

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

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
10 December 2009 (10.12.2009)

PCT

(10) International Publication Number
WO 2009/149319 A2

(51) International Patent Classification:
G01N 33/50 (2006.01)

(21) International Application Number:
PCT/US2009/046356

(22) International Filing Date:
5 June 2009 (05.06.2009)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
61/059,153 5 June 2008 (05.06.2008) US
61/084,787 30 July 2008 (30.07.2008) US
61/111,917 6 November 2008 (06.11.2008) US

(71) Applicant (for all designated States except US):
WYETH [US/US]; Five Giralda Farms, Madison, NJ 07940 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **O'TOOLE, Margot, Mary** [US/US]; 353 Albemarle Road, Newton, MA 02460 (US). **REDDY, Padmalatha, Sunkara** [US/US]; 42 Laconia Street, Lexington, MA 02420 (US). **HILL, Andrew, Arthur** [CA/CA]; C-205 Walden Street, Cambridge, MA 02140 (US). **DORNER, Andrew, Joseph** [US/US]; 20 Baskin Road, Lexington, MA 02421 (US). **MCKEE, Charlotte, Marie** [US/US]; 470 Commonwealth Avenue, Newton, MA 02459 (US). **LIU, Wei** [US/US]; 15 Sunny Knoll Terrace, Lexington, MA 02421 (US). **CHAUDHARY, Divya** [US/US]; 27 Jenkins Road, Andover, MA 01810 (US). **SILVER, Matthew, Ren** [US/US]; 3 Seagull Street, Rockport, MA 01966 (US). **IMMERMANN, Frederick, William** [US/US]; 194 Haverstraw Road, Suffern, NY 10910 (US). **RYAN, John, Louis** [US/US]; 200 E. Evergreen Ave., Philadelphia, PA 19118 (US). **CSIMMA, Cristina, Ileana** [US/US]; 16 Conant Rd., Lincoln, MA 01773 (US).

(74) Agents: **MORAN, Michael, J.** et al.; Wyeth, Patent Law Department, Five Giralda Farms, Madison, NJ 07940 (US).

(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, 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, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, 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, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (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, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

- as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))
- as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))

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: GENE EXPRESSION PROFILES ASSOCIATED WITH ASTHMA EXACERBATION ATTACKS

(57) Abstract: The present invention provides methods for the assessment, diagnosis, or prognosis of asthma exacerbation, by assessing the level of expression of asthma exacerbation gene products in a sample derived from a patient. The markers of the present invention can be used in methods to identify or evaluate agents capable of modulating marker expression levels in subjects with asthma.



WO 2009/149319 A2

GENE EXPRESSION PROFILES ASSOCIATED WITH ASTHMA EXACERBATION ATTACKS

BACKGROUND

The present invention relates to markers of acute asthma exacerbation and methods of
5 using the same for the prediction, diagnosis and prognosis of acute asthma exacerbation.

Asthma is a chronic inflammatory disease of the airways that is characterized by
recurrent episodes of reversible airway obstruction and airway hyperresponsiveness (AHR).
Typical clinical manifestations of acute asthma exacerbation (also known as asthma attack)
include shortness of breath, wheezing, coughing and chest tightness that can become life
10 threatening or fatal. Despite the considerable progress that has been made in elucidating the
pathophysiology of asthma, the prevalence, morbidity, and mortality of the disease has
increased during the past two decades. In 1995, in the United States alone, nearly 1.8
million emergency room visits, 466,000 hospitalizations and 5,429 deaths were directly
attributed to acute asthma exacerbation.

15 It is generally accepted that allergic asthma is initiated by an inappropriate inflammatory
reaction to airborne allergens. The lungs of asthmatics demonstrate an intense infiltration of
lymphocytes, mast cells and eosinophils. A large body of evidence has demonstrated this
immune response to be driven by CD4⁺ T-cells expressing a T_{H2} cytokine profile. Four major
pathophysiological responses seen in human asthma include upregulation of serum IgE
20 (atopy), eosinophilia, excessive mucus secretion, and AHR.

Current therapy for asthma includes use of bronchodilators, corticosteroids and
leukotriene inhibitors. The treatments share the same therapeutic goal of bronchodilation,
reducing inflammation and facilitating expectoration. Many of such treatments, however,
include undesired side effects and lose effectiveness after being used for a period of time.
25 Additionally, only limited agents for therapeutic intervention are available for decreasing the
airway remodeling process that occurs in asthmatics. Therefore, there remains a need for an
increased molecular understanding of asthma, and a need for the identification of novel
therapeutic strategies to combat these complex diseases.

SUMMARY

30 In one aspect, the invention provides a method for determining the molecular signature
of asthma exacerbation attack of a subject, comprising the steps of determining the level of
at least one biomarker in said subject prior to an exacerbation attack; determining the level
of the at least one biomarker in said subject during an asthma exacerbation attack; and

ascertaining the difference between the level of the biomarker prior to the attack and the level during the attack. The difference in the level of a particular biomarker or plurality of biomarkers (i.e., a change in expression of one or more biomarkers) indicates the molecular signature, which in turn indicates the type of asthma exacerbation attack. In some
5 embodiments, the levels of biomarkers are determined from a sample obtained from the subject. In one embodiment, the sample is a blood sample comprising peripheral blood mononuclear cells (PBMCs). In some embodiments, the type of asthma exacerbation attack is one of innate immunity (subgroup X), as indicated e.g. by a change in expression of one or more biomarkers listed in Tables 4, 6 and 9. In some embodiments, the type of asthma
10 exacerbation attack is one of cognate immunity (subgroup Y), as indicated e.g. by a change in expression of one or more biomarkers listed in Tables 5 and 10. In some embodiments, the type of asthma exacerbation attack is coextensive with an airway infection, as indicated e.g. by a change in expression of one or more biomarkers listed in Tables 11 and 12. In yet other embodiments, the type of asthma exacerbation attack does not involve an airway
15 infection, as indicated by a change in expression of biomarkers selected from a group comprising interferon induced with helicase C domain 1 (IFIH1; e.g. SEQ ID NO:60), leukotriene A4 hydrolase (LTA4H; e.g. SEQ ID NO:61) and open reading frame number 25 of human chromosome 6 (C6ORF25; SEQ ID NO:62). In some embodiments, the biomarkers are nucleic acids. In other embodiments, the biomarkers are polypeptides.

20 In another aspect, the invention provides a method for selecting a treatment for asthma exacerbation in a patient, comprising the steps of determining the type of asthma exacerbation based on the molecular signature in the patient (*supra*), then selecting a treatment corresponding to the type of asthma exacerbation. In some embodiments, the therapies are tailored to stopping T and/or B cell cognate immunity, innate immunity and/or
25 airway infection. In some embodiments, the blood of the patient is monitored to ascertain a change in the levels of one or more biomarkers to assess the effectiveness of treatment and to revise therapy as indicated.

In one aspect, the invention provides a method for identifying individuals at risk for asthma, by identifying an individual who does not yet exhibit symptoms of asthma, measuring the level of at least one product in a sample obtained from the individual,
30 comparing that level to a reference level of the product, and optionally providing the result of the comparison to a user. The product is the product of at least one gene that is differentially expressed in individuals having an acute exacerbation of asthma versus those not having an acute exacerbation of asthma. A difference between the reference level and
35 the level of the product indicates that the individual is at risk for asthma.

In another aspect, the invention provides a method for identifying individuals at risk for asthma exacerbation, by identifying an individual who is a known asthmatic, measuring the

level of at least one product in a sample obtained from the individual, comparing that level to a reference level of the product, and optionally providing the result of the comparison to a user. The product is the product of at least one gene that is differentially expressed in individuals having an acute exacerbation of asthma versus those not having an acute
5 exacerbation of asthma. A difference between the reference level and the level of the product indicates that the individual is at risk for acute exacerbation of asthma.

In some embodiments, the invention provides a method of identifying individuals at risk for asthma or asthma exacerbation, comprising: (a) identifying an individual who does not exhibit symptoms of asthma; (b) measuring the level of at least one product in a sample
10 obtained from the individual, wherein the product is produced from a gene which is differentially expressed during asthma exacerbation; and (c) comparing said level of step (a) to a reference level of said product, wherein a difference between said level of step (a) and the reference level indicates that the individual is at risk for asthma or asthma exacerbation. In one embodiment, the individual has exhibited one or more symptoms of asthma
15 previously. In another embodiment, the individual has not exhibited one or more symptoms of asthma previously.

In another aspect, the invention provides an array for use in assessing the risk for asthma or asthma exacerbation in a patient, comprising a plurality of discrete regions or addresses, each of which comprises a target molecule disposed thereon, wherein a subset
20 of the plurality of discrete regions has disposed thereon target molecules that can specifically detect a marker of asthma exacerbation. In some embodiments, the subset of the plurality of discrete regions that can specifically detect a marker of asthma exacerbation is at least 5%, 15%, 20%, 25%, 30%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 90%, 95%, or 99% of the total discrete regions on the array. In some embodiments, the
25 target molecules are single stranded polynucleotides that hybridize to polynucleotides obtained from a sample. In other embodiments, the target molecules are peptide recognition moieties, such as for example antibodies or antibody fragments, aptamers, cognate ligands or receptors, and the like. In some embodiments, the sample is obtained from an individual. In some embodiments, the sample from the individual is a blood sample which contains
30 peripheral blood mononuclear cells.

In some embodiments of the aforementioned aspects, the genes or markers that are differentially expressed during asthma exacerbation are depicted in Tables 2-6 and 8-12. In other embodiments, the genes or markers are involved in interleukin-15 (IL-15) signaling, (B-cell receptor) BCR signaling, toll-like receptor (TLR) signaling, interferon (IFN) signaling
35 and/or interferon regulatory factor (IRFs) pathways.

In any one or more of the foregoing aspects, the reference levels of gene products that are differentially expressed during asthma exacerbation are levels of those gene products

that are expressed in individuals free of asthma symptoms or in an asthma quiet period. In some embodiments, the reference level is an average of levels obtained from symptom free or asthma quiet individuals. In other embodiments, the reference level is obtained during an asthma quiet period from the same individual who is being tested.

5 In another aspect, the invention provides a combination of polynucleotides comprising at least 2 or more, or at least 10 substantially purified and isolated polynucleotides, wherein each polynucleotide comprises at least 22 contiguous nucleotides of a gene selected from the group comprising the genes set forth in Table 2, Table 3, Table 4, Table 5, Table 6, Table 8, Table 9, Table 10, Table 11, Table 12 and SEQ ID NOs: 1-77, or the complements
10 and fragments thereof. In one embodiment, the combination of polynucleotides is attached to a substrate to form an array.

In another aspect, the invention provides a kit comprising a detection reagent which binds to the gene product of one or more genes that are differentially expressed in a sample obtained from an individual having an asthma exacerbation versus a sample obtained from
15 an individual having an asthma quiet period. In some embodiments, the one or more genes are selected from the group consisting of the genes set forth in Tables 1-6 and 8-12, and SEQ ID NOs:1-59. In some embodiments, the sample obtained from an individual having an asthma exacerbation is a blood sample. In some embodiments, the gene product comprises a polypeptide and the detection reagent comprises an antibody or an aptamer. In other
20 embodiments, the gene product comprises a polynucleotide and the detection reagent comprises an oligonucleotide or a polynucleotide.

In any one or more of the foregoing aspects, the samples obtained from individuals can be any cell, tissue or fluid. In some embodiments, the sample is a blood sample, which contains peripheral blood mononuclear cells (PBMCs). In other embodiments, the sample is
25 serum.

In another aspect, the invention provides a method of discovering a compound that is effective for treating asthma exacerbation, comprising: providing a candidate compound; determining whether said compound inhibits IL-15 activity, wherein inhibition of IL-15 activity indicates that said compound is effective for treating acute exacerbation of asthma.

30 In one embodiment, the methods for determining the molecular signature of asthma exacerbation comprise combining a sample from a patient with one or more agents capable of reacting with one or more markers in the sample, and detecting a reaction.

DETAILED DESCRIPTION

Asthma Exacerbation Markers

The present invention provides a new class of markers that are differentially expressed in acute exacerbation of asthma, particularly in peripheral blood mononuclear cells and/or serum. Specifically, the markers of the present invention upregulate or downregulate their expression in individuals having an asthma attack. The present invention provides methods for assessing the state-of-health as it relates to asthma in an individual by comparing the expression level of one or more markers with a reference expression level of the one or more markers. The present invention also provides methods for asthma diagnosis, prognosis, or assessment in which the expression level of one or more markers of the present invention is compared to a reference level of the one or more markers.

A study was conducted to investigate the transcriptomics and proteomics of asthma exacerbation. The study was intended to identify potential new targets and/or markers for asthma, particularly asthma exacerbation. The approach to the answers to these questions involved seeking to identify differences between the asthma quiet and asthma exacerbation phenotypes at the molecular level.

The inventors have discovered that particular sets of genes are differentially expressed in individuals during asthma exacerbation as compared to during an asthma quiet time. A subset of those genes that are differentially expressed during exacerbation versus quiet, and which have a false discovery rate of less than 0.05 are listed in Table 2. The study individuals were clustered into three subgroups, based upon their exacerbation molecular profile: subgroup X, subgroup Y and subgroup Z.

For subgroup X individuals, Table 4 depicts 1081 genes having an exacerbation versus quiet expression differential with a false discovery rate of less than 0.05. The subgroup X differentially expressed genes include many well-defined interferon (IFN)–inducible genes and transcription factors, such as IFN α , IFN β , ISGF3G, IRF7, IRF1, SP100, OAS1, OAS2, MX1, MX2, ISG15, IFITM1, NM1, IR27, IR6, IR30, GBP1, GBP2, SP110, IRF4, IFITM2, and IFI16. The subgroup X differentially expressed genes also include genes linked to IFN, such as for example FGL2, LGALS, IL23A, ARTS-1, STAT1, STAT2, IRF1, IRF4, IRF7, ISGF3G, and the like. The subgroup X differentially expressed genes also include those genes driven by interferon regulatory factors (IRFs), such as OAS2, STAT2, IL15, TAP1, CTSS, IFIT3, OAS1, EIF2AK2, PSMB10, CYBB, CASP7, BCL2, STAT1, PSMB9, CASP8, CDKN1A, CASP1, HLA-G, VIL2, GATA3, GBP1, CXCR4, MS4A1, DNASE2, CCL5, TAP2, TEGT, PLSCR1, ISG15, and TNFSF10. The subgroup X differentially expressed genes also

include those genes regulated by interleukin-15 (IL-15), which are listed for example in Table 6.

The differential expression of one or more subgroup X differentially expressed genes in a sample of an individual comprises a molecular profile of an asthma exacerbation that indicates that the asthma exacerbation involves innate immunity. The innate immune system is generally known in the art to be involved in the recruitment of immune cells to sites of infection and inflammation through the production of cytokines, the activation of the complement cascade, the identification and removal of foreign substances by leukocytes, and the activation of the adaptive (cognate) immune system via antigen presentation.

For subgroup Y individuals, Table 5 depicts 574 genes having an exacerbation versus quiet expression differential with a false discovery rate of less than 0.05. The B-cell receptor (BCR) pathway was identified as a canonical pathway specific to subgroup Y, which includes genes CD72, CD19, CD79B, Syk, BLNK, Rac/Cdc42, MEKKs, and IKK. For subgroup Z individuals, the Toll-like receptor - Toll-IL-1 receptor domain-containing adaptor inducing interferon- β (TLR-TRIF)-induced intracellular signaling pathway was identified as a canonical pathway specific to subgroup Z genes.

The differential expression of one or more subgroup Y differentially expressed genes in a sample of an individual comprises a molecular profile of an asthma exacerbation that indicates that the asthma exacerbation involves cognate immunity. Cognate (adaptive) immunity is generally known in the art to involve the generation and/or elicitation of a specific B-cell (antibody) and T-cell (T-cell receptor) response to antigens and is triggered when a pathogen or other foreign agent evades the innate immune system and generates a threshold level of antigen. Activation of the cognate system integrates with the innate system through antigen presenting cells.

"Asthma exacerbation," "acute exacerbation of asthma" "exacerbation attack" and "asthma attack" are phrases that are used interchangeably. "Asthma quiet," "asthma quiet period," "quiet asthma period," and "quiet visits," are phrases that are used interchangeably and generally refer to asthma symptomless periods. In some cases, the air passages of individuals with asthma are inflamed during a quiet period.

The terms "molecular signature," "expression profile" and "gene expression profile" refer to two or more genes or gene products which represent a particular state of health of an individual. Alternatively, the molecular signature represents a collection of expression values for a plurality (e.g., at least two, but frequently about 10, about 100, about 1000, or more) of members of a library of genes or gene products. In some embodiments, the molecular signature represents the expression pattern for all of the nucleotide sequences in a library or array of nucleotide sequences or genes. Alternatively, the molecular signature represents the expression pattern for one or more subsets of a library of genes or gene

products. In some embodiments, the molecular signature indicates the asthma status of an individual, such as e.g. a quiet period or an exacerbation. In some embodiments, the molecular signature is a molecular signature of asthma exacerbation for an individual with asthma, which indicates the type of exacerbation. Types of exacerbation include e.g. exacerbation involving innate immunity, exacerbation involving cognate or adaptive immunity, exacerbation associated with an infection and exacerbation not associated with any infection.

Various aspects of the invention are described in further detail in the following subsections. The use of subsections is not meant to limit the invention. Each subsection may apply to any aspect of the invention.

Identification of Asthma Exacerbation Markers

As discussed earlier, expression level of markers of the present invention can be used as an indicator and/or predictor of asthma exacerbation. Detection and measurement of the relative amount of an asthma-associated gene, marker or gene product (polynucleotide or polypeptide) of the invention (generally referred to as "marker" or "biomarker") can be by any method known in the art.

Methodologies for peptide detection include protein extraction from a cell or tissue sample, followed by binding of an antibody specific for the target protein to the protein sample, and detection of the antibody. Antibodies are generally detected by the use of a labeled secondary antibody. The label can be a radioisotope, a fluorescent compound, an enzyme, an enzyme co-factor, or ligand. Such methods are well understood in the art.

Detection of specific polynucleotide molecules may be assessed by gel electrophoresis, column chromatography, or direct sequencing, quantitative PCR, RT-PCR, or nested PCR among many other techniques well known to those skilled in the art.

Detection of the presence or number of copies of all or part of a marker as defined by the invention may be performed using any method known in the art. It is convenient to assess the presence and/or quantity of a DNA or cDNA by Southern analysis, in which total DNA from a cell or tissue sample is extracted, is hybridized with a labeled probe (i.e., a complementary DNA molecule), and the probe is detected. The label group can be a radioisotope, a fluorescent compound, an enzyme, or an enzyme co-factor. Other useful methods of DNA detection and/or quantification include direct sequencing, gel electrophoresis, column chromatography, and quantitative PCR, as would be understood by one skilled in the art.

Methodologies for detection of a transcribed polynucleotide can include RNA extraction from a cell or tissue sample, followed by hybridization of a labeled probe (i.e., a

complementary polynucleotide molecule) specific for the target RNA to the extracted RNA and detection of the probe (e.g., Northern blotting).

Diagnosis, Prognosis, and Assessment of Asthma Exacerbation

The markers disclosed in the present invention can be employed in the prediction, diagnosis and/or prognosis of asthma exacerbation comprising the steps of (a) detecting an expression level of an asthma exacerbation marker in a patient; (b) comparing that expression level to a reference expression level of the same asthma exacerbation marker; (c) and diagnosing a patient has having asthma or an asthma exacerbation event, based upon the comparison made. This can be achieved by comparing the expression profile of one or more asthma exacerbation markers in a subject of interest to at least one reference expression profile of the asthma exacerbation markers. The reference expression profile(s) can include an average expression profile or a set of individual expression profiles each of which represents the gene expression of the asthma exacerbation markers in a particular asthma patient during a quiet period or in a disease-free individual.

In many embodiments, one or more asthma exacerbation markers, which are selected from any one or more of Tables 2-6 and 8-12 and SEQ ID NOs:1-77, can be used for asthma diagnosis or disease monitoring. In one embodiment, each asthma exacerbation marker has a p-value of less than 0.01, 0.005, 0.001, 0.0005, 0.0001, or less. In another embodiment, the asthma exacerbation marker comprises a gene having a log2 difference between asthma exacerbation and asthma quiet of $\geq |0.25|$ (absolute value of 0.25).

The asthma exacerbation markers of the present invention can be used alone, or in combination with other clinical tests, for asthma diagnosis, prognosis or monitoring. Conventional methods for detecting or diagnosing asthma include, but are not limited to, blood tests, chest X-ray, biopsies, skin tests, mucus tests, urine/excreta sample testing, physical exam, or any and all related clinical examinations known to the skilled artisan. Any of these methods, as well as any other conventional or non-conventional method, can be used, in addition to the methods of the present invention, to improve the accuracy of asthma diagnosis, prognosis or monitoring.

The expression profile of a patient of interest (which by definition comprises the level of at least one marker in a sample obtained from an individual) can be compared to one or more reference expression profiles. The reference expression profiles (which by definition comprise a reference level of the marker) can be determined concurrently with the expression profile of the patient of interest. The reference expression profiles can also be predetermined or prerecorded in electronic or other types of storage media.

The reference expression profiles can include average expression profiles, or individual profiles representing gene expression patterns in particular patients. In one embodiment, the reference expression profiles used for a prediction or diagnosis of asthma exacerbation include an average expression profile of the marker(s) in tissue samples, such as peripheral
5 blood samples, of healthy volunteers or individuals during an asthma quiet period. In one embodiment, the reference expression profiles include an average expression profile of the marker(s) in tissue samples, such as peripheral blood samples, of reference asthma patients who have known or determinable disease status. Any averaging method may be used, such as arithmetic means, harmonic means, average of absolute values, average of log-
10 transformed values, or weighted average. In one example, the reference asthma patients have the same disease assessment. In another example, the reference patients are healthy volunteers used in a diagnostic method. In another example, the reference asthma patients can be divided into at least two classes, each class of patients having a different respective disease assessment. The average expression profile in each class of patients constitutes a
15 separate reference expression profile, and the expression profile of the patient of interest is compared to each of these reference expression profiles.

Other types of reference expression profiles can also be used in the present invention. In yet another embodiment, the present invention uses a numerical threshold as a control level. The numerical threshold may comprise a ratio, including, but not limited to, the ratio of
20 the expression level of a marker in an asthma patient in relation to the expression level of the same marker in a healthy or asthma quiet individual; or the ratio between the expression levels of the marker in an asthma patient both before and after an exacerbation event. The numerical threshold may also be a ratio of marker expression levels between patients with differing disease assessments.

25 The expression profile of the patient of interest and the reference expression profile(s) can be constructed in any form. In one embodiment, the expression profiles comprise the expression level of each marker used in outcome prediction. The expression levels can be absolute, normalized, or relative levels. Suitable normalization procedures include, but are not limited to, those used in nucleic acid array gene expression analyses or those described
30 in Hill, et al., (Hill (2001) Genome Biol. 2:research0055.1-0055.13). In one example, the expression levels are normalized such that the mean is zero and the standard deviation is one. In another example, the expression levels are normalized based on internal or external controls, as appreciated by those skilled in the art. In still another example, the expression levels are normalized against one or more control transcripts with known abundances in
35 blood samples. In many cases, the expression profile of the patient of interest and the reference expression profile(s) are constructed using the same or comparable methodologies.

In another embodiment, each expression profile being compared comprises one or more ratios between the expression levels of different markers. An expression profile can also include other measures that are capable of representing gene expression patterns or protein levels.

5

Samples

The peripheral blood samples used in the present invention can be either whole blood samples, samples comprising enriched PBMCs, or serum. In one example, the peripheral blood samples used for preparing the reference expression profile(s) comprise enriched or purified PBMCs, and the peripheral blood sample used for preparing the expression profile
10 of the patient of interest is a whole blood sample. In another example, all of the peripheral blood samples employed in outcome prediction comprise enriched or purified PBMCs. In many cases, the peripheral blood samples are prepared from the patient of interest and reference patients using the same or comparable procedures.

Other types of blood samples can also be employed in the present invention, such as
15 serum, which contains protein biomarkers; and the gene or protein expression profiles in these blood samples are statistically significantly correlated with patient outcome.

Assays

Construction of the expression profiles typically involves detection of the expression level of each marker used in the prediction, diagnosis, prognosis or monitoring of asthma
20 exacerbation. Numerous methods are available for this purpose. For instance, the expression level of a gene can be determined by measuring the level of the RNA transcript(s) of the gene(s). Suitable methods include, but are not limited to, quantitative RT-PCR, Northern blot, in situ hybridization, slot-blotting, nuclease protection assay, and nucleic acid array (including bead array). The expression level of a gene can also be determined by
25 measuring the level of the polypeptide(s) encoded by the gene. Suitable methods include, but are not limited to, immunoassays (such as ELISA, RIA, FACS, or Western blot), 2-dimensional gel electrophoresis, mass spectrometry, or protein arrays.

In one aspect, the expression level of a marker is determined by measuring the RNA transcript level of the gene in a tissue sample, such as a peripheral blood sample. RNA can
30 be isolated from the peripheral blood or tissue sample using a variety of methods. Exemplary methods include guanidine isothiocyanate/acidic phenol method, the TRIZOL® Reagent (Invitrogen), or the Micro-FastTrack™ 2.0 or FastTrack™ 2.0 mRNA Isolation Kits (Invitrogen). The isolated RNA can be either total RNA or mRNA. The isolated RNA can be amplified to cDNA or cRNA before subsequent detection or quantitation. The amplification

can be either specific or non-specific. Suitable amplification methods include, but are not limited to, reverse transcriptase PCR (RT-PCR), isothermal amplification, ligase chain reaction, and Q-beta replicase.

In one embodiment, the amplification protocol employs reverse transcriptase. The isolated mRNA can be reverse transcribed into cDNA using a reverse transcriptase, and a primer consisting of oligo (dT) and a sequence encoding the phage T7 promoter. The cDNA thus produced is single-stranded. The second strand of the cDNA is synthesized using a DNA polymerase, combined with an RNase to break up the DNA/RNA hybrid. After synthesis of the double-stranded cDNA, T7 RNA polymerase is added, and cRNA is then transcribed from the second strand of the doubled-stranded cDNA. The amplified cDNA or cRNA can be detected or quantitated by hybridization to labeled probes. The cDNA or cRNA can also be labeled during the amplification process and then detected or quantitated.

In another embodiment, quantitative RT-PCR (such as TaqMan, ABI) is used for detecting or comparing the RNA transcript level of a marker of interest. Quantitative RT-PCR involves reverse transcription (RT) of RNA to cDNA followed by relative quantitative PCR (RT-PCR).

In PCR, the number of molecules of the amplified target DNA increases by a factor approaching two with every cycle of the reaction until some reagent becomes limiting. Thereafter, the rate of amplification becomes increasingly diminished until there is not an increase in the amplified target between cycles. If a graph is plotted on which the cycle number is on the X axis and the log of the concentration of the amplified target DNA is on the Y axis, a curved line of characteristic shape can be formed by connecting the plotted points. Beginning with the first cycle, the slope of the line is positive and constant. This is said to be the linear portion of the curve. After some reagent becomes limiting, the slope of the line begins to decrease and eventually becomes zero. At this point the concentration of the amplified target DNA becomes asymptotic to some fixed value. This is said to be the plateau portion of the curve.

The concentration of the target DNA in the linear portion of the PCR is proportional to the starting concentration of the target before the PCR is begun. By determining the concentration of the PCR products of the target DNA in PCR reactions that have completed the same number of cycles and are in their linear ranges, it is possible to determine the relative concentrations of the specific target sequence in the original DNA mixture. If the DNA mixtures are cDNAs synthesized from RNAs isolated from different tissues or cells, the relative abundances of the specific mRNA from which the target sequence was derived may be determined for the respective tissues or cells. This direct proportionality between the concentration of the PCR products and the relative mRNA abundances is true in the linear range portion of the PCR reaction.

The final concentration of the target DNA in the plateau portion of the curve is determined by the availability of reagents in the reaction mix and is independent of the original concentration of target DNA. Therefore, in one embodiment, the sampling and quantifying of the amplified PCR products are carried out when the PCR reactions are in the linear portion of their curves. In addition, relative concentrations of the amplifiable cDNAs can be normalized to some independent standard, which may be based on either internally existing RNA species or externally introduced RNA species. The abundance of a particular mRNA species may also be determined relative to the average abundance of all mRNA species in the sample.

In one embodiment, the PCR amplification utilizes internal PCR standards that are approximately as abundant as the target. This strategy is effective if the products of the PCR amplifications are sampled during their linear phases. If the products are sampled when the reactions are approaching the plateau phase, then the less abundant product may become relatively over-represented. Comparisons of relative abundances made for many different RNA samples, such as is the case when examining RNA samples for differential expression, may become distorted in such a way as to make differences in relative abundances of RNAs appear less than they actually are. This can be improved if the internal standard is much more abundant than the target. If the internal standard is more abundant than the target, then direct linear comparisons may be made between RNA samples.

