cg25606201	447878
-0.111		8:141490124	cg15842218	292164
-0.111	IPMK	10:59949191	cg09039685	174085
-0.111	CCDC129	7:31685368	cg02943305	59917
-0.111		5:1645640	cg11628972	218045
-0.111	CDHR3	7:105596715	cg27099486	472857
-0.111	DCX	X:110654011	cg11031647	208426
-0.111	PLA2G4D	15:42371967	cg02760164	56222
-0.111	ANKRD34C	15:79576704	cg14577319	271361
-0.110		1:161391807	cg00056433	1344
-0.110	FHL3;SF3A3	1:38460950	cg05202204	103487
-0.110		5:72485634	cg14727987	274140
-0.110		11:41481578	cg24638253	432227
-0.110		6:27521330	cg26264769	458241
-0.110		5:177592761	cg25087499	439729
-0.110		14:103783717	cg10559742	200586
-0.110	ARL4C	2:235406291	cg05308656	105595

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
-0.112	FZD1	7:90895894	cg08714590	168374
-0.112	CLCN7	16:1524255	cg08008072	155549
-0.112	CRX	19:48324309	cg06945747	135695
-0.112		1:91227319	cg08895590	171690
-0.112	KALRN	3:124232190	cg06690085	130439
-0.112		9:128799328	cg13946341	258251
-0.112	IL34;MTSS1L	16:70688171	cg02602352	52989
-0.112	TMEM171	5:72431891	cg01170694	24642
-0.112		17:42706084	cg14836839	275934
-0.112	RASGEF1C	5:179634671	cg12408990	231108
-0.112	DOK7	4:3486116	cg00752263	15898
-0.112	ANAPC2;GRI N1;LRRC26; MIR3621	9:140062197	cg03206445	65043
-0.111	OR6Q1;OR9 Q1	11:57792403	cg18886347	342489
-0.111	BAI1	8:143580823	cg05758861	113684
-0.111		2:121280002	cg00314115	6610
-0.111	MUC22	6:30980847	cg27292220	475981
-0.111	AGAP1	2:236773924	cg15981851	294380
-0.111		6:55774999	cg19318364	348791

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
-0.110	CLDN4;WBS CR27	7:73256416	cg03781731	76399
-0.110	SNRPN	15:25123381	cg08560373	165668
-0.109	FBXL16;MET RN	16:757149	cg07644125	149038
-0.109	EIF2D	1:206786170	cg21155316	377647
-0.109		8:135726252	cg00057272	1361
-0.109		13:112979998	cg20620751	369432
-0.109	DHRS7	14:60629192	cg06898279	134753
-0.109	EFS;IL25	14:23835595	cg17205324	315223
-0.109	PALMD	1:100111727	cg07960762	154721
-0.109		10:79470169	cg19094530	345528
-0.109	ARHGEF6	X:135863582	cg01134144	23879
-0.109	DUS3L	19:5799340	cg20467412	367204
-0.109	RGMA	15:93633408	cg04697454	93855
-0.109	VWA5B1	1:20608736	cg16713551	307396
-0.109		14:106791268	cg14042931	260352
-0.109		19:1673498	cg10697737	202878
-0.109	GPR4;OPA3	19:46097075	cg16620032	305585
-0.109	LOC388630	1:48452740	cg07202054	140866
-0.108	HK3;UNC5A	5:176314628	cg06783121	132285

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
-0.110	HHIP;LOC64 6576	4:145566595	cg02524475	51415
-0.110	C11orf9	11:61545187	cg07136108	139453
-0.110	PCDHA1;PCDHA10;PCDHA11;PCDHA2;PCDHA3;PCDHA4;PCDHA5;PCDHA6;PCDHA7;PCDHA8;PCDHA9	5:140238079	cg18906028	342772
-0.110	LOC151171	2:239463229	cg10182060	193967
-0.110		14:22385890	cg16138400	296975
-0.110	MAGIX;PLP2;PRICKLE3	X:49027884	cg22366498	395712
-0.110	COL1A1	17:48288538	cg06769994	132032
-0.110	FAM70A	X:119443941	cg26583344	463923
-0.110	CXCR2	2:219001517	cg10819992	204935
-0.110		16:66162203	cg26798936	467489
-0.110	CCHCR1;PSORS1C2	6:31105872	cg03034365	61773
-0.110		3:36675685	cg12870891	238511
-0.110	DEFB135;DEFB136	8:11838843	cg12807628	237566
-0.110	MDC1;TUBB	6:30684572	cg10925640	206607

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
-0.107	GUCY2E;LR RC32	11:76381800	cg19752094	355941
-0.107	LOC440910	2:132057004	cg07051654	137739
-0.107	NAPSA	19:50861262	cg12273319	229159
-0.107	TRIM69	15:45028270	cg10439456	198368
-0.107	CHTOP;S100A1;S100A13	1:153599831	cg02331910	47613
-0.107		5:132938694	cg19005955	344221
-0.107	ACOT11;FA M151A	1:55096622	cg22619910	399357
-0.107	CRYBA2;FEV;LOC151300	2:219851181	cg18664514	338819
-0.107	C10orf96	10:118084504	cg13836550	255997
-0.107	SORCS3	10:106749483	cg26349484	459830
-0.107	ZEB2;ZEB2-AS1	2:145273345	cg04640885	92836
-0.107	GALNT6	12:51786489	cg15127250	280846
-0.107		3:137187558	cg24821307	435362
-0.107	ADORA1	1:203086869	cg18811731	341246
-0.107	OR1J4;OR1N1	9:125289357	cg14598387	271804
-0.107	CARTPT	5:71012177	cg11927345	223348
-0.107	HCRT;KCNH4	17:40330907	cg06514003	127062

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
-0.108		6:12342070	cg03519011	71096
-0.108	C12orf73;TDG	12:104350162	cg22927789	404375
-0.108	CDH22	20:44882514	cg25558663	447055
-0.108		6:18752614	cg00664117	14044
-0.108	ARHGEF25;B4GALNT1;DTX3;SLC26A10	12:58011837	cg00700412	14808
-0.108	SHANK2	11:70564414	cg13080721	241684
-0.108	LOC154449	6:170571686	cg18698681	339306
-0.108	KCNH2	7:150644459	cg01559770	32264
-0.108	TMEM132D	12:130384734	cg08261450	160299
-0.108	DUOX1;DUOX1A1	15:45427034	cg14918338	277309
-0.108	DNAJB13	11:73661250	cg02070028	42486
-0.108	PSMD7	16:74331618	cg09313046	178793
-0.108	LGR6	1:202172778	cg04811114	95994
-0.108		13:69557960	cg18586262	337639
-0.108		1:201316444	cg26233753	457728
-0.108		1:37139265	cg20745381	371614
-0.108		10:121837310	cg10087780	192116
-0.108		15:98196234	cg08064292	156507

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
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-0.106	SGPP2	2:223288637	cg11300809	212887
-0.106	DLC1	8:13373090	cg00933411	19610
-0.106	PRSS55	8:10386222	cg10657228	202268
-0.106	ZIC1;ZIC4	3:147120248	cg13897134	257142
-0.106	DKFZp434L192	7:56563742	cg17876758	325825
-0.106	C11orf10;C11orf9	11:61548003	cg19617373	353600
-0.106		6:99075228	cg05593122	110762
-0.106		14:104787388	cg05210671	103662
-0.106	HHLA2	3:108041508	cg24769830	434575
-0.106	LOC100506012;PNMAL2	19:46999055	cg03969996	79829
-0.106	BEX5	X:101411275	cg03993934	80323
-0.106		15:98196333	cg11023328	208285
-0.105	ZIC5	13:100605441	cg10523198	199939
-0.105	TIGIT	3:114009756	cg05943254	117166
-0.105	CTNND2	5:11589049	cg17415451	318667
-0.105	MGC27382	1:78693899	cg22559013	398527
-0.105	DLC1	8:13372483	cg08768218	169300

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
-0.107	SNRPN	15:25093366	cg02171545	44484
-0.107	C2orf28;CAD;SLC5A6	2:27434262	cg14242246	264531
-0.107	HOXA3;HOXA4;LOC100133311	7:27170552	cg16651126	306141
-0.107		15:20562413	cg03344283	67729
-0.106	PLA2G7	6:46703670	cg12854458	238255
-0.106	MAG	19:35790951	cg25443560	445295
-0.106	HLA-DRB1	6:32552022	cg10765922	203924
-0.106	FAM83H;MA PK15	8:144801088	cg05626536	111385
-0.106		3:193987757	cg16282892	299443
-0.106	POU4F2	4:147573410	cg05710982	112882
-0.106	DKFZp434J0226	19:46712075	cg00537984	11421
-0.106	GPR31	6:167571630	cg25285053	442729
-0.106	PCDHA1;PCDHA10;PCDHA11;PCDHA12;PCDHA2;PCDHA3;PCDHA4;PCDHA5;PCDHA6;PCDHA7;PCDHA8;PCDHA	5:140248610	cg25024993	438807

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
-0.105	DKFZp434L192	7:56555482	cg21720373	386268
-0.105		22:50482250	cg10146330	193299
-0.105	PKD1L2	16:81254209	cg07091758	138538
-0.104		2:75136334	cg12269972	229112
-0.104		6:30433749	cg07017214	137090
-0.104	SLC38A4	12:47226005	cg08005660	155507
-0.104	XPNPEP1	10:111683631	cg17201651	315167
-0.104	MYH11	16:15931580	cg03737209	75526
-0.104	FLOT1;TUBB	6:30696029	cg22024120	390747
-0.104		5:170763941	cg26497768	462323
-0.104	KCNK3	2:26916575	cg20955989	374545
-0.104	TRIM31	6:30080230	cg17048834	312621
-0.104	ABCA7;HMH A1	19:1064938	cg26576206	463804
-0.104	PRKCB	16:23850404	cg26562691	463553
-0.104	GAPDHS;LO C100506469; SBSN	19:36024313	cg25681177	449001
-0.104	CDSN;PSOR S1C1;PSORS 1C2	6:31096204	cg03880216	78131
-0.104	MORC2;MOR	22:31316184	cg26278151	458506

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
-0.105	F10;F7	13:113783990	cg25796986	450780
-0.105	SOX2-OT	3:181417613	cg06283493	123126
-0.105		13:54898133	cg18817396	341362
-0.105	KIAA1143;KIF15	3:44802566	cg17546649	320901
-0.105	CRYAA	21:44593708	cg21895314	388915
-0.105	FOXS1	20:30437731	cg05366561	106738
-0.105	FIBIN	11:27015592	cg02565993	52210
-0.105	CLC	19:40228820	cg04764056	95048
-0.105		15:84974881	cg06813100	132909
-0.105	FBXO47	17:37123767	cg10600889	201304
-0.105	C14orf23;FOXG1	14:29240992	cg03472898	70248
-0.105	STK10	5:171541827	cg11334870	213456
-0.105	HLA-DPA1;HLA-DPB1	6:33041697	cg00798281	16870
-0.105	P2RX5	17:3598755	cg13375828	246413
-0.105	LOC100506012;PNMAL2	19:46998383	cg06484000	126528
-0.105	CMBL	5:10308785	cg26878318	468990
-0.105	MYO7A	11:76903134	cg24852442	435899

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
-0.103	ABHD8;DDA1;MRPL34	19:17420304	cg10664184	202380
-0.103	SLC9A3	5:501938	cg22572362	398700
-0.103	C1QTNF8;LO C146336;SST R5	16:1133074	cg03327829	67387
-0.103	HCN4	15:73639105	cg11831431	221705
-0.103		3:27638612	cg14143723	262354
-0.103	BST2	19:17516712	cg01329005	27706
-0.103		4:115649889	cg14855679	276322
-0.103	TMEM136	11:120187999	cg09120934	175365
-0.103	IRS4	X:107980846	cg21111568	376933
-0.103		7:55072042	cg13490352	248855
-0.103	NCKAP5	2:134326172	cg18984282	343881
-0.103	NCR1	19:55417496	cg17804112	324505
-0.103	FHL3;SF3A3	1:38461687	cg17077180	313040
-0.102	SEMA5B	3:122712224	cg04830808	96325
-0.102	SLCO1B1	12:21324585	cg04579507	91754
-0.102		22:39323204	cg07123855	139180
-0.102		5:134881662	cg12613020	234541
-0.102		2:220352476	cg20456243	367005

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
-0.104	C2-AS1			
-0.104	PCDH5	5:140515736	cg15120855	280719
-0.104		6:68849256	cg09531389	182666
-0.104	WNT10A	2:219763642	cg16582803	304901
-0.104		14:56471704	cg05314124	105693
-0.104	MMRN2;SNC G	10:88717623	cg07436701	145067
-0.104		1:31280493	cg25204088	441555
-0.104	RFTN2	2:198540621	cg08373610	162365
-0.104	C1QTNF8	16:1152474	cg04004158	80525
-0.104	LOC1005074 63;PSMB8;T AP1;TAP2	6:32805692	cg26685246	465648
-0.104	THOC2	X:122867073	cg08100265	157187
-0.104	PDLIM4	5:131589552	cg14815361	275561
-0.103	HHATL;KBTB D5	3:42727489	cg25129124	440393
-0.103	LOC84931	2:121223847	cg21406402	381501
-0.103	MACROD2	20:15177509	cg09937190	189621
-0.103	FAM163A	1:179713828	cg24460126	429325
-0.103	LOC1005060 12;PNMAL2	19:46988034	cg14128773	262082

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
-0.102	LRRC10B;MI R4488;SYT7	11:61273282	cg15263021	282930
-0.102	FBXO7	22:32870150	cg21023126	375623
-0.102		13:112985463	cg17655970	322387
-0.102		15:74060182	cg26579616	463866
-0.102		6:28781594	cg00176718	3961
-0.102	PLK5	19:1542897	cg00392196	8275
-0.102		6:156983315	cg00269725	5770
-0.102	LOC1005067 76	7:38403507	cg05460050	108373
-0.102		5:15385947	cg00105403	2447
-0.102	CKMT1A	15:43984922	cg26247942	457947
-0.102		1:14462810	cg16164607	297377
-0.102	CDH22	20:44838981	cg07296387	142575
-0.102		10:133156015	cg09005971	173513
-0.101	CHRD1	X:110038954	cg07653640	149177
-0.101		6:79339334	cg11074783	209107
-0.101	C1orf159	1:1052600	cg10126324	192906
-0.101	RINL;SIRT2	19:39360313	cg02711397	55211
-0.101	ZFP41	8:144339106	cg19504605	351705
-0.101		16:85981336	cg10274029	195601

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
-0.102	BA11	8:143581070	cg25473866	445797
-0.102	PCDHB17;PC DHB6	5:140528785	cg26866168	468766
-0.102	GABBR2	9:101192792	cg14523238	270180
-0.102		5:74908170	cg00601450	12858
-0.102	OCA2	15:28053339	cg24943998	437498
-0.102	DPF1	19:38721070	cg23480284	413571
-0.102	TRAPPC12;T SSC1	2:3383257	cg12447832	231782
-0.102	FGF8;NPM3	10:103532798	cg16079364	296042
-0.102	CHRNA1;PRS S56	2:233384489	cg25571880	447246
-0.102	APCDD1	18:10456115	cg14623989	272309
-0.102		X:119151476	cg22956922	404868
-0.102		5:88991074	cg04117076	82698
-0.102		2:131010522	cg13302869	245147
-0.102		13:19243756	cg08628006	166844
-0.102	GCM2;SYCP 2L	6:10881782	cg18187244	331085
-0.102		7:158243632	cg23859303	419493
-0.102	C16orf91;CC DC154	16:1478718	cg09615056	184112

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
	XL1			
-0.101		21:10888524	cg19433175	350575
-0.101	WDSUB1	2:160142643	cg00168785	3783
-0.101	CYP26B1	2:72357937	cg15160709	281412
-0.101		6:74965323	cg11654562	218523
-0.101	AAAS;SP7	12:53715148	cg23032316	406156
-0.101	ZNF718	4:124693	cg15792688	291287
-0.101		11:120387302	cg06995068	136607
-0.101		7:147500722	cg17372101	317966
-0.101		2:3044737	cg11902863	222986
-0.101		14:77519601	cg13576669	250680
-0.101	PDE11A	2:178770927	cg04628174	92633
-0.101	CCDC64B;H CFC1R1;THO C6;TNFRSF1 2A	16:3079708	cg07868599	153015
-0.101	HLA- DPA1;HLA- DPB1	6:33044510	cg00750366	15857
-0.101	ZNF767	7:149323101	cg08744726	168908
-0.100	LOC1005060 12;PNMAL2	19:46999224	cg11410682	214729
-0.100	SDC3	1:31368797	cg00658151	13923

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
-0.101		11:2212225	cg08241307	159919
-0.101		15:98196022	cg00744413	15733
-0.101		5:9119047	cg17608082	321764
-0.101	DPYSL5	2:27068081	cg08806184	169893
-0.101	GP6	19:55526208	cg27154418	473807
-0.101	C16orf61;CE NPN	16:81039227	cg08265926	160397
-0.101	LOC1001296 20;LPPR5	1:99471295	cg03593336	72666
-0.101	HLA- DPA1;HLA- DPB1	6:33040610	cg20617328	369385
-0.101	CD3EAP;ER CC1;PPP1R1 3L	19:45901453	cg08884571	369385
-0.101	NALCN	13:102060580	cg22191606	393258
-0.101	MGLL	3:127473936	cg15694422	289708
-0.101		2:121279886	cg23405152	412432
-0.101	DNAH17;PG S1	17:76417995	cg22290140	394680
-0.101	PALM2;PALM 2-AKAP2	9:112593847	cg13893012	257062
-0.101	CHAT;SLC18 A3	10:50816262	cg04730768	94454
-0.101	CCBL2;RBM	1:89459658	cg23627354	415857

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.100	MLNR	13:49795541	cg06476591	126402
0.100	ZNF542	19:56879662	cg03146949	63935
0.100	KY	3:134369987	cg12307306	229684
0.100	TMEM200B	1:29449356	cg00866556	18256
0.100	ERICH1	8:687384	cg01200640	25242
0.100	HOXA5;HOXA6;HOXA7;L OC10013331 1	7:27187372	cg04265576	85698
0.100	LOC386758;Z NF582	19:56904901	cg09568464	183339
0.100	ISM1	20:13200973	cg06262436	122823
0.100		10:100109635	cg23078268	407013
0.100	AQPEP	5:115298720	cg25044651	439130
0.100	AJAP1	1:4714672	cg12475759	232236
0.100		15:78112847	cg09369863	179831
0.100	HOXC4	12:54441509	cg10366797	197193
0.100	C7orf50;CYP 2W1	7:1029594	cg22505411	397678
0.100	SLC22A3	6:160769116	cg07883823	153297
0.100	CDH8	16:62070086	cg06831576	133330
0.100	CCDC164;EP T1	2:26625047	cg13255216	244382

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
-0.100	CILP2;NDUF A13;YJEFN3	19:19643534	cg09935271	189575
-0.100	HOXD3;LOC 401022	2:177028804	cg10304824	196084
-0.100	PCDHGA1;P CDHGA10;P CDHGA11;P CDHGA12;P CDHGA2;PC DHGA3;PCD HGA4;PCDH GA5;PCDHG A6;PCDHGA 7;PCDHGA8; PCDHGA9;P CDHGB1;PC DHGB2;PCD HGB3;PCDH GB4;PCDHG B5;PCDHGB 6;PCDHGB7; PCDHGB8P	5:140807225	cg21929183	389472
-0.100	SCN7A	2:167350889	cg06038864	118973
-0.100	CEBPZ;LOC1 00505876;SU LT6B1	2:37424015	cg23687288	417012
-0.100		15:101389354	cg25878441	451879
0.100		20:690915	cg12338552	230066
0.100	KIRREL3- AS3	11:126873181	cg08668551	167552

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.101	CNGB1	16:57915850	cg07029201	137333
0.101	HTR4	5:148033708	cg12825070	237836
0.101	C1orf201;NIP AL3	1:24741723	cg21298759	380184
0.101		7:158286570	cg23618588	415687
0.101		5:4942612	cg11468819	215620
0.101		5:56595244	cg19985056	359969
0.101	FLJ23152	6:17102678	cg05312353	105662
0.101	TCHH	1:152080543	cg04938315	98550
0.101	DCC	18:49868477	cg01839464	37773
0.101	FAM155A	13:108519752	cg064446668	125897
0.101	LOC285548; NKX3-2	4:13546151	cg27438798	478567
0.101		6:29818300	cg22473097	397165
0.101	PSKH2	8:87082023	cg20982735	375026
0.101	UTP14A	X:129065551	cg02699127	54944
0.101	FAM169A	5:74161231	cg07222505	141302
0.101	PLS1	3:142314493	cg00063773	1512
0.101	RUNX1T1	8:93115504	cg01806520	37028
0.101		2:133106819	cg12792250	237266
0.101	LOC654342	2:91848218	cg24829460	435500

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.100	GHSR	3:172167445	cg04851268	96789
0.100		2:213402433	cg08042975	156156
0.100	TCHH	1:152081002	cg05523911	109583
0.100	ERBB2	17:37856378	cg26111030	455565
0.100		9:13278626	cg14655855	272946
0.100	EPGN;MTHF D2L	4:75174080	cg07643762	149031
0.100	ISL2;SCAPE R	15:76634887	cg02245004	45800
0.100	UGGT2	13:96705123	cg08797194	169739
0.100	TBL1XR1	3:176827739	cg22160300	392814
0.100	LMO3	12:16762831	cg05355757	106496
0.101		17:25676440	cg07143451	139627
0.101	MYF5;MYF6	12:81110706	cg14067873	260821
0.101	EVX2;HOXD1 3	2:176948693	cg01749491	35793
0.101	OR7G3	19:9238958	cg03494634	70624
0.101	PON2;PON3	7:95025905	cg15927196	293537
0.101	TP73;WRAP7 3	1:3567986	cg24073122	423203
0.101		1:148854572	cg11818631	221440
0.101	ASCL2	11:2292000	cg13930892	257925

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.101		8:41004167	cg09091657	174922
0.101		14:28733613	cg01840183	37791
0.101	CDK6	7:92442568	cg05278074	104986
0.101	FLJ42875;PRDM16	1:2990490	cg17001566	311833
0.102		7:53286906	cg10502121	199449
0.102	IQGAP3;TTC24	1:156542103	cg12262564	229022
0.102	DEAF1;DRD4	11:640606	cg20411756	366324
0.102		12:29303160	cg23787937	418459
0.102	FOXF1;LOC400550	16:86548895	cg08589354	166151
0.102		18:44787492	cg18074954	329008
0.102	KANK3	19:8398300	cg17490089	319937
0.102	PRDM12	9:133534961	cg13465477	248295
0.102	GLRA1	5:151304817	cg25352328	443801
0.102	GRIA2	4:158141570	cg00699993	14796
0.102	ADNP2;LOC100130522;PAR6G	18:77905119	cg18973878	343754
0.102	TBL1X	X:9432900	cg10839723	205305
0.102	LOC255480;TBX5	12:114845868	cg21907579	389107

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.101		5:2915236	cg21081803	376494
0.101	THR3	3:24536252	cg02333852	47654
0.101	SNAP91	6:84418789	cg16334314	300384
0.101	SGK1	6:134497247	cg03400131	68781
0.101	LOC729852;RPA3	7:7726202	cg26804611	467608
0.101	ILF2;NPR1	1:153651568	cg04484579	89880
0.101	LOC643714;T3X	16:52581551	cg02709321	55162
0.101	EYA4	6:133562475	cg20787173	372221
0.101	DBNDD2;PIGT	20:44035850	cg03172947	64447
0.101	PAK3	X:110187421	cg06455967	126034
0.101	HCN1	5:45695922	cg06498267	126802
0.101	ZIC4	3:147111120	cg27606499	481395
0.101	MAGI2-AS3	7:79082531	cg14592474	271684
0.101	WTIP	19:34972358	cg11869770	222476
0.101	UCP1	4:141490153	cg19346645	349167
0.101	COL23A1	5:178017853	cg26996818	471137
0.101	ZC3H12C	11:109964976	cg11758932	220367
0.101	SYT9	11:7273498	cg08185661	158874