A problem inherent in clinical samples is that they are of variable quantity or quality. This problem can be overcome if the RT-PCR is performed as a relative quantitative RT-PCR with an internal standard in which the internal standard is an amplifiable cDNA fragment that is larger than the target cDNA fragment and in which the abundance of the mRNA encoding the internal standard is roughly 5-100 fold higher than the mRNA encoding the target. This assay measures relative abundance, not absolute abundance of the respective mRNA species.

In another embodiment, the relative quantitative RT-PCR uses an external standard protocol. Under this protocol, the PCR products are sampled in the linear portion of their amplification curves. The number of PCR cycles that are optimal for sampling can be empirically determined for each target cDNA fragment. In addition, the reverse transcriptase products of each RNA population isolated from the various samples can be normalized for equal concentrations of amplifiable cDNAs. While empirical determination of the linear range of the amplification curve and normalization of cDNA preparations are tedious and time-consuming processes, the resulting RT-PCR assays may, in certain cases, be superior to those derived from a relative quantitative RT-PCR with an internal standard.

In yet another embodiment, nucleic acid arrays (including bead arrays) are used for detecting or comparing the expression profiles of a marker of interest. The nucleic acid arrays can be commercial oligonucleotide or cDNA arrays. They can also be custom arrays comprising concentrated probes for the markers of the present invention. In many
5 examples, at least 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, or more of the total probes on a custom array of the present invention are probes for asthma exacerbation markers. These probes can hybridize under stringent or nucleic acid array hybridization conditions to the RNA transcripts, or the complements thereof, of the corresponding markers.

10 "Nucleic acid array hybridization conditions" refer to the temperature and ionic conditions that are normally used in nucleic acid array hybridization. These conditions include 16-hour hybridization at 45°C., followed by at least three 10-minute washes at room temperature. The hybridization buffer comprises 100 mM MES, 1 M Na⁺, 20 mM EDTA, and 0.01% Tween 20. The pH of the hybridization buffer preferably is between 6.5 and 6.7. The wash buffer is
15 6X SSPET, which contains 0.9 M NaCl, 60 mM NaH₂PO₄, 6 mM EDTA, and 0.005% Triton X-100. Under more stringent nucleic acid array hybridization conditions, the wash buffer can contain 100 mM MES, 0.1 M Na⁺, and 0.01% Tween 20.

As used herein, "stringent conditions" are at least as stringent as, for example, conditions G-L shown in Table 7. "Highly stringent conditions" are at least as stringent as conditions A-
20 F shown in Table 7. Hybridization is carried out under the hybridization conditions (Hybridization Temperature and Buffer) for about four hours, followed by two 20-minute washes under the corresponding wash conditions (Wash Temp. and Buffer).

In one example, a nucleic acid array of the present invention includes at least 2, 5, 10, or more different probes. Each of these probes is capable of hybridizing under stringent or
25 nucleic acid array hybridization conditions to a different respective marker of the present invention. Multiple probes for the same marker can be used on the same nucleic acid array. The probe density on the array can be in any range.

The probes for a marker of the present invention can be a nucleic acid probe, such as, DNA, RNA, PNA (peptide nucleic acid), or a modified form thereof. The nucleotide residues
30 in each probe can be either naturally occurring residues (such as deoxyadenylate, deoxycytidylate, deoxyguanylate, deoxythymidylate, adenylate, cytidylate, guanylate, and uridylate), or synthetically produced analogs that are capable of forming desired base-pair relationships. Examples of these analogs include, but are not limited to, aza and deaza pyrimidine analogs, aza and deaza purine analogs, and other heterocyclic base analogs,
35 wherein one or more of the carbon and nitrogen atoms of the purine and pyrimidine rings are substituted by heteroatoms, such as oxygen, sulfur, selenium, and phosphorus. Similarly, the polynucleotide backbones of the probes can be either naturally occurring (such as

through 5' to 3' linkage), or modified. For instance, the nucleotide units can be connected via non-typical linkage, such as 5' to 2' linkage, so long as the linkage does not interfere with hybridization. For another instance, peptide nucleic acids, in which the constitute bases are joined by peptide bonds rather than phosphodiester linkages, can be used.

5 The probes for the markers can be stably attached to discrete regions on a nucleic acid array. By "stably attached," it means that a probe maintains its position relative to the attached discrete region during hybridization and signal detection. The position of each discrete region on the nucleic acid array can be either known or determinable. All of the methods known in the art can be used to make the nucleic acid arrays of the present
10 invention. Hybridization probes or amplification primers for the markers of the present invention can be prepared by using any method known in the art.

In another embodiment, nuclease protection assays are used to quantitate RNA transcript levels in peripheral blood samples. There are many different versions of nuclease protection assays. The common characteristic of these nuclease protection assays is that
15 they involve hybridization of an antisense nucleic acid with the RNA to be quantified. The resulting hybrid double-stranded molecule is then digested with a nuclease that digests single-stranded nucleic acids more efficiently than double-stranded molecules. The amount of antisense nucleic acid that survives digestion is a measure of the amount of the target RNA species to be quantified. Examples of suitable nuclease protection assays include the
20 RNase protection assay provided by Ambion, Inc. (Austin, Texas).

In one embodiment, the probes/primers for a marker significantly diverge from the sequences of other markers. This can be achieved by checking potential probe/primer sequences against a human genome sequence database, such as the Entrez database at the U.S. National Center for Biotechnology Information ("NCBI"). One algorithm suitable for
25 this purpose is the BLAST algorithm. This algorithm involves first identifying high scoring sequence pairs (HSPs) by identifying short words of length W in the query sequence, which either match or satisfy some positive-valued threshold score T when aligned with a word of the same length in a database sequence. T is referred to as the neighborhood word score threshold. The initial neighborhood word hits act as seeds for initiating searches to find
30 longer HSPs containing them. The word hits are then extended in both directions along each sequence to increase the cumulative alignment score. Cumulative scores are calculated using, for nucleotide sequences, the parameters M (reward score for a pair of matching residues; always >0) and N (penalty score for mismatching residues; always <0). The BLAST algorithm parameters W, T, and X determine the sensitivity and speed of the
35 alignment. These parameters can be adjusted for different purposes, as appreciated by those skilled in the art.

In another embodiment, the probes for markers can be polypeptide in nature, such as, antibody probes. The expression levels of the markers of the present invention are thus determined by measuring the levels of polypeptides encoded by the markers. Methods suitable for this purpose include, but are not limited to, immunoassays such as ELISA, RIA, 5 FACS, dot blot, Western Blot, immunohistochemistry, and antibody-based radio-imaging. In addition, high-throughput protein sequencing, 2-dimensional SDS-polyacrylamide gel electrophoresis, mass spectrometry, or protein arrays can be used.

In one embodiment, ELISAs are used for detecting the levels of the target proteins. In an exemplifying ELISA, antibodies capable of binding to the target proteins are immobilized 10 onto selected surfaces exhibiting protein affinity, such as wells in a polystyrene or polyvinylchloride microtiter plate. Samples to be tested are then added to the wells. After binding and washing to remove non-specifically bound immunocomplexes, the bound antigen(s) can be detected. Detection can be achieved by the addition of a second antibody which is specific for the target proteins and is linked to a detectable label. Detection can 15 also be achieved by the addition of a second antibody, followed by the addition of a third antibody that has binding affinity for the second antibody, with the third antibody being linked to a detectable label. Before being added to the microtiter plate, cells in the samples can be lysed or extracted to separate the target proteins from potentially interfering substances.

In another exemplifying ELISA, the samples suspected of containing the target proteins 20 are immobilized onto the well surface and then contacted with the antibodies. After binding and washing to remove non-specifically bound immunocomplexes, the bound antigen is detected. Where the initial antibodies are linked to a detectable label, the immunocomplexes can be detected directly. The immunocomplexes can also be detected using a second antibody that has binding affinity for the first antibody, with the second 25 antibody being linked to a detectable label.

Another exemplary ELISA involves the use of antibody competition in the detection. In this ELISA, the target proteins are immobilized on the well surface. The labeled antibodies are added to the well, allowed to bind to the target proteins, and detected by means of their labels. The amount of the target proteins in an unknown sample is then determined by 30 mixing the sample with the labeled antibodies before or during incubation with coated wells. The presence of the target proteins in the unknown sample acts to reduce the amount of antibody available for binding to the well and thus reduces the ultimate signal.

Different ELISA formats can have certain features in common, such as coating, incubating or binding, washing to remove non-specifically bound species, and detecting the 35 bound immunocomplexes. For instance, in coating a plate with either antigen or antibody, the wells of the plate can be incubated with a solution of the antigen or antibody, either overnight or for a specified period of hours. The wells of the plate are then washed to

remove incompletely adsorbed material. Any remaining available surfaces of the wells are then "coated" with a nonspecific protein that is antigenically neutral with regard to the test samples. Examples of these nonspecific proteins include bovine serum albumin (BSA), casein and solutions of milk powder. The coating allows for blocking of nonspecific
5 adsorption sites on the immobilizing surface and thus reduces the background caused by nonspecific binding of antisera onto the surface.

In ELISAs, a secondary or tertiary detection means can be used. After binding of a protein or antibody to the well, coating with a non-reactive material to reduce background, and washing to remove unbound material, the immobilizing surface is contacted with the
10 control or clinical or biological sample to be tested under conditions effective to allow immunocomplex (antigen/antibody) formation. These conditions may include, for example, diluting the antigens and antibodies with solutions such as BSA, bovine gamma globulin (BGG) and phosphate buffered saline (PBS)/Tween and incubating the antibodies and antigens at room temperature for about 1 to 4 hours or at 40 C overnight. Detection of the
15 immunocomplex is facilitated by using a labeled secondary binding ligand or antibody, or a secondary binding ligand or antibody in conjunction with a labeled tertiary antibody or third binding ligand.

Following all incubation steps in an ELISA, the contacted surface can be washed so as to remove non-complexed material. For instance, the surface may be washed with a
20 solution such as PBS/Tween, or borate buffer. Following the formation of specific immunocomplexes between the test sample and the originally bound material, and subsequent washing, the occurrence of the amount of immunocomplexes can be determined.

To provide a detecting means, the second or third antibody can have an associated label
25 to allow detection. In one embodiment, the label is an enzyme that generates color development upon incubating with an appropriate chromogenic substrate. Thus, for example, one may contact and incubate the first or second immunocomplex with a urease, glucose oxidase, alkaline phosphatase or hydrogen peroxidase-conjugated antibody for a period of time and under conditions that favor the development of further immunocomplex
30 formation (e.g., incubation for 2 hours at room temperature in a PBS-containing solution such as PBS-Tween).

After incubation with the labeled antibody, and subsequent washing to remove unbound material, the amount of label can be quantified, e.g., by incubation with a chromogenic substrate such as urea and bromocresol purple or 2,2'-azido-di-(3-ethyl)-benzthiazoline-6-
35 sulfonic acid (ABTS) and H₂O₂, in the case of peroxidase as the enzyme label. Quantitation can be achieved by measuring the degree of color generation, e.g., using a spectrophotometer.

Another method suitable for detecting polypeptide levels is RIA (radioimmunoassay). An exemplary RIA is based on the competition between radiolabeled-polypeptides and unlabeled polypeptides for binding to a limited quantity of antibodies. Suitable radiolabels include, but are not limited to, ^{125}I . In one embodiment, a fixed concentration of ^{125}I -labeled polypeptide is incubated with a series of dilution of an antibody specific to the polypeptide. When the unlabeled polypeptide is added to the system, the amount of the ^{125}I -polypeptide that binds to the antibody is decreased. A standard curve can therefore be constructed to represent the amount of antibody-bound ^{125}I -polypeptide as a function of the concentration of the unlabeled polypeptide. From this standard curve, the concentration of the polypeptide in unknown samples can be determined. Protocols for conducting RIA are well known in the art.

Suitable antibodies for the present invention include, but are not limited to, polyclonal antibodies, monoclonal antibodies, chimeric antibodies, humanized antibodies, single chain antibodies, Fab fragments, or fragments produced by a Fab expression library. Neutralizing antibodies (e.g., such as those which inhibit dimer formation) can also be used. Methods for preparing these antibodies are well known in the art. In one embodiment, the antibodies of the present invention can bind to the corresponding marker gene products or other desired antigens with binding affinities of at least 10^4 M^{-1} , 10^5 M^{-1} , 10^6 M^{-1} , 10^7 M^{-1} , or more.

The antibodies of the present invention can be labeled with one or more detectable moieties to allow for detection of antibody-antigen complexes. The detectable moieties can include compositions detectable by spectroscopic, enzymatic, photochemical, biochemical, bioelectronic, immunochemical, electrical, optical or chemical means. The detectable moieties include, but are not limited to, radioisotopes, chemiluminescent compounds, labeled binding proteins, heavy metal atoms, spectroscopic markers such as fluorescent markers and dyes, magnetic labels, linked enzymes, mass spectrometry tags, spin labels, electron transfer donors and acceptors, and the like.

The antibodies of the present invention can be used as probes to construct protein arrays for the detection of expression profiles of the markers. Methods for making protein arrays or biochips are well known in the art. In many embodiments, a substantial portion of probes on a protein array of the present invention are antibodies specific for the marker products. For instance, at least 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, or more probes on the protein array can be antibodies specific for the marker gene products.

In yet another aspect, the expression levels of the markers are determined by measuring the biological functions or activities of these genes. Where a biological function or activity of a gene is known, suitable in vitro or in vivo assays can be developed to evaluate the function or activity. These assays can be subsequently used to assess the level of expression of the marker.

After the expression level of each marker is determined, numerous approaches can be employed to compare expression profiles. Comparison of the expression profile of a patient of interest to the reference expression profile(s) can be conducted manually or electronically. In one example, comparison is carried out by comparing each component in one expression profile to the corresponding component in a reference expression profile. The component can be the expression level of a marker, a ratio between the expression levels of two markers, or another measure capable of representing gene expression patterns. The expression level of a gene can have an absolute or a normalized or relative value. The difference between two corresponding components can be assessed by fold changes, absolute differences, or other suitable means.

Comparison of the expression profile of a patient of interest to the reference expression profile(s) can also be conducted using pattern recognition or comparison programs, such as the k-nearest-neighbors algorithm as described in Armstrong, et al., (Armstrong (2002) Nature Genetics 30:41-47), or the weighted voting algorithm as described below. In addition, the serial analysis of gene expression (SAGE) technology, the GEMTOOLS gene expression analysis program (Incyte Pharmaceuticals), the GeneCalling and Quantitative Expression Analysis technology (Curagen), and other suitable methods, programs or systems can be used to compare expression profiles.

Multiple markers can be used in the comparison of expression profiles. For instance, 2, 4, 6, 8, 10, 12, 14, or more markers can be used. In addition, the marker(s) used in the comparison can be selected to have relatively small p-values (e.g., two-sided p-values). In many examples, the p-values indicate the statistical significance of the difference between gene expression levels in different classes of patients. In many other examples, the p-values suggest the statistical significance of the correlation between gene expression patterns and clinical outcome. In one embodiment, the markers used in the comparison have p-values of no greater than 0.05, 0.01, 0.001, 0.0005, 0.0001, or less. Markers with p-values of greater than 0.05 can also be used. These genes may be identified, for instance, by using a relatively small number of blood samples.

Similarity or difference between the expression profile of a patient of interest and a reference expression profile is indicative of the class membership of the patient of interest. Similarity or difference can be determined by any suitable means. The comparison can be qualitative, quantitative, or both.

In one example, a component in a reference profile is a mean value, and the corresponding component in the expression profile of the patient of interest falls within the standard deviation of the mean value. In such a case, the expression profile of the patient of interest may be considered similar to the reference profile with respect to that particular

component. Other criteria, such as a multiple or fraction of the standard deviation or a certain degree of percentage increase or decrease, can be used to measure similarity.

In another example, at least 50% (e.g., at least 60%, 70%, 80%, 90%, or more) of the components in the expression profile of the patient of interest are considered similar to the corresponding components in a reference profile. Under these circumstances, the expression profile of the patient of interest may be considered similar to the reference profile. Different components in the expression profile may have different weights for the comparison. In some cases, lower percentage thresholds (e.g., less than 50% of the total components) are used to determine similarity.

The marker(s) and the similarity criteria can be selected such that the accuracy of the diagnostic determination or the outcome prediction (the ratio of correct calls over the total of correct and incorrect calls) is relatively high. For instance, the accuracy of the determination or prediction can be at least 50%, 60%, 70%, 80%, 90%, or more.

Screening Methods

The invention also provides methods (also referred to herein as "screening assays") for identifying agents capable of modulating marker expression ("modulators"), i.e., candidate or test compounds or agents comprising therapeutic moieties (e.g., peptides, peptidomimetics, peptoids, polynucleotides, small molecules or other drugs) which (a) bind to a marker gene product or (b) have a modulatory (e.g., upregulation or downregulation; stimulatory or inhibitory; potentiation/induction or suppression) effect on the activity of a marker gene product or, more specifically, (c) have a modulatory effect on the interactions of the marker gene product with one or more of its natural substrates, or (d) have a modulatory effect on the expression of the marker. Such assays typically comprise a reaction between the marker gene product and one or more assay components. The other components may be either the test compound itself, or a combination of test compound and a binding partner of the marker gene product.

The test compounds of the present invention are generally either small molecules or biomolecules. Small molecules include, but are not limited to, inorganic molecules and small organic molecules. Biomolecules include, but are not limited to, naturally-occurring and synthetic compounds that have a bioactivity in mammals, such as polypeptides, polysaccharides, and polynucleotides. In one embodiment, the test compound is a small molecule. In another embodiment, the test compound is a biomolecule. One skilled in the art will appreciate that the nature of the test compound may vary depending on the nature of the protein encoded by the marker of the present invention.

The test compounds of the present invention may be obtained from any available source, including systematic libraries of natural and/or synthetic compounds. Test compounds may also be obtained by any of the numerous approaches in combinatorial library methods known in the art, including: biological libraries; peptoid libraries (libraries of molecules having the functionalities of peptides, but with a novel, non-peptide backbone which are resistant to enzymatic degradation but which nevertheless remain bioactive; see, e.g., Zuckerman et al. (Zuckerman (1994) J. Med. Chem. 37:2678-85); spatially addressable parallel solid phase or solution phase libraries; synthetic library methods requiring deconvolution; the "one-bead, one-compound" library method; and synthetic library methods using affinity chromatography selection. The biological library and peptoid library approaches are applicable to peptide, non-peptide oligomers or small molecule libraries of compound (Lam (1997) Anticancer Drug Des. 12:145).

The invention provides methods of screening test compounds for inhibitors of the marker gene products of the present invention. The method of screening comprises obtaining samples from subjects diagnosed with or suspected of having asthma, contacting each separate aliquot of the samples with one or more of a plurality of test compounds, and comparing expression of one or more marker gene products in each of the aliquots to determine whether any of the test compounds provides a substantially decreased level of expression or activity of a marker gene product relative to samples with other test compounds or relative to an untreated sample or control sample. In addition, methods of screening may be devised by combining a test compound with a protein and thereby determining the effect of the test compound on the protein.

In addition, the invention is further directed to a method of screening for test compounds capable of modulating with the binding of a marker gene product and a binding partner, by combining the test compound, the marker gene product, and binding partner together and determining whether binding of the binding partner and the marker gene product occurs. The test compound may be either a small molecule or a biomolecule.

Modulators of marker gene product expression, activity or binding ability are useful as therapeutic compositions of the invention. Such modulators (e.g., antagonists or agonists) may be formulated as pharmaceutical compositions, as described herein below. Such modulators may also be used in the methods of the invention, for example, to diagnose, treat, or prognose asthma.

The invention provides methods of conducting high-throughput screening for test compounds capable of inhibiting activity or expression of a marker gene product of the present invention. In one embodiment, the method of high-throughput screening involves combining test compounds and the marker gene product and detecting the effect of the test compound on the marker gene product.

A variety of high-throughput functional assays well-known in the art may be used in combination to screen and/or study the reactivity of different types of activating test compounds. Since the coupling system is often difficult to predict, a number of assays may need to be configured to detect a wide range of coupling mechanisms. A variety of
5 fluorescence-based techniques is well-known in the art and is capable of high-throughput and ultra high throughput screening for activity, including but not limited to BRET™ (bioluminescence resonance energy transfer) or FRET™ (fluorescence resonance energy transfer) (both by Packard Instrument Co., Meriden, Conn.). The ability to screen a large volume and a variety of test compounds with great sensitivity permits for analysis of the
10 therapeutic targets of the invention to further provide potential inhibitors of asthma. The BIACORE™ system (a plasmon resonance system) may also be manipulated to detect binding of test compounds with individual components of the therapeutic target, to detect binding to either the encoded protein or to the ligand.

Therefore, the invention provides for high-throughput screening of test compounds for
15 the ability to inhibit activity of a protein encoded by the marker gene products listed in Tables 2, 3, 4, 5, 6, 8, 9, 10, 11, 12 and/or SEQ ID NOs:1-77, by combining the test compounds and the protein in high-throughput assays such as BIACORE™, or in fluorescence-based assays such as FRET or BRET™. In addition, high-throughput assays may be utilized to identify specific factors which bind to the encoded proteins, or alternatively, to identify test
20 compounds which prevent binding of the receptor to the binding partner. In the case of orphan receptors, the binding partner may be the natural ligand for the receptor. Moreover, the high-throughput screening assays may be modified to determine whether test compounds can bind to either the encoded protein or to the binding partner (e.g., substrate or ligand) which binds to the protein.

25 In one embodiment, the high-throughput screening assay detects the ability of a plurality of test compounds to bind to a marker gene product selected from the group consisting of the markers listed in Tables 2, 3, 4, 5, 6, 8, 9, 10, 11, 12 and/or SEQ ID NOs:1-77. In another specific embodiment, the high-throughput screening assay detects the ability of a plurality of a test compound to inhibit a binding partner (such as a ligand) to bind to a marker gene
30 product selected from the group consisting of the markers listed in Tables 2, 3, 4, 5, 6, 8, 9, 10, 11, 12 and/or SEQ ID NOs:1-77. In yet another specific embodiment, the high-throughput screening assay detects the ability of a plurality of a test compounds to modulate signaling through a marker gene product selected from the group consisting of the markers listed in Tables 2, 3, 4, 5, 6, 8, 9, 10, 11, 12 and/or SEQ ID NOs:1-77.

Nucleic Acid Arrays

Polynucleotide probes that correspond to the genes/markers of the present invention can be used to make nucleic acid arrays. A typical nucleic acid array includes at least one substrate support. The substrate support includes a plurality of discrete regions or
5 addresses. The location of each discrete region is either known or determinable. The discrete regions can be organized in various forms or patterns. For instance, the discrete regions can be arranged as an array of regularly spaced areas on the surface of the substrate. Other patterns, such as linear, concentric or spiral patterns, can be used. In one embodiment, a nucleic acid array of the present invention is a bead array which includes a
10 plurality of beads stably associated with the polynucleotide probes of the present invention.

Polynucleotide probes can be stably attached to their respective discrete regions through covalent and/or non-covalent interactions. By "stably attached" or "stably associated," it means that during nucleic acid array hybridization the polynucleotide probe maintains its position relative to the discrete region to which the probe is attached. Any suitable method
15 can be used to attach polynucleotide probes to a nucleic acid array substrate. In one embodiment, the attachment is achieved by first depositing the polynucleotide probes to their respective discrete regions and then exposing the surface to a solution of a cross-linking agent, such as glutaraldehyde, borohydride, or other bifunctional agents. In another embodiment, the polynucleotide probes are covalently bound to the substrate via an
20 alkylamino-linker group or by coating the glass slides with polyethylenimine followed by activation with cyanuric chloride for coupling the polynucleotides. In yet another embodiment, the polynucleotide probes are covalently attached to a nucleic acid array through polymer linkers. The polymer linkers may improve the accessibility of the probes to their purported targets.

25 In addition, the polynucleotide probes can be stably attached to a nucleic acid array substrate through non-covalent interactions. In one embodiment, the polynucleotide probes are attached to the substrate through electrostatic interactions between positively charged surface groups and the negatively charged probes. In another embodiment, the substrate is a glass slide having a coating of a polycationic polymer on its surface, such as a cationic
30 polypeptide. The probes are bound to these polycationic polymers. In yet another embodiment, the methods described in U.S. Pat. No. 6,440,723, which is incorporated herein by reference, are used to attach the probes to the nucleic acid array substrate(s).

Various materials can be used to make the substrate support. Suitable materials include, but are not limited to, glasses, silica, ceramics, nylons, quartz wafers, gels, metals, and
35 papers. The substrates can be flexible or rigid. In one embodiment, they are in the form of a

tape that is wound up on a reel or cassette. Two or more substrate supports can be used in the same nucleic acid array.

The surfaces of the substrate support can be smooth and substantially planar. The surfaces of the substrate can also have a variety of configurations, such as raised or depressed regions, trenches, v-grooves, mesa structures, and other irregularities. The surfaces of the substrate can be coated with one or more modification layers. Suitable modification layers include inorganic and organic layers, such as metals, metal oxides, polymers, or small organic molecules. In one embodiment, the surface(s) of the substrate is chemically treated to include groups such as hydroxyl, carboxyl, amine, aldehyde, or sulfhydryl groups.

The discrete regions on the substrate can be of any size, shape and density. For instance, they can be squares, ellipsoids, rectangles, triangles, circles, other regular or irregular geometric shapes, or any portion or combination thereof. In one embodiment, each of the discrete regions has a surface area of less than 10^{-1} cm², such as less than 10^{-2} , 10^{-3} , 10^{-4} , 10^{-5} , 10^{-6} , or 10^{-7} cm². In another embodiment, the spacing between each discrete region and its closest neighbor, measured from center-to-center, is in the range of from about 10 to about 400 μm. The density of the discrete regions may range, for example, between 50 and 50,000 regions/cm².

All of the methods known in the art can be used to make the nucleic acid arrays of the present invention. For instance, the probes can be synthesized in a step-by-step manner on the substrate, or can be attached to the substrate in pre-synthesized forms. Algorithms for reducing the number of synthesis cycles can be used. In one embodiment, a nucleic acid array of the present invention is synthesized in a combinational fashion by delivering monomers to the discrete regions through mechanically constrained flowpaths. In another embodiment, a nucleic acid array of the present invention is synthesized by spotting monomer reagents onto a substrate support using an ink jet printer. In yet another embodiment, polynucleotide probes are immobilized on a nucleic acid array of the present invention by using photolithography techniques.

The nucleic acid arrays of the present invention can also be bead arrays which comprise a plurality of beads. Polynucleotide probes can be stably attached to each bead using any of the above-described methods.

In one embodiment, a substantial portion of all polynucleotide probes on a nucleic acid array of the present invention can hybridize under stringent or nucleic acid array hybridization conditions (Table 7) to genes that are differentially expressed in samples from individuals having asthma exacerbation versus an asthma quiet period. In some embodiments, at least 5%, 10%, 15%, 20%, 25%, 35%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, 99% or more of all polynucleotide probes on the nucleic acid

array can hybridize to asthma exacerbation differentially expressed genes. The probes for these genes can be concentrated on one substrate support. They can also be attached to two or more substrate supports, such as in the bead arrays.

Any number of polynucleotide probes can be included in a nucleic acid array of the present invention. For instance, the nucleic acid array can include at least 2, 5, 10, 20, 30, 40, 50, 100, 200, 300, 400, 500, 1,000 or more different probes, and each probe can hybridize under stringent or nucleic acid array hybridization conditions to a different respective gene selected from asthma exacerbation genes. In one embodiment, a nucleic acid array of the present invention includes a first set of probes which are capable of hybridizing under stringent or nucleic acid array hybridization conditions to different respective asthma exacerbation genes. In yet another embodiment, a nucleic acid array of the present invention includes at least 2, 5, 10, 20, 30, 40, 50, 100, 200, 300, 400, 500, 1,000, 2,000, 3,000, 4,000, 5,000, or more different probes, and each probe can hybridize under stringent or nucleic acid array hybridization conditions to a different respective target sequence selected from any one or more of Tables 2-6 and 8-12, and SEQ ID NOs:1-77, or the complement thereof.

Multiple probes can be included in the nucleic acid arrays of the present invention for detecting the same target sequence. For instance, at least 2, 5, 10, 15, 20, 25, 30 or more different probes can be used for detecting the same target sequence selected from any one or more of Tables 2-6 and 8-12, and SEQ ID NOs:1-77. In one embodiment, a nucleic acid array of the present invention includes at least 30, 40, 50, or 60 different probes for each target sequence of interest. In another embodiment, a nucleic acid array of the present invention includes 25-39 probes for each target sequence of interest.

Each probe can be attached to a different respective discrete region on a nucleic acid array. Alternatively, two or more different probes can be attached to the same discrete region. The concentration of one probe with respect to the other probe or probes in the same region may vary according to the objectives and requirements of the particular experiment. In one embodiment, different probes in the same region are present in approximately equimolar ratio.

In some embodiments, probes for different tiling or target sequences are attached to different discrete regions on a nucleic acid array. In some applications, probes for different tiling or target sequences are attached to the same discrete region.

The length of each probe on a nucleic acid array of the present invention can be selected to achieve the desirable hybridization effects. For instance, each probe can include or consist of 15, 20, 25, 30, 35, 40, 45, 50, 60, 70, 80, 90, 100 or more consecutive nucleotides. In one embodiment, each probe consists of 25 consecutive nucleotides.

The nucleic acid arrays of the present invention can also include control probes which can hybridize under stringent or nucleic acid array hybridization conditions to respective control sequences, or the complements thereof.

Kits for prognosis, diagnosis, or selection of treatment of asthma

5 In addition, the present invention features kits useful for the diagnosis or selection of treatment of asthma. Each kit includes or consists essentially of at least one probe for an asthma exacerbation marker. Reagents or buffers that facilitate the use of the kit can also be included. Any type of probe can be used in the present invention, such as hybridization probes, amplification primers, antibodies, or any and all other probes commonly used and
10 known to the skilled artisan. In one embodiment, the asthma exacerbation markers are selected from Table 2, Table 3, Table 4, Table 5, Table 6, Table 8, Table 9, Table 10, Table 11, Table 12 and/or SEQ ID NOs:1-77.

In one embodiment, a kit of the present invention includes or consists essentially of at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or more polynucleotide probes or primers. Each
15 probe/primer can hybridize under stringent conditions or nucleic acid array hybridization conditions to a different respective asthma exacerbation marker. As used herein, a polynucleotide can hybridize to a gene if the polynucleotide can hybridize to an RNA transcript, or complement thereof, of the gene. In another embodiment, a kit of the present invention includes one or more antibodies, each of which is capable of binding to a
20 polypeptide encoded by a different respective asthma prognostic or disease gene/marker.

In one example, a kit of the present invention includes or consists essentially of probes (e.g., hybridization or PCR amplification probes or antibodies) for at least 1, 2, 3, 4, 5, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, or more genes selected from Tables 2, 3, 4, 5, 6, 8, 9, 10, 11, 12 and/or SEQ ID NOs:1-77. In another embodiment, the kit can contain
25 nucleic acid probes and antibodies to 1, 2, 3, 4, 5, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, or more genes selected from Tables 2, 3, 4, 5, 6, 8, 9, 10, 11, 12 and/or SEQ ID NOs:1-77.

The probes employed in the present invention can be either labeled or unlabeled. Labeled probes can be detectable by spectroscopic, photochemical, biochemical,
30 bioelectronic, immunochemical, electrical, optical, chemical, or other suitable means. Exemplary labeling moieties for a probe include radioisotopes, chemiluminescent compounds, labeled binding proteins, heavy metal atoms, spectroscopic markers such as fluorescent markers and dyes, magnetic labels, linked enzymes, mass spectrometry tags, spin labels, electron transfer donors and acceptors, and the like.

The kits of the present invention can also have containers containing buffer(s) or reporter means. In addition, the kits can include reagents for conducting positive or negative controls. In one embodiment, the probes employed in the present invention are stably attached to one or more substrate supports. Nucleic acid hybridization or immunoassays
5 can be directly carried out on the substrate support(s). Suitable substrate supports for this purpose include, but are not limited to, glasses, silica, ceramics, nylons, quartz wafers, gels, metals, papers, beads, tubes, fibers, films, membranes, column matrices, or microtiter plate wells. The kits of the present invention may also contain one or more controls, each representing a reference expression level of a marker detectable by one or more probes
10 contained in the kits.

It should be understood that the above-described embodiments and the following examples are given by way of illustration, not limitation. Various changes and modifications within the scope of the present invention will become apparent to those skilled in the art from the present description.

EXAMPLE 1: HUMAN SUBJECTS AND STUDY DESIGN

Adult subjects age 18 years or older with confirmed diagnosis of mild, moderate or severe persistent asthma were enrolled in a prospective 12-month non-interventional study of gene expression associated with asthma. Enrollment was stratified by severity of asthma as defined by NIH 1997 guidelines (NIH Publication No. 07-4051, originally printed July
20 1997).

A prospective, multi-center, non-interventional study, which included subjects having asthma, was conducted in five countries (Australia, Iceland, Ireland, U.K., and USA). Three types of study visits were conducted: (a) exacerbation visits, defined as taking place during exacerbation attacks and within 14 days of attack onset; (b) follow-up visits, defined as
25 taking place within 14 days after cessation of exacerbation attack; and (c) quiet visits, defined as taking place during stable disease at approximately 3 month intervals.

Blood samples were collected for gene expression analyses from each subject at each visit. Samples were collected into Vacutainer™ cell preparation tubes (CPT, Becton Dickinson). Samples were shipped overnight and cell differential counts taken using a Pentra
30 5™ (Horiba ABX). Peripheral blood mononuclear cells ("PBMCs") were purified according to manufacturer's instructions. Isolated PBMC pellets were stored at -80°C pending RNA purification. RLT lysis buffer (with 0.1% β -mercaptoethanol; Qiagen) was added to the frozen pellets. RNA was isolated from the lysate using RNeasy™ Mini Kit (Qiagen Catalog #74104) and DNase treated (Qiagen RNase-free DNase Kit Catalog #79254). The DNase
35 treated RNA preparation was further purified using a Phase Lock Gel™ column (Brinkman).

RNA quality was assessed as acceptable by Agilent Bioanalyzer™ gel (Model 2100), and quantified using SpectraMax™ (Molecular Devices).

Exacerbation Visit Samples: From the total of 357 enrolled subjects, at least one evaluable exacerbation visit sample was collected from each of 118 (59 severe, 51 moderate, and 8 mild) subjects. A total of 166 exacerbation visit samples were collected from these 118 subjects. Of these, 25% were collected on the day of exacerbation attack onset, 16% one day post onset, 18% two days post onset, 37% between 3 and 9 days post onset, and the remaining 4% between 10 and 14 days post-onset. 161 of the exacerbation samples were collected while the subjects were experiencing one or more of the following symptoms: wheezing, chest tightness, and/or shortness of breath, (with concomitant symptom of cough reported for 48% of samples). For the other 5 exacerbation samples, for which neither wheezing, chest tightness nor shortness of breath were reported, cough attributed by the physician to an exacerbation attack was noted. Symptoms of upper respiratory infections associated with exacerbation attack were reported for 23% of 166 exacerbation visit samples.

Follow-up Visit Samples: A total of 125 evaluable follow-up samples from 102 subjects were collected from the 118 exacerbation visit subjects.

Quiet Visit Samples: A total of 393 evaluable quiet visit samples were collected from the 118 subjects used in the comparison of quiet and exacerbation visits. A total of 345 evaluable quiet visit samples were collected from the 102 subjects used in analyses relating to follow-up visits.

EXAMPLE 2: DETERMINATION OF GENE EXPRESSION LEVELS

Gene expression levels in samples were determined using the U133A Affymetrix GENECHIP Array®. Quality control acceptance criteria are shown in Table 1. Samples that did not pass these quality control criteria were re-run, and samples that failed twice were excluded from analyses. A sample was considered evaluable if (a) GENECHIP quality control acceptance criteria were met, and (b) at least one exacerbation visit sample and at least one quiet visit sample was available from the same subject. Labeled target for oligonucleotide arrays were prepared using 2 µg of total RNA according to the Affymetrix protocol. Biotinylated cRNA was hybridized to the HG-U133A Affymetrix GENECHIP Array®. Raw intensity values were processed using Affymetrix MAS 5.0 software, which calculated signal expression levels and present/absent calls for each probe set.

Of the 22,283 probe sets present on the U133A array, a subset of 9,696 probe sets, which met the following two criteria, were analyzed: (a) those probe sets detected as being

present in at least 10% of the samples; and (b) those probe sets having a signal of at least 50 in at least 10% of the samples.

The clinical and gene expression databases were merged using SAS version 9.1. Correct association of GENECHIP data with sample donor was verified by determining that gender specific expression patterns correctly reflected the donor's gender, and by a consistent expression pattern of HLA marker genes in samples collected at different times from the same donor.

Analysis of covariance (ANCOVA) methods were used to adjust for covariates when testing for differences in expression levels between visit types. The ANCOVA models used log₂-transformed MAS 5.0 signal as the dependent variable and included terms for visit type, asthma severity defined by NIH guidelines, sex, age (18-39, 40-59, or 60-83), race, sample processing lab, maximum corticosteroid exposure (a 4-level variable reflecting corticosteroid exposure at time of visit, with systemic > inhaled > intranasal > no corticosteroid exposure), an indicator for use of leukotriene antagonist at time of visit, bactin-GAPDH ratio (an indicator of RNA quality), and monocyte/lymphocyte ratio. The visit type factor was limited to quiet visits and exacerbation visits in some analyses, while in others it included follow-up visits. Some analyses included an additional 3-level factor for exacerbation subgroup. In some analyses, pairwise contrasts were run between specific levels of factors with more than two levels. In such cases, the contrasts were performed using two-sided t-tests, with the denominator of the t-statistics derived from the ANCOVA error term. Separate ANCOVAs were run for each probe set. To adjust for the multiplicity of testing, false discovery rates were calculated across all probe sets, separately for each term in the ANCOVA model or pairwise contrast. All ANCOVAs and false discovery rate ("FDR"; Benjamini and Hochberg, *J. of the Royal Statistical Society, Series B*, 57:289-300 1995) adjustments for multiplicity of testing calculations were run using SAS version 9.1.

Complete linkage hierarchical analysis (SPOTFIRE version 8.1) was used to identify exacerbation visit samples with similar exacerbation associated patterns of gene expression. The difference between the log₂ expression level during each individual exacerbation visit and the mean log₂ expression level of quiet visits for the same subject was calculated for each of the 166 exacerbation visits for each probe set with an association with exacerbation $P < 0.05$. These log ratios were ordered by spectral bi-clustering analysis to organize the expression profiles of each exacerbation visit according to their level of similarity to each other. Based on the heterogeneity observed, iterative K-means clustering was used to assess the evidence for distinct visit subgroups (see, e.g., Hartigan and Wong, *Applied Statistics* 1979, 28:100-108.) Clustering of visits was executed for $K = 2, 3, 4$, and 8 clusters. For each clustering, the strength of the clustering was assessed by two complementary methods. First, the silhouette statistic (SW) was calculated for each cluster

(subgroup) and the overall clustering (see, e.g., Rousseeuw P, *J Comput Appl Math* 1987, 20:53-65.). Second, typical levels of gaussian experimental noise were injected into the expression data, 100 realizations of this noisy data were each clustered, and the weighted sum of the fraction of realizations where the same groups of visits were co-clustered was calculated to generate a robustness index, (R), which is closely related to the measures described in McShane, 2002 (McShane et al., *Bioinformatics* 2002, 18(11):1462-1469). For K = 2 clusters, there was a clear and robust separation into two clusters (SW = 0.19, R = 0.998). For K = 3 clusters, robust groupings were also found (SW = 0.08, R = 0.88). Beyond K = 3 clusters, the SW and R measures declined further, indicating little support for more than 3 subgroups. Based on these results, K means clustering using 3 clusters was used to segregate exacerbation visit samples into three subgroups designated as X, Y and Z. Analyses using data for all 9,696 probe sets were then conducted to compare subgroup exacerbation visit expression levels to quiet visit expression levels. Probe sets showing a within-subgroup exacerbation association of FDR < 0.05 and average fold change with exacerbation >1.2 were defined as meeting the criteria for association with exacerbation.

In order to track the biological pathways and functional networks implicated in exacerbation attacks, genes associated with exacerbation attack were analyzed using Ingenuity Pathway Analysis (IPA 3.1 release, Ingenuity® Systems, www.ingenuity.com; see e.g., Calvano *et al.*, 2005 *Nature* 437:1032-1037) to reveal relationships between them.

EXAMPLE 3: NUCLEIC ACID METHODS

Conversion of 2µg of total RNA from the above preparations to cDNA was accomplished using the Applied Biosystems High Capacity cDNA Archive Kit (Applied Biosystems Catalog #4322171) was performed according to the manufacturer's instructions. Pre-validated, QC tested gene specific primer-probe pairs, optimized for use on any ABI PRISM™ sequence detection system, were purchased from Applied Biosystems (ABI). Real-time quantitative gene expression assay kits were obtained from Applied Biosystems. The genes assayed were IFN α 1 (assay Hs00256882_s1), IFN β 1 (assay Hs00277188_s1), IFN γ (assay Hs00174143_m1), IL18 (assay Hs00155517_m1), IL13 (assay Hs00174379_m1), and the endogenous normalizer control, ZNF592 (assay Hs00206029_m1). All study samples were normalized to ZNF592 levels to determine relative concentration values.

Using the Taqman Assay-On-Demand ("AOD") product insert volume recommendations, a master mix was prepared using Taqman™ Universal PCR Master Mix (Catalog #4304437) and aliquoted into a 96 well plate (ABI Catalog #N801-0560 and caps #N801-0935) for a final volume of 50 µl/well. Duplicate wells for serially diluted standards and cDNA samples (50 ng/well) were assayed on an ABI PRISM 7700 Sequence detector (Sequence Detector

Software v1.7) using universal thermal cycling conditions of 50°C for 2 minutes, 95°C for 10 minutes and 40 cycles of 95°C for 15 seconds, 60°C for 1 minute.

Relative quantification of RNA transcript levels was performed following the guidelines described in ABI PRISM 7700 Sequence Detection System User Bulletin #2 using the relative standard curve method. Specifically, standard curves are calculated for target standards and endogenous control, input values determined for target and endogenous control using standard curves' slope and y-intercept, and target input values are normalized to endogenous control. Fold change is calculated using the 50 ng standard as a calibrator and relative concentration of sample is obtained by multiplying fold change by calibrator, then averaged. To utilize the standard curve method for RNA quantification, a tissue empirically determined to express the target gene was identified using Applied Biosystems Taqman AOD™. Standard curve tissue sources were: cervix tumor from Ambion for $\text{INF}\alpha$, activated human monocyte for $\text{INF}\beta$, activated human PBMC for $\text{INF}\gamma$ and IL18, and thymus from Ambion for IL13. Cycle threshold (Ct) values of >35 were considered below the limits of detection. For standard curve development, the goal was to achieve a Ct value between 18 and 25 for 100 ng of cDNA. This allowed for appropriate standard curve dynamic range. Standard curves consisted of two-fold serial dilutions of total cDNA from 100 ng/well to 1.5 ng/well. Standard curves were performed on each plate for every assay and were used for sample quantification and assay performance monitoring. Inter-plate % CV for standard curve points were $< 4.5\%$ for $\text{INF}\alpha$ and IL-13 and $< 3\%$ for interferon- β , $\text{INF}\beta$ and IL-18.

AOD for single exon gene targets ($\text{INF}\alpha$ 1 and $\text{INF}\beta$ 1) can produce inaccurate transcript expression values if the RNA preparations used for cDNA conversion contain genomic DNA. The following strategy was developed and employed to determine which cDNA samples contained genomic DNA.

Genomic sequence analysis was performed in the area of the human KIAA0644 gene product (accession #NM_014817) to determine predicted mRNA sequences using the Ensembl Gene Browser (see Fernandez Suarez and Schuster, "Using the Ensembl Genome Server to Browse Genomic Sequence Data," UNIT 1.15 in Current Protocols in Bioinformatics, Supplement 16, January 2007; and also <http://www.ensembl.org/index.html>). A Taqman primer/probe pair was designed (ABI Primer Express) from a predicted nontranslated sequence located approximately 1.5 Kb 3' of the KIAA0644 single exon gene product open reading frame on chromosome 7. In a Taqman assay, this primer/probe pair was shown to produce a strong signal, Ct value of 24.14, using a human genomic DNA preparation (Clontech catalog #6550-1) and no signal (Ct value of 40) using a commercially available purified RNA preparation from Ambion (human kidney, catalog #7976). Taqman analysis of all AOS cDNA preparations was performed using this primer/probe pair. Samples

producing a Ct value of 35 or greater were determined to not be contaminated with genomic DNA, while samples producing a Ct value of less than 35 were considered to be contaminated with genomic DNA. For single exon gene target results, samples containing genomic DNA were not included in the statistical analysis (12% of AOS samples).

5 Statistical analyses were conducted to compare gene expression for 5 preselected genes (IFN α 1, IFN β 1, IFN γ , IL13, and IL18) for exacerbated and quiet asthma periods. For each subgroup of patients (defined by K-means analysis described above), a mixed model analysis of variance was fit to the expression data to compare expression between exacerbation and quiet periods at the five percent significance level. The model included a
10 fixed effect for visit type (quiet or exacerbated) and a random effect for patient to account for multiple visits per patient.

Gene expression from the quiet periods were then combined for the two subgroups to estimate the between and within subject variability in expression for asthma patients during quiet periods. These variance components were also estimated for a set of 28 healthy
15 volunteers.

EXAMPLE 4: PBMC GENE EXPRESSION ASSOCIATED WITH EXACERBATION

By ANCOVA analysis of the 118 subjects comparing quiet (393 samples) and exacerbation (166 samples), 78 probe sets had changes in expression that were associated with exacerbation, based on a criterion of FDR < 0.05. The significance of the association
20 with exacerbation ranged from 5.16E-5 to 4.6E-2 (Table 2). A listing and annotation of these 78 probe sets and the significance of association is given in Table 2.

The comparison between exacerbation and quiet visits that identified the 78 sequences was based on 118 subjects, and for 16 of these subjects no evaluable follow-up visit samples were available. The ANCOVA comparing quiet and exacerbation visit gene
25 expression was rerun on visits only from the 102 subjects that also had follow-up visit data. The significant differences between quiet and exacerbation in the comparison based on 118 subjects also trend towards significance in the comparison based on 102 subjects, although, as predictable given the loss of statistical power, there are fewer probe sets with FDR < 0.05 in the analysis based on 102 donors (Table 2).

30 The ANCOVA comparing mean expression levels in quiet and follow-up genes indicated that gene expression levels associated with exacerbation had returned to quiet visit levels at follow-up visit (Table 2).

EXAMPLE 5: ASTHMA SUBGROUPS

To examine in more detail expression patterns associated with exacerbation, spectral bi-clustering analysis was performed using the difference between the log2 expression levels during each individual exacerbation visit and the mean log2 expression level of quiet visits for each of the 166 exacerbation visits. This analysis revealed significant heterogeneity between the expression profiles of exacerbation visits, and suggested that sub-grouping of visits might increase our power to detect transcripts that were differentially expressed only within specific subgroups. It was determined that K-means clustering using 3 clusters defined three relatively distinct and robust exacerbation associated gene expression patterns (see Methods section). K-means clustering was therefore used to assign each exacerbation sample to one of three subgroups (or clusters) designated as X (30 visits), Y (64 visits) and Z (72 visits). ANCOVA was performed on all 9,696 probe sets to compare mean expression levels in each exacerbation subgroup with mean quiet visit expression levels, thereby identifying sub-group specific expression profiles that might have been masked by heterogeneity when data from all exacerbation visits were lumped together.

Since the subgroups (or clusters) were defined based on minimizing variability among members of the same subgroup, the p-values and FDR values observed for specific exacerbation subgroup versus quiet visit comparisons for any given probe set can not be interpreted as numerically equivalent to p-values and FDRs obtained in the earlier analysis of quiet versus exacerbation expression levels. Rather the “within subgroup” FDR values are used primarily to rank the probe sets in terms of significance of differences between exacerbation and quiet expression levels. Therefore, FDR values generated from within subgroup analyses were designated as “comparative FDRs”. Therefore, in practical terms, a probe set with a comparative within subgroup X FDR of $< 1E-15$ is much more likely to be associated with exacerbation than the probe sets with comparative FDRs of > 0.05 , but the overall probability of association with exacerbation can not be stated to be $FDR < 1E-15$.

Within subgroup X, 1,081 probe sets had differences between exacerbation and quiet visit expression levels, as defined by comparative $FDR < 0.05$ and absolute average fold change > 1.2 , and 48% of these 1,081 probe sets had comparative $FDR < 1E-3$. Table 4 lists these probes sets along with their gene annotations and the strength of association with exacerbation as determined by comparative FDR. These findings indicate a very robust exacerbation associated gene expression profile within subgroup X. Analyses were then performed to determine the differences between quiet and follow-up visits within subgroup X. Of the 30 subgroup X exacerbation visits, evaluable follow-up samples were available for 22, resulting in 8 (26.6%) fewer samples in the analysis comparing quiet to follow-up visits within subgroup X. Even with this smaller sample size, ANCOVA comparing expression in quiet

visits and 22 exacerbation visits for which there was a corresponding follow-up visit, showed that 793 (74%) of the 1,081 exacerbation associated probes sets retained a comparative $FDR < 0.05$, indicating that a robust exacerbation associated expression profile was detectable even with a 26.6% decrease in sample size. In stark contrast, the ANCOVA
5 comparing quiet visits and 22 follow-up visits of subgroup X exacerbation visits for all 9,696 probe sets identified only 36 differences with $FCR < 0.05$, indicating that, unlike exacerbation samples, follow-up samples are very similar to quiet visit samples. Of the 793 probe sets significantly associated with exacerbation in the 22 visit analysis, only 2 had a significant difference between quiet and follow-up visits.

10 Many of the 1,081 exacerbation-associated subgroup X probe sets did not show even a slight trend towards association with exacerbation in subgroup Y, with 26% having a subgroup Y association $FDR > 0.5$ (50%). These data indicate significant qualitative gene expression differences in subgroup X and Y exacerbations. Overlap between subgroups was also observed, however, with 21% of the subgroup X probe sets showing an association
15 with exacerbation (comparative $FDR < 0.05$) within subgroup Y.

ANCOVA comparing exacerbation and quiet visit expression levels within sub-group Y identified 574 probe sets associated with exacerbation. For subgroup Y, there were 64 exacerbation visits in the analyses comparing quiet and exacerbation, and 51 in the analyses that included follow-up visits. As was seen in the both the conglomerate and
20 subgroup X analyses, for most probe sets subgroup Y expression levels had returned to quiet visit levels by follow-up. The list of the subgroup Y probe sets together with the metrics for association with exacerbation is given in Table 5. Of the probes sets associated with exacerbation in subgroup Y, 24% overlapped with subgroup X probe sets. In addition, subgroup Y probe sets include 39% that did not show even a slight trend with exacerbation
25 (comparative $FDR > 0.5$) in subgroup X. These data confirm the striking difference between subgroups X and Y exacerbations.

Subgroup Z contained the largest number of exacerbation visits (72) and the analyses that included follow-up visits contained 52 samples. The total number of exacerbation association probe sets in subgroup Z was 211, and the lowest relative FDR observed was
30 0.0004. No probe sets were identified in subgroup Z that did not also show a significant association with exacerbation in subgroup X and/or Y, indicating that subgroup Z does not represent a third qualitatively distinct exacerbation associated profile. Rather the data show that subgroup Z contains the visits that differ the least from quiet visits, and suggest that visits with weak to absent exacerbation associated profiles were assigned by the K-means
35 algorithm to this group.

Chi-square tests or ANOVAs were performed to determine if clinical or technical parameters could be identified that had a significant association with subgroup assignment.

A significant association between body mass index (BMI) and subgroup assignment was identified. Mean BMI was statistically significantly lower ($p = 0.006$) in subgroup X than subgroup Y, and was statistically suggestively lower ($p = 0.0501$) in subgroup Z than subgroup Y. Mean BMI was 28.4, 32.4, and 30.2 in subgroups X, Y and Z, respectively. Additionally, subgroup Y samples were somewhat less likely ($p = 0.042$) to be from fasting subjects at time of visit, with 30%, 22% and 29% fasting samples in subgroup X, Y and Z respectively. Subgroup Y samples tended to be from older patients (mean age 46.0 years) than those in subgroup X (mean age 39.1) or Z (mean age 43.5), and this difference was significant in the comparison of subgroups X and Y ($p = 0.03$).

No evidence was found for association between subgroup assignments and any of the following parameters: sex, race, country, disease severity, atopy status, respiratory infection, systemic, inhaled, intra-nasal corticosteroid or leukotriene inhibitor use, histamine H2 antagonist or PPI use, medical history of acid reflux, time between onset of exacerbation and sample collection, or sample processing lab. Also no evidence was found for association with FEV1 or IgE, but many values were missing in this analysis.

The mean number of days between quiet and exacerbation visits was significantly smaller for subgroup X (48.4 days) than for subgroup Y (62.7 days) and or Z (79.6 days). (The p-value of 0.03 is for the overall test comparing the means for the 3 subgroups; the p-value for X vs Z was 0.014; the p-value for X vs Y was > 0.05 .) While not wishing to be bound by theory, given the study design, this difference possibly indicates that subgroup X samples were more likely to be collected from subjects who sought medical attention due to symptoms of attack, whereas the samples in the other subgroups were more likely to include some samples collected during a scheduled visit whose exacerbation attack symptoms had not triggered the patient to come in for an exacerbation visit. Other explanations for this observed difference are also possible, including that the different types of exacerbation visits may just have different frequencies of occurrence. The associations between subgroup assignment and clinical parameters therefore suggest that exacerbations with the most acute attack symptoms (as defined by prompting the subject to seek more immediate medical attention) tended to be in subgroup X. Those with exacerbations (and asthma) associated the high BMI tended to be in subgroup Y, perhaps providing a molecular signature for the previously observed link between higher BMI and symptoms of asthma. Those in subgroup Z tended to display more mild form of exacerbation profile as apparently reflected in the significantly longer intervals between seeking medical attention and the very much less robust molecular signature.

EXAMPLE 6: GENES/MARKERS ASSOCIATED WITH ASTHMA EXACERBATION

To determine the biological pathways and functional networks implicated in exacerbation by gene expression patterns, genes were analyzed using Ingenuity Pathway Analysis. Various canonical pathways are specific to subgroups X and Y, respectively. For example, subgroup X canonical signaling pathways include e.g. natural killer cell, antigen presentation, leukocyte extravasation, JAK/Stat, interferon, GM-CSF, T cell receptor, toll-like receptor and IL-10 signaling. Subgroup Y canonical signaling pathways include e.g. IL-4, B cell receptor, death receptor, SAPK/JNK, IL-2, PTEN, circadian rhythm, IGF-1, actin cytoskeleton, PI3K/Akt and insulin receptor signaling. Many IFN-inducible genes were noted in subgroup X. These include the interferon regulatory factors (IRFs) that are known to drive the transcription of various IFN-inducible genes. IRF1, IRF7, IRF9 are upregulated in exacerbation while IRF4 is down in exacerbation.

Networks were built (using the Connect Tool) around these IRFs using the subgroup X associated genes and expression and/or transcription as the connectivity from IRFs to the subgroup X associated genes. Subgroup X associated genes for IRF1, IRF7 and IRF9 are also upregulated in exacerbation suggesting that these IRFs drive the expression of these exacerbation genes. Likewise, exacerbation genes in the IRF4 hub are down and so is IRF4 in exacerbation. A network centered around IL15 was also highly significant, suggesting that IL15 could be regulating the expression of several exacerbation genes. All subgroup X associated genes were connected to IL15 based on information available in IPA for IL15 regulation of gene expression using the Connect tool (Table 6).

Subgroup Y showed a robust signature for the canonical pathway for B cell signaling. While subgroup Z did not have a robust signature, pathway analysis identified TLR pathway as well represented among the genes that passed the significance filter in this subgroup.

Since interferon response elements were so strongly identified with exacerbations, and IFN γ is so strongly identified with a Th1 type response and IFN α and β more consistent with the Th2 response classically associated with asthma, TAQMAN analysis of a subset of samples from subgroups X and Y was performed to assess the association of each of these genes with subgroups X and Y. As shown in Table 3, the results indicate that elevated levels of IFN α and β were associated with subgroup X exacerbations. IFN γ did not differ significantly between quiet and exacerbation samples.

Comparison of quiet and exacerbation visit gene expression profiles identified significant exacerbation associated changes in gene expression levels. Expression levels had returned to quiet visit levels two weeks after the attack. Clustering algorithms identified three relatively distinct exacerbation phenotypes defined by PBMC gene expression profiles, and analysis showed that gene expression patterns identified by ANCOVA performed within

subgroups had also returned to quiet visit levels two weeks following an exacerbation, confirming that the within subgroup analysis did, indeed, identify genes significantly associated with exacerbation.

Pathway analysis for the three subgroups identified distinct pathways active within subgroups X, Y and Z. Many IFN-inducible genes such as OAS1, OAS3, MX1, IFITM3, IFIT3, IFI27, IFI35, IFIT1, et cetera are observed in subgroup X. These include interferon regulatory factors (IRFs), a family of transcription factors involved in the regulation of the interferon response. Of the nine known IRFs, IRF1, IRF7 and IRF9 are up-regulated in exacerbation, while IRF4 is down-regulated in exacerbation. The majority of the subgroup X genes that are regulated by IRF1 and IRF7 are also up-regulated in exacerbation. The majority of the subgroup X genes regulated by IRF4, such as CXCR4, MS4A, VIL2 and GATA3 are also down-regulated in exacerbation. IFN response in subgroup X is likely regulated by these IRFs and maybe either a Type I IFN (IFN α /IFN β and others, such as IFN- ω , - ϵ , and - κ) or a Type II IFN (IFN γ) response. Taqman data indicates that the subgroup X IFN pathway is driven by IFN α and IFN β . Data analysis indicates that the IFN pathway activation observed in the instant exacerbation samples are not attributable to respiratory infections, and that samples in this subgroup tend to have come from patients with normal BMI.