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.102	DLC1	8:13134166	cg20536983	368192
0.102		2:44312696	cg08613504	166550
0.102	ESR1	6:152085619	cg17741339	323560
0.102	CPLX2	5:175299035	cg06833732	133382
0.102		21:42218932	cg09880551	188645
0.102	CCDC108;CR YBA2;FEV;MI R375	2:219858146	cg24374738	427940
0.102	FBXL15;NFK B2;PSD	10:104170217	cg26089160	455163
0.102	PTPRZ1	7:121513695	cg10948929	206989
0.102		5:87979504	cg12991050	240324
0.102	RNF180	5:63461566	cg16485558	303034
0.102	ZDBF2	2:207140303	cg00410106	8675
0.103	CACNA1B	9:140917413	cg11827453	221623
0.103	CUL4B	X:119694554	cg22267947	394373
0.103	DUOX1;DUO XA1	15:45422054	cg24505618	430070
0.103	RUNX1T1	8:93114294	cg07622493	148653
0.103	GBX2	2:237078733	cg07014673	137017
0.103	HOXD4;MIR1 0B	2:177014949	cg27160395	473893

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.102	TDRD5	1:179555658	cg17138852	314056
0.102	GPR176	15:40212781	cg17497271	320059
0.102	CHST3	10:73724697	cg19731268	355545
0.102	SNAP91	6:84418659	cg15950068	293877
0.102	PDXK	21:45147292	cg02253535	45973
0.102		5:168728149	cg15927720	293550
0.102	PRDM13	6:100061111	cg17302155	316788
0.102	DLL4	15:41219238	cg16069079	295915
0.102	PDGFRA	4:55100025	cg24799620	435038
0.102	FAM190A	4:91049007	cg17275700	316281
0.102	FUT9	6:96463959	cg25114913	440174
0.102	MOXD2P;PR SS58	7:141951023	cg12970830	240011
0.102	HPS4;SRRD	22:26875563	cg27087377	472647
0.102		17:25676386	cg05977781	117874
0.102		15:96905554	cg00221709	4765
0.102	RARRES1	3:158450208	cg03269060	66248
0.102	KDR	4:55991701	cg25722465	449597
0.102	SOX17	8:55370579	cg26059468	454690
0.102		14:95330880	cg18939596	343247

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.103		12:130422172	cg01448115	30160
0.103	RBFOX3	17:77454437	cg25258515	442358
0.103	EPB41L3	18:5543945	cg16304950	299805
0.103		13:112759355	cg15415452	285112
0.103	PPYR1	10:47083426	cg02394955	48953
0.103	ANKRD20A8 P	2:95522902	cg08721908	168505
0.103	C2orf65	2:74813369	cg02102114	43172
0.103	MIR137;MIR2 682	1:98519101	cg09896412	188935
0.103	NR1D1;THRA	17:38255871	cg09161455	176141
0.103	RPTOR	17:78815421	cg02363653	48276
0.103	LOC1005058 06;SNORD12 3	5:9545976	cg11011938	208099
0.103	GRIN2A	16:10051500	cg06880615	134389
0.103		16:85369038	cg05877550	115832
0.103	CAPN1;SPD YC	11:64949878	cg25363789	444004
0.103		4:1407989	cg26860935	468675
0.103	THSD7A	7:11871690	cg26748945	466682
0.103	NEURL;SH3P XD2A	10:105344174	cg16311536	299928

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.103	GLRB	4:157997363	cg09688546	185354
0.103	DENND4C	9:19298547	cg19584733	353015
0.103	CASC4	15:44579510	cg00093643	2177
0.103		6:9399379	cg20876760	373416
0.103	GBX2	2:237076171	cg20804191	372465
0.103	LY6H	8:144240945	cg00831710	17537
0.103		6:28853021	cg24867279	436176
0.103	ALKBH7;CLP P	19:6362787	cg16848221	309550
0.103		5:1107837	cg22172143	393020
0.103	ZNF729	19:22469860	cg15413034	285081
0.103	TP73;WRAP7 3	1:3567412	cg16823083	309243
0.103	KBTBD11	8:1949342	cg25021970	438735
0.103	KLF16	19:1851995	cg11434705	215145
0.103	PEX5L	3:179670323	cg18765712	340436
0.103	NFIX	19:13107252	cg06197482	121707
0.103		2:9235972	cg04575202	91657
0.103	PCDHGA1;P CDHGA2	5:140712459	cg21722795	386305
0.103		1:32237923	cg04878000	97320

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.104	TRIM67	1:231296818	cg08855395	170825
0.104	RBP4	10:95361223	cg25793377	450725
0.104	EDIL3	5:83679941	cg07201620	140856
0.104	C10orf114; MIR1915	10:21789124	cg00580562	12369
0.104	CAMK1G	1:209759145	cg14034757	260152
0.104	NET1	10:5488500	cg14426660	268226
0.104	ACTL6B	7:100253914	cg08572611	165841
0.104	TEKT1	17:6734940	cg20663042	370096
0.104	LOC100271702	12:2030223	cg08621624	166700
0.104	OCRL	X:128674222	cg27633753	481846
0.104	ANKRD53; TEX261	2:71205891	cg18006568	327816
0.104	RAB32	6:146864752	cg23833452	419083
0.104	NCAM1	11:112833773	cg12040830	225223
0.104	C3orf26; FILIP1L	3:99595145	cg22092811	391783
0.104		14:95331232	cg00814780	17210
0.104	LOC100507043	14:96342365	cg01718322	35254
0.104	CPLX1	4:789505	cg12792086	237263

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.103	FREM3	4:144621385	cg04514249	90444
0.103	CRNDE; IRX5	16:54965084	cg02056682	42152
0.104	POLR1B; TTL	2:113298655	cg12937159	239513
0.104	PRKD1	14:30396845	cg08608974	166464
0.104	LAIR1	19:54876795	cg20117742	361985
0.104	CNTNAP2	7:145814152	cg16254309	298913
0.104	CRMP1	4:5894930	cg15448975	285648
0.104	ASIP	20:32857151	cg09775533	186730
0.104	RBFOX1	16:6623787	cg04671611	93373
0.104	PCDHA1; PCDHA2; PCDHA3; PCDHA4; PCDHA5; PCDHA6; PCDHA7	5:140207609	cg16987900	311601
0.104	TGIF1	18:3452302	cg12899157	238913
0.104	ADRBK2	22:25961523	cg15154002	281307
0.104	FBP1	9:97402452	cg14211930	263861
0.104	GABRG2	5:161494500	cg08566437	165741
0.104	SMAD2	18:45458243	cg03294491	66702
0.104	SHISA6	17:11143830	cg08169394	158589
0.104	ADAMTSL3	15:84322946	cg14230666	264293

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.105	SLC7A14	3:170303721	cg21884231	388773
0.105	GRIN2D;GRWD1	19:48946564	cg04419610	88694
0.105	STK24	13:99218657	cg17176619	314752
0.105	FAM159B	5:63986733	cg14004073	259441
0.105	LOC728723; SNORA47;ZBED3	5:76373719	cg03163459	64262
0.105	ZNF536	19:30866192	cg03758150	75925
0.105	PCDHA1;PCDHA10;PCDHA11;PCDHA12;PCDHA13;PCDHA2;PCDHA3;PCDHA4;PCDHA5;PCDHA6;PCDHA7;PCDHA8;PCDHA9;PCDHAC1;PCDHAC2	5:140346394	cg21537235	383480
0.105		11:43569269	cg13201808	243496
0.105	GLDN	15:51634039	cg09495418	182011
0.105	UGGT1	2:128953231	cg11873311	222541
0.105	TBX3	12:115129446	cg10297792	195985
0.105	GPR123	10:134902278	cg07779444	151406

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.104	LINC00327	13:24062873	cg08381620	162504
0.104	OLFM2	19:10024282	cg06911487	135026
0.104	FLJ41350;LBX1	10:102987257	cg12646649	235126
0.104	DUSP27	1:167090974	cg17801546	324462
0.104	PCDHA1;PCDHA10;PCDHA11;PCDHA12;PCDHA13;PCDHA2;PCDHA3;PCDHA4;PCDHA5;PCDHA6;PCDHA7;PCDHA8;PCDHA9;PCDHAC1;PCDHAC2	5:140346199	cg25500080	446199
0.104	ABCC3;CACNA1G	17:48712370	cg00081975	1883
0.104	ZBTB16	11:113953621	cg20268992	364195
0.104	TMEM179	14:105070864	cg10281977	195739
0.104	ASB10;GBX1	7:150870036	cg12649727	235202
0.105		11:79151811	cg09673208	185113
0.105	CA10	17:50235965	cg22702328	400704
0.105	SOX17	8:55371013	cg08044097	156179
0.105	PIWIL1	12:130822603	cg24838063	435641

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.105	FLJ12825;HOXC4	12:54454163	cg04024827	80948
0.105		6:125855124	cg02612397	53198
0.105	TP73;WRAP73	1:3567646	cg07382920	144177
0.105		4:165304540	cg21300373	380200
0.105	PRDM8	4:81118588	cg26299084	458882
0.106	ASIP	20:32857072	cg16655240	306231
0.106	TBX18	6:85474093	cg02106850	43270
0.106	THBD	20:23030250	cg09279949	178245
0.106	HOXD8;LOC100506783	2:177004015	cg18516557	336519
0.106	AQPEP	5:115298704	cg22010052	390518
0.106	WNT3A	1:228248013	cg26841013	468320
0.106	C14orf23;FOXG1	14:29236008	cg02681442	54626
0.106	COL4A1;COL4A2	13:110959428	cg06659727	129920
0.106	LOC100192378;ZFX4	8:77590322	cg09938511	189649
0.106	MAGI2-AS3	7:79083753	cg07448060	145248
0.106	CHRD1	X:110039536	cg00619443	13187
0.106	FAM174B	15:93199037	cg25864024	451730

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.105	IRX1	5:3592435	cg19814981	357062
0.105	HOTAIRM1;HOXA2;HOXA3	7:27142682	cg09871315	188506
0.105	PLK2	5:57756539	cg07479092	145902
0.105	TBX3	12:115123875	cg18573327	337428
0.105	ACTN2	1:236849994	cg20482698	367438
0.105	LOC388499;LRRC8E	19:7953281	cg27615578	481540
0.105	THRB	3:24536889	cg26146027	456200
0.105	GRIA2	4:158141542	cg10410142	197887
0.105	FN3K;FN3KRP	17:80693076	cg03077331	62673
0.105	OPA3;VASP	19:46032528	cg26958124	470450
0.105	HOXD1;LOC401022	2:177053274	cg03450948	69796
0.105	VWVC2	7:49813088	cg01893212	38794
0.105		1:241520331	cg13849378	256225
0.105	DLX6-AS1	7:96622709	cg18502142	336304
0.105		4:180979631	cg12950911	239731
0.105	DNAH8	6:38683221	cg03166753	64319
0.105	NETO1	18:70536461	cg13644317	252077

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.106	ZNF362	1:33721234	cg03767970	76126
0.106	FGFR1OP;MI R3939	6:167409842	cg02634327	53695
0.106	PCDH8	13:53419963	cg07847863	152703
0.106	HS6ST3	13:96742421	cg08612100	166526
0.106	ARMS2;HTR A1	10:124220367	cg09576143	183453
0.106		3:64430940	cg11236526	211855
0.106	CHST9	18:24765490	cg21895526	388922
0.106	C14orf132	14:96505722	cg16539629	304057
0.106		5:72596646	cg01050429	22138
0.106		8:61823275	cg06011086	118514
0.106	ST6GAL2	2:107502679	cg19412467	350247
0.106	CHAT;SLC18 A3	10:50818299	cg11389172	214354
0.106	SLC6A1	3:11033866	cg00375819	7950
0.107	CLEC2L	7:139208852	cg08832906	170404
0.107	CCDC27;TP7 3-AS1	1:3663435	cg10634619	201918
0.107	ZNF90	19:20188803	cg03317517	67181
0.107	GBP1	1:89523325	cg11083157	209272
0.107	OSR2	8:99961874	cg01581084	32753

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.106	CNPY1	7:155301734	cg05944137	117184
0.106	PIGZ	3:196695320	cg23484358	413640
0.106	WNT7B	22:46372742	cg17179568	314808
0.106	TPRSS3;U BASH3A	21:43824071	cg00134539	3054
0.106	EPHA5;LOC1 00144602	4:66534218	cg23193365	408770
0.106	DGKI	7:137125473	cg13734282	253993
0.106	UNC5C	4:96470286	cg11723848	219719
0.106		10:35256135	cg16738929	307860
0.106	NRG1	8:32504919	cg14663451	273089
0.106	HOTTIP;HOX A13	7:27246799	cg25720795	449560
0.106	LMF1;SOX8	16:1030619	cg05520409	109522
0.106	CRMP1	4:5894923	cg07963234	154775
0.106	HOTAIR;HOX C12;HOXC13	12:54349169	cg26931862	469970
0.106	FOXI2	10:129535186	cg25539045	446751
0.106		1:41350014	cg13472192	248463
0.106		6:39740405	cg14173968	262984
0.106		20:690693	cg02217786	45276
0.106	PRSS3	9:33750687	cg14369648	267044

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.107	CBLN4	20:54579084	cg01729827	35479
0.107	HOXD10;HOXD8;HOXD9	2:176989349	cg09173768	176359
0.107	MIR196A1	17:46713962	cg13769834	254628
0.107	CRAMP1L	16:1665094	cg06810647	132860
0.107	ANGPT1	8:108511174	cg09443479	181117
0.107	DRD1	5:174871289	cg18190187	331134
0.107		1:227729906	cg11846112	221996
0.107	TGFB1	5:135364556	cg03625177	73315
0.107	TRMT2B	X:100307142	cg11708328	219456
0.107	HOXD4;MIR10B	2:177014966	cg12215739	228288
0.107		X:39548267	cg11712793	219521
0.107	DEAF1;DRD4;SCT	11:637035	cg23501406	413927
0.107	ZNF578	19:52956683	cg14582763	271490
0.107	KITLG	12:88974161	cg25741452	449928
0.107	BIRC5;TMEM235	17:76228233	cg09473315	181656
0.107	DMRTA2	1:50884480	cg10512745	199703
0.107	TMEM132C	12:128752040	cg04475027	89694
0.107	INPP5A;NKX	10:134600675	cg15304699	283459

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.107	KCNA7;NTF4	19:49575475	cg26923490	469807
0.107	ISL1	5:50678925	cg01587896	32872
0.107	NEFH	22:29876945	cg23353952	411659
0.107		7:149744935	cg15058253	279644
0.107	DDX25;HYLS1;PUS3	11:125774406	cg19792599	356708
0.107	CBWD1;FOX D4	9:113530	cg01237333	25956
0.107	MIR1253	17:2659081	cg08457011	163741
0.107	TAS2R1	5:9623366	cg01984802	40719
0.107	TBX18	6:85474090	cg07028914	137326
0.107	ARL5C;CAC NB1	17:37321631	cg20555674	368474
0.107	CNTNAP2	7:145813413	cg05749717	113523
0.107		2:165698949	cg21639287	385195
0.107	DNAJC6	1:65775570	cg26885220	469135
0.107	LILRA2	19:55084269	cg16893868	310220
0.107	CRNDE;IRX5	16:54965100	cg06191898	121610
0.107	PRKAR1B	7:751962	cg12441126	231659
0.107	ARHGEF10; MIR596	8:1772116	cg22880677	403671
0.107		5:143978290	cg02030403	41637

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.108	GABRA2	4:46391392	cg25145765	440699
0.108	KLF16	19:1851882	cg13382072	246526
0.108	CATSPER2P1; PDIA3	15:44035561	cg15437748	285428
0.108	TRAF3IP2;T RAF3IP2-AS1	6:111926749	cg15772366	291005
0.108	PCDHA1;PCDHA10;PCDHA11;PCDHA12;PCDHA13;PCDHA2;PCDHA3;PCDHA4;PCDHA5;PCDHA6;PCDHA7;PCDHA8;PCDHA9;PCDHAC1;PCDHAC2	5:140345966	cg04454086	89312
0.108	VWV2	7:49813486	cg18206027	331413
0.108		6:157264715	cg16455339	302565
0.108	FAM110C	2:46465	cg14255256	264798
0.108	ZNF148	3:125076480	cg22895305	403903
0.108	ADAMTS16	5:5139874	cg16508480	303412
0.108	LOC100506757;MGC16121;MIR424;MIR450A1;MIR450A2;MIR450	X:133678716	cg19112977	345819

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.107	6-2			
0.108	FGF8;MGEA5;NPM3	10:103536342	cg25209842	441648
0.108	SLC22A20	11:64993335	cg23930334	420666
0.108	DIP2C	10:601816	cg06279296	123066
0.108	PRKD1	14:30396515	cg01588388	32879
0.108	EYA4	6:133562332	cg01328892	27704
0.108	PTPRM	18:7566781	cg16474170	302867
0.108	FAM129C	19:17650009	cg12585966	234024
0.108	CD247	1:167409054	cg06900257	134801
0.108	DRD5	4:9783206	cg04597433	92065
0.108	ISCA2;LTBP2	14:74959018	cg26195881	457091
0.108	HOXC4;HOXC5;HOXC6;HOXC8	12:54408091	cg14569644	271205
0.108	FAM5C	1:190447290	cg23010538	405785
0.108	LRP12	8:105601696	cg00662122	14007
0.108	SFRP1	8:41166990	cg24319902	427005
0.108		13:24270087	cg10885151	205995
0.108	SVEP1	9:113341525	cg13606569	251311
0.108		3:181444563	cg04859466	96950

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.109	C3orf25;MBD4	3:129147397	cg17468185	319549
0.109	SRCIN1	17:36718549	cg20090283	361564
0.109	LOC400657	18:72263688	cg20276402	364322
0.109	C14orf23;FOXG1	14:29237480	cg16804284	308960
0.109	GABRG2	5:161494515	cg09220361	177083
0.109		8:72468820	cg24809973	435221
0.109		7:87974722	cg27221053	474880
0.109	NXPH2	2:139537745	cg10989763	207734
0.109	SGPL1	10:72594465	cg09140723	175742
0.109	FGF18	5:170848123	cg01392179	28917
0.109	ZNF300	5:150284796	cg21228005	379112
0.109	ZNF329;ZSCAN18	19:58629828	cg03145999	63909
0.109	LOC255480	12:114852091	cg01184975	24931
0.109	LPHN3	4:62383028	cg16225703	298417
0.109		7:156409058	cg16771407	308382
0.109	UNCX	7:1271236	cg18629009	338270
0.109		6:28945500	cg24126967	424128
0.109	MSX1	4:4860061	cg15092343	280260

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.108	B;MIR503;MIR542			
0.108	SNX9	6:158243833	cg26845300	468408
0.108	TMEM181	6:158957433	cg00590036	12606
0.108		3:75661206	cg24573207	431170
0.108	PSKH2	8:87082014	cg04470072	89611
0.108	C10orf140;MLLT10	10:21814313	cg03891590	78352
0.108	MIR1258;ZNF385B	2:180726035	cg24575676	431204
0.108	UBD	6:29521501	cg20723129	371254
0.108		13:112759386	cg21054521	376149
0.108	NTNG2	9:135118406	cg14408447	267814
0.108	PTPRT	20:41818356	cg13168820	242965
0.109	SOX1	13:112722333	cg15466862	285977
0.109	RSPO1	1:38100467	cg13448605	247923
0.109	FGF8;MGEA5;NPM3	10:103536348	cg06169131	121199
0.109	HOXB2;HOXB3	17:46618919	cg21780393	387140
0.109	SYT7	11:61335254	cg03200166	64948
0.109	SPATA18	4:52918471	cg17031543	312329

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.110	ODZ1	X:124097806	cg24761295	434425
0.110		6:78359965	cg10264012	195459
0.110		7:4921827	cg04816699	96082
0.110	MDGA1	6:37616598	cg03062252	62373
0.110	GJD2	15:35046760	cg21053529	376133
0.110	RLF;TMCO2; ZMPSTE24	1:40714009	cg06776907	132164
0.110	HS3ST6	16:1968232	cg14936269	277598
0.110	DKFZp434J0226	19:46713473	cg21629821	385058
0.110	ANO1	11:69934109	cg05846633	115247
0.110	KIAA1755	20:36889364	cg14003035	259413
0.110	CORIN;NFXL1	4:47840011	cg26018901	454082
0.110	GLT1D1	12:129337897	cg04054313	81425
0.110		9:13279482	cg06202228	121794
0.110	CADM1	11:115069145	cg05125455	102021
0.110	DPYS	8:105479058	cg10303487	196069
0.110	KDM2B	12:122019080	cg17452615	319270
0.110	FOXI2	10:129535509	cg09614415	184092
0.110	ARHGEF4	2:131673894	cg12910906	239117

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.109	SOX1	13:112721789	cg02547394	51873
0.109	CHST8	19:34112991	cg19594305	353222
0.109	BMP4	14:54413548	cg27302539	476206
0.109	FUT9	6:96463902	cg01758512	35982
0.109		2:240153778	cg25746499	450027
0.109	CCDC50;UTS2D	3:191047240	cg25235397	442049
0.109	PAX1	20:21686282	cg08448701	163575
0.110	UBQLN2	X:56589768	cg02587153	52704
0.110		10:13425015	cg18675735	338977
0.110		18:6414958	cg22058122	391310
0.110	CSMD1	8:4852036	cg12258042	228965
0.110	ASPG;MIR203;MIR3545	14:104583067	cg23960324	421202
0.110	RACGAP1	12:50426901	cg19796532	356768
0.110		13:20875915	cg14472366	269103
0.110		14:95330984	cg19453488	350906
0.110	ZNF385D	3:21792857	cg26077378	454997
0.110	MBNL2	13:98002933	cg03372334	68296
0.110	ENO4	10:118608698	cg01035689	21828
0.110	CRHBP	5:76249502	cg04306063	86503

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.111	TMEM131	2:98613076	cg02995664	61036
0.111	DLX5;DLX6;D LX6-AS1	7:96647021	cg23262036	410160
0.111	RAX	18:56940333	cg06676637	130191
0.111	COLEC12	18:500979	cg19461621	351026
0.111	MIR618	12:81331486	cg23441441	412989
0.111		7:64407743	cg24002887	421987
0.111	ST6GALNAC 5	1:77334045	cg23243867	409762
0.111	MIR618	12:81331469	cg17061244	312814
0.111	LAMA1	18:7117680	cg07846220	152681
0.111	LOC1005060 12;PNMAL1	19:46975062	cg21988244	390260
0.111	FGF12	3:192127330	cg16376000	301109
0.111		4:85403915	cg25174438	441100
0.111	GALR1	18:74961968	cg20872937	373368
0.111	LRIT1;RGR	10:86001254	cg14034858	260156
0.111	LAG3;PTMS	12:6888035	cg11429292	215067
0.111	PDE1C	7:32110523	cg14604568	271937
0.111	ZNF503;ZNF 503-AS2	10:77156218	cg20659435	370034
0.111	CDH8	16:62069337	cg02172312	44501

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.110	CPNE7	16:89654085	cg10499753	199387
0.110	CBLN1	16:49315302	cg08464190	163914
0.110	ADAM33;ATR N;GFRA4	20:3641641	cg25164624	440992
0.110	LIMK2	22:31644160	cg15504662	286549
0.110	FLT3	13:28673762	cg26472910	461940
0.110	BANK1	4:102712397	cg14855874	276324
0.110		12:34500585	cg19457237	350958
0.110	KDM2B	12:122018897	cg09151742	175965
0.111		2:130763641	cg08857994	170896
0.111	PAX6	11:31819380	cg26029734	454240
0.111	HMGCLL1	6:55443868	cg06401021	125152
0.111	ZNF578	19:52956832	cg25763393	450297
0.111	TRPC4	13:38444134	cg15696906	289754
0.111	PLEKHA6	1:204256846	cg25407979	444757
0.111	C5orf38;IRX2	5:2743601	cg26195356	457077
0.111	EP400;PUS1	12:132433838	cg26147845	456245
0.111	MLLT3	9:20339790	cg21222426	379016
0.111	CTTNBP2	7:117513348	cg17112089	313639
0.111	EFHD1	2:233499460	cg06842071	133579