Another likely player in subgroup X exacerbations is IL15. IL15 is a TH1 cytokine that activates T-cells in a T-cell receptor independent manner. TCR α , TCR ζ and CD3D, which is associated with TCR, are down-regulated in exacerbation along with CD8B, a co-receptor for MHC class I as well as downstream signaling proteins such as ITK, PLC γ 1, TEC, SOS2, PIK3R1 and CALM1. IL15 is up-regulated in exacerbation and so is IL2RG, the shared signaling component of IL15R. So likely subgroup X type exacerbations involve IL15 activation of T-cells in a TCR – independent manner. IRF1 induces IL15, and IFNs may activate CD8T-cells via IL15.

TLRs trigger IFN-responses. TLR-signal transduction occurs either in a MYD-88 dependent manner through the recruitment of IRAK1/4, TRAF6, TAB1/2, TAK1 or in a MYD-88 independent manner that involves TRAM, TRIF, TBK-1, IKK-e and other signaling molecules. TLR3 and TLR4 are the only Toll receptors that utilize the MYD-88 independent signaling pathway. TLR1, TLR2, TLR4 are all expressed at significantly higher levels in exacerbation as well as MYD88, MD-2, CD14 and a downstream kinase EIF2AK1

MDA5/IFIH, which is a cytosolic receptor for intracellular viral RNAs and synthetic dsRNAs, and which mediates TLR-independent induction of type I IFN genes, is also upregulated in subgroup X suggesting that both TLR-dependent and independent pathways are activated in subgroup X.

Additional pathways regulated in subgroup X include, for example, the NK-cell signaling pathway and the antigen presentation pathway.

The NK-cell signaling pathway is common to subgroup Y as well. Subgroup Y genes involved in NK activation such as FCER1 and FCGR3 are expressed at higher levels in
 5 exacerbation, as well as the downstream signaling molecules LCK, SYK, LAT, RAC and RRAS, but not PIK3C1 and PIK3RA1. On the NK-inhibition side, receptors LILRB1, LAIR1, AIRM1, as well some downstream signaling molecules, are up-regulated in exacerbation, suggesting compensatory mechanisms in place for NK signaling. Some parallels and some differences in both arms of NK signaling can be noted for subgroup X. Actin-cytoskeletal
 10 structural genes such as ARPC5, PFN, CYFIP1, ARPC1B, but not VIL2, are upregulated in Subgroup Y. Some of these trend in the opposite direction for Subgroup X.

The expression levels of TLRs, IRFs, IL15 do not significantly change in subgroup Y compared to the quiescents. Few genes common to the TLR, IFN, IL15 pathways in subgroup X such as for example MDA5, IFI35, ICAM2, CCR2, and IL2RG are also seen in Subgroup Y,
 15 and almost all trend in the same direction.

Additionally, different genes with similar functions showed sub-group specificity. For example, phospholipase scramblase 1 (PSCR1) is elevated in subgroup X (FDR = 7.13E-13) but not in sub-group Y (FDR = 0.509), whereas phospholipase scramblase 3 (PSCR3) is elevated in sub-group Y (FDR = 0.003) but not in subgroup X (FDR = 0.99).

20 The following tables, which are referenced in the foregoing description, are herein incorporated in their entirety.

EXAMPLE 7: SERUM MARKERS OF EXACERBATION

Plasma samples from asthmatic donors during either previously scheduled or random exacerbation visits, and healthy volunteer donors were analyzed by ELISA for the presence
 25 of various cytokines, sST2 protein, which is the soluble form of ST2, an IL-1 receptor family member and cognate receptor for IL-33 (see Sanada et al., J. Clin. Invest., 117:1538-1548, 2007, which is incorporated herein by reference,) and chitinase 3-like 1 protein (YKL-40, CHI3L1) (see Table 8.) CHI3L1 showed a significant difference in expression in the sera of asthmatics versus healthy volunteers, indicating its usefulness as an asthma-associated
 30 biomarker.

Serum sST2 concentrations were found to be significantly higher in (a) asthmatics versus healthy donors ($p < 0.05$); (b) asthmatics during exacerbation versus asthmatics during scheduled visits ($p < 0.05$); and (c) asthmatics during exacerbation versus healthy volunteers ($p < 0.0005$). Specifically, the concentration of sST2 in sera was observed to be
 35 elevated upon exacerbation (90 pg/mL) relative to normal controls (55 pg/mL) (p value <

0.0001). It was further observed that, upon asthma exacerbation, males have higher sST2 concentration in the sera (126 pg/mL) relative to females (78 pg/mL) (p value <0.01).

The question of whether sST2 is induced in response to G-protein coupled receptor (GPCR) activation was examined in a human mast cell line (HMC-1; see Versluis et al., Int. Immunopharmacol., 8:866-873, 2008.) We observed strong induction of sST2 mRNA and protein expression upon cell activation with asthma associated anaphylatoxin C5a and adenosine analog NECA, that activate GPCR signaling via C5a and adenosine receptor, respectively. Thus, sST2 is a useful asthma and exacerbation biomarker for the clinic.

EXAMPLE 8: INTRA-SUBJECT VARIABILITY OF BIOMARKERS

We have shown that there are significant differences in PBMC gene expression profiles of asthma exacerbation subjects and asthma quiet or healthy subjects. In this example, we have shown that the expression level of many asthma associated genes can vary over time (e.g. between visits separated by time) within a subject, and can range from close to healthy to very different from healthy, and that differences between subjects are not necessarily greater than differences within subjects. The result of such an analysis will enable the selection of more optimal asthma and asthma exacerbation biomarker candidates that have higher incidences of deviation from healthy and quiet, respectively, on a per visit basis, as well as lower intra-subject deviations. (See copending US Patent Application No. 60/879,994, which is herein incorporated by reference.) Non-limiting examples of such more optimal biomarkers for exacerbation include BLVRA (biliverdin reductase A), CSE1L (chromosome segregation 1-like), CTSC (cathepsin C), FCN1 (ficolin 1), GRN (granulin), LAMP2 (lysosomal-associated membrane protein 2), PECAM1 (platelet/endothelial cell adhesion molecule-1), S100A9 (S100 calcium binding protein A9) and SP110 (SP110 nuclear body protein). Exacerbation biomarkers having low intra-subject variability and high deviation from quiet or healthy are also shown in Table 9 and Table 10 for cluster X and cluster Y subgroups, respectively. These markers can be used to predict an exacerbation event in asthma sufferers.

To demonstrate this intra-subject variability, a first analysis was run on GeneChips from the first visit for each subject and a second analysis was run on GeneChips from the second visit for each subject (subsequent analysis looked at later visits.) Using all subjects and analyzing data from all visits analysis, 438 probesets, which were significantly associated with asthma, were selected. For each probeset, the log2 fold change was calculated for each asthma sample (including exacerbation asthma samples) over average healthy (all subjects, all visits). A quantitative scale was devised, which indicates the "distance" between an individual asthma (asthma exacerbation) profile and the mean healthy profile.

Then the range of distance of asthma or asthma exacerbation from healthy was analyzed on a subject-by-subject basis.

The first and second visit analyses gave the same results, including the same cluster structure, same asthma genes, and almost the same fold change in expression level.
 5 However, it was noted that the subjects move between a subcluster that is very different from healthy and a subcluster that is close to healthy, showing that some asthma-associated and exacerbation-associated genes vary within a subject over time.

EXAMPLE 9: BIOMARKERS FOR INFLAMMATORY DISEASES

The 438 probesets used for asthma profile (supra) were examined for their association
 10 with other inflammatory diseases. Approximately 155 of those markers were significantly associated with asthma and not with multiple sclerosis (MS) or inflammatory bowel disease (IBD). 164 were associated with asthma and MS, with an additional 112 at least trending to significance in MS. 16 markers were associated with asthma and Crohn's disease, 10 of which did not also associated with MS. Nine (9) markers were associated with asthma and
 15 ulcerative colitis (UC).

The majority of genes common to MS and asthma changed in the same direction relative to normal or healthy in both diseases, with the following exceptions: IL21R (interleukin 21 receptor) was up in MS, down in asthma, and down more in severe asthma; CUTL1 (Cut-like 1, CCAAT displacement protein) was up in MS, down in asthma, down more in severe
 20 asthma; DGKD (Diacylglycerol kinase, delta 130kDa) was up in MS, down in asthma, down more in severe asthma; and KIAA0528 (hypothetical protein LOC9847) was up in MS, down in asthma, and down more in severe asthma.

EXAMPLE 10: EXACERBATION DURING RESPIRATORY INFECTIONS

Of the 166 exacerbation samples, 39 occurred during a respiratory system infection and
 25 127 occurred with out symptoms of infection. To identify probe sets that showed association with exacerbation only in the presence of infection, an ANCOVA was performed comparing the 39 samples collected during infection with the quiet vists from the same patients. 54 probesets were identified with FDR<0.05 (Table 11) Of note among the 54 were 16 of the 54 probe sets showed an association with exacerbation in the presence of infection, but did
 30 not show a significant association in the analysis comparing the mixed group of 166 exacerbations (with and without infection) and quiet samples (Table 12). Consistent with this finding, none of these 16 was significantly associated with exacerbations in the absence of infection. These data indicate that there were some probe sets whose association with exacerbation was detectable only in the presence of a concomitant infection.

EXAMPLE 11: EXACERBATION IN THE ABSENCE OF INFECTION

At least three probe sets were observed to be associated with exacerbation in the absence of infection (i.e. not associated with exacerbation in the presence of infection). Those probes sets include: (a) interferon induced with helicase C domain 1 (IFIH1; e.g. SEQ ID NO:60), (b) leukotriene A4 hydrolase (LTA4H; e.g. SEQ ID NO:61) and (c) open reading
5 frame number 25 of human chromosome 6 (C6ORF25; SEQ ID NO:62). These probe sets can serve as biomarkers of exacerbation triggered by inert non-infectious agents.

Table 1: Quality Control Criteria for Inclusion of GENECHIP in Analysis

1	Defect on visual inspection	
2	Bactin Gapdh Freq Avg Exp	> 0.6
3	Genechip Raw Q Exp	< 7
4	Qc P Prob Freq Exp	< 20
5	Qc P Prob Avg Diff Exp	< 205
6	Qc Sensitivity Exp	< 6.1
7	Scale Factor Exp	< 4 and > 0.25

1	Defect on visual inspection: Patterns in chip fluorescence visible after the chip has been run that reveal scratches, uneven staining or other defects.	
2	Ratio of signal portion of the gene. A measure of the integrity of the RNA sample.	
3	Raw Q: measure of the noise level of the array, it is the degree of pixel-to-pixel variation among the probe cells used to calculate the background.	
4	QCP probability average difference: signal value for which there is a 70% probability of a Present call.	
5	QCP probability frequency: QCP probability average difference expressed in ppm units.	
6	Chip sensitivity: concentration level, in ppm, at which there is a 70% probability of obtaining a Present call.	
7	Scale factor: the value required to obtain a trimmed mean intensity indicated by the target value. For all data in this study, the target value was set to a value of 100 and the scale factor was determined by dividing the trimmed mean of all probe sets by the target value.	

Table 2: Exacerbation Genes and Metrics

AFFYMETRIX HG-U133A Probe set ID	Gene Name	Gene Description	Exemplar Entrez GeneID:	FDR Quiet v. Exacer'n, N = 118	FDR Quiet v. Exacer'n N = 102	Mean $\Delta\log 2$ Quiet v. Exacer'n
200057_s_at	NONO	non-POU domain containing, octamer-binding	4841	2.97E-03	1.15E-04	0.32
200661_at	CTSA	cathepsin A	5476	2.97E-03	1.64E-04	0.86
200962_at	RPL31	ribosomal protein L31	6160	2.43E-02	3.39E-04	0.47
200986_at	SERPING1	serpin peptidase inhibitor, clade G (C1 inhibitor), member 1, (angioedema, hereditary)	710	5.40E-04	1.33E-03	0.37
201064_s_at	PABPC4	poly(A) binding protein, cytoplasmic 4 (inducible form)	8761	4.61E-02	1.33E-03	0.28
201256_at	COX7A2L	cytochrome c oxidase subunit VIIa polypeptide 2 like	9167	4.05E-02	1.33E-03	-0.15
201315_x_at	IFITM2	interferon induced transmembrane protein 2 (1-8D)	10581	1.79E-02	1.33E-03	0.34
201600_at	PHB2	prohibitin 2	11331	4.22E-02	1.47E-03	0.41
201601_x_at	IFITM1	interferon induced transmembrane protein 1 (9-27)	8519	4.52E-04	1.59E-03	0.30
201649_at	UBE2L6	ubiquitin-conjugating enzyme E2L 6	9246	4.38E-02	1.66E-03	0.21
201762_s_at	PSME2	proteasome (prosome, macropain) activator subunit 2 (PA28 beta)	5721	9.51E-03	1.69E-03	-0.14
201939_at	PLK2	polo-like kinase 2 (Drosophila)	10769	3.29E-02	3.39E-03	0.22
202086_at	MX1	myxovirus (influenza virus) resistance 1, interferon- inducible protein p78 (mouse)	4599	1.56E-03	3.67E-03	0.46
202087_s_at	CTSL1	cathepsin L1	1514	4.17E-02	3.67E-03	0.34
202145_at	LY6E	lymphocyte antigen 6 complex, locus E	4061	7.62E-04	3.67E-03	-0.15
202374_s_at	RAB3GAP2	RAB3 GTPase activating protein subunit 2 (non-catalytic)	25782	4.63E-02	3.98E-03	0.16
202411_at	IFI27	interferon, alpha-inducible protein 27	3429	8.17E-05	1.75E-02	-0.11
202503_s_at	KIAA0101	KIAA0101	9768	4.38E-02	1.80E-02	-0.11
202589_at	TYMS	thymidylate synthetase	7298	2.75E-02	1.80E-02	-0.10
203153_at	IFIT1	interferon-induced protein with tetratricopeptide repeats 1	3434	4.61E-02	2.02E-02	0.30
204043_at	TCN2	transcobalamin II; macrocytic anemia	6948	1.01E-04	2.04E-02	-0.14
204415_at	IFI6	interferon, alpha-inducible protein 6	2537	1.47E-04	2.52E-02	-0.07
204698_at	ISG20	interferon stimulated exonuclease gene 20kDa	3669	6.28E-03	2.52E-02	0.20
204747_at	IFIT3	interferon-induced protein with tetratricopeptide repeats 3	3437	2.97E-03	2.52E-02	0.24
204858_s_at	ECGF1	endothelial cell growth factor 1 (platelet-derived)	1890	2.02E-02	2.52E-02	0.27

AFFYMETRIX HG-U133A Probe set ID	Gene Name	Gene Description	Exemplar Entrez GeneID:	FDR Quiet v. Exacer'n, N = 118	FDR Quiet v. Exacer'n N = 102	Mean $\Delta\log 2$ Quiet v. Exacer'n
204972_at	OAS2	2'-5'-oligoadenylate synthetase 2, 69/71kDa	4939	2.75E-02	2.52E-02	0.15
205055_at	ITGAE	integrin, alpha E (antigen CD103, human mucosal lymphocyte antigen 1; alpha polypeptide)	3682	1.54E-02	2.52E-02	0.30
205483_s_at	ISG15	ISG15 ubiquitin-like modifier	9636	7.24E-05	2.52E-02	0.23
205552_s_at	OAS1	2',5'-oligoadenylate synthetase 1, 40/46kDa	4938	2.30E-02	2.58E-02	0.25
205660_at	OASL	2'-5'-oligoadenylate synthetase- like	8638	2.38E-03	3.39E-02	0.17
206111_at	RNASE2	ribonuclease, RNase A family, 2 (liver, eosinophil-derived neurotoxin)	6036	2.75E-02	3.50E-02	0.26
206332_s_at	IFI16	interferon, gamma-inducible protein 16	3428	2.98E-03	3.50E-02	0.15
206513_at	AIM2	absent in melanoma 2	9447	4.63E-02	3.50E-02	0.16
208436_s_at	IRF7	interferon regulatory factor 7	3665	2.68E-02	4.94E-02	0.36
208631_s_at	HADHA	hydroxyacyl-Coenzyme A dehydrogenase/3-ketoacyl- Coenzyme A thiolase/enoyl- Coenzyme A hydratase (trifunctional protein), alpha subunit	3030	1.12E-02	4.98E-02	0.33
208805_at	PSMA6	proteasome (prosome, macropain) subunit, alpha type, 6	5687	4.71E-02	5.23E-02	0.25
208966_x_at	IFI16	interferon, gamma-inducible protein 16	3428	1.36E-02	5.23E-02	0.16
209009_at	ESD	esterase D/formylglutathione hydrolase	2098	1.04E-02	5.98E-02	0.10
209207_s_at	SEC22B	SEC22 vesicle trafficking protein homolog B (S. cerevisiae)	9554	2.43E-02	5.98E-02	0.15
209313_at	XAB1	XPA binding protein 1, GTPase	11321	4.61E-02	5.98E-02	0.20
209417_s_at	IFI35	interferon-induced protein 35	3430	2.75E-02	6.05E-02	-0.11
209684_at	RIN2	Ras and Rab interactor 2	54453	7.66E-03	7.35E-02	-0.11
209906_at	C3AR1	complement component 3a receptor 1	719	2.75E-02	7.85E-02	-0.09
210027_s_at	APEX1	APEX nuclease (multifunctional DNA repair enzyme) 1	328	4.09E-03	8.27E-02	-0.12
210797_s_at	OASL	2'-5'-oligoadenylate synthetase- like	8638	4.09E-03	9.32E-02	0.18
210873_x_at	APOBEC3A	apolipoprotein B mRNA editing enzyme, catalytic polypeptide- like 3A	200315	5.88E-04	9.32E-02	0.16
211937_at	EIF4B	eukaryotic translation initiation factor 4B	1975	1.24E-03	9.48E-02	0.15
211938_at	EIF4B	eukaryotic translation initiation factor 4B	1975	2.54E-04	1.11E-01	0.21
211954_s_at	RANBP5	RAN binding protein 5	3843	2.75E-02	1.21E-01	0.18

AFFYMETRIX HG-U133A Probe set ID	Gene Name	Gene Description	Exemplar Entrez GeneID:	FDR Quiet v. Exacer'n, N = 118	FDR Quiet v. Exacer'n N = 102	Mean $\Delta\log 2$ Quiet v. Exacer'n
212063_at	CD44	CD44 molecule (Indian blood group)	960	1.54E-02	1.21E-01	0.21
212145_at	MRPS27	mitochondrial ribosomal protein S27	23107	2.43E-02	1.21E-01	0.13
212203_x_at	IFITM3	interferon induced transmembrane protein 3 (1-8U)	10410	5.17E-06	1.21E-01	0.23
212658_at	LHFPL2	lipoma HMGIC fusion partner-like 2	10184	4.61E-02	1.21E-01	-0.08
213293_s_at	TRIM22	tripartite motif-containing 22	10346	1.27E-02	1.24E-01	0.17
213294_at	HUMPEIF2A	P1/eIF-2a protein kinase	NP_002750.1	4.24E-02	1.24E-01	0.12
214022_s_at	IFITM1	interferon induced transmembrane protein 1 (9-27)	8519	6.01E-03	1.36E-01	0.30
214290_s_at	HIST2H2AA3	histone cluster 2, H2aa3 /// histone cluster 2, H2aa4	723790 /// 8337	2.98E-02	1.55E-01	-0.11
214442_s_at	PIAS2	protein inhibitor of activated STAT, 2	9063	4.54E-02	1.72E-01	0.24
214453_s_at	IFI44	interferon-induced protein 44	10561	1.65E-04	1.72E-01	0.19
216565_x_at	LOC391020	interferon induced transmembrane protein pseudogene	391020	6.59E-05	1.76E-01	-0.12
216598_s_at	CCL2	chemokine (C-C motif) ligand 2	6347	2.43E-02	1.76E-01	0.22
216950_s_at	FCGR1A	Fc fragment of IgG, high affinity Ia, receptor (CD64)	2209	4.63E-02	1.76E-01	-0.09
217719_at	EIF3EIP	eukaryotic translation initiation factor 3, subunit E interacting protein	51386	1.82E-04	1.76E-01	0.61
217846_at	QARS	glutamyl-tRNA synthetase	5859	4.36E-03	1.87E-01	0.07
218232_at	C1QA	complement component 1, q subcomponent, A chain	712	9.51E-03	2.14E-01	0.54
218280_x_at	HIST2H2AA3	histone cluster 2, H2aa3 /// histone cluster 2, H2aa4	723790 /// 8337	4.61E-02	2.17E-01	-0.07
218400_at	OAS3	2'-5'-oligoadenylate synthetase 3, 100kDa	4940	9.51E-03	2.23E-01	0.18
218458_at	GMCL1	germ cell-less homolog 1 (Drosophila)	64395	2.74E-02	2.30E-01	0.14
219014_at	PLAC8	placenta-specific 8	51316	2.43E-02	2.33E-01	-0.07
219209_at	IFIH1	interferon induced with helicase C domain 1	64135	2.76E-02	2.33E-01	-0.09
219863_at	HERC5	hect domain and RLD 5	51191	9.51E-03	2.33E-01	-0.12
221476_s_at	RPL15	ribosomal protein L15	6138	2.62E-03	2.44E-01	0.16
221726_at	RPL22	ribosomal protein L22	6146	1.29E-03	2.52E-01	-0.08
221741_s_at	YTHDF1	YTH domain family, member 1	54915	4.61E-02	2.52E-01	-0.10
221875_x_at	HLA-F	major histocompatibility complex, class I, F	3134	2.75E-02	2.68E-01	0.14
222154_s_at	DNAPTP6	viral DNA polymerase-transactivated protein 6	26010	3.42E-02	2.84E-01	-0.07
33304_at	ISG20	interferon stimulated exonuclease gene 20kDa	3669	9.51E-03	3.10E-01	-0.24

AFFYMETRIX HG-U133A Probe set ID	Gene Name	Gene Description	Exemplar Entrez GeneID:	FDR Quiet v. Exacer'n, N = 118	FDR Quiet v. Exacer'n N = 102	Mean $\Delta\log_2$ Quiet v. Exacer'n
44673_at	SIGLEC1	sialic acid binding Ig-like lectin 1, sialoadhesin	6614	1.65E-04	3.30E-01	0.16

5

Table 3: Results of Mixed Model Analysis Comparing Exacerbation vs Quiet Visits

Subgroup	Gene	Estimate ¹	Standard Error	P Value	95% Confidence Interval	
					Lower	Upper
X	IFN α 1	16.97	5.82	0.0047*	5.37	28.57
	IFN β 1	2.51	0.82	0.0031*	0.88	4.15
	IFN γ	-0.19	0.15	0.2310	-0.49	0.12
	IL13	-11.01	6.89	0.1133	-24.69	2.67
	IL18	-100.34	148.52	0.5010	-395.33	194.64
Y	IFN α 1	-6.40	8.51	0.4537	-23.27	10.47
	IFN β 1	-0.04	0.24	0.8502	-0.51	0.42
	IFN γ	-0.01	0.21	0.9514	-0.42	0.40
	IL13	-4.98	3.54	0.1626	-11.99	2.03
	IL18	162.40	84.82	0.0576	-5.34	330.26

10

¹Estimated Difference for Exacerbation Expression - Quiet Expression.

* Gene expression for exacerbation visit is statistically different from that observed at quiet visits at 5 % significance level.

Table 4: Subgroup X Genes and Metrics

AFFYMETRIX HG-U133A Probe set ID	IPA-Gene Symbol	FDR Exacerbation versus quiet 30 visit analysis	FDR Exacerbation versus quiet, 22 visit analysis	FDR Follow-up Versus Quiet 22 visit analysis	Average log2 difference exacerbation versus quiet	SEQ ID NO:
202411_at	IFI27	1.00E-13	1.00E-13	0.314342283	3.2264742	SEQ ID NO:51
218943_s_at	DDX58	1.00E-13	2.28786E-10	0.418656737	1.257131388	
216950_s_at	FCGR1A	1.00E-13	4.37509E-11	0.543105461	0.868556644	
219014_at	PLAC8	1.00E-13	1.00E-13	0.547460786	0.87127678	
211938_at	EIF4B	1.00E-13	1.00E-13	0.576368551	-0.723426408	
201762_s_at	PSME2	1.00E-13	4.12266E-12	0.576624724	0.870211608	
221476_s_at	RPL15	1.00E-13	1.23025E-13	0.62004893	-0.463678293	
205552_s_at	OAS1	1.00E-13	2.71458E-12	0.625905427	1.698977288	
203153_at	IFIT1	1.00E-13	9.56864E-13	0.632763895	3.237554236	
208012_x_at	SP110	1.00E-13	6.0713E-10	0.663534687	0.72768352	
204698_at	ISG20	1.00E-13	3.3066E-11	0.677299865	0.894249544	
214511_x_at	FCGR1A	1.00E-13	1.03296E-09	0.713883189	0.85734853	
210797_s_at	OASL	1.00E-13	9.01233E-13	0.726031892	1.112482705	
202270_at	GBP1	1.00E-13	5.25108E-13	0.745247946	1.568665304	
216565_x_at		1.00E-13	1.00E-13	0.764947366	1.456897986	
217846_at	QARS	1.00E-13	9.56864E-13	0.770211009	-0.49716941	
217719_at	EIF3EIP	1.00E-13	1.00E-13	0.804966785	-0.585342786	
212203_x_at	IFITM3	1.00E-13	1.00E-13	0.804966785	1.398071666	
201649_at	UBE2L6	1.00E-13	1.00E-13	0.804966785	0.981987226	
200887_s_at	STAT1	1.00E-13	8.19311E-10	0.806943262	0.871530247	
213294_at		1.00E-13	1.00E-13	0.808403299	1.06592408	
219209_at	IFIH1	1.00E-13	3.10885E-09	0.809600216	0.985007302	
211937_at	EIF4B	1.00E-13	1.00E-13	0.816104227	-0.689405283	
218986_s_at	FLJ20035	1.00E-13	2.26626E-13	0.82330521	1.291531957	
204994_at	MX2	1.00E-13	1.00E-13	0.823670503	0.979758523	
205241_at	SCO2	1.00E-13	1.00E-13	0.8250555	1.126907874	
208966_x_at	IFI16	1.00E-13	3.40484E-11	0.825177207	0.687857558	
33304_at	ISG20	1.00E-13	1.23025E-13	0.826503176	0.708565248	
213293_s_at	TRIM22	1.00E-13	1.00E-13	0.833074897	0.863567736	
209762_x_at	SP110	1.00E-13	7.81859E-11	0.838299238	0.688848248	
209417_s_at	IFI35	1.00E-13	1.00E-13	0.844024603	1.340312324	
204929_s_at	VAMP5	1.00E-13	9.01233E-13	0.845163449	0.767890787	
206332_s_at	IFI16	1.00E-13	3.3066E-11	0.864992216	0.746245403	
217933_s_at	LAP3	1.00E-13	2.26626E-13	0.87331579	0.904969621	
205660_at	OASL	1.00E-13	1.00E-13	0.89701828	1.452000093	
218400_at	OAS3 (includes EG:4940)	1.00E-13	1.00E-13	0.899088585	1.773759512	
204439_at	IFI44L	1.00E-13	1.00E-13	0.903665108	3.343964203	SEQ ID NO:52
202145_at	LY6E (includes EG:4061)	1.00E-13	1.00E-13	0.906012249	2.022298855	SEQ ID NO:53
218543_s_at	PARP12	1.00E-13	1.00E-13	0.906722412	0.769313779	
204415_at	IFI6	1.00E-13	1.00E-13	0.911573276	1.766313456	
200628_s_at	WARS	1.00E-13	8.81825E-09	0.920178258	0.674972037	
202086_at	MX1	1.00E-13	1.00E-13	0.92335789	1.933302682	
204858_s_at	ECGF1	1.00E-13	2.26626E-13	0.926416412	1.091960902	