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.112		11:110627909	cg04297660	86337
0.112	DNMT3A	2:25474327	cg10749994	203678
0.112		19:23185714	cg24911113	436942
0.112	CCT8L2,TPT EP1	22:17083482	cg00816224	17246
0.112	SLC35F3	1:234040781	cg09424759	180776
0.112	EPHB2,MIR4 684	1:23038177	cg27573841	480859
0.112	HOXC8,HOX C9	12:54398518	cg08254359	160184
0.112	PRDM8	4:81118794	cg06307913	123528
0.112		22:33454324	cg05206884	103569
0.112	CR1L	1:207842927	cg20264068	364122
0.112	DNAF2:LRR 1:MGAT2,RP L36AL	14:50085410	cg24149364	424560
0.112	MAPK14	6:36076933	cg20559215	368537
0.112	ISL2	15:76630209	cg23513966	414134
0.112	F10,PROZ	13:113807384	cg10067723	191777
0.112	C1orf229,ZNF 124,ZNF669	1:247275344	cg23695504	417170
0.112	HOOK1	1:60280809	cg23996071	421845
0.112	ZNF83	19:53142304	cg17132967	313971

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.111	ISL1	5:50678913	cg17412886	318628
0.111	THRB	3:24537469	cg08123277	157665
0.111	HOXD10;HO XD11;HOXD1 2	2:176972068	cg05500840	109127
0.111	ADAMTS16	5:5140003	cg03209854	65125
0.111		2:200524012	cg27211284	474729
0.111	SLC16A2	X:73641955	cg06805513	132754
0.111	HOXC4;HOX C5;HOXC6;M IR615	12:54424964	cg10005224	190710
0.111	PTPRZ1	7:121513058	cg05931096	116896
0.111	SOX17	8:55370434	cg15186181	281779
0.112	ZNF536	19:30866194	cg06000994	118339
0.112		1:17199104	cg20168927	362799
0.112	STAC2	17:37381475	cg14328457	266291
0.112	CLMP	11:123008408	cg12995113	240381
0.112	CADPS	3:62860224	cg13514230	249338
0.112	TAPBPL,VAM P1	12:6572482	cg22129323	392333
0.112		13:112849184	cg20681688	370443
0.112	OR51A2;OR5 1A4	11:4977924	cg07589078	148007

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.113	NLRP14;ZNF214	11:7041549	cg22867063	403403
0.113		6:28921805	cg22489957	397412
0.113	AMPD3;MIR4485;MTRNR2L8;RNF141	11:10531596	cg18489034	336073
0.113	PALLD	4:169525923	cg24784416	434791
0.113	KHDRBS2	6:62996119	cg26715952	466174
0.113	PTGER2	14:52780158	cg21502048	382905
0.113	CTNNA2	2:79739863	cg08119884	157578
0.113	PRKAR1B	7:751833	cg00356183	7541
0.113	GPR125	4:22517094	cg08141192	158041
0.113	SLC6A17	1:110693237	cg11885396	222730
0.113	FAT1	4:187645120	cg27475132	479115
0.113	KIAA0748	12:55371892	cg24536818	430655
0.113	TRIM31	6:30071394	cg23642250	416154
0.113	DPP6	7:153584582	cg06495961	126761
0.113		8:142276422	cg25461290	445593
0.113	MRPS15;OSCP1	1:36912487	cg26030770	454254
0.113	EPPK1	8:144952929	cg18153977	330494
0.113		3:184231385	cg15718583	290162

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.112	TACR1	2:75292272	cg14054283	260559
0.112		15:29862568	cg13942157	258175
0.112		4:165305050	cg10453719	198622
0.112	SPAG6	10:22634218	cg12377139	230587
0.112	GRM6	5:178422071	cg23003783	405665
0.112	AQP12A;AQP12B	2:241623436	cg08049592	156267
0.112		16:15219673	cg04381865	87943
0.112	KIAA0182	16:85648263	cg07301329	142673
0.112	HOXC4;HOXC5;HOXC6;HOXC8	12:54413384	cg15772924	291010
0.112	TCF15	20:591083	cg25984671	453527
0.112	C5orf38;IRX2	5:2751550	cg18371475	334040
0.113	ST6GAL2	2:107503672	cg21649258	385387
0.113	PTPRT	20:41818574	cg27625055	481684
0.113	PRKCG	19:54402455	cg02849693	57883
0.113		8:41754181	cg17331296	317296
0.113	SOX11	2:5836231	cg18897632	342660
0.113		17:55213656	cg11030264	208410
0.113	DPP6	7:153584597	cg14523847	270200

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.114	MACROD2;S EL1L2	20:13976143	cg06571075	128176
0.114	CNN3;LOC72 9970	1:95393096	cg18344652	333645
0.114	DUSP27	1:167090757	cg11236550	211856
0.114	MEGF6	1:3447348	cg17163527	314497
0.114		20:12809929	cg12505343	232775
0.114	CHST8	19:34112683	cg27058486	472166
0.114	PUS1;ULK1	12:132410932	cg24221398	425685
0.114	C14orf23;FO XG1	14:29244278	cg21195256	378436
0.114		1:88928467	cg02664812	54315
0.114	SLC44A2	19:10713016	cg05567294	110272
0.114	LOC1001297 94	14:37641462	cg25051529	439230
0.114	CRNDE;IRX5	16:54966471	cg16642791	305999
0.114	STAT3;STAT 5A	17:40464780	cg25500196	446200
0.114	FGF18	5:170878209	cg02125316	43605
0.114		7:127775630	cg19871348	358070
0.114		7:158380884	cg22282410	394574
0.114		16:1048069	cg11978890	224277

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.113	HAND2;NBLA 00301	4:174453166	cg15234400	282488
0.113	EGLN3	14:34420292	cg24665290	432653
0.113	HOXD1;LOC4 01022	2:177053297	cg19180624	346696
0.113	LINC00472	6:72130209	cg10039188	191305
0.113	DMRTA2	1:50886949	cg25191628	441334
0.113	KIT	4:55524199	cg10087973	192117
0.114		15:87892167	cg02693157	54811
0.114	NXPH1	7:8482235	cg12597389	234250
0.114	CACNG6;CA CNG8;MIR93 5	19:54486058	cg02574502	52401
0.114	HOXD11;HO XD12;HOXD1 3	2:176964720	cg03964958	79739
0.114		7:127910927	cg08234689	159796
0.114	SPAG6	10:22634226	cg18247055	332095
0.114	FAM104B	X:55187561	cg15824287	291790
0.114	FOXQ1	6:1313211	cg26422161	461072
0.114		11:91957992	cg07603330	148311
0.114	UTF1;VENTX	10:135050619	cg25577463	447348
0.114	ARL9;SRP72	4:57371607	cg06922635	135243

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.115		7:52156489	cg18793404	340916
0.115	KCNK18	10:118976677	cg27455890	478852
0.115	UPK3A	22:45680879	cg07021644	137193
0.115	SLC6A2	16:55689865	cg10362591	197113
0.115		4:104918078	cg05123845	101996
0.115	PON2;PON3	7:95025836	cg08828819	170325
0.115	PROX1	1:214160860	cg17954152	327012
0.115	THRB	3:24536562	cg24120841	424012
0.115	CDK5R2	2:219826870	cg27638196	481940
0.115	TMEM17	2:62732892	cg10848792	205426
0.115	RBFOX1	16:6533163	cg14642432	272661
0.115	PSMD14;TBR1	2:162270993	cg08184652	158859
0.115	FKBP5	6:35654363	cg03546163	71700
0.115	LOC100188947	10:93058376	cg17402294	318468
0.115	KIF26B	1:245820634	cg11424312	214996
0.115	ELAVL4	1:50513766	cg05697849	112668
0.115	KIAA0748	12:55376897	cg25486399	445985
0.115	VAX1	10:118896755	cg11398452	214514
0.115	RFX8	2:102091269	cg12291728	229438

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.114	RGAG4	X:71352048	cg03056321	62257
0.114	ZNF83	19:53142146	cg25793430	450728
0.114	FRYL;SLC10A4;ZAR1	4:48492304	cg14249348	264663
0.115	HES6;LOC151174;LOC643387	2:239140182	cg23497383	413854
0.115		6:28911938	cg25005112	438404
0.115	RBFOX1	16:6070188	cg08015447	155664
0.115	CHST8	19:34113214	cg06399302	125117
0.115	PRKG1	10:52752476	cg11175150	210715
0.115	CRNDE;IRX5	16:54965142	cg09641689	184540
0.115	EMX2;EMX2OS	10:119303225	cg15373239	284408
0.115	ATOH1	4:94749865	cg00335712	7088
0.115	DSC3	18:28622474	cg14719951	274021
0.115	IDH1;PIKFYVE	2:209128590	cg06177665	121341
0.115	CAMKK2;P2RX4	12:121678558	cg09297514	178526
0.115	GABRB3	15:27018037	cg18026588	328201
0.115	GNA15	19:3136430	cg01032675	21764
0.115	DPP6	7:153749736	cg18940047	343252

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.116	CBWD2;FOX D4L1	2:114256781	cg10602757	201345
0.116	HES6;LOC151174;LOC643387	2:239140024	cg13957874	258474
0.116	OPRK1	8:54164296	cg13405783	247011
0.116	NKX2-1;SFTA3	14:36992233	cg04224064	84867
0.116	CCNA1	13:37005273	cg24297049	426624
0.116		2:91671535	cg02109405	43319
0.116		15:32607923	cg00943360	19827
0.116	PTPRG	3:61547130	cg09472360	181640
0.116	GLRB	4:157998201	cg10146199	193292
0.116	C1orf53;LHX9	1:197875080	cg12578211	233875
0.116	NPTX2	7:98246006	cg08315202	161360
0.116	GDF7	2:20871195	cg10553204	200490
0.116		8:61835848	cg06445016	125876
0.116	PRMT8	12:3600106	cg27316886	476555
0.116	ADAMTS16	5:5139878	cg04136610	83123
0.116	ZNF503;ZNF503-AS2	10:77163383	cg18510056	336418
0.116		6:28911902	cg13293729	244984

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.115		6:28677112	cg14234426	264370
0.115	MTNR1A	4:187476455	cg25107254	440048
0.115	ID2	2:8817010	cg21946006	389750
0.115	HTR1A	5:63257847	cg09698471	185520
0.115	SORCS3	10:106401319	cg10778841	204179
0.116		14:74100987	cg14527456	270289
0.116	FLRT2	14:85996499	cg01711160	35095
0.116	SHANK1	19:51198381	cg07060551	137922
0.116	ALLC;COLEC11	2:3699195	cg13452994	248021
0.116	GRM6	5:178421711	cg12483476	232367
0.116		3:22413960	cg06062984	119382
0.116	LRRC36;TPP P3;ZDHHC1	16:67427339	cg07355841	143680
0.116	HOTAIR;HOXC12	12:54355476	cg19188855	346817
0.116	TACSTD2	1:59042275	cg24851854	435890
0.116	NPY2R	4:156130016	cg21512644	383071
0.116	KIRREL3-AS3	11:126873379	cg00373707	7906
0.116	HS6ST3	13:96743087	cg27176138	474164
0.116	UBD	6:29521228	cg15814717	291599

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.117	MMP17	12:132312461	cg03570417	72216
0.117	ADAT1;KARS	16:75661691	cg01921773	39352
0.117	FIGLA	2:71017541	cg22650617	399823
0.117	CNPY1	7:155324691	cg09090582	174907
0.117	BDNF	11:27740876	cg05733135	113285
0.117	LINC00467	1:211590292	cg20802616	372441
0.117	OXTR	3:8813493	cg08449558	163593
0.117	DNAJB13	11:73668626	cg20737388	371474
0.117	SLC34A2	4:25657365	cg19766441	356236
0.117	LINC00461;MIR9-2	5:87968528	cg14636534	272541
0.117	PIWIL1	12:130822286	cg13861644	256478
0.117	DSC3	18:28622593	cg15439862	285459
0.117	UBD	6:29521046	cg18342026	333604
0.117	GABRA2	4:46391929	cg23160016	408245
0.117	DUSP8;MOB2	11:1575607	cg05280206	105032
0.117	PHACTR2	6:143998958	cg26846959	468429
0.117	FAM47E;SCARB2	4:77134471	cg19050061	344935
0.117	SPG7	16:89600764	cg08905080	171867

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.116	DMRT1;DMRT3	9:971480	cg07173635	140295
0.116		6:170686343	cg01061164	22368
0.116		5:4942469	cg18101138	329470
0.116	FBN2	5:127874466	cg25532099	446652
0.116	PPM1L	3:160475090	cg04056576	81465
0.116	11-Mar	5:16179210	cg03705912	74857
0.116	SOX11	2:5837057	cg15989068	294511
0.116	INTU	4:128544255	cg16654911	306224
0.116	FAM20C	7:193262	cg08782337	169501
0.116	SLC15A3	11:60719947	cg26980692	470832
0.116	RBFOX1	16:6068835	cg19378133	349684
0.116		14:95826734	cg05162306	102773
0.116	SOX1	13:112717244	cg09469566	181584
0.117	PRPH	12:49689463	cg14029489	260043
0.117	MLXIPL	7:73038859	cg10092878	192247
0.117	ATP4A	19:36048943	cg19715414	355233
0.117	MANEAL;YRDC	1:38261057	cg24433287	428889
0.117	KCNA4	11:30038677	cg15310492	283522
0.117		3:54119792	cg03494612	70623

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.118	CADPS	3:62861055	cg15957055	293976
0.118	KCNQ1DN	11:2891082	cg25203481	441543
0.118	ZFPM2	8:106332119	cg10868817	205750
0.118		3:171543413	cg11639615	218225
0.118	PXDN	2:1748112	cg12164282	227454
0.118	TIGD7,ZNF75A	16:3355553	cg05540369	109851
0.118	SP8	7:20824770	cg27618240	481572
0.118		15:96905729	cg11157253	210450
0.118	ADRA1D	20:4202378	cg04293085	86242
0.118	LOC100130298	8:61880392	cg04882213	97419
0.118	DYNLT1;SYTL3	6:159068210	cg27278961	475791
0.118	PCDHA1;PCDHA2;PCDHA3;PCDHA4;PCDHA5;PCDHA6	5:140201656	cg11781306	220669
0.119	DPP6	7:153584416	cg22620221	399362
0.119	ZNF468	19:53361164	cg08531263	165137
0.119	CNTNAP5	2:124782831	cg08790440	169635
0.119	FBN2	5:127873106	cg17564775	321142

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.117	BBX	3:107244746	cg02321062	47394
0.117	ALDH1L1	3:125899370	cg01566526	32429
0.117		3:4856199	cg08998950	173407
0.117	LTBP3	11:65325158	cg08965235	172854
0.118		16:85203635	cg00942219	19808
0.118	PIPOX	17:27369780	cg06144905	120806
0.118	LMNB2	19:2446487	cg18087306	329215
0.118	GUSBP4	6:58263193	cg17976157	327360
0.118	ISL1	5:50679149	cg08734740	168746
0.118	BAALC;C8orf56	8:104153627	cg18168101	330737
0.118		1:65534742	cg20301308	364692
0.118		9:136474735	cg03262554	66122
0.118	ZC3H8	2:113012627	cg27242549	475215
0.118	ZNF148	3:125076233	cg12508343	232821
0.118	MGC45800	4:183064388	cg00053393	1279
0.118	NRG2;PSD2	5:139223811	cg08682153	167769
0.118	HOXA5;HOXA6;HOXA7;LOC100133311	7:27187269	cg06237983	122446

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.119	EPHA6	3:96533511	cg11410023	214721
0.119	HOXA5;HOXA6;HOXA7;L OC10013331 1	7:27188364	cg19816811	357110
0.119	PDGFC	4:157892765	cg22451233	396868
0.119	HCG4B	6:29895005	cg01519225	31476
0.119	ATP2C2	16:84402160	cg08974450	173017
0.119		4:187037318	cg05379002	107021
0.119	TRIM71	3:32860178	cg12338417	230063
0.119	POU6F2	7:39125198	cg02367316	48362
0.119	RBP1	3:139258295	cg12497564	232636
0.119	EF3;IL25	14:23834909	cg13011388	240610
0.119	MYRIP	3:39851788	cg07892785	153449
0.119	RAB38	11:87908783	cg01568784	32481
0.119	TBX4	17:59532306	cg14823851	275680
0.119	TOX2	20:42544794	cg03011535	61343
0.120	DLC1	8:13134144	cg03304380	66890
0.120	SNED1	2:241938436	cg08233654	159775
0.120	KIF25	6:168436019	cg12003941	224653
0.120	C1orf35;MRP	1:228297864	cg22163199	392875

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.119	CDH8	16:62070184	cg01718742	35267
0.119	COX19;CYP2 W1	7:1018969	cg01823585	37440
0.119	LPHN2	1:82267931	cg02243785	45777
0.119	LOC1001301 55;MIR124-2	8:65290484	cg07792478	151647
0.119	LHX8	1:75595970	cg22694818	400568
0.119	LOC339529;Z NF238	1:244213616	cg19698993	354930
0.119	OLFML2A	9:127531952	cg14046477	260419
0.119	EPHA1;LOC2 85965	7:143108841	cg16618979	305561
0.119	AZU1;LPPR3; MIR3187	19:822086	cg21928701	389466
0.119	OSBPL3	7:25005464	cg07110009	138907
0.119		7:52155829	cg11342198	213584
0.119	PREX2	8:68864769	cg06617456	128991
0.119	CHRNA4	20:61992494	cg01743841	35695
0.119	ISLR2;LOC28 3731	15:74425552	cg01178680	24810
0.119	UNC5D	8:35092823	cg08000065	155421
0.119	PRKAR1B	7:751830	cg27331241	476807
0.119	MAP7	6:136847359	cg18421949	334865

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
	HGC5			
0.121	HOXA10;HOXA10- HOXA9;HOXA7;HOXA9;L OC10013331 1;MIR196B	7:27204894	cg27009703	471328
0.121	DLG5	10:79622515	cg11063088	208886
0.121	KDM2B	12:122019076	cg15234492	282489
0.121	IRF6	1:209979733	cg21951975	389837
0.121	ACTL6B	7:100254149	cg16024950	295200
0.121	ONECUT2	18:55095177	cg05735180	113314
0.121	WDR17	4:176987020	cg08095852	157102
0.121	CLEC14A	14:38725312	cg08139247	158007
0.121	HOXD4;MIR10B	2:177014555	cg19519747	352000
0.121	UTRN	6:144608500	cg15785898	291201
0.121	MFSD7;MYL5	4:682834	cg24693053	433212
0.121	GABRA5	15:27112430	cg10652393	202197
0.121	PLSCR2	3:146187706	cg02128651	43681
0.121	PENK	8:57358590	cg21694941	385984
0.121	FBN2	5:127873283	cg05209584	103634

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
	L55			
0.120	CTNNA2	2:79739278	cg18806140	341143
0.120	ALOX5	10:45869702	cg27243389	475225
0.120	NAALAD2	11:89867976	cg21500966	382886
0.120	NLRP2	19:55477755	cg17760849	323892
0.120	AIM1	6:106957995	cg20796467	372352
0.120	ZFPM2	8:106331995	cg15449956	285663
0.120	ISL1	5:50679290	cg11711420	219504
0.120	C3orf15	3:119422161	cg08145590	158129
0.120		4:82965250	cg04643822	92882
0.120	FGFR1	8:38323059	cg13278539	244735
0.120	SRRM4	12:119591747	cg27010159	471336
0.120	UGP2	2:64069682	cg19915305	358803
0.120	GLI4	8:144361073	cg11240062	211921
0.120	TOX2	20:42544792	cg13459498	248157
0.120	AQP4;CHST9-AS1	18:24445692	cg12445775	231741
0.120	NKX6-1	4:85418265	cg12076463	225925
0.121	PCDHGA12;P CDHGC3;PC DHGC4;PCD	5:140871385	cg24619378	431928

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.122	CCDC146	7:76747831	cg02901065	58990
0.122	ZFP42	4:188916581	cg15718581	290161
0.122		2:225306901	cg10193763	194181
0.122	HOXD10;HOXD11;HOXD12	2:176972581	cg24633978	432153
0.122	ENTPD6	20:25177340	cg00926318	19472
0.122	TSHZ1;ZADH2	18:72917387	cg22088248	391726
0.122	POLG	15:89879190	cg24365117	427793
0.122		7:43291318	cg02964324	60381
0.122	NETO1	18:70534298	cg23883696	419843
0.122	POU4F1	13:79170283	cg24221648	425692
0.122	GNAS;GNAS-AS1	20:57427650	cg02890368	58752
0.122	PDE2A	11:72301724	cg26268145	458304
0.122	ARL9;SRP72	4:57372356	cg14775423	274866
0.122	HLCS	21:38353114	cg22777062	401811
0.122	TP73;WRAP73	1:3568210	cg20677901	370380
0.122		2:190192866	cg25550823	446916
0.122	SNX31	8:101661788	cg10715223	203178

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.121	PAX1	20:21686293	cg01783070	36501
0.121		18:6414602	cg083336641	161747
0.121	NRG1	8:31497464	cg24946597	437530
0.121	FBXO39;XAF1	17:6679564	cg02374745	48515
0.121	WNT2	7:116963259	cg07697895	149945
0.121		8:142413013	cg06830360	133304
0.121	SNORA76;SNORD104;TEX2	17:622222808	cg20969675	374778
0.121	EHP1;LOC100132215;OTX1	2:63275602	cg27344587	477023
0.121	IRX1	5:3599686	cg01294808	27051
0.121	CADM2	3:85008587	cg13331200	245621
0.121	FAT1	4:187647690	cg12769506	236972
0.121		10:131762052	cg11757357	220344
0.122	ADAM12	10:128077307	cg05237641	104212
0.122	CLVS2	6:123317569	cg08194879	159033
0.122		12:127940654	cg16065021	295854
0.122	SLC6A3	5:1446208	cg14502484	269687
0.122	ASPG;MIR203;MIR3545	14:104583071	cg03401997	68837

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.123	C1QL1	17:43044660	cg24042242	422692
0.123	PCDHGA1;P CDHGA2	5:140711852	cg05580809	110540
0.123	VSTM5	11:93583693	cg14291919	265581
0.123	ZFP2;ZNF454	5:178367827	cg24843380	435721
0.123	KLHDC10	7:129781152	cg07026433	137279
0.123	SLIT2	4:20257590	cg19940312	359283
0.123	IRF6	1:209979665	cg22029157	390830
0.123		11:71350975	cg13009111	240573
0.123	PITX1	5:134367394	cg23064601	406786
0.123	PLSCR2	3:146187740	cg21569635	384039
0.124	SKAP2	7:26897685	cg03730533	75381
0.124	CABYR;TTC3 9C	18:21719433	cg26349976	459840
0.124	TSHZ1;ZADH 2	18:72916776	cg02750262	56023
0.124	ZNF835	19:57183118	cg08146323	158144
0.124	TBX15	1:119535928	cg24035245	422569
0.124	OSGIN1	16:83986941	cg07978099	155051
0.124	PRKD1	14:30396444	cg10501704	199443
0.124	SCRT2	20:644758	cg12590600	234112

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.122	ARHGEF10; MIR596	8:1771973	cg10964367	207265
0.122	B3GNT4;DIA BLO;LRRC43	12:122688787	cg23445859	413050
0.122	TRPC4	13:384444227	cg16409955	301745
0.122	KCNA1	12:5020693	cg08832227	170388
0.122	EXT2	11:44118094	cg24662154	432585
0.123	ADAMTSL3	15:84363061	cg14598478	271807
0.123	STK32B	4:5053504	cg08323075	161506
0.123	DKFZp434J0 226	19:46713446	cg21100328	376752
0.123	RNF180	5:63461803	cg09839635	187877
0.123	CYB561D2;N PRL2;RASSF 1;TMEM115;Z MYND10	3:50383175	cg00460268	9723
0.123	RNF207;RPL 22	1:6269448	cg25286333	442745
0.123		17:2627661	cg12187586	227838
0.123	P2RY12	3:151058783	cg13229867	243994
0.123	DUSP4	8:29210592	cg05128656	102084
0.123	HTR4	5:148034045	cg04091563	82145
0.123	TMEM164	X:109246494	cg04926827	98346

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.125		8:61823027	cg20904475	373766
0.125	PRDM8	4:81118188	cg03463411	70030
0.125	INSR	19:7294093	cg26532951	462966
0.125	HOXD4;MIR10B	2:177014959	cg17104824	313519
0.125	PON2;PON3	7:95025740	cg23230584	409500
0.125	TFAP4	16:4324280	cg00021532	522
0.125	CRNDE;IRX5	16:54965087	cg05870072	115671
0.125		14:103673450	cg26579556	463863
0.125	NXPH2	2:139537824	cg18150439	330428
0.125		13:42002627	cg25532201	446653
0.125	KLHL4	X:86772364	cg15554694	287280
0.125	MALL;NPHP1	2:110873396	cg01615704	33421
0.125	HAAO	2:43020264	cg17246140	315873
0.125	DPP6	7:153584609	cg27032232	471703
0.125	LHFPL4	3:9594385	cg04061117	81564
0.125	EGFL7	9:139551542	cg13900767	257221
0.125	COX16;SYNJ2BP;SYNJ2B P-COX16	14:70827109	cg13099429	241974
0.125	LHX6	9:124990456	cg13817952	255647

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.124	TRPM4	19:49713828	cg10951975	207052
0.124		5:53564	cg22807585	402379
0.124	DUOX2;DUOX1;DUOX2	15:45405103	cg04222582	84830
0.124		14:99584667	cg23683254	416925
0.124	FEZF1;LOC154860	7:121940216	cg27393010	477821
0.124	NELF;PNPLA7	9:140348828	cg14384158	267359
0.124	PTPN13	4:87515467	cg15543566	287079
0.124	KCTD14;NDUFC2-KCTD14	11:77734206	cg16769152	308350
0.124	GBX2	2:237076811	cg21426003	381745
0.124	PON2;PON3	7:95025829	cg08520743	164919
0.124	CPEB1	15:83316223	cg27578811	480950
0.124	NTM	11:131780492	cg15617814	288391
0.124	ATP9A	20:50385371	cg01900832	38931
0.124		13:36705475	cg25724283	449620
0.124		10:21462441	cg17426273	318854
0.124	ALX1	12:85674296	cg07780095	151415
0.124		6:106441441	cg03942932	79300
0.125	HECW1	7:43152254	cg08039116	156084

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.126	CXCL2	4:74965262	cg23244559	409786
0.126	MIR1469;NIR2 F2	15:96884187	cg07016184	137060
0.126	EGLN2;RAB4 B-EGLN2	19:41319790	cg01282508	26784
0.126	TMEM132C	12:128751460	cg03530754	71358
0.126	PDZRN4	12:41582349	cg21926708	389441
0.126	EFCAB1	8:49647734	cg08258526	160240
0.126	PIN4	X:71401384	cg23905908	420234
0.126	RP11-165H20.1	1:111813690	cg07197785	140790
0.126	LOC645249	7:156814491	cg00024086	585
0.126	ATHL1;FITM 5;NLRP6	11:288305	cg08829299	170335
0.126	GALR1	18:74961966	cg03659519	73996
0.126		1:2738746	cg10105681	192507
0.126	RGAG4	X:71351980	cg20347665	365414
0.126	RNF180	5:63461574	cg14591786	271667
0.127	EOMES	3:27772805	cg11642106	218279
0.127	HOXB9;MIR1 96A1	17:46711017	cg23690166	417069
0.127	ARMC5;TGF B11	16:31484032	cg10995380	207836

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.125	KCNK16;KCN K17	6:39281885	cg08315770	161367
0.125	CCT8L2;TPT EP1	22:17082770	cg14505585	269757
0.125	FAM135B	8:139509672	cg23294090	410690
0.125	GDA	9:74764428	cg211170041	377969
0.126	IL1RAPL1	X:28604661	cg06927864	135328
0.126	CIDEA	18:12254551	cg07204280	140912
0.126	NPAS3	14:33403862	cg08117309	157524
0.126	ENPP2	8:120650994	cg02534163	51618
0.126		7:156400711	cg16561657	304460
0.126	STXBP5L	3:120627406	cg05293820	105268
0.126	CNTN1	12:41086680	cg14625113	272330
0.126	IRF6	1:209979283	cg25192855	441351
0.126	CAST	5:96038614	cg24742349	434137
0.126	FBN2	5:127874463	cg11965976	224052
0.126	ATXN2	12:112035212	cg08273772	160571
0.126	PDE4D	5:59189120	cg03323696	67297
0.126	TOX2	20:42544663	cg06779449	132219
0.126	BCOR	X:40005177	cg12737514	236481
0.126	KIAA1530	4:1366597	cg23921777	420508

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.128		2:71115370	cg10954469	207096
0.128	ZNF347;ZNF415	19:53635967	cg18301583	332927
0.128	SNED1	2:241938321	cg21384492	381197
0.128	VSTM2A	7:54614477	cg06584494	128412
0.128	MEIS2	15:37388540	cg00691830	14602
0.128	NLRP14;ZNF214	11:7041930	cg17228942	315646
0.128	KCNV1	8:110988043	cg23291534	410667
0.128	MAGI2-AS3	7:79081666	cg06809544	132847
0.128	FBXO39;XAF1	17:6679348	cg00376544	7966
0.128	PTF1A	10:23481176	cg22746058	401390
0.128	TAL1	1:47691160	cg10810752	204761
0.128	FBRSL1	12:133137479	cg03621470	73255
0.128	CCDC36;LOC646498	3:49236946	cg03540175	71588
0.128	CXXC4	4:105412800	cg22604213	399113
0.128	MSX1	4:4864902	cg11078084	209175
0.128	FLJ45983;GATA3	10:8097641	cg17124583	313810
0.128	ADRA1B	5:159343549	cg07011172	136949

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.127	PON2;PON3	7:95025855	cg04685170	93636
0.127	PRSS3	9:33749216	cg22410499	396383
0.127	CPNE4	3:131246097	cg08151596	158229
0.127	GABRG3	15:27216529	cg11651237	218458
0.127	B4GALNT2	17:47209827	cg20233029	363633
0.127	MSX1	4:4864488	cg21538208	383498
0.127	ARHGEF4	2:131673771	cg09015973	173696
0.127	PCDHA1;PCDHA10;PCDHA11;PCDHA12;PCDHA13;PCDHA2;PCDHA3;PCDHA4;PCDHA5;PCDHA6;PCDHA7;PCDHA8;PCDHA9	5:140261663	cg02051771	42046
0.127	ASPG;MIR203;MIR3545	14:104583048	cg13673833	252679
0.127	MAGI2-AS3	7:79083507	cg02523844	51402
0.127	IRX2	5:2739602	cg21573200	384101
0.127	NUP210	3:13431720	cg17336044	317388
0.128		2:132088801	cg14001664	259383
0.128	CCDC130;MR11	19:13875137	cg14272688	265161

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.129	LOC1005070 55:P2RX2;PO LE	12:133195094	cg00058329	1387
0.129	CCDC164;EP T1	2:26624934	cg14273450	265175
0.129	ISM1	20:13200929	cg22588144	398900
0.129	EGR2	10:64578919	cg22903908	404041
0.129	GSDMD;ZC3 H3	8:144626190	cg09422696	180737
0.129	KCNK9	8:140715802	cg21415530	381621
0.129		3:94243571	cg16274205	299307
0.129	UNC80	2:210636539	cg24938830	437420
0.129	CABLES2;RP S21	20:60958108	cg14168305	262866
0.129		11:124324477	cg03252499	65933
0.129	FAT1	4:187645144	cg24410535	428521
0.129	PPP1R14A;S PINT2	19:38747378	cg02571816	52340
0.130	ASIP	20:32856898	cg05267394	104806
0.130	CCDC144A	17:16593885	cg02879122	58511
0.130	CRISPLD1	8:75896720	cg15953602	293925
0.130	KAL1	X:8700172	cg18396832	334461
0.130	CELF1	11:47528955	cg13308137	245225

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.128	UBD	6:29521272	cg22762215	401614
0.128	TGFB1	5:135364568	cg15146621	281189
0.128	CHST8	19:34112825	cg26565021	463587
0.128	JPH1	8:75234269	cg23599843	415405
0.128	ACSS1	20:25039707	cg03321508	67252
0.128	BASP1;LOC2 85696	5:17218778	cg14306451	265851
0.128		11:79148502	cg05454619	108297
0.128	NLRP14;ZNF 214	11:7041752	cg11838299	221836
0.128		2:9235898	cg20610452	369302
0.129	PCDHA1;PC DHA10;PCDH A11;PCDHA1 2;PCDHA13; PCDHA2;PC DHA3;PCDH A4;PCDHA5; PCDHA6;PC DHA7;PCDH A8;PCDHA9; PCDHAC1;P CDHAC2	5:140346236	cg12832313	237924
0.129	C8orf42	8:495736	cg05142982	102391
0.129		11:70962935	cg11263364	212293
0.129	CDH12	5:21751337	cg23404351	412413

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.130	LOC643714;T OX3	16:52580987	cg26817217	467846
0.131	UNCX	7:1265851	cg15591276	287897
0.131	RARRES1	3:158450251	cg142226182	264214
0.131	PRDM8	4:81118500	cg19409579	350194
0.131	DQX1;PCGF1 ;TLX2	2:74742786	cg19656282	354267
0.131	STL	6:125283245	cg24822696	435377
0.131	CPNE4	3:131756545	cg12981577	240178
0.131	UBD	6:29521407	cg03402459	68848
0.131	HLCS	21:38362725	cg14785464	275096
0.131	SHROOM2	X:9753940	cg26318441	459244
0.131	FTSJ2;NUDT 1;SNX8	7:2289054	cg17467898	319545
0.131	PCDHB10;PC DHB16;PCDH B7;PCDHB8; PCDHB9	5:140562738	cg21081817	376495
0.131	NOS1	12:117798954	cg04883903	97454
0.131	CHL1	3:238615	cg07746943	150879
0.131	SGPP2	2:223289277	cg00043095	1074
0.131	TUSC1	9:25678015	cg13985784	259065
0.131	NKX2-8	14:37051417	cg10530851	200070

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.130	HOXC4;HOX C5;HOXC6;H OXC8;HOXC 9	12:54404315	cg13545297	249972
0.130	DOCK1;FAM 196A	10:128994608	cg25984344	453521
0.130	LOC1005072 66	4:4577273	cg07914772	153870
0.130	KCNS2	8:99440279	cg14486338	269395
0.130		5:3093070	cg20428720	366575
0.130	HOXA10;HOX A10- HOXA9;HOX A7;HOXA9;L OC10013331 1;MIR196B	7:27204981	cg26521404	462738
0.130	RNF180	5:63461582	cg06776999	132168
0.130	MTRNR2L4;O R2C1	16:3415077	cg09999114	190605
0.130	PENK	8:57358312	cg12877723	238608
0.130	NETO1	18:70534767	cg18448581	335334
0.130	TTC40	10:134650467	cg25403174	444670
0.130	ASXL3	18:31158234	cg24880056	436440
0.130	DEAF1;DRD4 ;SCT	11:637038	cg15861585	292487
0.130	GLT1D1	12:129337910	cg06419750	125449

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.132	NEFM	8:24771326	cg07552803	147256
0.132	HMGCLL1	6:55443757	cg11907729	223067
0.132	WNT2B	1:113051846	cg27181253	474270
0.132	RADIL	7:4869981	cg00469380	9930
0.132	NRXN1	2:50574196	cg14875171	276641
0.133	CTNNA2	2:79740208	cg04670857	93356
0.133	DOCK1;FAM196A	10:128994605	cg12204732	228111
0.133		12:132146956	cg24533007	430572
0.133	CBLN2	18:70209432	cg13478228	248599
0.133	PIEZO2	18:11149470	cg03686593	74481
0.133	NELL1	11:20690957	cg17371081	317950
0.133	SLC34A2	4:25657381	cg03738352	75550
0.133		3:74663796	cg00735667	15563
0.133		5:132947501	cg23236554	409620
0.133	LRRRC4C	11:40315392	cg17949440	326949
0.133	CHST9	18:24765485	cg16933181	310893
0.133		6:168147405	cg07147204	139710
0.134	CNTNAP2	7:145813417	cg11592503	217489
0.134	ENTPD2;NPD C1	9:139943146	cg14024893	259944

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.132	FRYL;SLC10A4;ZAR1	4:48492225	cg22773661	401769
0.132	LOC402160;RNF4	4:2464050	cg21722242	386297
0.132	CHL1	3:239207	cg21145524	377484
0.132		18:73167671	cg12975230	240067
0.132	SALL1	16:51188697	cg00683332	14419
0.132	FAM19A5	22:48972349	cg06273376	122999
0.132	GRM6	5:178422128	cg00582971	12427
0.132	RTBDN	19:12936512	cg07583894	147890
0.132	HOXA10-HOXA9;HOXA5;HOXA6;HOXA7;HOXA9;LOC100133311	7:27192656	cg23263937	410186
0.132	TMEM45B	11:129685751	cg27274706	475714
0.132	NRK	X:105066526	cg07674139	149532
0.132	NRG1	8:31497829	cg26267340	458285
0.132	NAALAD2	11:89867653	cg01577414	32669
0.132	SMTNL2	17:4488345	cg07888347	153363
0.132	CHRN1;FGF11;TMEM102	17:7341641	cg25563256	447126

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
	A11;PCDHA1 2;PCDHA13; PCDHA2;PC DHA3;PCDH A4;PCDHA5; PCDHA6;PC DHA7;PCDH A8;PCDHA9			
0.135	SSTR1	14:38678420	cg18443253	335246
0.136	KCNQ4	1:41248881	cg16294363	299640
0.136	DUSP27	1:167090646	cg17104258	313508
0.136		4:170696239	cg18912209	342859
0.136	CXCL5	4:74864165	cg27109129	473022
0.136	LHX8	1:75602412	cg08146483	158147
0.136	CCR6	6:167559913	cg16338365	300452
0.136	KIF17;SH2D5	1:21044101	cg09793172	187028
0.136	ANKRD26P3; LINC00421	13:19918586	cg06722407	131065
0.136	ZFP42	4:188916875	cg10242602	195098
0.136	UBD	6:29521430	cg15818307	291669
0.136	HOXD1;LOC4 01022	2:177053292	cg05099387	101608
0.136	ISM1	20:13200944	cg14060111	260677
0.136	NMBR	6:142409507	cg20747266	371647

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.134	MAGI2-AS3	7:79083445	cg04652097	93018
0.134	TACR3	4:104640662	cg18538958	336883
0.134	NXNL2	9:91150537	cg14347199	266666
0.134	COX6B2;FAM 71E2;IL11;SU V420H2	19:55866087	cg20106459	361820
0.134	DPRXP4;RNF 135	17:29297391	cg01347228	28034
0.134	GPR6	6:110300573	cg26252167	458027
0.134	MAN1C1	1:25944514	cg10706230	203035
0.135	TJP1	15:30114474	cg19965221	359674
0.135	SSPO	7:149484798	cg16516272	303562
0.135	C3orf25;MBD 4	3:129147541	cg14779951	274962
0.135		13:50701501	cg23104954	407495
0.135	LRP3	19:33685817	cg10276227	195631
0.135	HOXD10;HO XD8;HOXD9; LOC1005067 83	2:176994448	cg14473102	269120
0.135	SNAP91	6:84418433	cg24190603	425243
0.135	ISL1	5:50679147	cg16318053	300061
0.135	PCDHA1;PC DHA10;PCDH	5:140261653	cg19876814	358160

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.137	OR2H1	6:29427519	cg05111645	101800
0.137	HAS1;LINC00085	19:52206667	cg17519645	320492
0.137	TGFBI	5:135364580	cg09873933	188549
0.138	NAALAD2	11:89867637	cg16886581	310118
0.138		14:95331190	cg03459776	69950
0.138	FOXF2	6:1390622	cg12221475	228386
0.138	THRB	3:24537050	cg27526665	479998
0.138		7:156400779	cg18584424	337608
0.138	MIR3663	10:118922493	cg24234899	425848
0.138	PITX1	5:134364387	cg00396667	8373
0.138	DRD5	4:9783198	cg03045635	62021
0.138	SIK3	11:116857794	cg09458566	181396
0.138		13:109147921	cg03994318	80330
0.138	IGF2BP1	17:47075880	cg02745847	55935
0.138	SKINTL	1:48559803	cg08871545	171173
0.138	LMX1A	1:165204796	cg09118258	175320
0.138	GATA6	18:19756877	cg12615165	234584
0.138	CYB561D2;N PRL2;RASSF 1;TMEM115;Z	3:50383079	cg20881888	373460

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.137		7:1287065	cg12560987	233619
0.137	STL	6:125283953	cg10621825	201643
0.137	FAM181B	11:82444798	cg09617579	184158
0.137	DACH2	X:85402643	cg16259355	299014
0.137		13:21872234	cg11317459	213174
0.137	IRX4	5:1882885	cg14507560	269807
0.137	FGD3	9:95737070	cg14263098	264963
0.137		7:157477846	cg04207084	84494
0.137	AATF;LHX1	17:35300010	cg19760241	356113
0.137	HES6;LOC151174;LOC643387;PER2	2:239149859	cg24127874	424152
0.137	HOXD4;MIR10B	2:177014962	cg00014998	368
0.137	C5orf63	5:126409308	cg21113900	376968
0.137	SLC16A11;SLC16A13	17:6946059	cg19639560	354003
0.137	ZBTB44	11:130185651	cg14482569	269324
0.137	ARHGEF4	2:131674140	cg07815799	152125
0.137	DAXX;TAPBP;ZBTB22	6:33280424	cg26083458	455084
0.137	DPP10;LOC389023	2:115919829	cg01718116	35249

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.139	H2AFY	5:134735637	cg15613420	288307
0.139	PLD3	19:40871823	cg08360726	162147
0.140	KIRREL3;ST3 GAL4	11:126286828	cg12804791	237513
0.140	ASIP	20:32856846	cg16440058	302309
0.140	NKAIN3	8:63161609	cg15858239	292441
0.140	SMAD3	15:67396487	cg19193595	346888
0.140	ALPK3	15:85360655	cg25895948	452116
0.140	C8orf83	8:93977794	cg16560711	304445
0.140	MSX1	4:4864532	cg09748975	186296
0.140	ACTN3;CTSF	11:66326798	cg05475524	108647
0.141	DPP6	7:153584873	cg14564076	271091
0.141	CTNNA2	2:79740185	cg19707040	355066
0.141	SOX1	13:112721325	cg24604013	431705
0.141	DOCK1;FAM 196A	10:128994297	cg06525651	127283
0.141	SLC6A18;SL C6A19	5:1222847	cg04248937	85368
0.141	C14orf23;FO XG1	14:29236898	cg07489048	146092
0.141	NANS	9:100819928	cg13527921	249630
0.141		11:44545144	cg13759632	254444

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
	MYND10			
0.138	NXNL1;TME M221	19:17559217	cg18380550	334165
0.138	C12orf53	12:6818384	cg23877043	419727
0.138	TAL1	1:47691158	cg10380348	197448
0.139	ALPK3	15:85360664	cg20318166	364967
0.139	VSTM2A	7:54614620	cg06139908	120728
0.139		15:26108391	cg03419058	69144
0.139	OPCML	11:132813563	cg18710784	339517
0.139	HOXA5;HOX A6;HOXA7;L OC10013331 1	7:27187560	cg14044640	260386
0.139		6:27525678	cg20494374	367603
0.139	KDM1A;MIR3 115	1:23361764	cg25002551	438359
0.139	RLF	1:40626599	cg18646240	338570
0.139	NRSN2	20:328035	cg21192095	378373
0.139	MSX1	4:48644430	cg24840099	435675
0.139	FLJ16779;NK AIN4	20:61886079	cg08111446	157414
0.139	DUSP4	8:29210154	cg13635007	251899
0.139	MAGI2-AS3	7:79083509	cg24021956	422308

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.142	RNF207;RPL22	1:6269260	cg15731815	290408
0.142	LOC100188947	10:93058549	cg04285822	86104
0.142	HOOK1	1:60280812	cg15900248	293091
0.142	DRD5	4:9783196	cg23847712	419333
0.142	CNTN4	3:2140256	cg04222358	84827
0.142		3:159818742	cg07617768	148563
0.142	GLRB	4:157997367	cg16269431	299215
0.143		2:68917482	cg18670846	338907
0.143		8:41624841	cg07162571	140077
0.143	MTUS2	13:30055092	cg05122437	101967
0.143	FAM110B	8:59058254	cg13247663	244256
0.143		2:92027943	cg27311294	476418
0.143	TNR	1:175568559	cg24932457	437299
0.143	TNIP3	4:122078348	cg26832294	468154
0.143	C5orf63	5:126409007	cg10200291	194305
0.143	BCOR	X:40012100	cg06548617	127783
0.143		11:32008961	cg20019985	360529
0.143	OCRL	X:128674224	cg05032353	100321
0.143	CHST8	19:34113010	cg16190732	297843

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.141	LRP12	8:105601036	cg24098951	423650
0.141	COL23A1	5:178004091	cg08475953	164148
0.141	ASGR1	17:7077709	cg03975755	79935
0.141		11:133837265	cg23152235	408116
0.141	SIM2	21:38070671	cg26938272	470089
0.141	SCN2B;SCN4B	11:118023765	cg18718634	339649
0.141	FZD5	2:208631684	cg15714846	290094
0.141	DOCK1	10:128593946	cg23665778	416569
0.141	INPP5A;NKX6-2	10:134600701	cg17996619	327663
0.141	ONECUT2	18:55095249	cg15222899	282298
0.141	ZDHHC4	7:6616423	cg19149522	346313
0.141	OR10AD1	12:48592721	cg23748340	417996
0.142	NLRP2	19:55477759	cg19689876	354758
0.142	NXPH2	2:139537845	cg00804628	16987
0.142	FAIM3;IL24	1:207082828	cg06528575	127352
0.142	ZC3H3	8:144599125	cg13071618	241523
0.142	FAM84A	2:14775046	cg05602862	110952
0.142	FAM84A	2:14773973	cg16846645	309527
0.142	HMX3	10:124897048	cg15396686	284826

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.144	CYB561D2;N PRL2;RASSF 1;TMEM115;Z MYND10	3:50383118	cg11270070	212403
0.144	DPP6	7:153749756	cg15549927	287181
0.144	HCN1	5:45695643	cg18273840	332528
0.144	LHX8	1:75602167	cg08272731	160551
0.145	UBD	6:29521420	cg22305167	394855
0.145	ADAMTS20	12:43945892	cg19619405	353636
0.145	HAGH	16:1863053	cg00935504	19660
0.145	ISM1	20:13200931	cg04432319	88934
0.145	ANKS1B	12:99288805	cg03609960	73052
0.145	LHX3	9:139085579	cg04455058	89330
0.145		6:10382103	cg20906291	373785
0.145	FAM110B	8:59058273	cg12615766	234593
0.145	CYP1A1	15:75018852	cg20004910	360290
0.145	CACNB2	10:18429703	cg02456226	50000
0.145	SNTG2	2:1134065	cg16519574	303633
0.145	DPYS	8:105478855	cg16783744	308581
0.145		19:57618136	cg18384778	334232
0.145		2:200524189	cg20711639	371065