AFFYMETRIX HG-U133A Probe set ID	IPA-Gene Symbol	FDR Exacerbation versus quiet 30 visit analysis	FDR Exacerbation versus quiet, 22 visit analysis	FDR Follow-up Versus Quiet 22 visit analysis	Average log2 difference exacerbation versus quiet	SEQ ID NO:
202269_x_at	GBP1	1.00E-13	1.77141E-09	0.926416412	1.522330967	
200986_at	SERPING1	1.00E-13	1.00E-13	0.926817552	2.389898415	SEQ ID NO:54
204747_at	IFIT3	1.00E-13	1.00E-13	0.932963506	2.237939985	SEQ ID NO:55
201601_x_at	IFITM1	1.00E-13	1.00E-13	0.932963506	1.073969376	
202869_at	OAS1	1.00E-13	7.4694E-12	0.940129298	1.738328761	
219352_at	HERC6	1.00E-13	1.11447E-11	0.940468793	1.37694416	
44673_at	SIGLEC1	1.00E-13	1.00E-13	0.940613622	1.921070997	
201641_at	BST2	1.00E-13	3.80484E-11	0.947786651	0.866641592	
202688_at	TNFSF10	1.00E-13	1.72681E-10	0.971768475	1.107047024	
214022_s_at	IFITM1	1.00E-13	1.00E-13	0.977627636	0.916009634	
208436_s_at	IRF7	1.00E-13	1.00E-13	0.977971618	1.584740885	
210873_x_at	APOBEC3A	1.00E-13	1.00E-13	0.978184927	1.449174452	
202748_at	GBP2 (includes EG:2634)	1.00E-13	1.67719E-08	0.978184927	0.591465092	
217502_at	IFIT2	1.00E-13	1.33546E-09	0.979892081	1.189237002	
200629_at	WARS	1.00E-13	7.81759E-09	0.983061504	0.815198536	
205483_s_at	ISG15	1.00E-13	1.00E-13	0.9845525	2.458789526	SEQ ID NO:56
219863_at	HERC5	1.00E-13	1.00E-13	0.989252635	1.340107229	
214453_s_at	IFI44	1.00E-13	1.00E-13	0.989523303	2.06603506	SEQ ID NO:57
221726_at	RPL22	1.00E-13	4.30589E-13	0.99162365	-0.517692133	
53720_at	FLJ11286	1.00E-13	2.35906E-10	0.99162365	0.597380083	
222154_s_at	DNAPTP6	1.00E-13	1.00E-13	0.992470596	1.268255203	
212145_at	MRPS27	1.00E-13	1.00E-13	0.994302012	-0.62736433	
204972_at	OAS2	1.00E-13	1.23025E-13	0.994302012	1.128075814	
202687_s_at	TNFSF10	1.00E-13	2.18312E-08	0.994302012	0.98900227	
203964_at	NMI	1.26644E-13	4.2913E-10	0.652660658	0.669128866	
211623_s_at	FBL	1.87213E-13	3.31222E-13	0.833074897	-0.60033015	
204211_x_at	EIF2AK2	4.30589E-13	3.02612E-08	0.804966785	1.594408461	
204043_at	TCN2	9.09695E-13	9.227E-10	0.980726521	0.690121385	
202446_s_at	PLSCR1	1.01667E-12	2.64986E-08	0.85177202	0.755042505	
219062_s_at	ZCCHC2	1.5336E-12	8.91807E-09	0.896710842	0.687393544	
202307_s_at	TAP1	2.50207E-12	3.13346E-06	0.921239504	0.536758483	
203052_at	C2	3.55953E-12	1.7915E-09	0.992470596	0.857425826	
208751_at	NAPA	4.13592E-12	1.06049E-08	0.906012249	0.580955305	
219403_s_at	HPSE	5.4243E-12	5.89108E-09	0.915587288	0.80562162	
201315_x_at	IFITM2	7.23169E-12	2.60589E-09	0.748460361	0.836283869	
216598_s_at	CCL2	7.90321E-12	8.87013E-12	0.896257222	3.396641489	
213716_s_at	SECTM1	1.50706E-11	5.90667E-09	0.947058156	0.84862382	
214470_at	KLRB1	2.81743E-11	1.91211E-10	0.439510344	-0.793264263	
217497_at	ECGF1	3.50772E-11	3.28619E-07	0.897429484	0.781032998	
205055_at	ITGAE	4.17619E-11	2.31436E-09	0.825177207	-0.539147903	
202863_at	SP100	4.59295E-11	7.7357E-09	0.77858286	0.430558471	
203258_at	DRAP1	4.69595E-11	9.72445E-08	0.669240413	0.589634478	
202430_s_at	PLSCR1	6.83435E-11	1.79462E-07	0.972269431	0.845088924	
202087_s_at	CTSL1	7.25567E-11	6.54854E-12	0.594216566	1.306864024	
206133_at	BIRC4BP	9.81058E-11	2.19014E-07	0.662172655	1.636633862	

AFFYMETRIX HG-U133A Probe set ID	IPA-Gene Symbol	FDR Exacerbation versus quiet 30 visit analysis	FDR Exacerbation versus quiet, 22 visit analysis	FDR Follow-up Versus Quiet 22 visit analysis	Average log2 difference exacerbation versus quiet	SEQ ID NO:
203882_at	ISGF3G	1.18436E-10	5.965E-08	0.69958278	0.561582554	
221816_s_at	PHF11 (includes EG:51131)	1.32526E-10	5.58325E-08	0.978029446	0.400769775	
201030_x_at	LDHB	1.36369E-10	8.5811E-09	0.995153496	-0.459647176	
201064_s_at	PABPC4	1.3938E-10	1.77234E-07	0.377556356	-0.375919864	
206491_s_at	NAPA	1.82885E-10	4.51507E-08	0.654429654	0.527768347	
200705_s_at	EEF1B2	2.58537E-10	4.91623E-10	0.933418803	-0.45534209	
214329_x_at	TNFSF10	3.11293E-10	8.01708E-06	0.846591986	1.081146781	
210027_s_at	APEX1	3.68378E-10	8.83764E-08	0.842242847	-0.426855876	
209969_s_at	STAT1	3.7661E-10	1.00035E-05	0.996581247	1.22371884	
204279_at	PSMB9	5.56075E-10	3.43766E-06	0.633489787	0.723472351	
208631_s_at	HADHA	5.71422E-10	1.03033E-08	0.968104648	-0.439593818	
212657_s_at	IL1RN	6.59662E-10	1.25404E-06	0.980673033	1.117091191	
211729_x_at	BLVRA	9.49683E-10	1.679E-05	0.913332358	0.395647321	
201637_s_at	FXR1	1.08247E-09	5.18658E-07	0.867793855	-0.394212413	
201798_s_at	FER1L3	1.12058E-09	3.50361E-06	0.978012719	0.804547413	
202659_at	PSMB10	1.31884E-09	5.16183E-05	0.570133912	0.514936934	
206513_at	AIM2	1.32014E-09	9.75118E-08	0.577947358	0.874116153	
204224_s_at	GCH1	1.43325E-09	3.05898E-06	0.958976925	0.458470138	
214167_s_at	RPLP0 (includes EG:6175)	1.47044E-09	4.94913E-09	0.977971618	-0.545742349	
201812_s_at	TOMM7	1.81354E-09	2.44475E-07	0.997185403	-0.378798248	
213361_at	TDRD7	2.49844E-09	1.26415E-07	0.974654709	0.437970793	
209124_at	MYD88	2.53766E-09	1.00782E-05	0.899359693	0.344411265	
208697_s_at	EIF3E	2.611E-09	3.04635E-07	0.985020691	-0.359281275	
209761_s_at	SP110	3.12069E-09	1.19836E-06	0.865251659	0.758063399	
205875_s_at	TREX1 (includes EG:11277)	3.44688E-09	4.30558E-05	0.668804606	0.542376727	
34689_at	TREX1 (includes EG:11277)	3.56006E-09	1.04345E-06	0.706296724	0.40831158	
203582_s_at	RAB4A	5.80722E-09	1.85329E-09	0.882049407	-0.455069678	
201669_s_at	MARCKS (includes EG:4082)	5.99094E-09	6.23664E-08	0.896681815	0.887496769	
200036_s_at	RPL10A (includes EG:4736)	1.01645E-08	5.22692E-08	0.899991236	-0.439060404	
217988_at	CCNB1IP1	1.06098E-08	2.21844E-07	0.784207096	-0.476825911	
213762_x_at	RBMX	1.06768E-08	3.28619E-07	0.971652444	-0.350958082	
206584_at	LY96	1.07795E-08	8.54545E-07	0.770211009	0.740360256	
201600_at	PHB2	1.3624E-08	6.23664E-08	0.708968475	-0.346901246	
204834_at	FGL2	1.45774E-08	8.12098E-06	0.519109042	1.288816531	
200089_s_at	RPL4	1.46276E-08	1.65355E-07	0.988678861	-0.505446846	
203236_s_at	LGALS9	1.65314E-08	5.33164E-06	0.542658561	0.655449754	
200937_s_at	RPL5	1.69382E-08	1.45556E-07	0.991325836	-0.506636182	
209193_at	PIM1	1.77548E-08	2.40667E-07	0.971652444	0.452796841	

AFFYMETRIX HG-U133A Probe set ID	IPA-Gene Symbol	FDR Exacerbation versus quiet 30 visit analysis	FDR Exacerbation versus quiet, 22 visit analysis	FDR Follow-up Versus Quiet 22 visit analysis	Average log2 difference exacerbation versus quiet	SEQ ID NO:
218232_at	C1QA	1.78536E-08	3.20582E-06	0.970304109	0.827307093	
219356_s_at	CHMP5	2.08519E-08	2.44506E-06	0.940578006	0.637083293	
201670_s_at	MARCKS (includes EG:4082)	2.08619E-08	1.72623E-07	0.926350227	1.064785892	
200005_at	EIF3D	2.67828E-08	3.00878E-07	0.553496047	-0.343060011	
211710_x_at	RPL4	2.67828E-08	3.08059E-07	0.857260432	-0.428953368	
211666_x_at	RPL3	2.67828E-08	1.90854E-07	0.9722812	-0.440596971	
200814_at	PSME1	2.80502E-08	0.000272302	0.996581247	0.310736438	
200094_s_at	EEF2	3.0418E-08	2.24843E-05	0.676993566	-0.37012599	
201154_x_at	RPL4	3.06216E-08	2.38122E-07	0.995153496	-0.428958782	
208805_at	PSMA6	3.07928E-08	5.3051E-06	0.996581247	0.334500935	
204533_at	CXCL10	3.13289E-08	0.000169945	0.977971618	0.649918318	
213418_at	HSPA6	3.34632E-08	1.33215E-05	0.916817284	0.645613395	
219590_x_at	DPH5	3.54892E-08	3.39148E-07	0.984183933	-0.56634902	
205992_s_at	IL15	3.65239E-08	5.65213E-06	0.920139527	0.693000634	
211395_x_at	FCGR2C	3.79402E-08	2.64289E-05	0.949368864	0.504597766	
218660_at	DYSF	3.82874E-08	8.90393E-07	0.525380174	0.858852687	
212659_s_at	IL1RN	4.02669E-08	5.84398E-06	0.884660098	0.794747033	
204006_s_at	FCGR3A	4.05855E-08	1.00186E-05	0.926817552	1.139105262	
203595_s_at	IFIT5	4.15916E-08	0.000196146	0.927054575	0.462431585	
218168_s_at	CABC1	4.35065E-08	7.99186E-06	0.712482556	-0.434659676	
213564_x_at	LDHB	4.51081E-08	2.25956E-07	0.997185403	-0.338018026	
221875_x_at	HLA-F	4.51302E-08	6.87174E-05	0.843903188	0.252103695	
207040_s_at	ST13	4.6487E-08	5.74755E-06	0.806943262	-0.317357338	
215963_x_at	RPL3	5.43326E-08	5.22692E-08	0.739399013	-0.54170032	
204204_at	SLC31A2	5.58708E-08	4.86643E-05	0.899088585	0.503456523	
208892_s_at	DUSP6	5.80686E-08	2.25956E-07	0.745326368	0.931549428	
200660_at	S100A11 (includes EG:6282)	6.19255E-08	2.55682E-05	0.884660098	0.780649063	
218253_s_at	LGTM	6.58812E-08	1.4878E-06	0.954990264	-0.390068742	
204232_at	FCER1G	8.70985E-08	2.37802E-05	0.845163449	0.515516462	
213214_x_at	ACTG1	1.10815E-07	1.88018E-06	0.909279827	-0.286450562	
216243_s_at	IL1RN	1.10815E-07	4.71896E-05	0.932963506	0.733657533	
217969_at	C11ORF2	1.27636E-07	1.66268E-06	0.793520318	-0.468285993	
209009_at	ESD	1.62581E-07	3.86107E-05	0.983024519	-0.329837339	
201592_at	EIF3H	1.68399E-07	8.5382E-06	0.66341159	-0.347008103	
200086_s_at	COX4I1	1.7144E-07	1.60503E-06	0.254883603	-0.324425641	
218495_at	UXT	1.74894E-07	4.70865E-07	0.971652444	-0.389750956	
201400_at	PSMB3	1.85558E-07	0.000145002	0.978029446	0.306473442	
207614_s_at	CUL1	2.07029E-07	0.000251413	0.971652444	0.336153832	
221345_at	FFAR2	2.13477E-07	6.27001E-06	0.96226171	1.56455422	
201761_at	MTHFD2	2.40953E-07	7.61713E-05	0.971652444	0.456828545	
210470_x_at	NONO	2.54095E-07	7.97249E-05	0.572703468	-0.297512722	
204205_at	APOBEC3G	2.56556E-07	3.28891E-05	0.570133912	0.538643341	
210146_x_at	LILRB2	2.6892E-07	2.08727E-05	0.806943262	0.634455458	

AFFYMETRIX HG-U133A Probe set ID	IPA-Gene Symbol	FDR Exacerbation versus quiet 30 visit analysis	FDR Exacerbation versus quiet, 22 visit analysis	FDR Follow-up Versus Quiet 22 visit analysis	Average log2 difference exacerbation versus quiet	SEQ ID NO:
208912_s_at	CNP	2.90992E-07	0.001420257	0.97607782	0.346507294	
208717_at	OXA1L	3.17515E-07	5.33164E-06	0.627940295	-0.39144339	
201256_at	COX7A2L	3.48182E-07	1.35286E-06	0.920178258	-0.313875053	
201786_s_at	ADAR	3.61686E-07	0.000160373	0.983540219	0.332746832	
212761_at	TCF7L2	3.91925E-07	0.000507052	0.991516688	0.461601921	
212063_at	CD44	4.13799E-07	1.35286E-06	0.757136645	-0.328548578	
212995_x_at	FAM128B	4.43613E-07	7.62784E-07	0.980673033	-0.4525389	
208771_s_at	LTA4H	4.56734E-07	8.85437E-07	0.818684405	-0.505919359	
219528_s_at	BCL11B	5.16386E-07	5.54335E-06	0.931474938	-0.613739228	
221827_at	RBCK1	5.1805E-07	0.000500307	0.937972084	0.265058447	
201647_s_at	SCARB2	5.5928E-07	6.43719E-05	0.949462591	0.394796339	
209684_at	RIN2	6.1967E-07	4.20656E-05	0.996581247	0.615141074	
210992_x_at	FCGR2C	6.24826E-07	0.000516537	0.933364008	0.540639219	
208959_s_at	TXNDC4	6.27267E-07	8.01708E-06	0.989523303	0.358056192	
208796_s_at	CCNG1	6.30959E-07	0.000137277	0.998249748	-0.356027629	
214042_s_at	RPL22	6.56996E-07	4.9363E-06	0.940129298	-0.408753498	
200030_s_at	SLC25A3	6.59369E-07	6.65459E-05	0.514325032	-0.251827666	
206111_at	RNASE2	6.80154E-07	3.4304E-07	0.103154853	0.900316586	
213166_x_at	FAM128A	7.36947E-07	2.52156E-06	0.972604469	-0.459478297	
48531_at	TNIP2	7.59908E-07	2.64623E-05	0.948066734	0.304570703	
200715_x_at	RPL13A	8.12603E-07	1.679E-05	0.976541414	-0.325439068	
204563_at	SELL	8.35783E-07	9.86081E-06	0.542658561	0.570840007	
218429_s_at	FLJ11286	8.44404E-07	0.000290242	0.542658561	0.422610209	
209593_s_at	TOR1B	8.44404E-07	0.005088536	0.957267847	0.308269962	
218271_s_at	PARL	1.09568E-06	2.93579E-07	0.644078042	-0.358246135	
221475_s_at	RPL15	1.22492E-06	7.99186E-06	0.85740335	-0.426401885	
205819_at	MARCO	1.22492E-06	0.000149568	0.913862795	1.305945932	
204007_at	FCGR3B	1.24312E-06	5.36671E-05	0.460110071	1.328602783	
205170_at	STAT2	1.24744E-06	2.64623E-05	0.896710842	0.625304165	
208540_x_at	S100A11 (includes EG:6282)	1.25006E-06	0.000145182	0.858338088	0.486038424	
213002_at	MARCKS (includes EG:4082)	1.33961E-06	1.91357E-05	0.980673033	0.602740512	
208698_s_at	NONO	1.3502E-06	0.000153504	0.891670708	-0.261819767	
216032_s_at	ERGIC3	1.87633E-06	7.13495E-06	0.611156155	-0.371879627	
208826_x_at	HINT1	1.99657E-06	8.10441E-06	0.824385407	-0.355922859	
218854_at	DSE	2.11257E-06	9.63401E-08	0.741625882	0.834549374	
213988_s_at	SAT1	2.21005E-06	1.12606E-05	0.913332358	0.635144779	
207721_x_at	HINT1	2.4571E-06	6.05064E-05	0.842053841	-0.450360691	
201892_s_at	IMPDH2	2.52815E-06	1.33532E-05	0.504375257	-0.519690211	
218154_at	GSDMDC1	2.55311E-06	0.001157149	0.958976925	0.515052858	
212085_at	SLC25A6	2.55512E-06	2.12978E-05	0.893024231	-0.295997965	
221691_x_at	NPM1 (includes EG:4869)	2.89278E-06	2.76878E-05	0.952102861	-0.547195243	
208819_at	RAB8A	3.01224E-06	0.002328471	0.913292392	0.294688001	

AFFYMETRIX HG-U133A Probe set ID	IPA-Gene Symbol	FDR Exacerbation versus quiet 30 visit analysis	FDR Exacerbation versus quiet, 22 visit analysis	FDR Follow-up Versus Quiet 22 visit analysis	Average log2 difference exacerbation versus quiet	SEQ ID NO:
207697_x_at	LILRB2	3.01224E-06	0.000198214	0.998828056	0.42477032	
201368_at	ZFP36L2	3.49162E-06	0.00385991	0.554763569	-0.339565447	
218599_at	REC8	4.17798E-06	2.51425E-05	0.649255083	0.387711796	
217807_s_at	GLTSCR2	4.57745E-06	2.60872E-05	0.985775064	-0.321527374	
209620_s_at	ABCB7	4.59573E-06	3.71364E-05	0.838839885	-0.49253984	
207713_s_at	RBCK1	5.56529E-06	0.001230539	0.9722812	0.485489106	
207574_s_at	GADD45B	5.64844E-06	2.33291E-05	0.658621166	0.584857315	
200024_at	RPS5	5.74376E-06	2.32942E-05	0.980264971	-0.371099528	
212018_s_at	RSL1D1	5.75524E-06	5.2651E-05	0.852763334	-0.374756011	
211345_x_at	EEF1G	5.87551E-06	2.63616E-05	0.878694832	-0.332288405	
218561_s_at	LYRM4	6.35001E-06	0.000178513	0.927054575	-0.383313694	
209861_s_at	METAP2	6.61524E-06	0.000438021	0.950173591	-0.400293647	
214290_s_at	HIST2H2AA3	6.69398E-06	1.11005E-05	0.570133912	0.545713891	
200823_x_at	RPL29 (includes EG:6159)	7.27556E-06	1.00186E-05	0.959247226	-0.438585583	
221494_x_at	EIF3K	7.52644E-06	1.96128E-05	0.949368864	-0.313036928	
201922_at	TINP1	7.53268E-06	0.000111159	0.993864266	-0.304975325	
217436_x_at	HLA-A	7.54331E-06	0.000811135	0.926350227	0.288688983	
203561_at	FCGR2A	7.58179E-06	0.00140219	0.989523303	0.541054572	
203771_s_at	BLVRA	8.2961E-06	0.014081568	0.997185403	0.40479609	
200678_x_at	GRN	8.45692E-06	0.000536107	0.997185403	0.477018079	
222218_s_at	PILRA	8.80032E-06	0.000475117	0.811796229	0.50513639	
218280_x_at	HIST2H2AA3	9.23142E-06	1.12089E-05	0.504375257	0.537868991	
200661_at	CTSA	9.23142E-06	0.000204583	0.774402907	0.364971499	
219505_at	CECR1	9.40966E-06	0.00042371	0.997185403	0.57028576	
207181_s_at	CASP7	9.80392E-06	0.000222785	0.890400749	0.453533094	
219690_at	TMEM149	9.82898E-06	0.003896087	0.726031892	0.254732155	
206420_at	IGSF6	1.02608E-05	0.00042371	0.884660098	0.741966662	
215262_at	OXNAD1	1.03082E-05	7.9003E-05	0.915759954	-0.779468561	
210592_s_at	SAT1	1.03377E-05	9.85604E-05	0.870341928	0.304373382	
213958_at	CD6	1.19573E-05	0.000206884	0.558360244	-0.546783187	
218773_s_at	MSRB2	1.26553E-05	0.000282964	0.42752641	0.653901617	
214097_at	RPS21	1.27079E-05	2.78036E-05	0.957907274	-0.510530358	
214084_x_at	NCF1	1.30587E-05	0.000589823	0.480845338	0.634088365	
32069_at	N4BP1	1.32096E-05	1.50662E-05	0.83826875	0.548797525	
218919_at	ZFAND1	1.35464E-05	2.78026E-05	0.941532908	-0.440976806	
200962_at	RPL31 (includes EG:6160)	1.38143E-05	0.008278452	0.815013718	-0.228873204	
201217_x_at	RPL3	1.43294E-05	2.23558E-05	0.918228194	-0.365069349	
219938_s_at	PSTPIP2	1.46256E-05	0.000335844	0.603006862	0.50344177	
201369_s_at	ZFP36L2	1.46256E-05	0.007035026	0.745247946	-0.594951593	
211072_x_at	TUBA1B	1.48847E-05	0.000500307	0.957267847	0.287212702	
217752_s_at	CNDP2	1.54096E-05	0.001296308	0.739399013	0.501512566	
216342_x_at	Need to update annotation	1.55326E-05	2.32942E-05	0.706296724	-0.323819243	

AFFYMETRIX HG-U133A Probe set ID	IPA-Gene Symbol	FDR Exacerbation versus quiet 30 visit analysis	FDR Exacerbation versus quiet, 22 visit analysis	FDR Follow-up Versus Quiet 22 visit analysis	Average log2 difference exacerbation versus quiet	SEQ ID NO:
211336_x_at	LILRB1	1.60186E-05	0.001507031	0.922570226	0.447319539	
201433_s_at	PTDSS1	1.66951E-05	0.000199218	0.849443057	-0.298448249	
211284_s_at	GRN	1.74918E-05	0.002054495	0.904036627	0.455123958	
204119_s_at	ADK	1.88846E-05	0.002815734	0.926817552	-0.257696817	
202864_s_at	SP100	1.94278E-05	0.000673806	0.957267847	0.400984735	
201272_at	AKR1B1	1.97498E-05	8.5382E-06	0.824385407	-0.380485363	
220755_s_at	C6ORF48	2.00312E-05	0.006348967	0.813784664	-0.252143599	
200093_s_at	HINT1	2.00617E-05	8.29478E-05	0.927054575	-0.359178969	
216041_x_at	GRN	2.0389E-05	0.001563684	0.957267847	0.497052621	
205896_at	SLC22A4 (includes EG:6583)	2.04806E-05	8.71593E-05	0.964319867	0.478927514	
200063_s_at	NPM1 (includes EG:4869)	2.05577E-05	1.679E-05	0.933418803	-0.380986943	
207104_x_at	LILRB1	2.05577E-05	0.008495265	0.952168804	0.492361467	
209616_s_at	CES1 (includes EG:1066)	2.0569E-05	0.000196146	0.839175678	0.528248527	
200689_x_at	EEF1G	2.0569E-05	4.93084E-05	0.847283605	-0.334904567	
210501_x_at	EIF3K	2.15942E-05	0.000207377	0.976541414	-0.275759712	
216035_x_at	TCF7L2	2.27983E-05	0.016007945	0.937972084	0.356351135	
208918_s_at	NADK	2.35932E-05	0.002522694	0.558360244	0.494520309	
222163_s_at	SPATA5L1	2.35932E-05	0.000290242	0.885856306	0.352402229	
214280_x_at	HNRPA1	2.35932E-05	0.000589823	0.906012249	-0.334912016	
216570_x_at	RPL29 (includes EG:6159)	2.39804E-05	7.1509E-05	0.921230073	-0.446641707	
201033_x_at	RPLP0 (includes EG:6175)	2.39804E-05	5.68087E-05	0.948783771	-0.319753176	
218223_s_at	PLEKHO1	2.41851E-05	0.004700829	0.978184927	0.370133687	
218754_at	NOL9	2.42684E-05	0.001020355	0.722442937	-0.336999354	
219599_at	EIF4B	2.50822E-05	0.000438687	0.958855347	-0.562792124	
202469_s_at	CPSF6	2.51361E-05	5.23645E-05	0.983164326	-0.32609193	
211984_at	CALM1	2.79959E-05	2.98467E-05	0.667944101	-0.359804924	
205269_at	LCP2	2.91093E-05	0.000106144	0.826503176	0.464073202	
217995_at	SQRDL (includes EG:58472)	2.91093E-05	0.008300582	0.862781884	0.28577528	
211073_x_at	RPL3	2.96591E-05	0.000214153	0.959098102	-0.298765595	
213261_at	LBA1	3.11947E-05	0.005806222	0.896710842	0.276333078	
200652_at	SSR2	3.15124E-05	0.000150797	0.749293634	-0.282063207	
209282_at	PRKD2	3.15124E-05	0.002011765	0.967981598	0.343096169	
212313_at	CHMP7	3.15124E-05	0.000708686	0.996387193	-0.398559843	
203538_at	CAMLG	3.28125E-05	0.002274258	0.72033594	-0.258987523	
220942_x_at	C3ORF28	3.28713E-05	0.002357652	0.99162365	-0.318433955	
204959_at	MNDA	3.55057E-05	0.00099468	0.556263799	0.725578329	
220933_s_at	ZCCHC6	3.85292E-05	0.000113929	0.793788265	0.55076101	
212690_at	DDHD2	4.01316E-05	0.000121671	0.845163449	-0.385897611	

AFFYMETRIX HG-U133A Probe set ID	IPA-Gene Symbol	FDR Exacerbation versus quiet 30 visit analysis	FDR Exacerbation versus quiet, 22 visit analysis	FDR Follow-up Versus Quiet 22 visit analysis	Average log2 difference exacerbation versus quiet	SEQ ID NO:
200942_s_at	HSBP1	4.08133E-05	0.000566984	0.777646896	0.366713414	
211967_at	TMEM123	4.08133E-05	0.00123082	0.989523303	0.317676844	
218746_at	TAPBPL	4.15837E-05	0.005350708	0.570133912	0.413987811	
203492_x_at	CEP57	4.2409E-05	0.000535638	0.870852621	-0.325547339	
200008_s_at	GDI2	4.29585E-05	1.61347E-05	0.974685401	-0.375970405	
201422_at	IFI30	4.64093E-05	0.006089172	0.857260432	0.377761352	
117_at	HSPA6	4.91495E-05	0.003228567	0.87331579	0.513120601	
200877_at	CCT4	4.91495E-05	0.000267502	0.9722812	-0.320444714	
218747_s_at	TAPBPL	5.04997E-05	0.005239299	0.820704131	0.411214137	
206881_s_at	LILRA3	5.07001E-05	0.000727893	0.968104648	0.688073893	
203773_x_at	BLVRA	5.14119E-05	0.012307101	0.99162365	0.339155772	
211927_x_at	EEF1G	5.23546E-05	0.000714064	0.803159361	-0.287856256	
204780_s_at	FAS	5.23546E-05	0.000227842	0.971652444	0.488565671	
208856_x_at	RPLP0 (includes EG:6175)	5.27196E-05	3.78677E-05	0.939374883	-0.32035963	
205098_at	CCR1	5.34222E-05	7.90801E-05	0.708968475	0.904349461	
201939_at	PLK2	5.54204E-05	6.94986E-05	0.975695805	-0.991234778	
35254_at	TRAFD1	5.55383E-05	0.012001139	0.706089088	0.275742178	
200826_at	SNRPD2	5.58734E-05	8.96776E-05	0.989523303	-0.352157943	
201924_at	AFF1	5.68138E-05	0.003760437	0.525380174	0.294218003	
201743_at	CD14	5.80196E-05	0.000927887	0.926027044	0.532529524	
202646_s_at	CSDE1	5.85627E-05	0.001267314	0.703685034	-0.267474933	
211955_at	RANBP5	6.19023E-05	0.000269924	0.994302012	-0.361149345	
204745_x_at	MT1G	6.24714E-05	0.000535638	0.99162365	0.482758396	
208965_s_at	IFI16	6.26238E-05	0.00099468	0.921230073	0.685450957	
204187_at	GMPR	6.46454E-05	0.001633158	0.899991236	0.580973366	
218680_x_at	HYPK	6.51351E-05	0.003141727	0.741625882	0.244004498	
215693_x_at	DDX27	6.55698E-05	0.000150797	0.827347393	-0.34011042	
212348_s_at	AOF2	6.56031E-05	0.007108849	0.463553935	-0.257602593	
202592_at	BLOC1S1	6.7862E-05	0.001686828	0.994302012	0.286307236	
208581_x_at	MT1X	7.09165E-05	0.00100511	0.963348318	0.73046362	
212185_x_at	MT2A	7.09565E-05	0.000440646	0.97215811	0.667478886	
208891_at	DUSP6	7.35402E-05	4.45417E-05	0.741625882	0.924214277	
203042_at	LAMP2	7.35402E-05	0.005146761	0.749123103	0.413530001	
208594_x_at	LILRA6	7.42589E-05	0.009107667	0.970304109	0.274201604	
211971_s_at	LRPPRC	7.5771E-05	0.007283007	0.94123881	-0.251164739	
208664_s_at	TTC3	7.63081E-05	0.001537804	0.838371349	-0.769757056	
204493_at	BID	7.77238E-05	0.003938812	0.884660098	0.331998151	
208073_x_at	TTC3	8.21711E-05	0.000149568	0.908091808	-0.300142872	
220299_at	SPATA6	8.28224E-05	0.002267971	0.825527416	-0.337259357	
203416_at	CD53	8.3029E-05	0.000753618	0.776697234	0.337815779	
201324_at	EMP1	8.32129E-05	2.78036E-05	0.932963506	1.028302244	
208804_s_at	SFRS6	8.48247E-05	0.002747678	0.737884754	-0.235945586	
209201_x_at	CXCR4	8.48738E-05	0.009918127	0.554763569	-0.352992299	
218764_at	PRKCH	8.51435E-05	2.78011E-05	0.651124512	-0.509978449	