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.143	UBD	6:29520774	cg08065408	156530
0.143	PCDHGA1;P CDHGA10;P CDHGA2;PC DHGA3;PCD HGA4;PCDH GA5;PCDHG A6;PCDHGA7 ;PCDHGA8;P CDHGA9;PC DHGB1;PCD HGB2;PCDH GB3;PCDHG B4;PCDHGB5 ;PCDHGB6;P CDHGB7	5:140787430	cg07613945	148493
0.143	SYT15	10:46970625	cg09373037	179902
0.143	FOXI2	10:129535669	cg07918545	153959
0.144	LOC649133;P OU2F3	11:120110882	cg26357587	459979
0.144	CSMD1	8:4849827	cg23495279	413823
0.144	OSTalpha;ZD HHC19	3:195934355	cg26292150	458748
0.144	PITX1	5:134363877	cg04223420	84848
0.144	PDZRN4	12:41582362	cg16896079	310254
0.144	SH2D4B	10:82295864	cg15642854	288829
0.144	UNC80	2:210636560	cg04100532	82347

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.147	AGAP1	2:236412034	cg11045331	208636
0.147	KDM2B	12:122019006	cg07793808	151670
0.147	KIF12	9:116860650	cg14326196	266248
0.148	FAM150A	8:53477881	cg09442654	181101
0.148	ADAP1	7:968552	cg05904016	116371
0.148	DOCK1;FAM196A	10:128994644	cg03129384	63592
0.148	MAML2	11:95969587	cg05270552	104870
0.148	SP8	7:20824932	cg23093589	407294
0.148		12:119212248	cg22125805	392264
0.148	ZSCAN18	19:58609618	cg22721334	401040
0.148	FOSB	19:45976195	cg12542255	233333
0.148	ZSCAN18	19:58609602	cg25784220	450602
0.148	GALR1	18:74962672	cg06360427	124375
0.148		5:168728081	cg07136998	139473
0.148	ANKRD18A;FAM201A	9:38622559	cg21189438	378326
0.148	CSGALNACT2;RET	10:43633030	cg07178550	140402
0.148		13:53775410	cg13974192	258762
0.149	DIAPH1;PCDHGA12;PCD	5:140892822	cg08860070	170948

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.145	HLA-DPA1;HLA-DPB1	6:33053608	cg01991743	40852
0.146	GNG12;LOC100289178	1:68299409	cg13184736	243235
0.146	NAALAD2	11:89867679	cg18540157	336897
0.146		1:241520286	cg14156405	262603
0.146		18:4455337	cg25627226	448224
0.146	PLSCR2	3:146187126	cg24092307	423558
0.146	MAD2L1BP;RSPH9	6:43612908	cg17536595	320768
0.146	GALNT10	5:153569246	cg13372456	246337
0.146	KCNA4	11:30038675	cg08490115	164399
0.146		7:158380886	cg27392792	477814
0.146	KY	3:134369661	cg24675998	432827
0.146	IRF6	1:209979624	cg09509183	182272
0.147		7:156400881	cg27483342	479249
0.147	ZSCAN1	19:58545333	cg27391267	477779
0.147	NAALAD2	11:89867704	cg21817737	387693
0.147	NID1	1:236228741	cg07157830	139963
0.147	TCHH	1:152079713	cg16689481	306872
0.147	ZBTB44	11:130185670	cg05227350	103986

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.150	CLEC14A	14:38724648	cg16404157	301618
0.150	CACNA2D3	3:54155663	cg18143243	330278
0.151	BTG4;C11orf88;MIR34B;MIR34C	11:111383624	cg23211240	409137
0.151	GTF3A;MTIF3	13:28016624	cg26772116	467001
0.151		16:49499006	cg01517680	31431
0.151	CTTN	11:70262058	cg16629523	305772
0.151	CCDC106;U2AF2;ZNF580;ZNF581	19:56159485	cg08496742	164543
0.152	DQX1;PCGF1;TLX2	2:74743009	cg07203423	140895
0.152	KCNIP1	5:169960825	cg10931884	206704
0.152	MAL2	8:120220856	cg02225716	45426
0.152	GDF6	8:97173034	cg21859781	388371
0.152	HOXC4;HOXC5;HOXC6;MIR615	12:54424203	cg13826247	255805
0.152	NCAM1	11:112831501	cg21727486	386364
0.152	ZNF503;ZNF503-AS2	10:77156697	cg25023298	438769
0.152	MDGA1	6:37616803	cg24442454	429044

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.149	HGC3;PCDHGC4;PCDHGC5	14:50084155	cg22857670	403218
0.149	DNAAF2;LRR1;MGAT2;RPL36AL	20:13976096	cg01552272	32076
0.149	MYH13	17:10220829	cg13984289	259022
0.149		22:20284604	cg00192046	4240
0.149	CCDC148;PKP4	2:159312727	cg14426788	268232
0.149		1:23544995	cg19743168	355780
0.150	GLRB	4:157997360	cg22065614	391410
0.150		16:51671357	cg07302051	142686
0.150	ZFP42	4:188916943	cg14189571	263343
0.150	UBD	6:29520752	cg11935738	223492
0.150	CPSF3;IAH1	2:9614225	cg08047252	156223
0.150	GP9	3:128787213	cg20264543	364127
0.150	CCR6	6:167559851	cg02524205	51410
0.150	EFCAB1	8:49647809	cg11469098	215629
0.150	IRX4	5:1876397	cg14451382	268670
0.150	ARHGAP23	17:36666642	cg15825321	291821

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.155	ADAMTS16	5:5140001	cg229544449	404825
0.155	PITX1	5:134365728	cg18606375	337970
0.155		10:109674526	cg00157668	3542
0.155	TSHZ1;ZADH2	18:72916393	cg11568697	217092
0.155		2:240135921	cg18121901	329904
0.155	LYPD1;NCKA P5	2:133427612	cg25571189	447240
0.155	NAALAD2	11:89867809	cg12403137	230998
0.155	HOXC8;HOXC9	12:54396990	cg22679316	400266
0.155	ANKRD36B	2:98206733	cg23224356	409392
0.156	NKAIN3	8:63161589	cg08855288	170823
0.156	RPS7P5	1:240161445	cg21854408	388273
0.156		12:116354837	cg20169823	362815
0.156	GABRA5	15:27112902	cg03462380	70010
0.156	UNCX	7:1267228	cg11715858	219570
0.156	TNIP3	4:122078167	cg10061361	191660
0.156	CDH11	16:65157428	cg07537692	146986
0.156	DNAJB6	7:157192974	cg25039694	439065
0.156	DOCK1;FAM196A	10:128994432	cg03242819	65770

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.152	SHROOM2	X:9754927	cg05782106	114103
0.152		4:1515011	cg08480901	164253
0.153	NXPH2	2:139537826	cg14923640	277390
0.153	BDNF	11:27740813	cg13974632	258776
0.153		3:74663689	cg24346629	427487
0.153		4:1400189	cg24496475	429912
0.153		14:97058777	cg11871960	222513
0.154	ATP2C2	16:84402158	cg07507755	146441
0.154		7:32358540	cg27511599	479742
0.154	INTU	4:128544375	cg26114043	455622
0.154	PNLIPRP2	10:118387207	cg18699744	339327
0.154	WPI2	7:5271480	cg26660312	465112
0.154	GALNTL6	4:172734431	cg22153181	392677
0.154	MSI2	17:55362836	cg07249730	141786
0.154	LIN9;MIXL1	1:226411057	cg18564989	337293
0.154	GPR125	4:22520573	cg13702087	253322
0.155	MMP16	8:89340139	cg12818557	237751
0.155	11-Mar	5:16179660	cg09017434	173718
0.155		5:143978357	cg11527001	216436

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.159	FLJ31485;FZD10	12:130647004	cg21885046	388782
0.160	CBLN1	16:49316197	cg03389653	68591
0.160	GBX2	2:237076815	cg19761848	356155
0.160	BCOR	X:40035961	cg00016934	407
0.160	HS3ST2	16:22825046	cg09191731	176695
0.160	ZNF148	3:125076372	cg02970696	60506
0.160	PROZ	13:113819073	cg00898013	18847
0.160		2:130971164	cg08566455	165743
0.160		7:32467657	cg18961681	343589
0.160		7:152621979	cg08202754	159199
0.161	FEZF1;LOC154860	7:121946036	cg10485664	199138
0.161	NKAIN3	8:63161579	cg01906015	39032
0.161	PROCA1;RAB34;RPL23A;SNORD42A;SNORD42B;SNORD4A;SNORD4B;TLCD1	17:27044629	cg21816330	387671
0.161	DOCK1	10:128593922	cg06128198	120545
0.161	HTR4	5:148033882	cg11438011	215195

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.156	ADAMTSL1	9:18514052	cg14470762	269062
0.157	CPNE9;MTMR14	3:9745610	cg02741521	55842
0.157	KIF25	6:168436099	cg18319852	333241
0.157	PIN4	X:71401206	cg26578373	463841
0.157	ANKRD36BP2	2:89065379	cg02646394	53977
0.157	PXDN	2:1748132	cg25181651	441181
0.158	GPR78	4:8582227	cg18901644	342716
0.158	ADAMTS16	5:5139797	cg16670809	306536
0.158		18:6414974	cg18556788	337142
0.158	GRM7	3:6903019	cg27199820	474552
0.158	CBWD2;FOX D4L1	2:114261369	cg23850283	419371
0.158	DPP10;LOC389023	2:115919006	cg03753331	75826
0.158	MIR4634	5:174178693	cg12398645	230921
0.159	SEMA3C	7:80548456	cg03823904	77109
0.159	DHRS4L2	14:24476559	cg10926857	206629
0.159	WBSCR17	7:70597058	cg02300154	46944
0.159		11:2367787	cg20805368	372479
0.159	NTM	11:131781257	cg19717586	355276

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
	XD11;HOXD1 2			
0.164	NSUN4	1:46814106	cg15580309	287719
0.164	CYB561D2;N PRL2;RASSF 1;TMEM115;Z MYND10	3:50383167	cg09682796	185261
0.164	CHL1	3:239665	cg10603275	201352
0.164	MYOG;PPFIA 4	1:203045044	cg00805880	17008
0.165	GNAI1	7:79764178	cg25744767	449994
0.165	LOC649133;P OU2F3	11:120110887	cg17176573	314750
0.165	11-Mar	5:16179633	cg23479922	413567
0.165	PSMB9;TAP1	6:32829303	cg05062939	100976
0.165	TMEM229A	7:123673331	cg17025835	312249
0.165	CEND1;PDD C1;SLC25A22	11:783889	cg01741372	35661
0.166	DOCK1	10:128593943	cg22665692	400049
0.166	ATP6V1A	3:113502832	cg19924544	358964
0.166	C6orf147;KH DC1	6:74024628	cg02447304	49827
0.166		22:43168851	cg24694833	433260
0.167	FAT1	4:187645118	cg01244944	26097

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.161	PITX1	5:134363973	cg07274716	142211
0.161	UHRF1BP1	6:34760872	cg07306190	142760
0.161	IRX4	5:1887300	cg07565505	147521
0.161	SOX17	8:55370429	cg11214140	211422
0.161	GRHL2	8:102505986	cg03650674	73811
0.162	ABC11;G6P C2	2:169769616	cg05703053	112745
0.162		18:6729810	cg02824202	57399
0.162	GALR1	18:74962000	cg17911318	326333
0.162	KCNA4	11:30038672	cg15044957	279439
0.162	CNTNAP2	7:145813421	cg21126583	377176
0.162	NID1	1:236228744	cg04837025	96465
0.162	THRB	3:24536474	cg20985755	375077
0.162	COBL	7:51384371	cg12988534	240269
0.162	GDF7	2:20870362	cg07755735	151051
0.162	ARHGAP33;C 19orf55	19:36265700	cg18805164	341126
0.163		8:143070187	cg06573787	128217
0.163	ERG	21:40033163	cg12884169	238711
0.163	PON2;PON3	7:95025736	cg07121856	139138
0.163	HOXD10;HO	2:176972563	cg11546137	216732

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.171		18:6414976	cg14352983	266773
0.171	WBSCR17	7:70597065	cg03044249	61987
0.171	MYO16	13:109352806	cg24702069	433391
0.171	ANKRD36	2:97778927	cg12623145	234729
0.171		7:152622022	cg15818671	291676
0.171	SP8	7:20824706	cg01003961	21140
0.172	CTTNBP2	7:117513101	cg05951860	117342
0.172	NAT2	8:18244861	cg12174804	227617
0.172	WBSCR17	7:70597921	cg07143083	139618
0.172	THRB	3:24536478	cg13790603	255057
0.172		16:85368973	cg02418439	49379
0.173	UBD	6:29521356	cg21632158	385088
0.173	ADAMTSL3	15:84322584	cg04138185	83155
0.173	RAB32	6:146864885	cg26252281	458030
0.174	CLEC14A	14:38724675	cg05057720	100847
0.174	DOCK1;FAM196A	10:128994603	cg03070297	62543
0.174	MDGA1	6:37618009	cg26720545	466246
0.174	BAIAP2L1	7:98029266	cg08684580	167809
0.174	LRRRC4C	11:40314978	cg19849428	357643

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.167	LILRB3	19:54728037	cg23679434	416846
0.167	SYT14	1:210111561	cg19922137	358920
0.167	ZNF844	19:12175935	cg26827373	468055
0.167	EVX2;HOXD12;HOXD13	2:176957842	cg04415176	88629
0.167		10:131762462	cg07045241	137620
0.167	KLF8	X:56259243	cg06457357	126059
0.168	C5orf63	5:126408756	cg14340928	266559
0.168	MAGI2-AS3	7:79083408	cg22280038	394533
0.168		4:21950567	cg00688962	14541
0.169	SHISA6	17:11144043	cg13330559	245613
0.169	ARSG;SLC16A6	17:66287032	cg11879514	222640
0.169	RNF180	5:63461654	cg17370163	317926
0.169	DACH1	13:72439698	cg05510902	109333
0.169		7:55516724	cg03357999	68033
0.169	EPB41L3	18:5543801	cg00027083	665
0.170		11:67499431	cg02666610	54357
0.170	CCT8L2;TPT EP1	22:17082772	cg01660911	34237
0.171	UBTD1	10:99278449	cg10989317	207724

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.179	GDF7	2:20870812	cg14780466	274979
0.179	HOXA10;HOXA10- HOXA9;HOXA7;HOXA9;MIR196B	7:27206073	cg15506609	286583
0.179	TMCC3	12:94995915	cg09162806	176158
0.179	LOC91149;RAPGEF4	2:173600676	cg00997611	21009
0.179	PHACTR1	6:12749978	cg13246235	244239
0.180	GCK;MYL7	7:44184403	cg03812172	76924
0.181		9:98981500	cg21167269	377918
0.181	GDF7	2:20870087	cg09074113	174642
0.181	KCNE1	21:35832028	cg07321776	143076
0.181	KCNK2	1:215256262	cg18794839	340940
0.181	GPR123	10:134910540	cg13750264	254277
0.182	FTSJ2;NUDT1;SNX8	7:2289097	cg12017558	224816
0.182	KLF16	19:1852127	cg07355926	143681
0.182		2:154143768	cg18771570	340550
0.183		6:77563066	cg21291856	380079
0.184		17:54858770	cg07973125	154969
0.184	FGF12	3:192127457	cg08002883	155463

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.174		8:7079106	cg08498719	164579
0.174	FAM43B	1:20879547	cg12768681	236962
0.174	SEMA5B	3:122694286	cg07733481	150639
0.175	SGPP2	2:223289306	cg07357987	143728
0.175		8:76320150	cg26220018	457454
0.175	CDH2	18:25757710	cg14312538	265980
0.175	CR1L	1:207842917	cg17822947	324851
0.175	NOVA1	14:27067372	cg20478129	367360
0.176	CACNA1B	9:140917431	cg13610307	251390
0.176	TRAF3	14:103367591	cg10920224	206529
0.176	IRX1	5:3596207	cg10530883	200071
0.176	BTBD3	20:11871384	cg23944804	420919
0.177		10:111216962	cg16664405	306435
0.177		10:125751413	cg20250269	363883
0.178	IRS2	13:110438578	cg02320481	47382
0.178	EVX2;HOXD13	2:176948732	cg15133351	280970
0.178	PKDCC	2:42275740	cg12630082	234855
0.179	IL5RA	3:3152916	cg21594961	384489
0.179	C5orf63	5:126408806	cg17848407	325324

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.191	CLCA1	1:86968255	cg26829098	468093
0.191	HLA-A	6:29910755	cg11808100	221232
0.192		19:22444593	cg03692651	74585
0.192	SERTM1	13:37248244	cg09907509	189121
0.193	CNTN4	3:2140699	cg06598836	128644
0.193		15:29862517	cg04283162	86040
0.193		4:56023751	cg10360906	197083
0.193	KIAA1217;PRINS	10:24535410	cg04122385	82818
0.194	C5orf63	5:126409211	cg10812634	204796
0.194	LOC91149;RAPGEF4	2:173600362	cg14379854	267268
0.195	ZNF471	19:57019069	cg00674365	14254
0.195	AFG3L1P;DBNDD1	16:90070038	cg16380389	301186
0.195	SH2D4B	10:82296072	cg09981929	190306
0.196	C21orf67;ITGB2;LOC100505746	21:46349496	cg02464073	50169
0.196	NPTX2	7:98246633	cg18952796	343455
0.197	LHX6	9:124990276	cg00142257	3190
0.197	GDF7	2:20871401	cg04082016	81976

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.185	ILDR1	3:121714668	cg20356878	365522
0.185	SLC17A3	6:25882590	cg03517284	71065
0.186	FHOD3	18:34325827	cg07495405	146206
0.186	C1orf106	1:200860534	cg00909514	19113
0.186	HOXA5;HOXA6;HOXA7;LOC100133311	7:27187502	cg03529432	71326
0.186	SH2D4B	10:82295502	cg08506606	164700
0.186	KNDC1;UTF1;VENTX	10:135044114	cg09053680	174307
0.186	GSC2	22:19137874	cg23774356	418306
0.186	CLCA1	1:86968087	cg19807991	356943
0.187	SCTR	2:120281999	cg07176264	140350
0.187	PITX1	5:134363562	cg02037307	41774
0.187	FTSJ2;NUDT1;SNX8	7:2288716	cg13550401	250077
0.188		8:7543899	cg12174280	227610
0.189	CLCA1	1:86968543	cg04896168	97717
0.190	NAALAD2	11:89867911	cg14304817	265815
0.190	LHX6	9:124989294	cg21469772	382370
0.190	KLF16	19:1852165	cg05006231	99848

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.210		1:239550283	cg13985485	259057
0.210		9:96623674	cg13679303	252812
0.210	DRD5	4:9783192	cg26296488	458826
0.210	NETO1	18:70535005	cg18651870	338661
0.211	MDGA1	6:37617124	cg00807871	17056
0.212	FAM75C1	9:90531866	cg21265404	379726
0.213	TNS3	7:47621692	cg06352730	124250
0.214		2:16484904	cg23905015	420220
0.214		7:32358064	cg13207630	243593
0.216	PROZ	13:113819100	cg18105134	329535
0.216	TSHZ1;ZADH 2	18:72917101	cg18449964	335368
0.217	C5orf63	5:126409310	cg15405432	284960
0.218	ZNF468	19:53361448	cg15721243	290213
0.219	FAT1	4:187644739	cg16248329	298797
0.220	CTTNBP2	7:117513835	cg16913250	310581
0.220	HES6;LOC15 1174;LOC643 387	2:239139911	cg06102419	120125
0.221	MAL2	8:120220882	cg06822816	133139
0.222	C5orf63	5:126409227	cg02304092	47036

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.197	CR1L	1:207842833	cg03408135	68966
0.198	DKFZP686115 217;NQO2	6:2991147	cg06195525	121679
0.199	PCDH7	4:30723855	cg261133769	455996
0.199	IFITM1;IFITM 3	11:320956	cg14885742	276796
0.199	GNAS;GNAS- AS1	20:57414274	cg23732978	417791
0.201	NAALAD2	11:89867819	cg05500015	109117
0.202	CPNE4	3:131246020	cg01966816	40359
0.204	EFHA2	8:16885000	cg12097222	226305
0.204	CRMP1	4:5894691	cg035444320	71665
0.205	UNC5D	8:35092876	cg06010588	118507
0.206	WTIP	19:34972145	cg10771931	204037
0.207	DNAH2;EFNB 3;WRAP53	17:7613764	cg22098780	391853
0.207	CR1L	1:207843084	cg21106486	376853
0.207	CR1;CR2	1:207669922	cg10021878	191017
0.207		13:21872349	cg14456004	268764
0.207	LOC645249	7:156814480	cg09858188	188213
0.208		13:50701619	cg01803928	36963
0.208	GALR1	18:74962133	cg03502002	70747

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.252	LHX6	9:124990165	cg03363289	68128
0.253	GDF7	2:20870211	cg05481257	108752
0.253	SH2D4B	10:82295723	cg24440658	429013
0.254	GDF7	2:20869434	cg27141850	473604
0.254	TSNARE1	8:143376371	cg24849373	435844
0.254	AGAP1	2:236579469	cg03451670	69806
0.255		1:41350183	cg08870646	171150
0.255	LHX6	9:124989915	cg13862711	256498
0.256	IGF1R	15:99193247	cg03437748	69502
0.256	SDK1	7:4118583	cg22535849	398182
0.257	PM20D1	1:205819492	cg24503407	430027
0.258	CLCA1	1:86968184	cg10760651	203838
0.259	WDR17	4:176987009	cg11923920	223292
0.261	ACAN	15:89354338	cg02401352	49110
0.266	TSHZ1;ZADH2	18:72917163	cg03972071	79876
0.269	MDGA1	6:37617956	cg24796644	434985
0.272	C5orf63	5:126409153	cg27097438	472827
0.275	C11orf67;RSF1	11:77532707	cg22741595	401343
0.275		6:167195910	cg06330797	123893

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.224	LHX6	9:124988720	cg04282082	86021
0.226	HCG4;LOC554223	6:29759078	cg11036359	208507
0.229	C5orf63	5:126409061	cg18710053	339507
0.229	GPR78	4:8582249	cg01829241	37555
0.229	LHX6	9:124989337	cg13571460	250561
0.230	C5orf63	5:126409198	cg22905511	404065
0.231		2:154143677	cg07563363	147470
0.233	FCRLA	1:161675579	cg04888234	97564
0.233	FAM160B1	10:116634877	cg14964115	278020
0.235	PM20D1	1:205819251	cg14893161	276892
0.235	GDF7	2:20871279	cg07021052	137180
0.237	ANKRD27;RGS9BP	19:33165484	cg27413643	478153
0.238	MDGA1	6:37617864	cg20053110	361003
0.240		18:6414978	cg17688525	322822
0.244	ATP8B5P;RUSC2	9:35490515	cg15271616	283055
0.244	GDF7	2:20871002	cg10687131	202734
0.248		2:181987552	cg20685672	370518
0.252	ARHGAP33;C19orf55	19:36264029	cg16569309	304609

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
	61			
0.297	AVL9;LSM5	7:32526065	cg26856631	468599
0.300	PM20D1	1:205819088	cg26354017	459920
0.300	MIR182;MIR183;MIR96	7:129412730	cg16069065	295914
0.301	SCN1A	2:166930521	cg00881894	18574
0.305	RPSAP58;ZN F681	19:23941859	cg25958450	453100
0.305	CCDC130;MIR11	19:13875111	cg25755428	450171
0.317	PML	15:74345103	cg11399582	214535
0.318	C1orf109;CD CA8	1:38156652	cg06917450	135153
0.324	CELF4	18:34917603	cg20094343	361624
0.325	CLEC4F	2:71033156	cg02479782	50493
0.343	EHMT2;NEU1;SLC44A4	6:31838544	cg20370184	365714
0.344	NCOR2	12:124827315	cg23878260	419752
0.349	PCCA	13:100989375	cg20536971	368191
0.351	ANKRD26P3;LINC00421	13:19918525	cg08801017	169810
0.355	PPYR1	10:47083392	cg11861387	222311
0.358		5:5887642	cg26690407	465769

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.276	COL9A1	6:71022072	cg23974730	421453
0.276	INPP5A	10:134411480	cg12501287	232697
0.277	PM20D1	1:205818956	cg17178900	314798
0.277	FAM181A;FA M181A-AS1	14:94385395	cg20022541	360557
0.279		3:120151283	cg06378561	124751
0.280	LOC255411	12:49113738	cg00007810	182
0.280	CHAF1B	21:37761363	cg22871721	403496
0.281	ASB1	2:239330383	cg13295614	245013
0.282	TNFSF8	9:117694183	cg14361804	266932
0.284	DISC1	1:231820076	cg07134368	139412
0.285	DIP2C	10:593275	cg06051619	119189
0.286	ULK4P1;ULK 4P2	15:30861172	cg23804921	418678
0.287	TPO	2:1426786	cg01957222	40112
0.288	PM20D1	1:205819463	cg07167872	140186
0.290	PM20D1	1:205819179	cg14159672	262672
0.290	LOC200772	2:241896910	cg06193597	121647
0.291	PM20D1	1:205819406	cg11965913	224049
0.292	PPP2R2B	5:146253830	cg10926851	206628
0.294	LOC1001334	4:3683268	cg03965172	79742

OA - RA	Associated gene	CpG*	Locus	SEQ ID No.
0.363		13:79694063	cg24941469	437468
0.366	ALLC	2:3753297	cg05971102	117729
0.378	MIR3663	10:118931160	cg17723206	323281
0.388	SERPINB9	6:2888212	cg19577958	352915
0.399	NCOR2	12:124831017	cg07474670	145798
0.404		14:22370643	cg12819537	237764
0.408	SLC37A1	21:43989949	cg08407901	162897
0.413	MRPL1	4:78852682	cg15897435	293045
0.417	C7orf26;ZNF853	7:6653510	cg08693140	167967
0.431		14:22361282	cg16702660	307151
0.432	ITIH4;MUSTN1;TMEM110;TMEM110-MUSTN1	3:52869263	cg24629711	432072
0.442	MAGI2-AS3	7:79083056	cg14464244	268938
0.586	PPP1R16B	20:37438823	cg18674961	338963
*: UCSC hg19 Cytosine Coordinate of CpG (+ strand)				

[0228] The term “comprising” as used herein is synonymous with “including,” “containing,” or “characterized by,” and is inclusive or open-ended and does not exclude additional, unrecited elements or method steps.