AFFYMETRIX HG-U133A Probe set ID	IPA-Gene Symbol	FDR Exacerbation versus quiet 30 visit analysis	FDR Exacerbation versus quiet, 22 visit analysis	FDR Follow-up Versus Quiet 22 visit analysis	Average log2 difference exacerbation versus quiet	SEQ ID NO:
212807_s_at	SORT1	8.57713E-05	0.002522694	0.905358421	0.344965524	
203044_at	CHSY1	8.74059E-05	0.000335844	0.906012249	0.465640594	
216037_x_at	TCF7L2	9.17002E-05	0.018088923	0.927054575	0.293147345	
200096_s_at	ATP6V0E1	9.37476E-05	0.00437166	0.808788579	0.328205791	
200663_at	CD63	9.56515E-05	0.000223886	0.85740335	0.328258707	
210176_at	TLR1	9.76332E-05	0.000113929	0.922570226	0.597335658	
212560_at	C11ORF32	9.76332E-05	3.86107E-05	0.957267847	-0.405581852	
222010_at	TCP1	9.81152E-05	0.000773739	0.899088585	-0.308461921	
204683_at	ICAM2	0.000103459	0.003026185	0.725120606	0.384609385	
208072_s_at	DGKD	0.000103459	0.002560028	0.9404858	-0.411104014	
217906_at	KLHDC2	0.000104391	0.007884053	0.837193604	-0.300351283	
201456_s_at	BUB3	0.000105142	0.001148959	0.782350826	-0.417697398	
216841_s_at	SOD2	0.000121579	0.002479609	0.460110071	0.593305775	
202193_at	LIMK2	0.000129311	0.002641311	0.927054575	0.732622819	
208798_x_at	GOLGA8A	0.000130254	0.003361757	0.9845525	-0.36990332	
205270_s_at	LCP2	0.000133398	0.005239299	0.980264971	0.304580978	
215399_s_at	OS-9	0.000135232	0.04826413	0.976541414	0.192838334	
209575_at	IL10RB	0.000136707	0.004491629	0.903665108	0.391467267	
203396_at	PSMA4	0.000139905	0.006264569	0.922570226	0.246413994	
212820_at	DMXL2	0.000141003	0.010230962	0.921230073	0.370167057	
213969_x_at	RPL29 (includes EG:6159)	0.000142041	0.000342023	0.997185403	-0.300406883	
205842_s_at	JAK2	0.000144633	0.004506325	0.93869607	0.462990735	
217989_at	HSD17B11	0.000145778	2.32942E-05	0.951263967	-0.345467249	
207610_s_at	EMR2	0.000150007	0.001371535	0.901541785	0.52062863	
204804_at	TRIM21	0.000151208	0.012126009	0.770211009	0.238585468	
208630_at	HADHA	0.000151208	3.78677E-05	0.932963506	-0.419726556	
204102_s_at	EEF2	0.000153539	0.01306258	0.910685215	-0.237231825	
212039_x_at	RPL3	0.000156078	0.000516537	0.942974617	-0.312659646	
216336_x_at	MT1M	0.000156831	0.001761164	0.808230912	0.515017334	
201947_s_at	CCT2	0.000158973	0.006761486	0.993864266	-0.263439476	
204070_at	RARRES3	0.00016176	0.050940897	0.933418803	0.238144405	
208646_at	RPS14	0.000167286	0.000269924	0.852171473	-0.49321732	
200017_at	RPS27A	0.000167286	0.000106786	0.86861163	-0.389483016	
208638_at	PDIA6	0.000169202	0.022203936	0.921230073	0.216927173	
200000_s_at	PRPF8	0.000173098	0.001316885	0.710647678	-0.301065526	
213101_s_at	ACTR3	0.000173683	0.000126297	0.554763569	0.367744698	
221680_s_at	ETV7	0.000176285	0.008422522	0.809600216	0.422233187	
200811_at	CIRBP	0.000182308	0.000342023	0.576368551	-0.290815817	
214567_s_at	XCL2	0.000191679	6.73554E-05	0.906722412	-0.778832174	
201569_s_at	SAMM50	0.000192531	0.001774795	0.906722412	-0.342912382	
211954_s_at	RANBP5	0.000193131	0.00119833	0.861456705	-0.324324521	
218366_x_at	METT11D1	0.000193131	0.002021656	0.916817284	-0.400617253	
205686_s_at	CD86	0.000193853	0.019468497	0.69202515	0.292707371	
212953_x_at	CALR	0.000196693	0.002853479	0.913292392	0.24789854	

AFFYMETRIX HG-U133A Probe set ID	IPA-Gene Symbol	FDR Exacerbation versus quiet 30 visit analysis	FDR Exacerbation versus quiet, 22 visit analysis	FDR Follow-up Versus Quiet 22 visit analysis	Average log2 difference exacerbation versus quiet	SEQ ID NO:
210644_s_at	LAIR1	0.000197548	0.001737269	0.811796229	0.414456955	
218380_at	NLRP1	0.000197548	0.006418624	0.971652444	-0.237882256	
204961_s_at	NCF1	0.000198079	0.006735956	0.493067373	0.645196061	
201090_x_at	TUBA1B	0.000201993	0.007154623	0.995153496	0.246651583	
211135_x_at	LILRB2	0.000203553	0.005359237	0.82604375	0.604255867	
208763_s_at	TSC22D3	0.000205683	0.011915365	0.721257498	-0.265245905	
207023_x_at	KRT10	0.000220135	0.001523636	0.972604469	-0.282689951	
202524_s_at	SPOCK2	0.000224915	0.003256107	0.493067373	-0.424843553	
208886_at	H1FO	0.000229618	4.32561E-05	0.570133912	0.624500357	
206968_s_at	NFRKB	0.000232267	0.007671535	0.574996104	-0.252565265	
203113_s_at	EEF1D	0.00023918	0.000721381	0.989523303	-0.4416568	
208787_at	MRPL3	0.000240465	0.00093572	0.925734912	-0.36424026	
201653_at	CNIH	0.000249558	0.001369281	0.957267847	-0.371051819	
200941_at	HSBP1	0.00025073	0.000857478	0.653680011	0.336300609	
204089_x_at	MAP3K4	0.000252114	0.025031513	0.460110071	-0.289870986	
214150_x_at	ATP6V0E1	0.00027072	0.020501576	0.806943262	0.23805218	
221985_at	KLHL24	0.00027072	0.046675751	0.824385407	-0.274959819	
201356_at	SF3A1	0.000279263	0.002747678	0.436770009	-0.275540687	
210069_at	CPT1B	0.000285211	0.002170519	0.408299445	0.355909262	
221641_s_at	ACOT9	0.000285211	0.002306028	0.710824574	0.348957648	
215838_at	LILRA5	0.000285211	0.003027785	0.838371349	0.689814945	
221756_at	PIK3IP1	0.000287807	0.010073144	0.717703472	-0.45540524	
201646_at	SCARB2	0.000295746	0.005641363	0.884660098	0.294088056	
204249_s_at	LMO2	0.000299566	0.028108844	0.955997488	0.274672756	
218809_at	PANK2	0.00030108	0.013167345	0.275116383	0.226774944	
219243_at	GIMAP4	0.000302454	0.015295263	0.957267847	0.491082072	
211919_s_at	CXCR4	0.000303358	0.048977002	0.647246593	-0.284135188	
212647_at	RRAS	0.000303358	0.000756774	0.874249756	0.898538883	
205099_s_at	CCR1	0.000303358	0.006752633	0.980264971	0.997306148	
211058_x_at	TUBA1B	0.000305393	0.006761486	0.978991398	0.236121092	
214686_at	ZNF266	0.000319692	0.003137784	0.591222948	-0.347543601	
219049_at	CHGN	0.000336807	0.039771173	0.511801929	-0.284541914	
217868_s_at	METTL9	0.000339692	0.002020053	0.922570226	-0.357567284	
205681_at	BCL2A1	0.000344351	0.003364282	0.968649563	0.609541704	
212406_s_at	PCMTD2	0.000348623	0.001710167	0.998328856	-0.322403539	
211133_x_at	LILRB2	0.000360302	0.009405926	0.908091808	0.446173357	
216559_x_at	HNRPA1	0.000361214	0.000451118	0.97607782	-0.366507064	
200022_at	RPL18	0.000366884	0.000607336	0.942959418	-0.318836404	
216640_s_at	PDIA6	0.000383384	0.008422522	0.907894589	0.263013219	
219371_s_at	KLF2	0.000387198	0.008146602	0.952102861	-0.285987047	
221123_x_at	ZNF395	0.00039184	0.01465184	0.439510344	-0.350035271	
212380_at	KIAA0082	0.000394564	7.82029E-05	0.82604375	0.460014641	
202180_s_at	MVP	0.000394683	0.098664757	0.839137004	0.23899631	
212737_at	GM2A	0.000396843	0.00426447	0.804966785	0.349031287	
213102_at	ACTR3	0.000406755	0.000847512	0.493067373	0.38533818	

AFFYMETRIX HG-U133A Probe set ID	IPA-Gene Symbol	FDR Exacerbation versus quiet 30 visit analysis	FDR Exacerbation versus quiet, 22 visit analysis	FDR Follow-up Versus Quiet 22 visit analysis	Average log2 difference exacerbation versus quiet	SEQ ID NO:
204446_s_at	ALOX5	0.000409964	0.010730062	0.517633091	0.353559732	
214394_x_at	EEF1D	0.000411744	0.000885874	0.852969982	-0.362814581	
218458_at	GMCL1	0.000411744	0.018155896	0.927054575	-0.293518292	
202068_s_at	LDLR	0.000411744	0.000886343	0.976077352	0.563864068	
216945_x_at	PASK	0.000418874	0.040273221	0.926027044	-0.339768876	
203470_s_at	PLEK	0.000427191	0.005442512	0.991325836	0.529418531	
219646_at	FLJ20186	0.000433149	0.002781205	0.645055666	-0.330686962	
201298_s_at	MOBK1B	0.000435123	0.000463884	0.739477563	0.446942833	
218149_s_at	ZNF395	0.000435888	0.017767982	0.39977166	-0.343534668	
215346_at	CD40	0.000444998	0.00482122	0.943566129	0.484897905	
205898_at	CX3CR1	0.000454627	0.021988609	0.888078708	0.747111855	
202833_s_at	SERPINA1	0.000472262	0.024006884	0.811796229	0.348410728	
222217_s_at	SLC27A3	0.000472285	0.00752454	0.9404858	0.420872519	
55692_at	ELMO2	0.00048374	0.001905065	0.968649563	0.367590053	
209304_x_at	GADD45B	0.000490046	0.001112052	0.740342948	0.564383956	
211799_x_at	HLA-C	0.000490046	0.01330827	0.959098102	0.234282769	
212757_s_at	CAMK2G	0.000490046	0.000803479	0.998615467	-0.296177222	
206461_x_at	MT1H	0.000492013	0.001066545	0.980726521	0.737329152	
200803_s_at	TEGT	0.0005025	0.012797193	0.891670708	0.25065271	
217202_s_at	GLUL	0.000503252	0.000493023	0.997185403	0.631358384	
200042_at	C22ORF28	0.00051179	0.082077787	0.711933676	0.182344332	
217794_at	PRR13	0.000513337	0.007100635	0.761083429	0.291184619	
212462_at	Need to update annotation	0.000513337	0.010760912	0.811796229	-0.349376398	
216383_at	HCG 2040224	0.000513337	0.000552261	0.846751596	-0.543196644	
201952_at	ALCAM	0.000513337	0.017218526	0.973104905	-0.257642142	
213646_x_at	TUBA1B	0.000521447	0.009552139	0.939653852	0.242315436	
200810_s_at	CIRBP	0.000521834	0.004276434	0.689887873	-0.280606824	
210425_x_at	GOLGA8B	0.000527301	0.084397141	0.9404858	-0.25737113	
212014_x_at	CD44	0.000537985	0.004518647	0.404804753	-0.386035136	
209933_s_at	CD300A	0.000562336	0.004506325	0.974685401	0.484834372	
218987_at	ATF7IP	0.000575666	0.002021169	0.570133912	-0.337529831	
209835_x_at	CD44	0.000577792	0.001774795	0.233883948	-0.31988032	
212665_at	TIPARP	0.000577792	0.005350708	0.463553935	-0.337663556	
218535_s_at	RIOK2	0.000579363	0.006704494	0.622352164	-0.400136904	
203041_s_at	LAMP2	0.000579363	0.004440578	0.947792157	0.413824286	
204706_at	INPP5E	0.000583831	0.01306258	0.921387833	-0.244364287	
219108_x_at	DDX27	0.000588644	0.004037506	0.893325545	-0.324986959	
210633_x_at	KRT10	0.000591061	0.000516537	0.849563735	-0.415728601	
200666_s_at	DNAJB1	0.000606799	0.01454404	0.621038766	-0.357251555	
212495_at	JMJD2B	0.000606945	0.001458413	0.906722412	-0.450191108	
221483_s_at	ARPP-19	0.000613195	0.009953383	0.511801929	-0.248035301	
200858_s_at	RPS8	0.000613195	0.000327341	0.938509968	-0.369135153	
201576_s_at	GLB1	0.000623374	0.011973966	0.835997143	0.342339064	
216705_s_at	ADA	0.000632586	0.002781205	0.943771576	0.306990949	
211456_x_at	MT1P2	0.000639141	0.001401757	0.997185403	0.744016347	

AFFYMETRIX HG-U133A Probe set ID	IPA-Gene Symbol	FDR Exacerbation versus quiet 30 visit analysis	FDR Exacerbation versus quiet, 22 visit analysis	FDR Follow-up Versus Quiet 22 visit analysis	Average log2 difference exacerbation versus quiet	SEQ ID NO:
214442_s_at	PIAS2	0.000642096	0.011798434	0.006848914	-0.253731909	
200002_at	RPL35	0.00064429	0.001057167	0.980264971	-0.355531622	
221988_at	C19ORF42	0.000656502	0.000174071	0.980754763	-0.523975286	
213503_x_at	ANXA2	0.000659784	0.026353097	0.811796229	0.332837372	
203028_s_at	CYBA	0.000694018	0.006166017	0.676993566	0.331149854	
203410_at	AP3M2	0.000696278	0.038963638	0.806943262	-0.295470157	
200973_s_at	TSPAN3	0.000696278	0.011435535	0.9845525	-0.334248544	
210427_x_at	ANXA2	0.000706529	0.020819979	0.833074897	0.336200928	
200664_s_at	DNAJB1	0.000718995	0.014988565	0.481710884	-0.373826408	
201590_x_at	ANXA2	0.000722606	0.02939767	0.749123103	0.316243552	
218085_at	CHMP5	0.000723341	0.012687139	0.652660658	0.363761991	
211594_s_at	MRPL9	0.000751237	0.007394863	0.740342948	-0.399938201	
203454_s_at	ATOX1	0.00075348	0.039264525	0.994302012	0.38634657	
202644_s_at	TNFAIP3	0.000755493	0.045075126	0.706296724	-0.282282288	
221622_s_at	TMEM126B	0.000755957	0.003952573	0.563830701	0.33832929	
204924_at	TLR2	0.000763579	0.000631869	0.981976319	0.609317622	
218344_s_at	RCOR3	0.000765713	0.0274525	0.826503176	-0.310921835	
200965_s_at	ABLIM1	0.000767558	0.000210718	0.932963506	-0.418271022	
203276_at	LMNB1	0.000767975	0.004082556	0.890400749	0.580225782	
201760_s_at	WSB2	0.000767975	0.023975743	0.994302012	0.248294941	
210225_x_at	LILRB2	0.00076903	0.023630979	0.894898588	0.462366549	
202907_s_at	NBN	0.000769354	0.001521011	0.799693669	0.35193611	
201581_at	TXNDC13	0.000796894	0.00875001	0.83681131	-0.251541541	
213588_x_at	RPL14	0.000821928	0.003026707	0.937972084	-0.293914008	
210385_s_at	ARTS-1	0.000851116	0.076481332	0.739726094	0.263386249	
203471_s_at	PLEK	0.000855203	0.00920277	0.921964349	0.37671753	
211725_s_at	BID	0.000867216	0.013142031	0.717703472	0.316370725	
214315_x_at	CALR	0.000868206	0.037858967	0.892303998	0.260644273	
215001_s_at	GLUL	0.000868206	0.010361012	0.966599128	0.29235252	
219033_at	PARP8	0.000873331	0.018530669	0.804614382	-0.239294084	
202230_s_at	CHERP	0.000874383	0.007871094	0.493067373	-0.317436342	
38241_at	BTN3A3	0.000880045	0.045193355	0.654429654	0.299200503	
221221_s_at	KLHL3 (includes EG:26249)	0.00088145	0.019547173	0.992470596	-0.397613329	
203922_s_at	CYBB	0.000887	0.031820023	0.890400749	0.320794193	
209251_x_at	TUBA1C	0.000887316	0.011718661	0.614354446	0.282059782	
207275_s_at	ACSL1	0.000887316	0.001906965	0.940021472	0.65843976	
207224_s_at	SIGLEC7	0.000891971	0.00920277	0.809600216	0.476452984	
206983_at	CCR6	0.000898256	0.012660545	0.825177207	-0.482482474	
209787_s_at	HMGNA4	0.000898256	0.025538134	0.952168804	0.254826309	
210825_s_at	PEBP1	0.000898256	0.002930074	0.969968852	-0.313529462	
200888_s_at	RPL23	0.000904895	0.001710167	0.985775064	-0.301386866	
201607_at	PWP1	0.000925757	0.001341171	0.993864266	-0.324177277	
202405_at	TIAL1	0.000930351	0.04826413	0.82693078	-0.24098632	
218654_s_at	MRPS33	0.000938023	0.001170572	0.882218308	-0.395220925	

AFFYMETRIX HG-U133A Probe set ID	IPA-Gene Symbol	FDR Exacerbation versus quiet 30 visit analysis	FDR Exacerbation versus quiet, 22 visit analysis	FDR Follow-up Versus Quiet 22 visit analysis	Average log2 difference exacerbation versus quiet	SEQ ID NO:
213241_at	PLXNC1	0.000945389	0.016609627	0.518649529	0.477531003	
210582_s_at	LIMK2	0.000945389	0.010429417	0.980192601	0.536975779	
210113_s_at	NLRP1	0.000949494	0.003695966	0.933418803	-0.332340611	
201172_x_at	ATP6V0E1	0.000962774	0.007953975	0.989523303	0.26719857	
208864_s_at	TXN	0.000967186	0.011435535	0.726166985	0.292113103	
211250_s_at	SH3BP2	0.000970367	0.000635992	0.996581247	0.414609016	
200843_s_at	EPRS	0.000988133	0.003026185	0.649255083	-0.303517149	
203494_s_at	CEP57	0.001009764	0.000516499	0.903665108	-0.354629675	
201241_at	DDX1	0.001013717	0.002084072	0.784412478	-0.414030979	
204019_s_at	SH3YL1	0.001030022	0.003361757	0.574996104	-0.389856408	
209901_x_at	AIF1	0.001030022	0.016164027	0.891454344	0.379496405	
207387_s_at	GK	0.001030022	0.021186181	0.932963506	0.654457685	
200074_s_at	RPL14	0.00103668	0.001703809	0.97793068	-0.329340666	
221666_s_at	PYCARD	0.00105502	0.018530669	0.885856306	0.379709728	
211429_s_at	SERPINA1	0.001065102	0.019119967	0.903665108	0.313891813	
208195_at	TTN	0.001085516	0.014960098	0.997537915	-0.303979146	
217826_s_at	UBE2J1	0.001091763	0.00869776	0.971652444	0.295813149	
216511_s_at	TCF7L2	0.001092487	0.04316627	0.99162365	0.33019635	
202367_at	CUTL1	0.001117484	0.041002541	0.377556356	0.276851206	
218357_s_at	TIMM8B	0.001117484	0.035658714	0.570645923	0.224141838	
202020_s_at	LANCL1	0.001117484	0.010158376	0.68704615	-0.300078637	
218476_at	POMT1	0.001117484	0.003925287	0.989523303	-0.452181221	
210070_s_at	CPT1B	0.001146661	0.003947253	0.892303998	0.306480967	
202414_at	ERCC5	0.001170122	0.004276434	0.969487152	-0.306685713	
200701_at	NPC2	0.001202659	0.032221551	0.655141739	0.216264415	
218298_s_at	C14ORF159	0.00122103	0.010766065	0.525380174	0.468319482	
204998_s_at	ATF5	0.00122103	0.116529465	0.806943262	0.228359114	
208680_at	PRDX1	0.001246093	0.019133444	0.849784409	0.285755256	
212859_x_at	MT1E	0.00125981	0.00428389	0.9404858	0.496034508	
209536_s_at	EHD4	0.001271367	0.000862146	0.602107351	0.500016127	
209733_at	LOC286440	0.001294607	0.005972081	0.66764821	-0.389101037	
201470_at	GSTO1	0.001298045	0.003675484	0.959247226	0.277751923	
204175_at	ZNF593	0.001312859	0.008383113	0.570133912	0.273324989	
211985_s_at	CALM1	0.001332095	0.002522694	0.957267847	-0.32859565	
208944_at	TGFB2	0.001345505	0.028000613	0.920178258	-0.261960571	
208822_s_at	DAP3	0.001354808	0.004585775	0.716959241	-0.294784118	
212285_s_at	AGRN	0.001356035	0.014751333	0.896710842	0.365172385	
219316_s_at	FLVCR2	0.001376113	0.007295947	0.704384868	0.488143001	
213018_at	GATAD1	0.001386955	0.004923299	0.798376788	-0.355469919	
200932_s_at	DCTN2	0.001411155	0.001035731	0.913292392	-0.324444916	
202767_at	ACP2	0.001430865	0.003957353	0.658726886	0.314860329	
203428_s_at	ASF1A	0.001430865	0.013167345	0.909501667	-0.395078596	
212440_at	RY1	0.00143871	0.000380111	0.460110071	-0.414104645	
213534_s_at	PASK	0.001446238	0.041171417	0.755657054	-0.354090552	
202912_at	ADM	0.001457959	0.001675882	0.995153496	0.709207627	

AFFYMETRIX HG-U133A Probe set ID	IPA-Gene Symbol	FDR Exacerbation versus quiet 30 visit analysis	FDR Exacerbation versus quiet, 22 visit analysis	FDR Follow-up Versus Quiet 22 visit analysis	Average log2 difference exacerbation versus quiet	SEQ ID NO:
219439_at	C1GALT1	0.001467726	0.008550305	0.570133912	0.335781258	
203127_s_at	SPTLC2 (includes EG:9517)	0.001467726	0.080807694	0.940578006	0.204545861	
209647_s_at	SOCS5	0.001481468	0.003633372	0.86219885	-0.364123725	
218734_at	NAT11	0.001499671	0.018530669	0.658621166	-0.246005267	
203610_s_at	TRIM38	0.001499671	0.009107667	0.741625882	0.355751974	
217165_x_at	MT1F	0.001582759	0.011718661	0.87331579	0.468426853	
219315_s_at	C16ORF30	0.001584536	0.013085216	0.884660098	-0.257539313	
202910_s_at	CD97	0.001584536	0.005547328	0.931474938	0.356334383	
202250_s_at	WDR42A	0.001623004	0.038995938	0.931474938	-0.265826992	
202122_s_at	M6PRBP1	0.001632577	0.01173034	0.647302266	0.274962463	
219343_at	CDC37L1	0.001640474	0.05270375	0.679835233	-0.338595411	
202832_at	GCC2	0.001640474	0.052684705	0.911573276	-0.283445314	
213095_x_at	AIF1	0.001640474	0.019258047	0.995153496	0.349424159	
204568_at	KIAA0831	0.00165125	0.00948745	0.608791366	-0.31832152	
201326_at	CCT6A	0.001700329	0.020501576	0.626064956	-0.29412661	
205831_at	CD2	0.001700329	0.027031678	0.933615651	-0.286425887	
204793_at	GPRASP1	0.001730888	0.038034197	0.926027044	-0.353562469	
204794_at	DUSP2	0.001744444	0.004369135	0.496888495	-0.474603942	
203642_s_at	COBL1	0.001744444	0.006424855	0.717703472	-0.422705467	
222139_at	KIAA1466	0.001744444	0.007001124	0.957267847	0.550595052	
212206_s_at	H2AFV	0.001752486	0.06884886	0.670488531	-0.242099204	
202179_at	BLMH	0.001807502	0.002599745	0.884660098	-0.670098186	
209305_s_at	GADD45B	0.001808823	0.005641363	0.861984472	0.458240739	
218611_at	IER5	0.001808823	0.038758876	0.867588284	0.266027709	
218999_at	TMEM140	0.001831038	0.032642302	0.745326368	0.299391846	
201237_at	CAPZA2	0.001831038	0.01085208	0.811151638	0.276258879	
200692_s_at	HSPA9	0.001831038	0.011175217	0.952271823	-0.340807584	
209185_s_at	IRS2	0.001844782	0.021416843	0.974685401	-0.336365573	
208885_at	LCP1	0.001847763	0.028151767	0.963348318	0.247481673	
210784_x_at	LILRB2	0.001864354	0.034519224	0.927054575	0.430331821	
213615_at	MBOAT5	0.001867904	0.036924797	0.884660098	-0.256709194	
205321_at	EIF2S3	0.001867904	0.005997244	0.997185403	-0.535802439	
208018_s_at	HCK	0.001906005	0.036087451	0.613727458	0.443368869	
203814_s_at	NQO2	0.001931351	0.019119967	0.658726886	0.482908465	
46665_at	SEMA4C	0.00193228	0.044723957	0.158947458	-0.32734474	
202447_at	DEC1	0.001942864	0.027841001	0.852019395	0.306751151	
218231_at	NAGK	0.001949758	0.048981958	0.670889982	0.330588322	
200648_s_at	GLUL	0.00198354	0.00527049	0.913332358	0.697474204	
213122_at	TSPYL5	0.00198354	0.022687088	0.945676894	-0.277246833	
205126_at	VRK2	0.001984886	0.018685204	0.983352528	0.274539756	
204494_s_at	C15ORF39	0.001988327	0.028151767	0.806943262	0.26199721	
212812_at	SERINC5	0.002021718	0.101514284	0.929312703	-0.2760828	
208893_s_at	DUSP6	0.002036658	0.006319223	0.937164918	1.281497985	
208982_at	PECAM1	0.002048249	0.079270267	0.997185403	0.224737326	

AFFYMETRIX HG-U133A Probe set ID	IPA-Gene Symbol	FDR Exacerbation versus quiet 30 visit analysis	FDR Exacerbation versus quiet, 22 visit analysis	FDR Follow-up Versus Quiet 22 visit analysis	Average log2 difference exacerbation versus quiet	SEQ ID NO:
210949_s_at	EIF3C	0.002067967	0.000975446	0.999684232	-0.360444341	
208816_x_at	ANX2P2	0.002083728	0.007890896	0.83681131	0.323780056	
209751_s_at	TRAPPC2	0.002100409	0.018977796	0.878184512	-0.309223681	
208623_s_at	VIL2	0.002112139	0.017267896	0.82330521	-0.377393449	
204098_at	RBMX2	0.002115591	0.019160876	0.994302012	-0.30492075	
201380_at	CRTAP	0.002180282	0.007726118	0.949315993	-0.304642718	
213607_x_at	NADK	0.002249929	0.038312345	0.827347393	0.377743985	
212578_x_at	RPS17 (includes EG:6218)	0.002249929	0.021857135	0.994302012	-0.252639434	
206687_s_at	PTPN6	0.002295934	0.012698387	0.748460361	0.275839516	
211893_x_at	CD6	0.002328916	0.076173873	0.684438087	-0.42156473	
211048_s_at	PDIA4	0.002374482	0.079390663	0.614354446	0.254948869	
213527_s_at	ZNF688	0.002375008	0.046069362	0.992470596	0.238402052	
216199_s_at	MAP3K4	0.00237884	0.021520834	0.940578006	-0.30913149	
203567_s_at	TRIM38	0.00244585	0.007856926	0.92632367	0.510133358	
212467_at	DNAJC13	0.002463344	0.021954471	0.339878792	0.412169546	
202906_s_at	NBN	0.002463344	0.008603033	0.895350322	0.47762565	
204781_s_at	FAS	0.002463344	0.002374667	0.9546428	0.331757378	
212675_s_at	CEP68	0.002508306	0.061221458	0.976541414	-0.317506099	
208074_s_at	AP2S1	0.002512384	0.025202689	0.906722412	0.243247711	
211900_x_at	CD6	0.002555068	0.099688256	0.627940295	-0.380349746	
210046_s_at	IDH2	0.002558945	0.131639009	0.963348318	0.179725917	
202747_s_at	ITM2A	0.002580928	0.07366103	0.882599341	-0.314112044	
207001_x_at	TSC22D3	0.002612245	0.071884369	0.775565942	-0.423736994	
213274_s_at	CTSB	0.002632035	0.027841001	0.937972084	0.33677359	
201850_at	CAPG	0.002695412	0.018295566	0.708363394	0.381728667	
209207_s_at	SEC22B	0.002713692	0.005415056	0.717703472	0.333034778	
206492_at	FHIT	0.002713692	0.020576696	0.989523303	-0.288495472	
219817_at	C12ORF47	0.002720658	0.007459361	0.970166679	-0.304423811	
214909_s_at	DDAH2	0.002764927	0.024531252	0.964319867	0.27355178	
221757_at	PIK3P1	0.002779628	0.058129054	0.756328383	-0.321192532	
202523_s_at	SPOCK2	0.002783903	0.02715706	0.463523306	-0.34716225	
205382_s_at	CFD	0.002809191	0.102540247	0.87331579	0.268032323	
203413_at	NELL2	0.002818871	0.027815279	0.980673033	-0.379895837	
200766_at	CTSD	0.002839836	0.00340538	0.544104436	0.353066091	
202374_s_at	RAB3GAP2	0.002839836	0.160685179	0.864671393	-0.176697263	
207857_at	LILRA2	0.00284801	0.051395894	0.735106887	0.278419117	
200782_at	ANXA5	0.00284801	0.021627048	0.96226171	0.299232848	
218494_s_at	SLC2A4RG	0.002864755	0.009115983	0.862432274	-0.319185279	
205256_at	ZBTB39	0.002901176	0.002930074	0.677299865	-0.32847357	
219055_at	SRBD1	0.002939152	0.044631413	0.613727458	0.310356543	
205237_at	FCN1	0.002977119	0.026100589	0.92335789	0.316019186	
221011_s_at	LBH	0.002980455	0.026851131	0.903552974	-0.300333828	
208862_s_at	CTNND1	0.003019451	0.090262707	0.090242763	-0.311168415	
218026_at	CCDC56	0.003116567	0.026774511	0.525711859	0.289130576	

AFFYMETRIX HG-U133A Probe set ID	IPA-Gene Symbol	FDR Exacerbation versus quiet 30 visit analysis	FDR Exacerbation versus quiet, 22 visit analysis	FDR Follow-up Versus Quiet 22 visit analysis	Average log2 difference exacerbation versus quiet	SEQ ID NO:
203140_at	BCL6	0.003116567	0.017549829	0.903325227	0.327171653	
217118_s_at	C22ORF9	0.003171274	0.051652279	0.902614556	0.322645076	
209155_s_at	NT5C2	0.003171274	0.137127736	0.915663453	0.207641141	
205129_at	NPM3	0.003189118	0.083885368	0.931474938	-0.201727885	
215051_x_at	AIF1	0.003220648	0.042501273	0.978012719	0.263344748	
202610_s_at	MED14	0.003228283	0.009000926	0.940578006	-0.35183311	
219788_at	PILRA	0.003234559	0.071289231	0.582517878	0.353600361	
213227_at	PGRMC2	0.003249496	0.083818883	0.554763569	-0.276589537	
205568_at	AQP9	0.003318349	0.01209333	0.94466883	0.660912235	
213570_at	EIF4E2	0.003370592	0.006232883	0.400416235	-0.300252785	
209375_at	XPC	0.00337838	0.066025213	0.846591986	-0.266873767	
209906_at	C3AR1	0.003419893	0.002321226	0.933418803	0.819839706	
205633_s_at	ALAS1	0.003421631	0.003633372	0.945733557	0.357107375	
217379_at	Need to update annotation	0.00348547	0.003301103	0.929312703	-0.395568974	
204651_at	NRF1	0.003562633	0.002034121	0.825177207	-0.343940015	
213348_at	CDKN1C	0.00361125	0.359989751	0.339878792	0.17004092	
206335_at	GALNS	0.003616738	0.009972197	0.997185403	0.341076825	
202387_at	BAG1	0.003666577	0.011175217	0.932963506	0.375692854	
211100_x_at	LILRA2	0.003758821	0.046711074	0.937686659	0.295017549	
210212_x_at	MTCP1	0.003770255	0.065330152	0.971652444	-0.242830116	
208919_s_at	NADK	0.003770388	0.015298913	0.815777859	0.443867875	
210119_at	KCNJ15	0.003788475	0.010539381	0.460110071	1.090969266	
215905_s_at	WDR57 (includes EG:9410)	0.003796022	0.034214155	0.946102625	-0.266456759	
201963_at	ACSL1	0.003829226	0.018963938	0.98230595	0.439072522	
220054_at	IL23A	0.003897951	0.081029058	0.706822729	-0.266216156	
209788_s_at	ARTS-1	0.003939996	0.102540247	0.814313307	0.405643872	
219700_at	PLXDC1	0.003939996	0.083844234	0.992470596	-0.26720345	
206631_at	PTGER2	0.003963935	0.025563375	0.937598763	0.365669176	
205068_s_at	ARHGAP26	0.004000498	0.012736339	0.896710842	0.380960494	
209407_s_at	DEAF1	0.004015257	0.053343511	0.903665108	-0.245833031	
217977_at	SEPX1	0.004077343	0.058629219	0.706822729	0.556329571	
215332_s_at	CD8B	0.004103592	0.026501749	0.711933676	-0.494046928	
214112_s_at	CXORF40A	0.004151672	0.253490893	0.803159361	-0.145135989	
209162_s_at	PRPF4	0.004278233	0.003695966	0.689887873	-0.49923349	
206296_x_at	MAP4K1	0.004289789	0.001681474	0.903665108	-0.74579783	
212696_s_at	RNF4	0.004309434	0.02939767	0.652902586	-0.376513628	
212669_at	CAMK2G	0.004309434	0.046716858	0.913332358	-0.266009209	
212068_s_at	KIAA0515	0.004343314	0.035073983	0.777646896	-0.501169346	
209357_at	CITED2	0.004351868	0.018723142	0.893518013	-0.387064354	
205329_s_at	SNX4	0.004376197	0.037305878	0.828414098	-0.25956829	
205599_at	TRAF1	0.004377463	0.071289231	0.855380438	-0.261039405	
219053_s_at	VPS37C	0.004423914	0.001959571	0.92335789	0.37798312	
218432_at	FBXO3	0.004423914	0.024609768	0.957288918	-0.361399133	
211750_x_at	TUBA1C	0.004450762	0.032221551	0.576624724	0.272705076	

AFFYMETRIX HG-U133A Probe set ID	IPA-Gene Symbol	FDR Exacerbation versus quiet 30 visit analysis	FDR Exacerbation versus quiet, 22 visit analysis	FDR Follow-up Versus Quiet 22 visit analysis	Average log2 difference exacerbation versus quiet	SEQ ID NO:
204992_s_at	PFN2	0.004534971	0.04006978	0.823670503	-0.251134207	
218315_s_at	CDK5RAP1	0.004605511	0.017641904	0.570645923	-0.291155276	
216274_s_at	SEC11A	0.004605511	0.000949277	0.825177207	-0.378159692	
209422_at	PHF20	0.004605511	0.017998525	0.935442363	-0.385257882	
36829_at	PER1	0.004625639	0.194358982	0.591499146	-0.236059027	
38340_at	HIP1R	0.004625681	0.048615893	0.899088585	-0.285830801	
212178_s_at	POM121	0.004729829	0.045193355	0.174921132	-0.250353794	
212602_at	WDFY3	0.004735822	0.022252697	0.8856292	0.475289863	
214219_x_at	MAP4K1	0.00474476	0.001157259	0.937164918	-0.954745175	
209177_at	C3ORF60	0.004748968	0.093442772	0.504375257	0.269283722	
211596_s_at	LRIG1	0.004762462	0.052606873	0.710647678	-0.306502009	
218329_at	PRDM4	0.004765228	0.025023243	0.557396992	-0.288865493	
202332_at	CSNK1E	0.004778822	0.056814203	0.906012249	-0.318476663	
221769_at	SPSB3	0.004874618	0.000873824	0.989523303	-0.473608464	
211210_x_at	SH2D1A (includes EG:4068)	0.004944449	0.050940897	0.947459717	-0.328965475	
218346_s_at	SESN1	0.004968862	0.182658265	0.982927437	-0.1925237	
206126_at	BLR1	0.004993954	0.10315335	0.932963506	-0.392408445	
203341_at	CEBPZ	0.005031823	0.021988609	0.800382255	-0.382726185	
209803_s_at	PHLDA2	0.005038526	0.040009654	0.896257222	0.485277576	
217823_s_at	UBE2J1	0.005109744	0.032982357	0.438252502	0.307047069	
209448_at	HTATIP2	0.005147167	0.039224073	0.557025701	0.391415598	
221484_at	B4GALT5	0.005160466	0.000422525	0.970304109	0.576135181	
203593_at	CD2AP	0.005170123	0.044631413	0.793788265	0.380848049	
219183_s_at	PSCD4	0.005170123	0.024712694	0.837193604	0.278800417	
208754_s_at	NAP1L1	0.005174786	0.008597407	0.504375257	-0.327955166	
210836_x_at	PDE4D	0.005177082	0.054963257	0.944102219	-0.278719955	
213497_at	ABTB2	0.005198329	0.080653538	0.983164326	0.273717046	
202703_at	DUSP11	0.005242435	0.018496832	0.542658561	-0.267153293	
202981_x_at	SIAH1	0.005244418	0.030827921	0.807579104	-0.329243885	
206877_at	MXD1	0.005244418	0.027139794	0.989523303	0.420763274	
201386_s_at	DHX15	0.005265833	0.100367382	0.594216566	-0.214370956	
208760_at	UBE2I	0.005299734	0.040716879	0.932963506	-0.248417224	
210031_at	CD247	0.005306398	0.009376411	0.376725352	-0.393876014	
218927_s_at	CHST12	0.005343153	0.05488334	0.933809558	0.409880547	
212658_at	LHFPL2	0.005343153	1.12606E-05	0.966121414	0.481980455	
201897_s_at	CKS1B	0.005355825	0.029128323	0.552322903	0.268726061	
210190_at	STX11	0.005358298	0.076481332	0.807579104	0.339889768	
204404_at	SLC12A2	0.005395374	0.026529648	0.833458294	-0.278528948	
212510_at	GPD1L	0.005395374	0.001992216	0.974685401	-0.548493813	
205312_at	SPI1	0.005444162	0.011756501	0.952168804	0.465937265	
213848_at	Need to update annotation	0.005469295	0.03290968	0.906012249	0.289533766	
211665_s_at	SOS2	0.005639289	0.080720349	0.62004893	-0.223059239	
208981_at	PECAM1	0.005654459	0.14859908	0.9404858	0.195110953	
202206_at	ARL4C	0.005746516	0.13182953	0.089058602	-0.242175972	

AFFYMETRIX HG-U133A Probe set ID	IPA-Gene Symbol	FDR Exacerbation versus quiet 30 visit analysis	FDR Exacerbation versus quiet, 22 visit analysis	FDR Follow-up Versus Quiet 22 visit analysis	Average log2 difference exacerbation versus quiet	SEQ ID NO:
204346_s_at	RASSF1	0.005746516	0.00567005	0.679835233	-0.316787126	
212218_s_at	FASN	0.005782194	0.032829207	0.654429654	-0.271838734	
210948_s_at	LEF1	0.005850693	0.053343511	0.848214323	-0.323253165	
203665_at	HMOX1	0.005926028	0.006435669	0.558360244	0.501438949	
207677_s_at	NCF4	0.005990637	0.04118555	0.518206857	0.444466999	
210423_s_at	SLC11A1	0.006072736	0.005255478	0.978029446	0.461627396	
218878_s_at	SIRT1	0.006099797	0.048486242	0.711933676	-0.252398797	
209782_s_at	DBP	0.006100528	0.002478215	0.926817552	-0.492805369	
206976_s_at	HSPH1	0.006112857	0.053406191	0.83948366	-0.386970539	
201367_s_at	ZFP36L2	0.006168213	0.200691332	0.99162365	-0.53621983	
209682_at	CBLB	0.006171548	0.014751333	0.480690341	-0.365162018	
210139_s_at	PMP22	0.006171548	0.053657896	0.558786143	-0.648429059	
221742_at	CUGBP1	0.006171548	0.229039457	0.906722412	-0.234867174	
205821_at	KLRK1	0.006240933	0.005483071	0.932963506	-0.365286687	
211806_s_at	KCNJ15	0.006269218	0.042359673	0.711933676	0.353421684	
204158_s_at	TCIRG1	0.00630195	0.024128392	0.843903188	0.283716907	
217987_at	ASNSD1	0.006347825	0.043738517	0.724798293	-0.247609028	
220175_s_at	CBWD5	0.006472153	0.262405096	0.824385407	0.23079063	
217914_at	TPCN1	0.006507875	0.020195013	0.911573276	-0.302077637	
220066_at	NOD2	0.006560891	0.014162131	0.844024603	0.414790172	
218312_s_at	ZSCAN18	0.006645837	0.037558025	0.793788265	-0.249159845	
201477_s_at	RRM1	0.006657771	0.152929649	0.925560488	-0.197192664	
205239_at	AREG	0.006662718	0.137330159	0.793788265	-0.561714888	
201529_s_at	RPA1	0.006677051	0.005239299	0.939374883	-0.319790627	
204550_x_at	GSTM1	0.00668529	0.006539863	0.519363959	-0.306251806	
210754_s_at	LYN	0.006743374	0.102540247	0.712482556	0.233277739	
214157_at	GNAS	0.006783131	0.180486724	0.937236314	-0.193755563	
202232_s_at	EIF3M	0.006851658	0.007992314	0.915587288	-0.350202481	
203640_at	MBNL2	0.006862456	0.025241455	0.973104905	-0.375480454	
200646_s_at	NUCB1	0.006865251	0.044355722	0.846488521	0.289261951	
210660_at	LILRA1	0.006865251	0.152193981	0.904447339	0.342439177	
208926_at	NEU1	0.006936416	0.01609353	0.660094786	0.309506084	
220370_s_at	USP36	0.006946096	0.036211188	0.558360244	-0.434914018	
202207_at	ARL4C	0.007130826	0.08975223	0.281969259	-0.211644383	
212706_at	RASA4	0.007130826	0.00204532	0.873092938	-0.340570127	
205049_s_at	CD79A	0.007212892	0.035658714	0.85740335	-0.327567934	
209240_at	OGT	0.007263415	0.015292598	0.838371349	-0.319554053	
219374_s_at	ALG9	0.007273424	0.090701484	0.462774646	-0.245867392	
212914_at	CBX7	0.007273424	0.124767142	0.705393437	-0.212077587	
201635_s_at	FXR1	0.007287471	0.062042268	0.926350227	-0.325358861	
207079_s_at	MED6	0.007339646	0.037804294	0.587867787	-0.343744921	
209602_s_at	GATA3	0.007371787	0.008525014	0.838839885	-0.495283623	
212589_at	SCP2	0.007495618	0.175147105	0.97607782	-0.315811594	
205353_s_at	PEBP1	0.007518218	0.015956229	0.926966603	-0.311886694	
215719_x_at	FAS	0.007558593	0.008422522	0.938509968	0.457875965	

AFFYMETRIX HG-U133A Probe set ID	IPA-Gene Symbol	FDR Exacerbation versus quiet 30 visit analysis	FDR Exacerbation versus quiet, 22 visit analysis	FDR Follow-up Versus Quiet 22 visit analysis	Average log2 difference exacerbation versus quiet	SEQ ID NO:
218017_s_at	HGSNAT	0.00756576	0.039403383	0.838839885	-0.370381753	
207005_s_at	BCL2	0.00760915	0.126644969	0.8856292	-0.251095968	
211339_s_at	ITK	0.00770117	0.127563619	0.845553812	-0.230103899	
210264_at	GPR35	0.00775976	0.002887818	0.82604375	0.36415151	
211530_x_at	HLA-G	0.00780468	0.039928129	0.906722412	0.347381355	
203182_s_at	SRPK2	0.007822228	0.007725788	0.824385407	-0.319818652	
202085_at	TJP2	0.007894163	0.019684146	0.968262217	0.367585114	
219806_s_at	C11ORF75	0.007934301	0.13556187	0.87331579	0.326283676	
209501_at	CDR2	0.007957413	0.073840644	0.971652444	-0.259508834	
212319_at	RUTBC1	0.007967542	0.039008412	0.570133912	-0.262148486	
201360_at	CST3	0.007967542	0.071289231	0.77858286	0.283221018	
221206_at	PMS2	0.007994284	0.014642114	0.753411615	-0.386445278	
208622_s_at	VIL2	0.008035758	0.178519882	0.518649529	-0.280919204	
206978_at	CCR2	0.008035758	0.057311059	0.792060926	0.303512327	
211744_s_at	CD58	0.008081567	0.007582799	0.906012249	0.431050257	
207723_s_at	KLRC3	0.008091871	0.00099468	0.749123103	-0.519195904	
212851_at	DCUN1D4	0.008222755	0.101868562	0.879699508	-0.218403278	
202988_s_at	RGS1	0.008232385	0.011435535	0.793788265	-0.815780929	
204769_s_at	TAP2	0.008273972	0.026353097	0.939653852	0.276805843	
211366_x_at	CASP1	0.008295672	0.182714573	0.725581316	0.218033461	
209476_at	TXNDC1	0.008307494	0.106919075	0.676993566	0.225606616	
213017_at	ABHD3	0.008358718	0.023223945	0.460110071	0.475746215	
200649_at	NUCB1	0.008407797	0.057311059	0.684376681	0.309553242	
221558_s_at	LEF1	0.008470173	0.022687088	0.927054575	-0.287620386	
204749_at	NAP1L3	0.008529966	0.017767982	0.765886782	-0.364788658	
204951_at	RHOH	0.008749703	0.125931231	0.801876388	-0.252265007	
202838_at	FUCA1	0.008837332	0.112301886	0.460110071	0.209117006	
203725_at	GADD45A	0.009040951	0.217913452	0.686191702	-0.225484265	
209569_x_at	D4S234E	0.009092541	0.017130768	0.983729727	-0.322718467	
209555_s_at	CD36	0.009208966	0.089960889	0.706296724	0.395342739	
207008_at	IL8RB	0.009246353	0.036211188	0.576624724	0.71152798	
202589_at	TYMS	0.009284264	0.080653538	0.014796277	0.384958451	
207270_x_at	CD300C	0.009349473	0.023705752	0.844024603	0.38303717	
207540_s_at	SYK	0.009362913	0.080653538	0.493618819	0.715540031	
203068_at	KLHL21	0.009415367	0.018151619	0.314342283	-0.616327633	
214366_s_at	ALOX5	0.00945614	0.047352479	0.726031892	0.327830344	
218718_at	PDGFC	0.009582838	0.02613039	0.717703472	-0.32514312	
206472_s_at	TLE3	0.009602301	0.022004396	0.81186408	0.381170905	
208190_s_at	LSR	0.009612752	0.177315023	0.970304109	-0.476797951	
201690_s_at	TPD52	0.009659332	0.023223945	0.242802241	-0.321170027	
203505_at	ABCA1	0.009659332	0.003633372	0.940578006	0.778682584	
217234_s_at	VIL2	0.009779784	0.099668492	0.686973252	-0.329869246	
209970_x_at	CASP1	0.0098609	0.204521053	0.613727458	0.214014925	
204957_at	ORC5L	0.009879341	0.059327291	0.937261364	-0.26845207	
213357_at	GTF2H5	0.010110733	0.041397161	0.086816858	0.3978722	

AFFYMETRIX HG-U133A Probe set ID	IPA-Gene Symbol	FDR Exacerbation versus quiet 30 visit analysis	FDR Exacerbation versus quiet, 22 visit analysis	FDR Follow-up Versus Quiet 22 visit analysis	Average log2 difference exacerbation versus quiet	SEQ ID NO:
201879_at	ARIH1	0.010263909	0.35973853	0.480690341	-0.139471305	
211138_s_at	KMO	0.010276714	0.088723342	0.809600216	0.290804418	
212439_at	IHPK1	0.010525524	0.127493222	0.677299865	-0.275597596	
214438_at	HLX	0.010594965	0.04826413	0.970304109	0.2904212	
214039_s_at	LAPTM4B	0.010716792	0.028151767	0.924278945	-0.287201922	
218636_s_at	MAN1B1	0.010849901	0.325367749	0.996248165	-0.242056143	
209369_at	ANXA3	0.010875364	0.032995797	0.01525423	0.640563446	
201749_at	ECE1	0.011154306	0.005050996	0.861456705	0.403999243	
202393_s_at	KLF10	0.011226627	0.084689941	0.922862728	0.303796756	
213278_at	MTMR9	0.011228946	0.023880247	0.793788265	-0.287287315	
204294_at	AMT (includes EG:275)	0.011246251	0.106919075	0.884660098	-0.218131032	
220086_at	IKZF5	0.011526475	0.12360589	0.671515228	-0.22770966	
215731_s_at	MPHOSPH9	0.011630638	0.00529338	0.867793855	-0.704486948	
204562_at	IRF4	0.011634495	0.088670705	0.454165885	-0.253054268	
203723_at	ITPKB	0.011634495	0.071289231	0.853800604	-0.340859709	
217957_at	C16ORF80	0.011680989	0.176732619	0.745247946	-0.306153713	
212447_at	KBTBD2	0.011756298	0.047553128	0.757749921	-0.261216593	
211991_s_at	HLA-DPA1	0.011756298	0.371927664	0.947786651	0.142001843	
204622_x_at	NR4A2	0.011798072	0.051467095	0.721821849	-0.408511875	
221826_at	ANGEL2	0.012244732	0.143126266	0.846591986	-0.229164026	
201301_s_at	ANXA4	0.012247414	0.049001016	0.570133912	0.858211651	
204336_s_at	RGS19	0.01228945	0.190075069	0.906722412	0.191451565	
213539_at	CD3D	0.012364628	0.006230433	0.937164918	-0.337874427	
213672_at	MARS (includes EG:4141)	0.012445306	0.038312345	0.850755602	-0.431723776	
210766_s_at	CSE1L	0.012544794	0.079390663	0.906012249	-0.253562708	
208890_s_at	PLXNB2	0.012572426	0.42023393	0.600791844	0.157960485	
211883_x_at	CEACAM1	0.012603414	0.060483745	0.54126922	0.312243791	
208880_s_at	PRPF6	0.012603414	0.016609627	0.921230073	-0.407193108	
213145_at	FBXL14	0.012736544	0.015214306	0.643328545	-0.300748427	
207419_s_at	RAC2	0.012755037	0.100111799	0.554763569	0.272077943	
215210_s_at	DLST	0.012789654	0.182456166	0.770047411	-0.221021784	
209773_s_at	RRM2	0.012867343	0.120778597	0.403965698	0.30763863	
206255_at	BLK	0.012961723	0.163040248	0.570133912	-0.43735596	
212346_s_at	MXD4	0.01304429	0.191875661	0.504375257	-0.227045717	
210818_s_at	BACH1	0.013249311	0.005483071	0.77678859	0.340649029	
202100_at	RALB	0.013424653	0.13940172	0.717703472	0.270826629	
221920_s_at	SLC25A37	0.013424653	0.039008412	0.825177207	0.499252449	
209845_at	MKRN1	0.013424653	0.055782899	0.970304109	0.37410074	
221569_at	AHI1	0.013470953	0.137381622	0.903665108	-0.202496009	
222026_at	RBM3	0.01350236	0.007642761	0.570133912	-0.450979832	
214455_at	HIST1H2BC	0.013533356	0.035658714	0.262239522	0.564730366	
202426_s_at	RXRA	0.013568315	0.058293142	0.554763569	0.330293309	
219089_s_at	ZNF576	0.013634698	0.081784947	0.878689864	-0.228182027	
201302_at	ANXA4	0.013697532	0.08084446	0.422140415	0.40111778	

AFFYMETRIX HG-U133A Probe set ID	IPA-Gene Symbol	FDR Exacerbation versus quiet 30 visit analysis	FDR Exacerbation versus quiet, 22 visit analysis	FDR Follow-up Versus Quiet 22 visit analysis	Average log2 difference exacerbation versus quiet	SEQ ID NO:
218645_at	ZNF277P	0.01375991	0.009000926	0.932963506	-0.332320974	
203678_at	MTMR15	0.014018481	0.014288107	0.809600216	-0.418966858	
208744_x_at	HSPH1	0.014027881	0.247709375	0.927054575	-0.435330989	
217967_s_at	FAM129A	0.014091343	0.346939576	0.82604375	0.214696528	
213204_at	PARC	0.014314457	0.126756122	0.884660098	-0.359478603	
207568_at	CHRNA6	0.01431841	0.010429417	0.830719817	-0.325429211	
209930_s_at	NFE2	0.01441225	0.034636644	0.891670708	0.400069337	
210224_at	MR1	0.014421369	0.20627165	0.649409254	0.218885928	
212231_at	FBXO21	0.014440182	0.108656399	0.567915232	-0.232315789	
214326_x_at	JUND	0.014553654	0.236385207	0.891953978	-0.251108764	
206118_at	STAT4	0.01470608	0.049001016	0.689229599	-0.266212673	
222115_x_at	N-PAC	0.014716395	0.051170918	0.819456917	-0.310590511	
213674_x_at	IGHD	0.014911014	0.039938777	0.695073101	-0.501844766	
219777_at	GIMAP6	0.015043577	0.144407805	0.570133912	0.326848663	
221601_s_at	FAIM3	0.015047614	0.027336598	0.885856306	-0.305777039	
209118_s_at	TUBA1A	0.015056809	0.128749695	0.962540421	0.233704948	
201695_s_at	NP	0.015304243	7.1509E-05	0.978029446	0.504320958	
214945_at	LOC202134	0.015493442	0.232239839	0.885856306	-0.237166546	
210629_x_at	LST1	0.015774191	0.183606534	0.906722412	0.197284912	
212569_at	SMCHD1	0.015774191	0.087852473	0.940595209	0.30797767	
205822_s_at	HMGCS1	0.015852397	0.059327291	0.997185403	-0.304518474	
209567_at	RRS1	0.015886509	0.083999076	0.980264971	-0.348378346	
219534_x_at	CDKN1C	0.015943545	0.463007545	0.866775981	0.200589944	
218309_at	CAMK2N1	0.015984508	0.009605583	0.320340002	-0.400982962	
201566_x_at	ID2	0.016142401	0.057909009	0.922875053	0.359282319	
201701_s_at	PGRMC2	0.016207876	0.02715706	0.902614556	-0.38800159	
205997_at	ADAM28	0.016219595	0.251515075	0.885856306	-0.255301646	
202201_at	BLVRB	0.016264535	0.040866126	0.90587437	0.387417159	
213839_at	KIAA0500	0.01628162	0.039648402	0.905763968	-0.396441068	
206011_at	CASP1	0.016827593	0.12414678	0.60494547	0.286452892	
221748_s_at	TNS1	0.016871581	0.017998525	0.973546798	0.488992364	
208621_s_at	VIL2	0.016908109	0.078950734	0.631444377	-0.34500341	
211367_s_at	CASP1	0.016963127	0.346529064	0.717703472	0.220770374	
202595_s_at	LEPROTL1	0.017055141	0.134342766	0.584976844	-0.246822942	
218517_at	PHF17	0.01729529	0.126277973	0.853800604	-0.229045499	
211902_x_at	TRA@	0.017446858	0.022184928	0.865251659	-0.380605249	
204860_s_at	NAIP	0.017450484	0.136220241	0.824328734	0.302867609	
211963_s_at	ARPC5	0.01776995	0.098966874	0.652902586	0.249707545	
213353_at	ABCA5	0.01776995	0.158870096	0.884660098	-0.23474082	
210116_at	SH2D1A (includes EG:4068)	0.01776995	0.065442642	0.936853005	-0.33592137	
222251_s_at	GMEB2	0.017802241	0.102730031	0.376725352	-0.234073959	
202626_s_at	LYN	0.017816929	0.211441079	0.552322903	0.195225713	
202943_s_at	NAGA	0.018177789	0.186012025	0.981360886	0.206473896	
203923_s_at	CYBB	0.018351402	0.168111748	0.552322903	0.303131083	