[0229] All numbers expressing quantities of ingredients, reaction conditions, and so forth used in the specification are to be understood as being modified in all instances by the term “about.” Accordingly, unless indicated to the contrary, the numerical parameters set forth herein are approximations that may vary depending upon the desired properties sought to be obtained. At the very least, and not as an attempt to limit the application of the doctrine of equivalents to the scope of any claims in any application claiming priority to the present application, each numerical parameter should be construed in light of the number of significant digits and ordinary rounding approaches.

[0230] The above description discloses several methods and materials of the present invention. This invention is susceptible to modifications in the methods and materials, as well as alterations in the fabrication methods and equipment. Such modifications will become apparent to those skilled in the art from a consideration of this disclosure or practice of the invention disclosed herein. Consequently, it is not intended that this invention be limited to the specific embodiments disclosed herein, but that it cover all modifications and alternatives coming within the true scope and spirit of the invention.

[0231] The following references are incorporated herein by reference in their entireties.

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[0232] All references cited herein, including but not limited to published and unpublished applications, patents, and literature references, are incorporated herein by reference in their entirety and are hereby made a part of this specification. To the extent publications and patents or patent applications incorporated by reference contradict the disclosure contained in the specification, the specification is intended to supersede and/or take precedence over any such contradictory material.

WHAT IS CLAIMED IS:

1. A method for diagnosing rheumatoid arthritis or osteoarthritis, determining a rheumatoid arthritis or osteoarthritis prognosis, or determining or predicting a response to treatment for rheumatoid arthritis or osteoarthritis in a subject comprising determining whether at least 2 nucleic acid loci or at least 2 genes in a sample from said subject have methylation states indicative of rheumatoid arthritis, osteoarthritis, a rheumatoid arthritis or osteoarthritis prognosis, or a response to treatment for rheumatoid arthritis or osteoarthritis.

2. The method of claim 1, further comprising comparing the methylation states of the at least 2 loci or at least 2 genes in the sample from said subject with the methylation states of the loci or genes in normal tissue, tissue from a subject without said known rheumatoid arthritis or osteoarthritis prognosis, or tissue from a subject without said known response to treatment for rheumatoid arthritis or osteoarthritis.

3. The method of claim 2, wherein an increase or decrease in the extent of methylation of at least 2 loci or at least 2 genes compared to the extent of methylation of the loci or genes in normal tissue, tissue from a subject without said known rheumatoid arthritis or osteoarthritis prognosis, or tissue from a subject without said known response to treatment for rheumatoid arthritis or osteoarthritis is indicative of the presence or absence of rheumatoid arthritis, osteoarthritis, a rheumatoid arthritis or osteoarthritis prognosis, or response to treatment for rheumatoid arthritis or osteoarthritis for the subject.

4. The method of any one of claims 1-3, wherein the methylation states of said at least 2 loci or at least 2 genes are determined in fibroblasts from said subject.

5. The method of any one of claims 1-3, wherein the methylation state of said at least 2 loci or at least 2 genes is determined in synoviocytes from said subject.

6. The method of any one of claims 1-3, wherein the methylation states of said at least 2 loci or at least 2 genes are determined in fibroblast-like synoviocytes from said subject.

7. The method of any one of claims 1-3, wherein the methylation states of said at least 2 loci or at least 2 genes are determined in rheumatoid arthritis fibroblast-like synoviocytes from said subject.

8. The method of any one of claims 1-3, wherein the methylation states of said at least 2 loci or at least 2 genes are determined in osteoarthritis fibroblast-like synoviocytes from said subject.

9. The method of any one of claims 1-3, wherein the methylation states of said at least 2 loci or at least 2 genes are determined in macrophage from said subject.

10. The method of any one of claims 1-3, wherein the methylation states of said at least 2 loci or at least 2 genes are determined in peripheral blood cells from said subject.
11. The method of claim 10, wherein the peripheral blood cell is selected from the group consisting of white blood cell, neutrophil, eosinophil, basophil, lymphocyte, B cell, plasma cell, T cell, natural killer cell, monocyte, and dendritic cell.
12. The method of any one of claims 1-11, wherein the sample is selected from the group consisting of a tissue sample, a frozen tissue sample, a biopsy specimen, a surgical specimen, a cytological specimen, whole blood, bone marrow, cerebral spinal fluid, peritoneal fluid, lymph fluid, serum, plasma, urine, stool, and nipple aspirate.
13. The method of any one of claims 1-12, wherein the at least 2 loci are selected from the group consisting of SEQ ID NO.s 1- 485512.
14. The method of any one of claims 1-13, wherein the at least 2 loci are selected from the group consisting of the loci listed in TABLE 6.
15. The method of any one of claims 1-13, wherein the at least 2 loci are selected from the group consisting of the loci listed in TABLE 7.
16. The method of any one of claims 1-13, wherein the at least 2 loci are selected from the group consisting of the loci listed in TABLE 8.
17. The method of any one of claims 1-12, wherein the at least 2 loci are selected from the group consisting of the loci listed in TABLE 3.
18. The method of any one of claims 1-17, wherein the methylation states of at least 5 nucleic acid loci or at least 5 genes in said sample are determined.
19. The method of any one of claims 1-18, wherein the methylation states of at least 10 nucleic acid loci or at least 10 genes in said sample are determined.
20. The method of any one of claims 1-19, wherein the methylation states of at least 20 nucleic acid loci or at least 20 genes in said sample are determined.
21. The method of any one of claims 1-20, wherein the methylation states of at least 50 nucleic acid loci or at least 50 genes in said sample are determined.
22. The method of any one of claims 1-21, wherein the methylation states of at least 100 nucleic acid loci or at least 100 genes are determined.
23. The method of any one of claims 1-22, wherein the subject is a mammal.
24. The method of any one of claims 1-23, wherein the subject is a human.
25. The method of any one of claims 1-24, wherein the nucleic acid loci are selected from the group consisting of the loci listed in TABLE 6.

26. The method of any one of claims 1-24, wherein the nucleic acid loci are selected from the group consisting of the loci listed in TABLE 7.

27. The method of any one of claims 1-24, wherein the nucleic acid loci are selected from the group consisting of the loci listed in TABLE 8.

28. A method for diagnosing rheumatoid arthritis or osteoarthritis, determining a rheumatoid arthritis or osteoarthritis prognosis, or determining or predicting a response to treatment for rheumatoid arthritis or osteoarthritis in a subject comprising:

determining the methylation states of a plurality of nucleic acid loci or the methylation states of a plurality of genes in a sample of said subject to obtain a methylation profile; and

determining whether said methylation profile is indicative of rheumatoid arthritis, osteoarthritis, a rheumatoid arthritis or osteoarthritis prognosis, or a response to treatment for rheumatoid arthritis or osteoarthritis.

29. The method of claim 28, further comprising comparing the methylation state of the plurality of nucleic acid loci or the methylation state of the plurality of genes in the sample from said subject with the methylation state of the plurality of nucleic acid loci or the methylation state of the plurality of genes in normal tissue, tissue from a subject without said known rheumatoid arthritis or osteoarthritis prognosis, or tissue from a subject without said known response to treatment for rheumatoid arthritis or osteoarthritis.

30. The method of claim 29, wherein an increase or decrease in the extent of methylation of plurality of nucleic acid loci or of the methylation state of the plurality of genes compared to the extent of methylation of the plurality of nucleic acid loci or the extent of methylation of the plurality of genes in normal tissue, tissue from a subject without said known rheumatoid arthritis or osteoarthritis prognosis, or tissue from a subject without said known response to treatment for rheumatoid arthritis or osteoarthritis is indicative of the presence or absence of rheumatoid arthritis, osteoarthritis, a rheumatoid arthritis or osteoarthritis prognosis, or response to treatment for rheumatoid arthritis or osteoarthritis for the subject.

31. The method of any one of claims 28-30, wherein the methylation state of said plurality of nucleic acid loci or said plurality of genes is determined in fibroblasts from said subject.

32. The method of any one of claims 28-30, wherein the methylation state of said plurality of nucleic acid loci or said plurality of genes is determined in synoviocytes from said subject.

33. The method of any one of claims 28-30, wherein the methylation state of said plurality of nucleic acid loci or said plurality of genes is determined in fibroblast-like synoviocytes from said subject.

34. The method of any one of claims 28-30, wherein the methylation state of said plurality of nucleic acid loci or said plurality of genes is determined in rheumatoid arthritis fibroblast-like synoviocytes from said subject.

35. The method of any one of claims 28-30, wherein the methylation state of said plurality of nucleic acid loci or said plurality of genes is determined in osteoarthritis fibroblast-like synoviocytes from said subject.

36. The method of any one of claims 28-30, wherein the methylation state of said plurality of nucleic acid loci or said plurality of genes is determined in macrophage from said subject.

37. The method of any one of claims 28-30, wherein the methylation state of said plurality of nucleic acid loci or said plurality of genes is determined in peripheral blood cells from said subject.

38. The method of claim 37, wherein the peripheral blood cell is selected from the group consisting of white blood cell, neutrophil, eosinophil, basophil, lymphocyte, B cell, plasma cell, T cell, natural killer cell, monocyte, and dendritic cell.

39. The method of any one of claims 28-38, wherein the sample is selected from the group consisting of a tissue sample, a frozen tissue sample, a biopsy specimen, a surgical specimen, a cytological specimen, whole blood, bone marrow, cerebral spinal fluid, peritoneal fluid, lymph fluid, serum, plasma, urine, stool, and nipple aspirate.

40. The method of any one of claims 28-39, wherein the plurality of nucleic acid loci is selected from the group consisting of SEQ ID NO.s 1- 485512

41. The method of any one of claims 28-40, wherein the plurality of nucleic acid loci is selected from the group consisting of the loci listed in TABLE 6.

42. The method of any one of claims 28-40, wherein the plurality of nucleic acid loci is selected from the group consisting of the loci listed in TABLE 7.

43. The method of any one of claims 28-40, wherein the plurality of nucleic acid loci is selected from the group consisting of the loci listed in TABLE 8.

44. The method of any one of claims 28-39, wherein the plurality genes is selected from the group consisting of the loci listed in TABLE 3.

45. The method of any one of claims 28-44, wherein the methylation states of at least 5 nucleic acid loci or at least 5 genes in said sample are determined.

46. The method of any one of claims 28-45, wherein the methylation states of at least 10 nucleic acid loci or at least 10 genes in said sample are determined.

47. The method of any one of claims 28-46, wherein the methylation states of at least 20 nucleic acid loci or at least 20 genes in said sample are determined.

48. The method of any one of claims 28-47, wherein the methylation states of at least 50 nucleic acid loci or at least 50 genes in said sample are determined.

49. The method of any one of claims 28-48, wherein the methylation states of at least 100 nucleic acid loci or at least 100 genes are determined.

50. The method of any one of claims 28-49, wherein the subject is a mammal.

51. The method of any one of claims 28-50, wherein the subject is a human.

52. A method of identifying a methylation profile indicative of rheumatoid arthritis, osteoarthritis, a rheumatoid arthritis or osteoarthritis prognosis, or a response to treatment for rheumatoid arthritis or osteoarthritis comprising:

determining the methylation states of a plurality of nucleic acid loci or the methylation states of a plurality of genes in a sample from a test subject with rheumatoid arthritis, osteoarthritis, a particular rheumatoid arthritis or osteoarthritis prognosis, or a particular response to treatment for rheumatoid arthritis or osteoarthritis;

determining the methylation states of said plurality of nucleic acid loci or said plurality of genes in a sample from a control subject without rheumatoid arthritis, without osteoarthritis, without said rheumatoid arthritis or osteoarthritis prognosis or without said response to treatment for rheumatoid arthritis or osteoarthritis; and

identifying loci or genes which are hypermethylated or hypomethylated in said sample from said test subject relative to said sample from said control subject to identify said methylation profile indicative of rheumatoid arthritis, osteoarthritis a rheumatoid arthritis or osteoarthritis prognosis, or a response to treatment for rheumatoid arthritis or osteoarthritis.

53. The method of Claim 52, further comprising storing data representing said loci or said genes which are hypermethylated or hypomethylated in said sample from said test subject relative to said sample from said control subject on a non-transitory computer readable medium.

54. The method of claim 53, further comprising comparing the methylation states of a plurality of nucleic acid loci or the methylation states of a plurality of genes in a sample from a test subject with rheumatoid arthritis, osteoarthritis, a particular rheumatoid arthritis or osteoarthritis prognosis, or a particular response to treatment for rheumatoid arthritis or osteoarthritis with the methylation states of said plurality of nucleic acid loci or the methylation

states of said plurality of genes in a sample from a control subject without rheumatoid arthritis, without osteoarthritis, without said rheumatoid arthritis or osteoarthritis prognosis or without said response to treatment for rheumatoid arthritis or osteoarthritis.

55. The method of any one of claims 52-54, wherein the methylation state of said plurality of nucleic acid loci or said plurality of genes in a sample from said test subject or said control subject is determined in fibroblasts from said test subject or said control subject.

56. The method of any one of claims 52-54, wherein the methylation state of said plurality of nucleic acid loci or said plurality of genes in a sample from said test subject or said control subject is determined in synoviocytes from said test subject or said control subject.

57. The method of any one of claims 52-54, wherein the methylation state of said plurality of nucleic acid loci or said plurality of genes in a sample from said test subject or control subject is determined in fibroblast-like synoviocytes from said test subject or said control subject.

58. The method of any one of claims 52-54, wherein the methylation state of said plurality of nucleic acid loci or said plurality of genes in a sample from said test subject or control subject is determined in rheumatoid arthritis fibroblast-like synoviocytes from said test subject or control subject.

59. The method of any one of claims 52-54, wherein the methylation state of said plurality of nucleic acid loci or said plurality of genes in a sample from said test subject or control subject is determined in osteoarthritis fibroblast-like synoviocytes from said test subject or control subject.

60. The method of any one of claims 52-54, wherein the methylation state of said plurality of nucleic acid loci or said plurality of genes in a sample from said test subject or control subject is determined in macrophage from said test subject or control subject.

61. The method of any one of claims 52-54, wherein the methylation state of said plurality of nucleic acid loci or said plurality of genes in a sample from said test subject or control subject is determined in peripheral blood cells from said test subject or control subject.

62. The method of claim 61, wherein the peripheral blood cell is selected from the group consisting of white blood cell, neutrophil, eosinophil, basophil, lymphocyte, B cell, plasma cell, T cell, natural killer cell, monocyte, and dendritic cell.

63. The method of any one of claims 52-62, wherein the sample is selected from the group consisting of a tissue sample, a frozen tissue sample, a biopsy specimen, a surgical specimen, a cytological specimen, whole blood, bone marrow, cerebral spinal fluid, peritoneal fluid, lymph fluid, serum, plasma, urine, stool, and nipple aspirate.

64. The method of any one of claims 52-63, wherein the methylation states of at least 5 nucleic acid loci or at least 5 genes are determined.

65. The method of any one of claims 52-64, wherein the methylation states of at least 10 nucleic acid loci or at least 10 genes are determined.

66. The method of any one of claims 52-65, wherein the methylation states of at least 20 nucleic acid loci or at least 20 genes are determined.

67. The method of any one of claims 52-66, wherein the methylation states of at least 50 nucleic acid loci or at least 50 genes are determined.

68. The method of any one of claims 52-67, wherein the methylation states of at least 100 nucleic acid loci or at least 100 genes are determined.

69. The method of any one of claims 52-68, wherein the subject is a mammal.

70. The method of any one of claims 52-69, wherein the subject is a human.

71. A method for diagnosing rheumatoid arthritis or osteoarthritis, determining a rheumatoid arthritis or osteoarthritis prognosis, or determining or predicting a response to treatment for rheumatoid arthritis or osteoarthritis in a subject comprising:

accessing first data representing the methylation status of nucleic acid loci or the methylation status of at least one gene which are differentially methylated in individuals with rheumatoid arthritis, osteoarthritis a rheumatoid arthritis or osteoarthritis prognosis, or a response to treatment for rheumatoid arthritis or osteoarthritis wherein said data is stored on a non-transitory computer readable medium;

instructing a computer to compare said first data to second data representing the methylation status of said nucleic acid loci or said at least one gene in a sample taken from said subject, wherein said data representing the methylation status of said nucleic acid loci or said at least one gene in a sample taken from said subject is stored on a non-transitory computer readable medium; and

instructing said computer to provide an output indicating whether said comparison indicates that said subject has rheumatoid arthritis or osteoarthritis, has a positive or negative prognosis for rheumatoid arthritis or osteoarthritis prognosis, or indicates a positive or negative prediction for the subject's response to treatment for rheumatoid arthritis or osteoarthritis.

72. The method of claim 71, further comprising diagnosing rheumatoid arthritis or osteoarthritis, determining a rheumatoid arthritis or osteoarthritis prognosis, or determining or predicting a response to treatment for rheumatoid arthritis or osteoarthritis in said subject if said first data representing the methylation status of said nucleic acid loci or said at least one gene in a

sample taken from said subject are significantly similar to said second data representing nucleic acid loci or genes which are differentially methylated in individuals with rheumatoid arthritis, osteoarthritis a rheumatoid arthritis or osteoarthritis prognosis, or a response to treatment for rheumatoid arthritis or osteoarthritis.

73. A method for diagnosing rheumatoid arthritis or osteoarthritis, determining a rheumatoid arthritis or osteoarthritis prognosis, or determining or predicting a response to treatment for rheumatoid arthritis or osteoarthritis in a subject comprising: determining the methylation states of at least 2 loci selected from the group consisting of SEQ ID NO.s 1-485512 in a sample obtained from the subject.

74. The method of claim 73, further comprising comparing the methylation states of the at least 2 loci in the sample with the methylation states of the loci in normal tissue, tissue from a subject with a known prognosis, or tissue from a subject with a known response to treatment.

75. The method of claim 74, wherein an increase or decrease in the extent of methylation of at least 2 loci compared to the extent of methylation of the loci in normal tissue, tissue from a subject with a known prognosis, or tissue from a subject with a known response to treatment is indicative of the presence or absence of rheumatoid arthritis, prognosis, or response to treatment for the subject.

76. The method of any one of claims 73-75, wherein the methylation states of said at least 2 loci are determined in fibroblasts from said subject.

77. The method of any one of claims 73-75, wherein the methylation states of said at least 2 loci are determined in synoviocytes from said subject.

78. The method of any one of claims 73-75, wherein the methylation states of said at least 2 loci are determined in fibroblast-like synoviocytes from said subject.

79. The method of any one of claims 73-75, wherein the methylations state of said at least 2 loci are determined in rheumatoid arthritis fibroblast-like synoviocytes from said subject.

80. The method of any one of claims 73-75, wherein the methylation states of said at least 2 loci are determined in osteoarthritis fibroblast-like synoviocytes from said subject.

81. The method of any one of claims 73-75, wherein the methylation states of said at least 2 loci are determined in macrophage from said subject.

82. The method of any one of claims 73-75, wherein the methylation states of said at least 2 loci are determined in peripheral blood cells from said subject.

83. The method of claim 82, wherein the peripheral blood cell is selected from the group consisting of white blood cell, neutrophil, eosinophil, basophil, lymphocyte, B cell, plasma cell, T cell, natural killer cell, monocyte, and dendritic cell.

84. The method of any one of claims 73-83, wherein the sample is selected from the group consisting of a tissue sample, a frozen tissue sample, a biopsy specimen, a surgical specimen, a cytological specimen, whole blood, bone marrow, cerebral spinal fluid, peritoneal fluid, lymph fluid, serum, plasma, urine, stool, and nipple aspirate.

85. The method of any one of claims 73-84, wherein the at least 2 loci are selected from the group consisting of the loci listed in TABLE 6.

86. The method of any one of claims 73-84, wherein the at least 2 loci are selected from the group consisting of the loci listed in TABLE 7.

87. The method of any one of claims 73-84, wherein the at least 2 loci are selected from the group consisting of the loci listed in TABLE 8.

88. The method of any one of claims 73-84, wherein the methylation states of at least 5 loci selected from the group consisting of the loci listed in TABLE 6, TABLE 7, and TABLE 8 are determined.

89. The method of any one of claims 73-84, wherein the methylation states of at least 10 loci selected from the group consisting of the loci listed in TABLE 6, TABLE 7, and TABLE 8 are determined.

90. The method of any one of claims 73-84, wherein the methylation states of at least 20 loci selected from the group consisting of the loci listed in TABLE 6, TABLE 7, and TABLE 8 are determined.

91. The method of any one of claims 73-84, wherein the methylation states of at least 50 loci selected from the group consisting of the loci listed in TABLE 6, TABLE 7, and TABLE 8 are determined.

92. The method of any one of claims 73-84, wherein the methylation states of at least 100 loci selected from the group consisting of the loci listed in TABLE 6, TABLE 7, and TABLE 8 are determined.

93. The method of any one of claims 73-92, wherein the subject is a mammal.

94. The method of any one of claims 73-93, wherein the subject is a human.

95. A method for identifying a therapeutic agent for treating rheumatoid arthritis or osteoarthritis comprising:

contacting a cell with a test agent; and

determining the methylation states in the contacted cell of at least 2 loci which have differential extents of methylation in individuals with rheumatoid arthritis or osteoarthritis relative to individuals without rheumatoid arthritis or osteoarthritis.

96. The method of claim 95, further comprising:

comparing the methylation states of the at least 2 loci in the contacted cell with the methylation states of the loci in a cell which was not contacted with the test agent; and selecting a test agent that increases or decreases the extent of methylation of the at least 2 loci in the cell contacted with the test agent compared to the extent of methylation of the at least 2 loci in a cell which was not contacted with the test agent such that the extent of methylation of the at least 2 loci in the cell contacted with the test agent is a methylation states associated with the absence of rheumatoid arthritis or osteoarthritis or with a reduction in the symptoms associated with rheumatoid arthritis osteoarthritis.

97. The method of any one of claims 95-96, wherein at least 2 loci are selected from the group consisting of SEQ ID NO.s 1-485512.

98. The method of any one of claims 95-97, wherein the at least 2 loci are selected from the group consisting of the loci listed in TABLE 6.

99. The method of any one of claims 95-97, wherein the at least 2 loci are selected from the group consisting of the loci listed in TABLE 7.

100. The method of any one of claims 95-97, wherein the at least 2 loci are selected from the group consisting of the loci listed in TABLE 8.

101. The method of any one of claims 95-97, wherein the methylation states of at least 5 loci selected from the group consisting of the loci listed in TABLE 6, TABLE 7, and TABLE 8 are determined.

102. The method of any one of claims 95-97, wherein the methylation states of at least 10 loci selected from the group consisting of the loci listed in TABLE 6, TABLE 7, and TABLE 8 are determined.

103. The method of any one of claims 95-97, wherein the methylation states of at least 20 loci selected from the group consisting of the loci listed in TABLE 6, TABLE 7, and TABLE 8 are determined.

104. The method of any one of claims 95-97, wherein the methylation states of at least 50 loci selected from the group consisting of the loci listed in TABLE 6, TABLE 7, and TABLE 8 are determined.

105. The method of any one of claims 95-97, wherein the methylation states of at least 100 loci selected from the group consisting of the loci listed in TABLE 6, TABLE 7, and TABLE 8 are determined.

106. The method of any one of claims 95-105, wherein the cell comprises a fibroblast.

107. The method of any one of claims 95-105, wherein the cell comprises a synoviocyte.

108. The method of any one of claims 95-105, wherein the cell comprises a fibroblast-like synoviocyte.

109. The method of any one of claims 95-105, wherein the cell comprises a rheumatoid arthritis fibroblast-like synoviocyte.

110. The method of any one of claims 95-105, wherein the cell comprises an osteoarthritis fibroblast-like synoviocyte.

111. The method of any one of claims 95-105, wherein the cell comprises a macrophage.

112. The method of any one of claims 95-105, wherein the cell comprises a peripheral blood cell.

113. The method of claim 112, wherein the peripheral blood cell is selected from the group consisting of white blood cell, neutrophil, eosinophil, basophil, lymphocyte, B cell, plasma cell, T cell, natural killer cell, monocyte, and dendritic cell.

114. The method of any one of claims 95-113, wherein the cell is mammalian.

115. The method of any one of claims 95-114, wherein the cell is a human.

116. The method of any one of claims 95-115, wherein a sample comprises the cell, the sample selected from the group consisting of a tissue sample, a frozen tissue sample, a biopsy specimen, a surgical specimen, a cytological specimen, whole blood, bone marrow, cerebral spinal fluid, peritoneal fluid, lymph fluid, serum, plasma, urine, stool, and nipple aspirate.

117. A kit for diagnosing rheumatoid arthritis or osteoarthritis, determining a rheumatoid arthritis or osteoarthritis prognosis, or determining or predicting a response to treatment for rheumatoid arthritis or osteoarthritis in a subject comprising: a reagent for determining the methylation states of at least 2 loci which have differential extents of methylation in individuals with rheumatoid arthritis or osteoarthritis relative to individuals without rheumatoid arthritis or osteoarthritis.

118. The kit of claim 117, wherein the at least 2 loci are selected from the group consisting of SEQ ID NO.s 1 – 485512

119. The kit of claim 117 or 118, wherein the at least 2 loci are selected from the group consisting of the loci listed in TABLE 6, TABLE 7, and TABLE 8.

120. The kit of claim 117 or 118, further comprising at least one polynucleotide primer comprising a sequence hybridizing to at least a portion of the at least 2 loci selected from the group consisting of the loci listed in TABLE 6, TABLE 7, and TABLE 8.

121. The kit of any one of claims 117-120, wherein the reagent comprises a restriction enzyme.

122. The kit of any one of claims 117-121, wherein the at least 2 loci are selected from the group consisting of the loci listed in TABLE 6.

123. The kit of any one of claims 117-121, wherein the at least 2 loci are selected from the group consisting of the loci listed in TABLE 7.

124. The kit of any one of claims 117-121, wherein the at least 2 loci are selected from the group consisting of the loci listed in TABLE 8.

125. The kit of any one of claims 117-121, wherein the reagent can determine the methylation states of at least 5 loci selected from the group consisting of SEQ ID NO.s 1-485512.

126. The kit of any one of claims 117-121, wherein the reagent can determine the methylation states of at least 5 loci selected from the group consisting of the loci listed in TABLE 6, TABLE 7, and TABLE 8.

127. The kit of any one of claims 117-121, wherein the reagent can determine the methylation states of at least 10 loci selected from the group consisting of the loci listed in TABLE 6, TABLE 7, and TABLE 8.

128. The kit of any one of claims 117-121, wherein the reagent can determine the methylation states of at least 20 loci selected from the group consisting of the loci listed in TABLE 6, TABLE 7, and TABLE 8.

129. The kit of any one of claims 117-121, wherein the reagent can determine the methylation states of at least 50 loci selected from the group consisting of the loci listed in TABLE 6, TABLE 7, and TABLE 8.

130. The kit of any one of claims 117-121, wherein the reagent can determine the methylation states of at least 100 loci selected from the group consisting of the loci listed in TABLE 6, TABLE 7, and TABLE 8.

131. A method for determining whether an individual suffers from rheumatoid arthritis or osteoarthritis comprising determining the methylation states of at least 2 loci which have differential extents of methylation in individuals with rheumatoid arthritis or osteoarthritis relative to individuals without rheumatoid arthritis or osteoarthritis, wherein the individual is diagnosed with rheumatoid arthritis if the methylation state of said at least 2 loci are associated with rheumatoid arthritis and the individual is diagnosed with osteoarthritis if the methylation states of said at least 2 loci are associated with osteoarthritis.

132. The method of claim 131, wherein the at least 2 loci are selected from the group consisting of SEQ ID NO.s 1-485512.

133. The method of any one of claims 131-132, wherein the at least 2 loci are selected from the group consisting of the loci listed in TABLE 6.

134. The method of any one of claims 131-132, wherein the at least 2 loci are selected from the group consisting of the loci listed in TABLE 7.

135. The method of any one of claims 131-132, wherein the at least 2 loci are selected from the group consisting of the loci listed in TABLE 8.

136. The method of any one of claims 131-132, wherein the methylation states of at least 5 loci selected from the group consisting of the loci listed in TABLE 6, TABLE 7, and TABLE 8 are determined.

137. The method of any one of claims 131-132, wherein the methylation states of at least 10 loci selected from the group consisting of the loci listed in TABLE 6, TABLE 7, and TABLE 8 are determined.

138. The method of any one of claims 131-132, wherein the methylation states of at least 20 loci selected from the group consisting of the loci listed in TABLE 6, TABLE 7, and TABLE 8 are determined.

139. The method of any one of claims 131-132, wherein the methylation states of at least 50 loci selected from the group consisting of the loci listed in TABLE 6, TABLE 7, and TABLE 8 are determined.

140. The method of any one of claims 131-132, wherein the methylation states of at least 100 loci selected from the group consisting of the loci listed in TABLE 6, TABLE 7, and TABLE 8 are determined.

141. A method for diagnosing rheumatoid arthritis or osteoarthritis, determining a rheumatoid arthritis or osteoarthritis prognosis, or determining or predicting a response to treatment for rheumatoid arthritis or osteoarthritis in a subject comprising: determining the methylation states of at least 2 genes selected from the group consisting of the genes listed in TABLE 3 in a sample obtained from the subject.

142. The method of claim 141, further comprising comparing the methylation states of the at least 2 genes in the sample with the methylation states of the genes in normal tissue, tissue from a subject with a known prognosis, or tissue from a subject with a known response to treatment.

143. The method of claim 142, wherein an increase or decrease in the extent of methylation of at least 2 genes compared to the extent of methylation of the of the genes in normal tissue, tissue from a subject with a known prognosis, or tissue from a subject with a

known response to treatment is indicative of the presence or absence of rheumatoid arthritis, prognosis, or response to treatment for the subject.

144. The method of any one of claims 141-143, wherein the methylation states of said at least 2 loci are determined in fibroblasts from said subject.

145. The method of any one of claims 141-143, wherein the methylation states of said at least 2 loci are determined in synoviocytes from said subject.

146. The method of any one of claims 141-143, wherein the methylation states of said at least 2 loci are determined in fibroblast-like synoviocytes from said subject.

147. The method of any one of claims 141-143, wherein the methylation states of said at least 2 loci are determined in rheumatoid arthritis fibroblast-like synoviocytes from said subject.

148. The method of any one of claims 141-143, wherein the methylation states of said at least 2 loci are determined in osteoarthritis fibroblast-like synoviocytes from said subject.

149. The method of any one of claims 141-143, wherein the methylation states of said at least 2 loci are determined in macrophage from said subject.

150. The method of any one of claims 141-143, wherein the methylation states of said at least 2 loci are determined in peripheral blood cells from said subject.

151. The method of claim 150, wherein the peripheral blood cell is selected from the group consisting of white blood cell, neutrophil, eosinophil, basophil, lymphocyte, B cell, plasma cell, T cell, natural killer cell, monocyte, and dendritic cell.

152. The method of any one of claims 141-151, wherein the sample is selected from the group consisting of a tissue sample, a frozen tissue sample, a biopsy specimen, a surgical specimen, a cytological specimen, whole blood, bone marrow, cerebral spinal fluid, peritoneal fluid, lymph fluid, serum, plasma, urine, stool, and nipple aspirate.

153. The method of any one of claims 141-152, wherein the methylation states of at least 5 genes selected from the group consisting of the genes listed in TABLE 3 are determined.

154. The method of any one of claims 141-153, wherein the methylation states of at least 10 genes selected from the group consisting of the genes listed in TABLE 3 are determined.

155. The method of any one of claims 141-154, wherein the methylation states of at least 20 genes selected from the group consisting of the genes listed in TABLE 3 are determined.

156. The method of any one of claims 141-155, wherein the methylation states of at least 50 genes selected from the group consisting of the genes listed in TABLE 3 are determined.

157. The method of any one of claims 141-156, wherein the subject is a mammal.

158. The method of any one of claims 141-157, wherein the subject is a human.

159. A method for identifying a therapeutic agent for treating rheumatoid arthritis or osteoarthritis comprising:

contacting a cell with a test agent; and

determining the methylation states of at least 2 genes selected from the group consisting of the genes listed in TABLE 3 in the contacted cell.

160. The method of claim 159, further comprising:

comparing the methylation states of the at least 2 genes in the contacted cell with the methylation states of the genes in a cell which was not contacted with the test agent; and

selecting a test agent that increases or decreases the extent of methylation of the at least 2 genes in the cell contacted with the test agent compared to the extent of methylation of the at least 2 genes in a cell which was not contacted with the test agent such that the extent of methylation of the at least 2 genes in the cell contacted with the test agent is a methylation states associated with the absence of rheumatoid arthritis or osteoarthritis or with a reduction in the symptoms associated with rheumatoid arthritis or osteoarthritis.

161. The method of any one of claims 159-160, wherein the methylation states of at least 5 genes selected from the group consisting of the genes listed in TABLE 3 are determined.

162. The method of any one of claims 159-161, wherein the methylation states of at least 10 genes selected from the group consisting of the genes listed in TABLE 3 are determined.

163. The method of any one of claims 159-162, wherein the methylation states of at least 20 genes selected from the group consisting of the genes listed in TABLE 3 are determined.

164. The method of any one of claims 159-163, wherein the methylation states of at least 50 genes selected from the group consisting of the genes listed in TABLE 3 are determined.

165. The method of any one of claims 159-164, wherein the cell comprises a fibroblast.

166. The method of any one of claims 159-164, wherein the cell comprises a synoviocyte.

167. The method of any one of claims 159-164, wherein the cell comprises a fibroblast-like synoviocyte.

168. The method of any one of claims 159-164, wherein the cell comprises a rheumatoid arthritis fibroblast-like synoviocyte.

169. The method of any one of claims 159-164, wherein the cell comprises an osteoarthritis fibroblast-like synoviocyte.

170. The method of any one of claims 159-164, wherein the cell comprises a macrophage.

171. The method of any one of claims 159-164, wherein the cell comprises a peripheral blood cell.

172. The method of claim 171, wherein the peripheral blood cell is selected from the group consisting of white blood cell, neutrophil, eosinophil, basophil, lymphocyte, B cell, plasma cell, T cell, natural killer cell, monocyte, and dendritic cell.

173. The method of any one of claims 159-172, wherein the cell is mammalian.

174. The method of any one of claims 159-173, wherein the cell is a human.

175. The method of any one of claims 159-174, wherein a sample comprises the cell, the sample selected from the group consisting of a tissue sample, a frozen tissue sample, a biopsy specimen, a surgical specimen, a cytological specimen, whole blood, bone marrow, cerebral spinal fluid, peritoneal fluid, lymph fluid, serum, plasma, urine, stool, and nipple aspirate.

176. A kit for diagnosing rheumatoid arthritis or osteoarthritis, determining a rheumatoid arthritis or osteoarthritis prognosis, or determining or predicting a response to treatment for rheumatoid arthritis or osteoarthritis in a subject comprising: a reagent for determining the methylation states of at least 2 genes selected from the group consisting of the genes listed in TABLE 3.

177. The kit of claim 176, further comprising at least one polynucleotide primer comprising a sequence hybridizing to at least a portion of the at least 2 genes selected from the group consisting of the genes listed in TABLE 3.

178. The kit of any one of claims 176-177, wherein the reagent comprises a restriction enzyme.

179. The kit of any one of claims 176-178, wherein the reagent can determine the methylation states of at least 5 genes selected from the group consisting of the genes listed in TABLE 3.

180. The kit of any one of claims 176-179, wherein the reagent can determine the methylation states of at least 10 genes selected from the group consisting of the genes listed in TABLE 3.

181. The kit of any one of claims 176-180, wherein the reagent can determine the methylation states of at least 20 genes selected from the group consisting of the genes listed in TABLE 3.

182. The kit of any one of claims 176-181, wherein the reagent can determine the methylation states of at least 50 genes selected from the group consisting of the genes listed in TABLE 3.

183. A method for identifying a therapeutic agent for treating rheumatoid arthritis or osteoarthritis comprising:

contacting a cell with a test agent; and

determining the methylation states of at least 2 genes selected from a gene encoding a protein that acts in a pathway that includes a protein encoded by a gene that is differentially methylated in a rheumatoid arthritis cell or that is differentially methylated in an osteoarthritis cell compared to a normal cell.

184. The method of claim *, further comprising:

comparing the methylation states of the at least 2 genes in the contacted cell with the methylation states of the genes in a cell which was not contacted with the test agent; and

selecting a test agent that increases or decreases the extent of methylation of the at least 2 genes in the cell contacted with the test agent compared to the extent of methylation of the at least 2 genes in a cell which was not contacted with the test agent such that the extent of methylation of the at least 2 genes in the cell contacted with the test agent are methylation states associated with the absence of rheumatoid arthritis or methylation states associated with the absence of osteoarthritis with a reduction in the symptoms associated with rheumatoid arthritis.

185. The method of claim 184, wherein the pathway is selected from the group consisting of the pathways listed in TABLE 5.

186. The method of any one of claims 184-185, wherein the methylation states of at least 5 genes selected from genes encoding proteins that act in a pathway that includes a protein encoded by a gene that is differentially methylated in a rheumatoid arthritis cell compared to a normal cell or that is differentially methylated in an osteoarthritis cell compared to a normal cell.

187. The method of any one of claims 184-186, wherein the methylation states of at least 10 genes selected from genes encoding proteins that act in a pathway that includes a protein encoded by a gene that is differentially methylated in a rheumatoid arthritis cell compared to a normal cell or that is differentially methylated in an osteoarthritis cell compared to a normal cell.

188. The method of any one of claims 184-187, wherein the cell comprises a fibroblast.

189. The method of any one of claims 184-187, wherein the cell comprises a synovial cell.

190. The method of any one of claims 184-187, wherein the cell comprises a fibroblast-like synoviocyte.

191. The method of any one of claims 184-187, wherein the cell comprises a rheumatoid arthritis fibroblast-like synoviocyte.

192. The method of any one of claims 184-187, wherein the cell comprises an osteoarthritis fibroblast-like synoviocyte.

193. The method of any one of claims 184-187, wherein the cell comprises a macrophage.

194. The method of any one of claims 184-187, wherein the cell comprises a peripheral blood cell.

195. The method of claim 194, wherein the peripheral blood cell is selected from the group consisting of white blood cell, neutrophil, eosinophil, basophil, lymphocyte, B cell, plasma cell, T cell, natural killer cell, monocyte, and dendritic cell.

196. The method of any one of claims 184-195, wherein the cell is mammalian.

197. The method of any one of claims 184-196, wherein the cell is a human.

198. The method of any one of claims 184-197, wherein a sample comprises the cell, the sample selected from the group consisting of a tissue sample, a frozen tissue sample, a biopsy specimen, a surgical specimen, a cytological specimen, whole blood, bone marrow, cerebral spinal fluid, peritoneal fluid, lymph fluid, serum, plasma, urine, stool, and nipple aspirate.

199. A method for identifying therapeutic agents for treating rheumatoid arthritis or osteoarthritis comprising:

contacting a cell with a test agent; and

determining the activity of a protein encoded by a gene differentially methylated in a rheumatoid arthritis cell or that is differentially methylated in an osteoarthritis cell compared to a normal cell.

200. The method of claim 199, further comprising:

comparing the activity of the protein in the contacted cell with the activity of the protein in a cell which was not contacted with the test agent; and

selecting a test agent that increases or decreases the activity of protein in the cell contacted with the test agent compared to the activity of the protein in a cell which was not contacted with the test agent such that the activity of the protein in the cell contacted with the test agent is an activity associated with the absence of rheumatoid arthritis or an activity associated with the absence of osteoarthritis with a reduction in the symptoms associated with rheumatoid arthritis.

201. The method of any one of claims 199-200, wherein the protein is encoded by a gene selected from the group consisting of the genes listed in TABLE 3.

202. The method of any one of claims 199-201, wherein the cell comprises a fibroblast.

203. The method of any one of claims 199-201, wherein the cell comprises a synoviocyte.

204. The method of any one of claims 199-201, wherein the cell comprises a fibroblast-like synoviocyte.

205. The method of any one of claims 199-201, wherein the cell comprises a rheumatoid arthritis fibroblast-like synoviocyte.

206. The method of any one of claims 199-201, wherein the cell comprises an osteoarthritis fibroblast-like synoviocyte.

207. The method of any one of claims 199-201, wherein the cell comprises a macrophage.

208. The method of any one of claims 199-201, wherein the cell comprises a peripheral blood cell.

209. The method of claim 208, wherein the peripheral blood cell is selected from the group consisting of white blood cell, including neutrophil, eosinophil, basophil, lymphocyte, B cell, plasma cell, T cell, natural killer cell, monocyte, and dendritic cell.

210. The method of any one of claims 199-209, wherein the cell is mammalian.

211. The method of any one of claims 199-210, wherein the cell is a human.

212. A method of determining the methylation status of a plurality of human nucleic acid loci comprising:

contacting a nucleic acid sample from a human subject with a reagent capable of providing an indication of the methylation status of said loci, wherein said loci comprise at least 5 which have differential extents of methylation in individuals with rheumatoid arthritis or osteoarthritis relative to individuals without rheumatoid arthritis or osteoarthritis.

213. The method of claim 212, wherein said reagent is a restriction enzyme.

214. The method of claim 212, wherein said reagent is a primer.

215. The method of claim 212, wherein said reagent is a probe.

216. The method of claim 212, wherein said reagent comprises sodium bisulfite.

217. The method of any one of claims 212-216, wherein the at least 5 loci are selected from the group consisting of SEQ ID NO.s 1- 485512.

218. The method of any one of claims 212-217, wherein the at least 5 loci are selected from the group consisting of the loci listed in TABLE 6, TABLE 7, and TABLE 8.

219. A nucleic acid array consisting essentially of nucleic acids useful for diagnosing rheumatoid arthritis or osteoarthritis, determining a prognosis of rheumatoid arthritis or osteoarthritis, or determining or predicting a response to treatment of a subject being evaluated for or suffering from rheumatoid arthritis or osteoarthritis, wherein said nucleic acids comprise at least 5 loci which have differential extents of methylation in individuals with rheumatoid arthritis or osteoarthritis relative to individuals without rheumatoid arthritis or osteoarthritis.

220. The method of claim 219, wherein said nucleic acids comprise at least 5 loci selected from the group consisting of SEQ ID NO.s 1-485512.

221. The method of any one of claims 219-220, wherein said nucleic acids comprise at least 5 loci selected from the group consisting of the loci listed in TABLE 6, TABLE 7, and TABLE 8.

222. The method of any one of claims 219-221, wherein said nucleic acids comprise at least 10 loci selected from the group consisting of the loci listed in TABLE 6, TABLE 7, and TABLE 8.

223. The method of any one of claims 219-222, wherein said nucleic acids comprise at least 20 loci selected from the group consisting of the loci listed in TABLE 6, TABLE 7, and TABLE 8.

224. The method of any one of claims 219-223, wherein said nucleic acids comprise at least 50 loci selected from the group consisting of the loci listed in TABLE 6, TABLE 7, and TABLE 8.

225. A method of ameliorating rheumatoid arthritis or osteoarthritis comprising:

evaluating the methylation status of a plurality of human nucleic acid loci in a nucleic acid sample from a human subject having symptoms of rheumatoid arthritis or osteoarthritis, wherein said loci comprise at least 5 loci which have differential extents of methylation in individuals with rheumatoid arthritis or osteoarthritis relative to individuals without rheumatoid arthritis or osteoarthritis; and

administering a treatment for rheumatoid arthritis or osteoarthritis if said at least 5 loci have a methylation status indicative of rheumatoid arthritis or osteoarthritis.

226. The method of claim 225, wherein said nucleic acids comprise at least 5 loci selected from the group consisting of SEQ ID NO.s 1-485512.

227. The method of any one of claims 225-226, wherein said nucleic acids comprise at least 5 loci selected from the group consisting of the loci listed in TABLE 6, TABLE 7, and TABLE 8.

228. The method of any one of claims 225-227, wherein said nucleic acids comprise at least 10 loci selected from the group consisting of the loci listed in TABLE 6, TABLE 7, and TABLE 8.

229. The method of any one of claims 225-228, wherein said nucleic acids comprise at least 20 loci selected from the group consisting of the loci listed in TABLE 6, TABLE 7, and TABLE 8.

230. The method of any one of claims 225-229, wherein said nucleic acids comprise at least 50 loci selected from the group consisting of the loci listed in TABLE 6, TABLE 7, and TABLE 8.

231. A mixture comprising a plurality of human nucleic acid loci from a human subject having symptoms indicative of potential rheumatoid arthritis or osteoarthritis and a reagent capable of providing an indication of the methylation status of said loci, wherein said loci comprise at least 5 loci which have differential extents of methylation in individuals with rheumatoid arthritis or osteoarthritis relative to individuals without rheumatoid arthritis or osteoarthritis.

232. The mixture of claim 231, wherein said nucleic acids comprise at least 5 loci selected from the group consisting of SEQ ID NO.s 1-485512

233. The mixture of any one of claims 231-232, wherein said nucleic acids comprise at least 5 loci selected from the group consisting of the loci listed in TABLE 6, TABLE 7, and TABLE 8.

234. The mixture of any one of claims 231-233, wherein said nucleic acids comprise at least 10 loci selected from the group consisting of the loci listed in TABLE 6, TABLE 7, and TABLE 8.

235. The mixture of any one of claims 231-234, wherein said nucleic acids comprise at least 20 loci selected from the group consisting of the loci listed in TABLE 6, TABLE 7, and TABLE 8.

236. The mixture of any one of claims 231-235, wherein said nucleic acids comprise at least 50 loci selected from the group consisting of the loci listed in TABLE 6, TABLE 7, and TABLE 8.

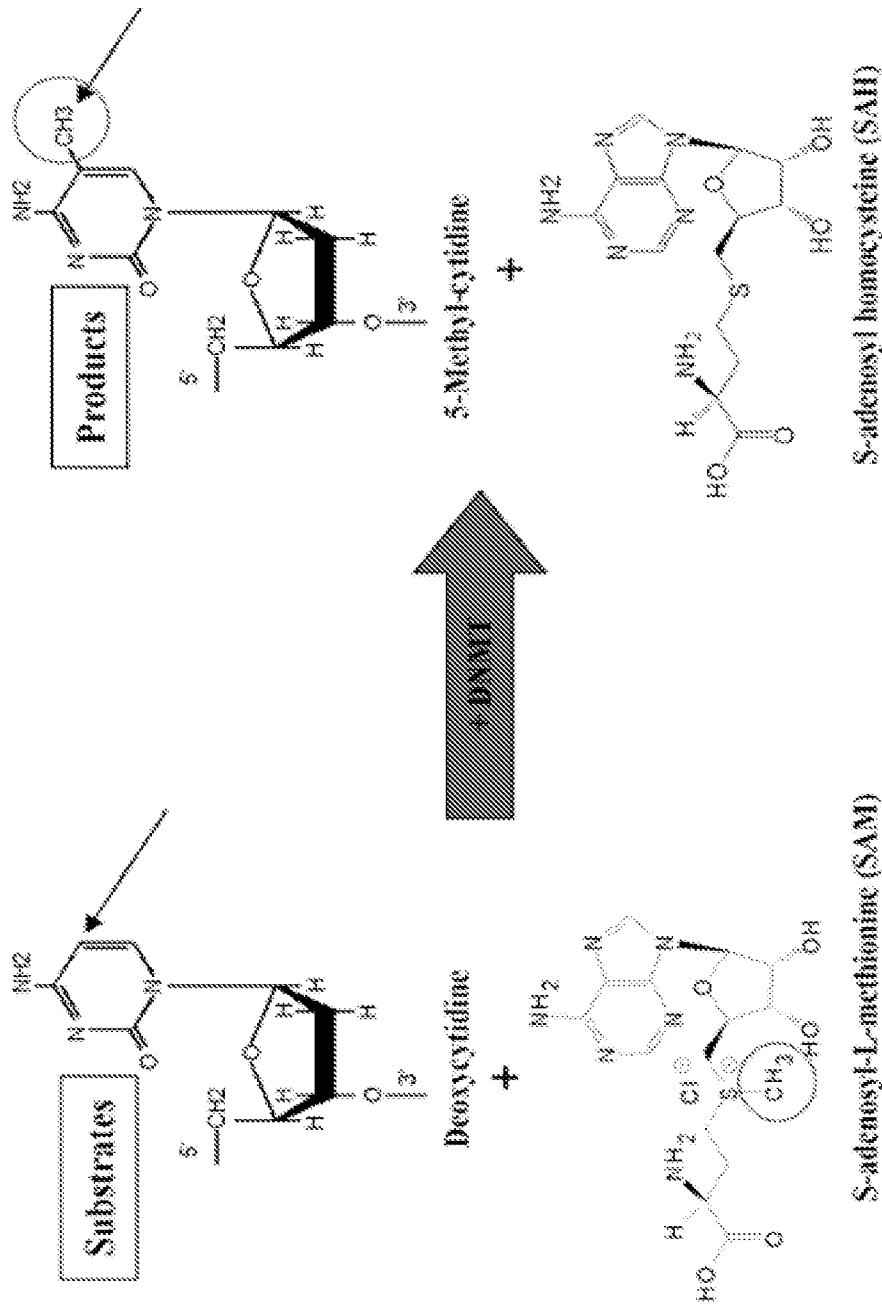


FIG. 1

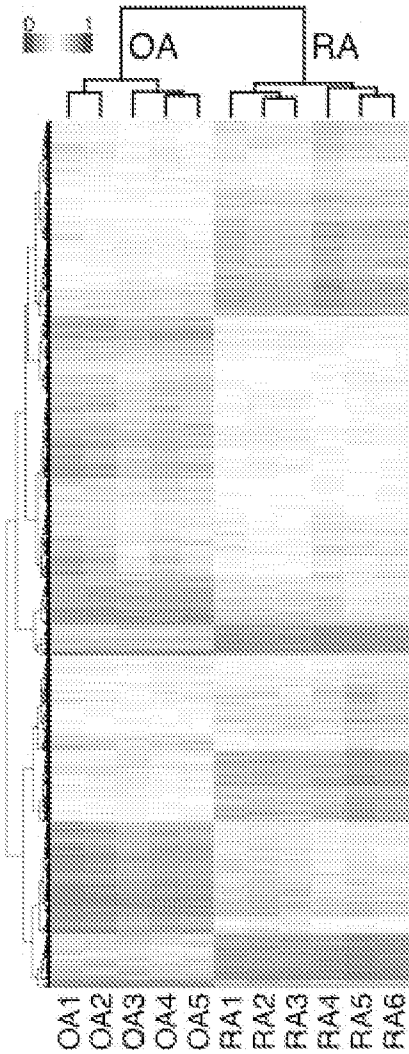


FIG. 2

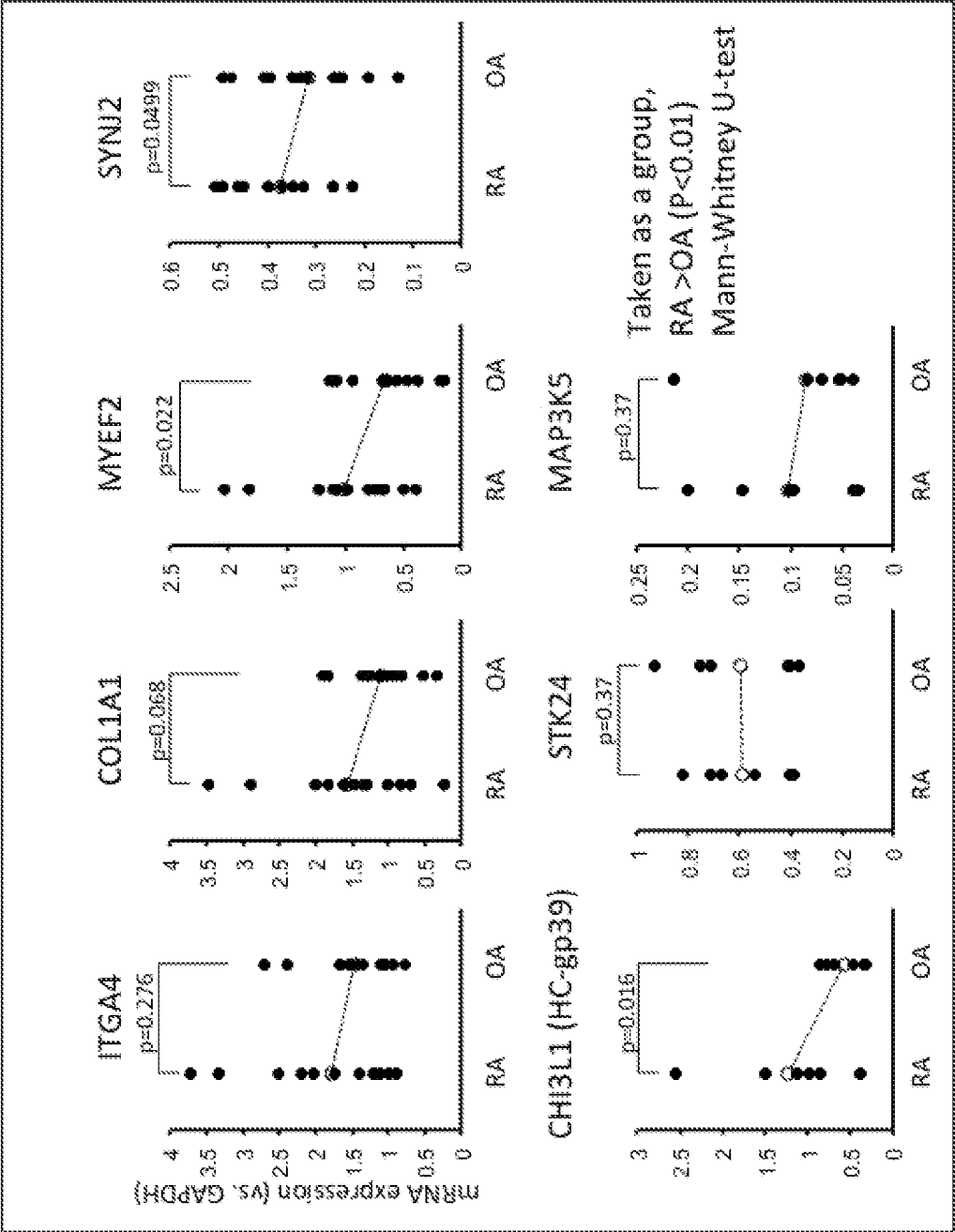
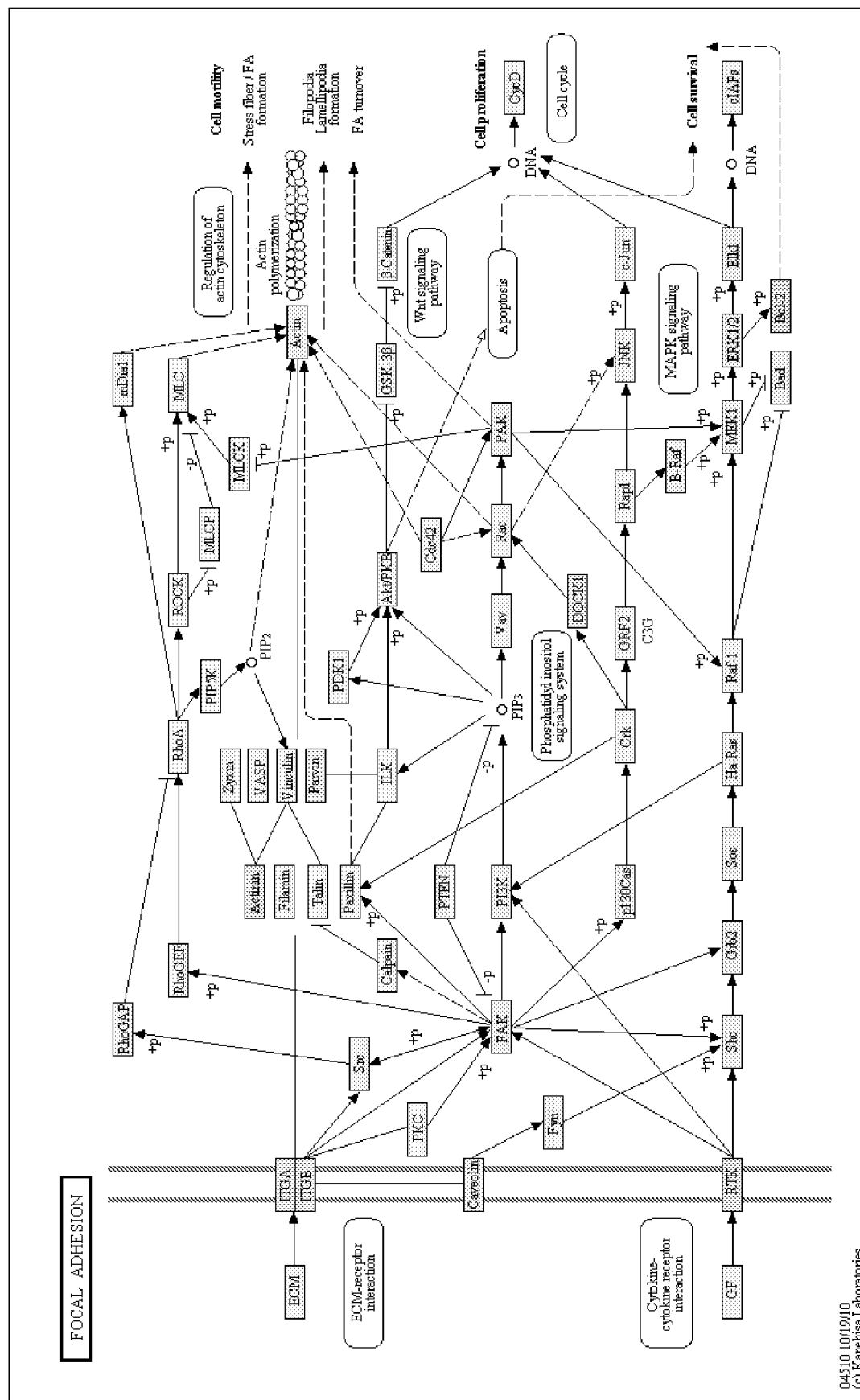


FIG. 3



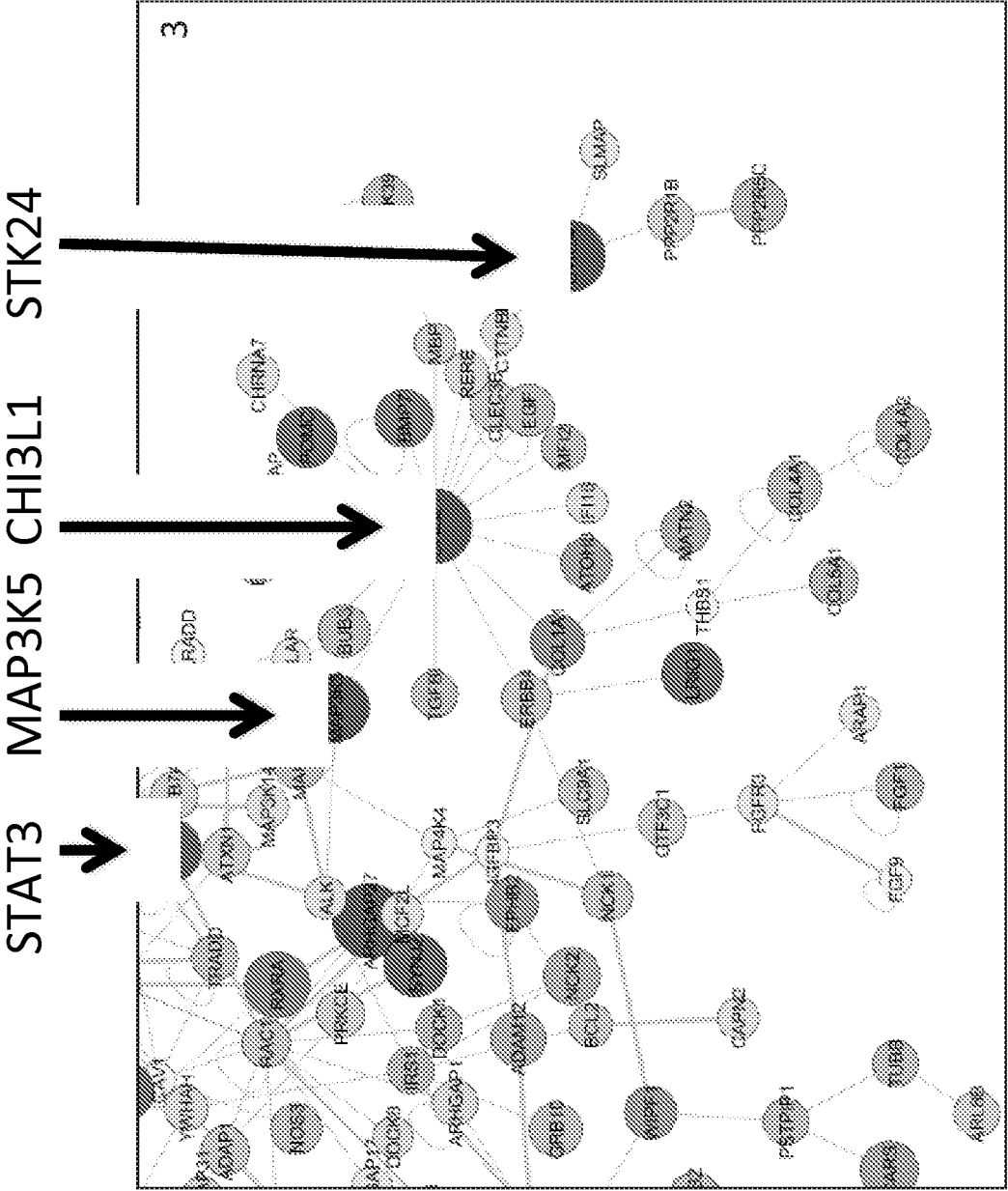


FIG. 5

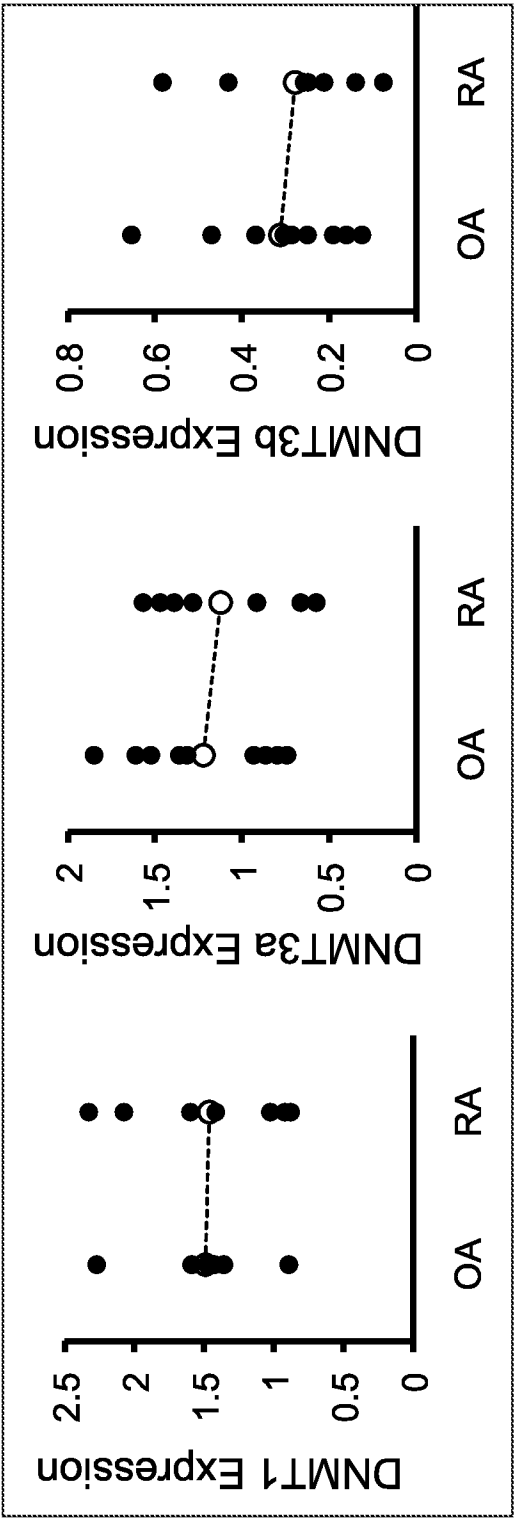


FIG. 6

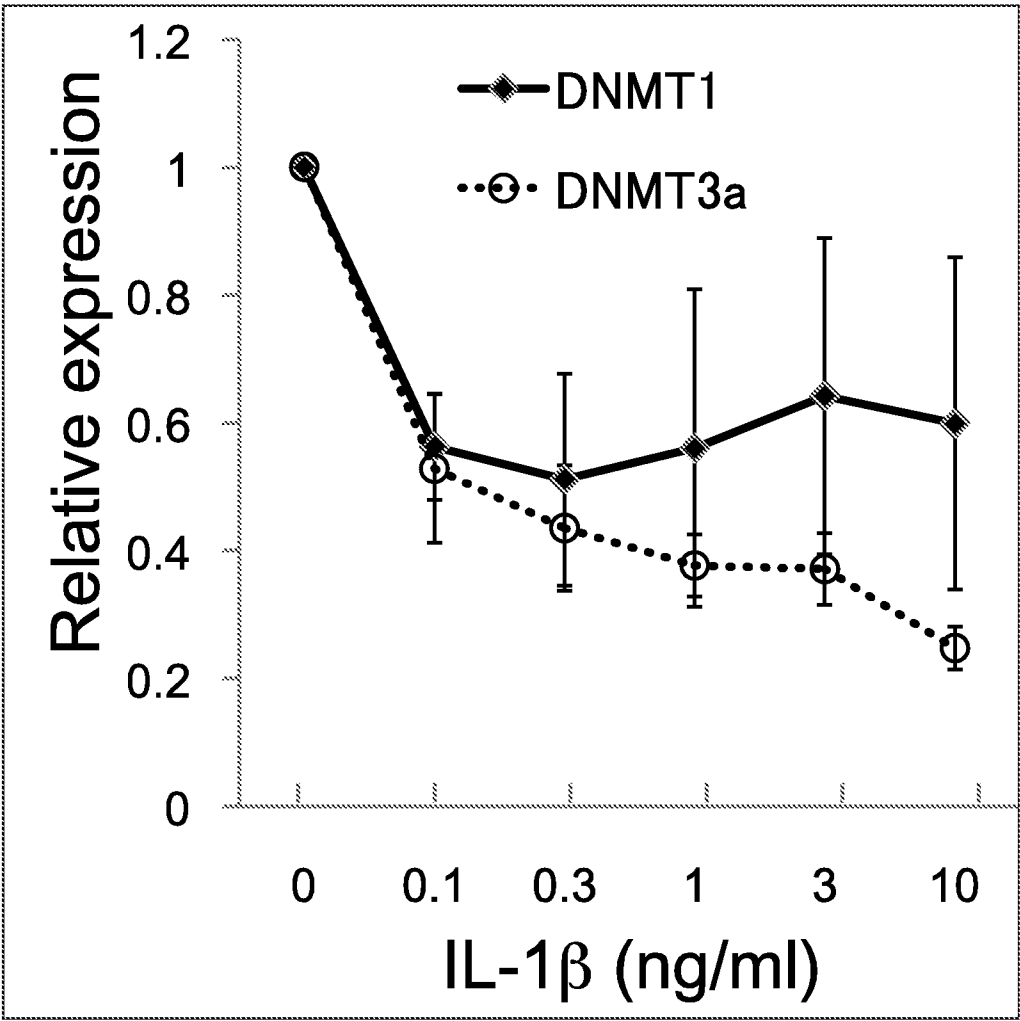


FIG. 7

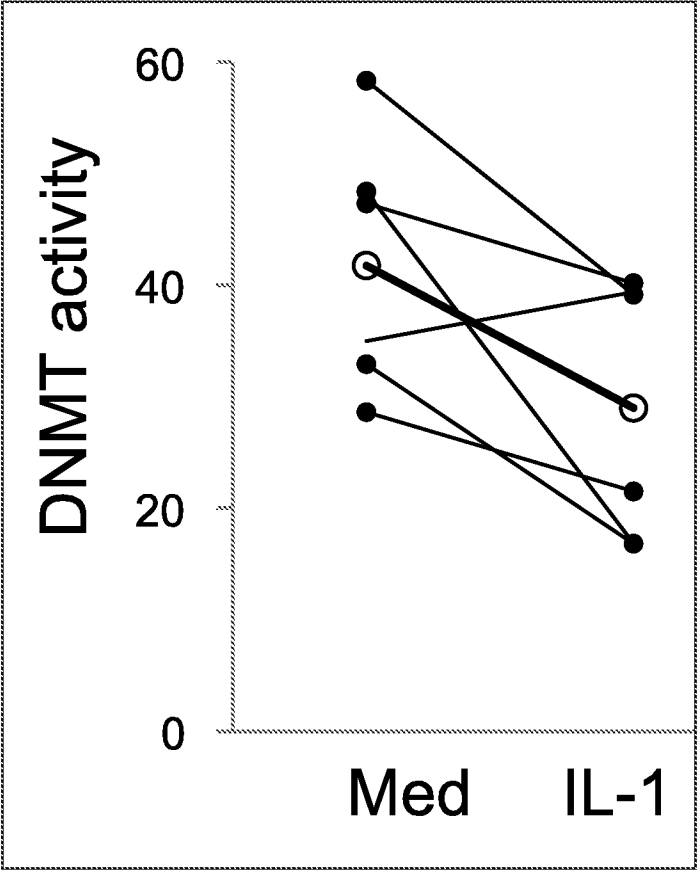


FIG. 8