AFFYMETRIX HG-U133A Probe set ID	IPA-Gene Symbol	FDR Exacerbation versus quiet 30 visit analysis	FDR Exacerbation versus quiet, 22 visit analysis	FDR Follow-up Versus Quiet 22 visit analysis	Average log2 difference exacerbation versus quiet	SEQ ID NO:
207075_at	NLRP3	0.018351402	0.013167345	0.915663453	0.591472979	
214744_s_at	RPL23	0.018351402	0.011123203	0.992169204	-0.334250799	
205745_x_at	ADAM17	0.018388943	0.005935136	0.827347393	0.374950593	
221485_at	B4GALT5	0.018388943	0.005379129	0.932963506	0.555017947	
201487_at	CTSC	0.018628959	0.151874357	0.943771576	0.249401114	
221653_x_at	APOL2	0.018694504	0.169194339	0.629434643	0.504841584	
212769_at	TLE3	0.01897878	0.039008412	0.846488521	0.342859284	
218130_at	C17ORF62	0.019043437	0.133051813	0.893435169	0.472265875	
206214_at	PLA2G7	0.019147471	0.442198685	0.803159361	0.190235824	
215786_at	RSF1	0.019151091	0.49890241	0.899991236	-0.188609275	
210792_x_at	SIVA1	0.019180223	0.070955978	0.45663747	-0.258975831	
203751_x_at	JUND	0.019180223	0.297742427	0.680969676	-0.210364435	
216942_s_at	CD58	0.019188421	0.042713549	0.940468793	0.361798864	
205173_x_at	CD58	0.019311744	0.032221551	0.907359477	0.412717957	
202104_s_at	SPG7	0.019426762	0.187298695	0.933418803	-0.229675114	
207490_at	TUBA4	0.019451966	0.128275331	0.864671393	0.236332987	
222315_at	Need to update annotation	0.019489922	0.004351803	0.845163449	-0.65783036	
210356_x_at	MS4A1	0.019789714	0.087296713	0.636658025	-0.363890781	
204655_at	CCL5	0.01983136	0.002547452	0.940129298	-0.435049716	
211560_s_at	ALAS2	0.01989019	0.026441636	0.980673033	0.946356737	
205292_s_at	HNRPA2B1	0.019939501	0.159812536	0.404804753	0.256446785	
203845_at	PCAF	0.020259923	0.067897502	0.775176914	0.269051192	
218522_s_at	MAP1S	0.020393984	0.013344213	0.613727458	0.328985626	
201780_s_at	RNF13	0.020532722	0.102540247	0.86194884	0.274624257	
221234_s_at	BACH2	0.020667873	0.062697542	0.923176795	-0.267014013	
203313_s_at	TGIF1	0.020895853	0.366896505	0.668753123	-0.165433985	
211101_x_at	LILRA2	0.020895853	0.10139137	0.996581247	0.250662434	
204821_at	BTN3A3	0.021021782	0.362114581	0.811510087	0.214935123	
210895_s_at	CD86	0.021148346	0.109013424	0.634508876	0.25389383	
202284_s_at	CDKN1A	0.02176265	0.108969489	0.436770009	0.264668049	
205987_at	CD1C	0.02176265	0.078348501	0.800382255	-0.503826416	
213475_s_at	ITGAL	0.02176265	0.53362722	0.808230912	0.124232857	
203092_at	TIMM44	0.02176265	0.223418785	0.859477285	-0.349971753	
217142_at	Need to update annotation	0.022030272	0.006421353	0.804966785	-0.614240987	
36564_at	IBRDC3	0.022043675	0.042251555	0.985411674	0.318898723	
214992_s_at	DNASE2	0.0221327	0.244921515	0.710824574	0.192600667	
207686_s_at	CASP8	0.022251637	0.293295305	0.761190158	-0.216609555	
217418_x_at	MS4A1	0.022292129	0.102810003	0.689284686	-0.381015062	
203535_at	S100A9	0.022328545	0.081536361	0.543044503	0.276794159	
218153_at	CARS2	0.022470077	0.368914376	0.646290307	0.150673741	
204445_s_at	ALOX5	0.022497073	0.160127618	0.542658561	0.224758249	
208782_at	FSTL1	0.022858433	0.174757062	0.983352528	-0.228315866	
216609_at	TXN	0.023172694	0.099122148	0.741144916	0.354826262	
210379_s_at	TLK1	0.023300636	0.044336207	0.93197518	-0.678196701	

AFFYMETRIX HG-U133A Probe set ID	IPA-Gene Symbol	FDR Exacerbation versus quiet 30 visit analysis	FDR Exacerbation versus quiet, 22 visit analysis	FDR Follow-up Versus Quiet 22 visit analysis	Average log2 difference exacerbation versus quiet	SEQ ID NO:
221210_s_at	NPL	0.023711476	0.082081555	0.654429654	0.429266523	
204168_at	MGST2	0.023788349	0.030439266	0.854833543	-0.379724773	
214790_at	SENP6	0.024264859	0.074582758	0.710647678	-0.2848028	
205639_at	AOAH	0.024264859	0.152121537	0.884660098	0.238715067	
209066_x_at	UQCRB (includes EG:7381)	0.024355364	0.051844029	0.994302012	-0.34577675	
201560_at	CLIC4	0.024378822	0.284723127	0.922875053	0.183824393	
209344_at	TPM4	0.024492869	0.018168174	0.954560682	0.35789861	
217580_x_at	ARL6IP2	0.024590772	0.032151111	0.99363955	-0.32492921	
201662_s_at	ACSL3	0.024628161	0.022571085	0.708542801	0.378306535	
218404_at	SNX10	0.024763042	0.173031608	0.613727458	0.257277393	
202789_at	PLCG1	0.024827653	0.08903096	0.927054575	-0.254047489	
210424_s_at	GOLGA8A	0.025087642	0.028000613	0.809600216	-0.426691788	
205715_at	BST1	0.025114072	0.150950206	0.804966785	0.307260943	
202599_s_at	NRIP1	0.025357862	0.019222851	0.966794706	0.486469213	
206765_at	KCNJ2	0.02570662	0.059497978	0.613727458	0.581853261	
201070_x_at	SF3B1	0.026391529	0.294935988	0.995153496	-0.221864528	
214244_s_at	ATP6V0E1	0.026394427	0.063783265	0.741625882	0.329307349	
213183_s_at	CDKN1C	0.026539963	0.274313528	0.726031892	0.226276402	
201348_at	GPX3	0.026686091	0.082081555	0.666831456	-0.365530362	
202861_at	PER1	0.026726313	0.2482877	0.658726886	-0.242651891	
202636_at	RNF103	0.027112829	0.293009431	0.706296724	-0.218783657	
215223_s_at	SOD2	0.027124769	0.100361826	0.927054575	0.329399145	
212894_at	SUPV3L1	0.027172687	0.073524055	0.460110071	-0.268038645	
214148_at	Need to update annotation	0.027444722	0.178491981	0.955997488	-0.212981318	
204520_x_at	BRD1	0.027460368	0.189992666	0.460110071	-0.255287237	
209671_x_at	TRA@	0.027947129	0.150767177	0.857260432	-0.308300427	
216015_s_at	NLRP3	0.028162825	0.086398294	0.633838349	0.436473324	
202746_at	ITM2A	0.028309925	0.232580835	0.980264971	-0.216105082	
214582_at	PDE3B	0.028389236	0.054662177	0.926914122	-0.303819563	
202901_x_at	CTSS	0.029554042	0.413823405	0.885856306	0.187087835	
206130_s_at	ASGR2	0.029889904	0.263030666	0.631444377	0.208922768	
205689_at	PCNXL2 (includes EG:80003)	0.029929092	0.069781211	0.980808943	-0.311434983	
209161_at	PRPF4	0.029963806	0.215112626	0.716868136	-0.206140316	
213370_s_at	SFMBT1	0.030436666	0.111978848	0.944102219	-0.273940987	
204642_at	EDG1	0.030530732	0.109209362	0.863302136	-0.333674522	
209561_at	THBS3	0.0307313	0.25458731	0.996581247	-0.205332375	
203148_s_at	TRIM14	0.03079373	0.15413446	0.493618819	0.369444372	
206700_s_at	JARID1D	0.03079373	0.03290968	0.974320691	-0.510194162	
211368_s_at	CASP1	0.031088222	0.351223201	0.587867787	0.194796989	
206715_at	TFEC	0.031692073	0.182305616	0.878184512	0.262716165	
220386_s_at	EML4	0.032071275	0.240072037	0.703685034	-0.232496456	
218152_at	HMG20A	0.032071275	0.025023243	0.87331579	-0.331804799	

AFFYMETRIX HG-U133A Probe set ID	IPA-Gene Symbol	FDR Exacerbation versus quiet 30 visit analysis	FDR Exacerbation versus quiet, 22 visit analysis	FDR Follow-up Versus Quiet 22 visit analysis	Average log2 difference exacerbation versus quiet	SEQ ID NO:
221428_s_at	TBL1XR1	0.032071275	0.218882785	0.926879061	-0.219118973	
205685_at	CD86	0.03213621	0.133433486	0.766023636	0.288434558	
203081_at	CTNNBIP1	0.032230779	0.070955978	0.955860316	-0.300167763	
215087_at	C15ORF39	0.032462237	0.137330159	0.929077542	0.249938638	
211702_s_at	USP32	0.032740923	0.019939423	0.944102219	0.329211319	
218711_s_at	SDPR	0.032753899	0.082301542	0.83826875	-0.307944714	
218963_s_at	KRT23	0.032909054	0.171437026	0.964140878	0.590754653	
219007_at	NUP43	0.033280508	0.040928464	0.542658561	-0.409889901	
213291_s_at	UBE3A	0.033740756	0.217913452	0.72033594	-0.228700873	
204326_x_at	MT1X	0.033740756	0.073126948	0.916817284	0.297075777	
217739_s_at	PBEF2	0.033740756	0.097661052	0.938509968	0.314295378	
217755_at	HN1	0.034086039	0.318045852	0.904036627	0.182399518	
217985_s_at	BAZ1A	0.03466727	0.206293395	0.83681131	0.546330304	
220939_s_at	DPP8	0.034720358	0.118168782	0.90275246	-0.283309897	
201313_at	ENO2	0.034816907	0.103747652	0.940613622	-0.263537736	
215533_s_at	UBE4B	0.034875223	0.071884369	0.966527259	-0.305565485	
204820_s_at	BTN3A3	0.035010794	0.234492658	0.570645923	0.233894373	
209604_s_at	GATA3	0.035010794	0.189352776	0.773450053	-0.343302452	
216153_x_at	RECK	0.035010794	0.242887888	0.92934451	0.256080351	
202643_s_at	TNFAIP3	0.035347675	0.288366984	0.636658025	-0.218475172	
218592_s_at	CECR5	0.035395293	0.026647711	0.856352566	-0.324706701	
209128_s_at	SART3	0.035427345	0.786783631	0.544104436	-0.060928286	
201297_s_at	MOBK1B	0.035484934	0.191007054	0.613727458	0.235466714	
218918_at	MAN1C1	0.035919274	0.126282967	0.937164918	-0.253876962	
219073_s_at	OSBPL10	0.036604792	0.093148343	0.33827973	-0.342811873	
202481_at	DHRS3	0.036854609	0.244931292	0.915663453	-0.218874569	
221060_s_at	TLR4	0.036961275	0.069577792	0.734889789	0.365264223	
205488_at	GZMA	0.037325756	0.294992587	0.460110071	0.337484953	
218532_s_at	FAM134B	0.037325756	0.226426426	0.690696537	-0.243620882	
202742_s_at	PRKACB	0.03742914	0.092656285	0.496888495	-0.295415741	
221698_s_at	CLEC7A	0.037452387	0.057086696	0.922190084	0.297635075	
204618_s_at	GABPB2	0.037591714	0.381825503	0.896710842	-0.218042909	
210972_x_at	TRA@	0.037637249	0.109209362	0.885856306	-0.286575049	
203046_s_at	TIMELESS	0.03767595	0.11248276	0.840058778	0.32358318	
201921_at	GNG10	0.037687753	0.252397888	0.630710872	0.224649839	
214152_at	CCPG1	0.037744945	0.162408905	0.74501549	0.276041521	
206267_s_at	MATK	0.037846145	0.047433804	0.711933676	-0.31260423	
214091_s_at	GPX3	0.038059023	0.22479257	0.710824574	-0.294139182	
212764_at	Need to update annotation	0.03856123	0.195211631	0.921230073	-0.397047724	
47560_at	LPHN1	0.039036499	0.40178772	0.745384696	-0.164877039	
204148_s_at	ZP3	0.039246736	0.144924218	0.867793855	-0.286257858	
204116_at	IL2RG	0.039543072	0.144407805	0.761190158	0.314711363	
214995_s_at	APOBEC3F	0.039953312	0.239878061	0.710647678	0.271497898	
212533_at	WEE1	0.040140137	0.115441586	0.846591986	-0.427512664	
201930_at	MCM6	0.040202104	0.135773151	0.878689864	-0.303067431	

AFFYMETRIX HG-U133A Probe set ID	IPA-Gene Symbol	FDR Exacerbation versus quiet 30 visit analysis	FDR Exacerbation versus quiet, 22 visit analysis	FDR Follow-up Versus Quiet 22 visit analysis	Average log2 difference exacerbation versus quiet	SEQ ID NO:
204491_at	PDE4D	0.040240856	0.353176062	0.543105461	-0.18749664	
211764_s_at	UBE2D1	0.040536755	0.195360834	0.80941741	0.221343709	
210837_s_at	PDE4D	0.040834283	0.123837945	0.631444377	-0.283111624	
202030_at	BCKDK	0.040834283	0.117548398	0.881158079	0.266327295	
216387_x_at	Need to update annotation	0.040910517	0.024403587	0.970304109	-0.472198243	
200596_s_at	EIF3A	0.041091878	0.076632972	0.998154228	-0.365016425	
202205_at	VASP	0.041506462	0.045384808	0.830933046	0.366499287	
202594_at	LEPROTL1	0.041603383	0.220538122	0.663534687	-0.215771141	
211575_s_at	UBE3A	0.041691347	0.224064374	0.702016627	-0.274002243	
209206_at	SEC22B	0.041816139	0.090689696	0.294369359	0.319067462	
203504_s_at	ABCA1	0.042178608	0.011718661	0.826503176	0.550771084	
213649_at	SFRS7	0.042304017	0.136220241	0.884660098	-0.259117862	
202723_s_at	FOXO1	0.042304017	0.21264104	0.927625491	-0.292781981	
209818_s_at	HABP4	0.042636263	0.33203729	0.945676094	-0.311322134	
208792_s_at	CLU	0.042931149	0.144123259	0.726166985	0.276378538	
216894_x_at	CDKN1C	0.042970438	0.297130477	0.814313307	0.293525643	
204572_s_at	PIN4	0.043371704	0.088869941	0.800734652	-0.294104374	
201909_at	RPS4Y1	0.04363416	0.663971605	0.896681815	-0.100566885	
204411_at	KIF21B	0.043854222	0.07765649	0.570133912	-0.427487501	
212239_at	PIK3R1	0.044194887	0.213451154	0.670488531	-0.287257475	
212484_at	FAM89B	0.044430061	0.06670052	0.852171473	0.344627775	
203542_s_at	KLF9	0.044646893	0.331308769	0.971652444	-0.218842169	
203005_at	LTBR	0.045172875	0.112342861	0.809600216	0.286047045	
203589_s_at	TFDP2	0.045666747	0.66361192	0.658726886	-0.107291109	
212003_at	C1ORF144	0.045996858	0.038203947	0.947479541	0.422374051	
202531_at	IRF1	0.04657947	0.196576193	0.997185403	0.23465268	
205147_x_at	NCF4	0.046735336	0.122418354	0.745384696	0.300343046	
210164_at	GZMB	0.046934401	0.479543269	0.939653852	0.183105831	
216248_s_at	NR4A2	0.047462798	0.123672921	0.708968475	-0.342837018	
201486_at	RCN2	0.047614506	0.189705454	0.980264971	-0.246724101	
41577_at	PPP1R16B	0.047627651	0.212046833	0.63027463	-0.278401921	
214257_s_at	SEC22B	0.048396634	0.17845009	0.281969259	0.247587803	
205019_s_at	VIPR1	0.048510692	0.168196372	0.943771576	-0.241780228	
206934_at	SIRPB1	0.049103457	0.213729478	0.761190158	0.366059397	
212309_at	CLASP2	0.049281475	0.261467089	0.983164326	-0.222347475	
202637_s_at	ICAM1	0.049617325	0.186713735	0.778166718	0.324877483	
201876_at	PON2	0.049717196	0.094257318	0.911573276	-0.285845859	
203408_s_at	SATB1	0.049974155	0.206310608	0.998615467	-0.239211025	

Table 5: Subgroup Y Genes and Metrics

AFFYMETRIX HG-U133A Probe set ID	Gene	FDR Exacer'n v Quiet, N = 64	FDR Exacer'n v Quiet, N = 51	FDR Exacer'n v Follow-up, N = 51	Mean $\Delta \log_2$ Exacer'n v Quiet
205267_at	POU2AF1	6.09889E-06	4.91347E-05	0.989449741	0.506602032
204571_x_at	PIN4	9.20878E-06	0.000269021	0.989449741	0.32332882
202546_at	VAMP8	9.20878E-06	0.000469175	0.989449741	0.271926692
204683_at	ICAM2	1.11155E-05	0.00029751	0.989449741	0.332416528
208680_at	PRDX1	1.11155E-05	0.000390432	0.989449741	0.296295802
213620_s_at	ICAM2	1.23038E-05	0.000307743	0.989449741	0.322945755
203259_s_at	HDDC2	1.56333E-05	0.000169818	0.989449741	0.296766769
200046_at	DAD1	1.78084E-05	0.000469175	0.989449741	0.273165135
201726_at	ELAVL1	1.78084E-05	0.00029751	0.989449741	0.345713605
208818_s_at	COMT	1.8168E-05	0.000725864	0.989449741	0.328690658
206111_at	RNASE2	1.8168E-05	0.000931464	0.989449741	0.445855302
201746_at	TP53	1.8168E-05	0.000228137	0.989449741	0.309465491
218747_s_at	TAPBPL	2.31671E-05	0.000269021	0.989449741	0.377510405
219505_at	CECR1	2.36519E-05	0.000713756	0.989449741	0.398952771
201240_s_at	SPCS2	2.57282E-05	0.000228137	0.989449741	0.470592216
210427_x_at	ANXA2	2.73645E-05	0.000937591	0.989449741	0.328866724
212577_at	SMCHD1	3.31201E-05	0.000689198	0.994302976	-0.319379373
204116_at	IL2RG	3.33315E-05	0.000206001	0.989449741	0.521996243
212827_at	IGHM	3.50226E-05	0.001238391	0.989449741	0.349524739
208858_s_at	FAM62A	3.91712E-05	0.00029751	0.989449741	0.487341826
209374_s_at	IGHM	3.91712E-05	0.001424129	0.989449741	0.360281972
200661_at	CTSA	4.21575E-05	0.001190689	0.989449741	0.233015986
213603_s_at	RAC2	4.21575E-05	0.000269021	0.989449741	0.283090983
203828_s_at	IL32	4.52678E-05	0.000635413	0.989449741	0.760887517
212175_s_at	AK2	4.68725E-05	0.000469175	0.989449741	0.281226543
201590_x_at	ANXA2	5.18784E-05	0.001415219	0.989449741	0.312862095
210644_s_at	LAIR1	5.18784E-05	0.000689198	0.989449741	0.321130978
32209_at	FAM89B	6.26777E-05	0.000760418	0.989449741	0.295826718
213503_x_at	ANXA2	6.47265E-05	0.001632865	0.989449741	0.317729923
216984_x_at	IGL@	7.43565E-05	0.000466147	0.989449741	0.642913797
201302_at	ANXA4	7.73652E-05	0.001190689	0.989449741	0.476997399
202655_at	ARMET	9.26164E-05	0.00048625	0.989449741	0.278663
201897_s_at	CKS1B	9.26164E-05	0.000390432	0.999875537	0.295834243
211645_x_at	0	9.30977E-05	0.001190689	0.989449741	0.465162816
200846_s_at	PPP1CA	9.30977E-05	0.000689198	0.989449741	0.324223639
204279_at	PSMB9	9.30977E-05	0.001922581	0.989449741	0.359917688
200789_at	ECH1	0.000107598	0.001922581	0.989449741	0.250183945
203466_at	MPV17	0.000113201	0.000713756	0.999875537	0.691493338
205488_at	GZMA	0.000120505	0.00029751	0.994317186	0.673401211
218026_at	CCDC56	0.000122403	0.001424129	0.989449741	0.279565664
204839_at	POP5	0.000122403	0.001190689	0.989449741	0.418721294
212569_at	SMCHD1	0.000122403	0.00325328	0.999875537	-0.331795389
218746_at	TAPBPL	0.000122403	0.001765977	0.989449741	0.321120498
204563_at	SELL	0.000133444	0.001424129	0.989449741	0.307941715

AFFYMETRIX HG-U133A Probe set ID	Gene	FDR Exacer'n v Quiet, N = 64	FDR Exacer'n v Quiet, N = 51	FDR Exacer'n v Follow-up, N = 51	Mean Δ log2 Exacer'n v Quiet
209539_at	ARHGEF6	0.000137065	0.001827858	0.999170597	0.247520218
38241_at	BTN3A3	0.000137065	0.001771005	0.999875537	0.303236768
205081_at	CRIP1	0.000137065	0.002477145	0.999170597	0.257126487
221081_s_at	DENND2D	0.000137065	0.001930541	0.989449741	0.464622601
204834_at	FGL2	0.000137065	0.002525693	0.989449741	0.648945004
213357_at	GTF2H5	0.000137065	0.001999151	0.989449741	0.39183635
210502_s_at	PPIE	0.000137065	0.001490239	0.989449741	0.271785205
218458_at	GMCL1	0.000137359	0.00634272	0.989449741	-0.226475248
211963_s_at	ARPC5	0.000140872	0.001415219	0.989449741	0.303544959
204232_at	FCER1G	0.000141945	0.001930541	0.989449741	0.277069582
202529_at	PRPSAP1	0.00015003	0.002461314	0.989449741	0.245784948
209702_at	FTO	0.000154806	0.001537436	0.989449741	0.264580463
203096_s_at	RAPGEF2	0.000154806	0.001775858	0.989449741	-0.326225528
212136_at	ATP2B4	0.00016222	0.001632865	0.989449741	0.384076656
221671_x_at	IGKC	0.00016222	0.001424129	0.989449741	0.365217597
219409_at	SNIP1	0.00016222	0.002442598	0.989449741	-0.253702874
201850_at	CAPG	0.000164212	0.00291282	0.989449741	0.319326031
204820_s_at	BTN3A3	0.000173406	0.001765977	0.989449741	0.359117268
212829_at	PIP5K2A	0.000173406	0.002437481	0.999875537	0.263400444
201284_s_at	APEH	0.000174099	0.003894405	0.989449741	0.34306097
218563_at	NDUFA3	0.000176874	0.002748357	0.989449741	0.235476452
204079_at	TPST2	0.000176874	0.001930541	0.989449741	0.293849427
203800_s_at	MRPS14	0.000180029	0.002229882	0.989449741	0.258068001
208998_at	UCP2	0.000193043	0.002692241	0.989449741	0.423766127
212613_at	BTN3A2	0.000199037	0.002705123	0.989449741	0.747702388
217286_s_at	NDRG3	0.000203249	0.001392062	0.999875537	0.368294346
200791_s_at	IQGAP1	0.0002203	0.00331601	0.989449741	0.357197839
207270_x_at	CD300C	0.000223695	0.003114079	0.989449741	0.329820875
212484_at	FAM89B	0.000227557	0.000807266	0.989449741	0.408397813
209879_at	SELPLG	0.000241035	0.00325328	0.989449741	0.393555874
202333_s_at	UBE2B	0.000241517	0.001763941	0.989449741	-0.276830195
1729_at	TRADD	0.000241723	0.008502132	0.996902938	0.296784617
202808_at	C10ORF26	0.000246633	0.003032572	0.999775135	0.371386316
203252_at	CDK2AP2	0.000248397	0.002477145	0.989449741	0.333028031
207108_s_at	NIPBL	0.000263483	0.007499776	0.999170597	-0.312838282
201548_s_at	JARID1B	0.000275345	0.001632865	0.989449741	-0.276402213
202659_at	PSMB10	0.000307326	0.00331601	0.989449741	0.272106446
200719_at	SKP1A	0.000311347	0.007670592	0.989449741	-0.23130029
213566_at	RNASE6	0.000312669	0.009062127	0.989449741	0.317555781
205718_at	ITGB7	0.000313372	0.001190689	0.992633412	0.2770242
204890_s_at	LCK	0.000313372	0.001922581	0.989449741	0.262915413
211637_x_at	LOC90925	0.000313372	0.0095183	0.989449741	0.494634585
218061_at	MEA1	0.000313372	0.003450279	0.989449741	0.274379136
212299_at	NEK9	0.000313372	0.001601914	0.989449741	0.361947717
206150_at	CD27	0.000314872	0.005418639	0.989449741	0.25560753
202033_s_at	RB1CC1	0.000314872	0.003927436	0.989449741	-0.283068359

AFFYMETRIX HG-U133A Probe set ID	Gene	FDR Exacer'n v Quiet, N = 64	FDR Exacer'n v Quiet, N = 51	FDR Exacer'n v Follow-up, N = 51	Mean $\Delta \log_2$ Exacer'n v Quiet
204233_s_at	CHKA	0.000327081	0.001415219	0.989449741	-0.587980802
203790_s_at	HRSP12	0.000327081	0.002727981	0.989449741	0.342224821
201413_at	HSD17B4	0.000327081	0.006359435	0.989449741	0.333084834
214677_x_at	IGL@	0.000327081	0.002692241	0.989449741	0.423884783
213918_s_at	NIPBL	0.000327081	0.00325328	0.995081416	-0.27071854
211005_at	LAT	0.000331555	0.000689198	0.992633412	0.312999176
205292_s_at	HNRPA2B1	0.000334082	0.004144142	0.989449741	0.315879927
206342_x_at	IDS	0.000336065	0.00372096	0.989449741	-0.245720985
203336_s_at	ITGB1BP1	0.000336065	0.001922581	0.989449741	0.304012724
221651_x_at	IGKC	0.00033855	0.001930541	0.989449741	0.352132457
218175_at	CCDC92	0.000346126	0.006359435	0.989449741	0.238586642
201331_s_at	STAT6	0.000346126	0.002727981	0.989449741	0.308582369
219032_x_at	OPN3	0.000357036	0.002748357	0.989449741	0.315457222
211986_at	AHNAK	0.000358691	0.003787898	0.989449741	0.319716188
205898_at	CX3CR1	0.000363049	0.002727981	0.989449741	0.64892969
201082_s_at	DCTN1	0.000380411	0.00325328	0.999875537	0.257862257
202845_s_at	RALBP1	0.0003886	0.007361396	0.989449741	0.387015183
39729_at	PRDX2	0.000390562	0.00457769	0.989449741	0.27918459
208018_s_at	HCK	0.000392544	0.006148992	0.989449741	0.371305637
200982_s_at	ANXA6	0.000410744	0.004431603	0.999875537	0.463842527
207419_s_at	RAC2	0.000414077	0.002933255	0.989449741	0.302920265
205297_s_at	CD79B	0.00042883	0.002441036	0.989449741	0.436193739
214259_s_at	AKR7A2	0.000435187	0.004726659	0.989449741	0.251578601
203341_at	CEBPZ	0.000435187	0.004992461	0.989449741	-0.307645978
220086_at	IKZF5	0.000435187	0.005091358	0.989449741	-0.253415901
205664_at	KIN	0.000435187	0.005952778	0.989449741	-0.240921176
200634_at	PFN1	0.000435187	0.009369724	0.999875537	0.232632614
204243_at	RLF	0.000435187	0.006968826	0.989449741	-0.254361688
218491_s_at	THYN1	0.000435187	0.002154763	0.989449741	0.328772135
221708_s_at	UNC45A	0.000435187	0.002727981	0.989449741	0.294145498
203990_s_at	UTX	0.000435187	0.001490239	0.989449741	-0.331952866
209138_x_at	IGL@	0.000443553	0.002810556	0.989449741	0.423688903
212315_s_at	NUP210	0.000443553	0.001632865	0.989449741	0.338828184
219014_at	PLAC8	0.000443553	0.003534516	0.989449741	0.255992476
202139_at	AKR7A2	0.000478035	0.003674925	0.989449741	0.257221263
201998_at	ST6GAL1	0.000478035	0.006229039	0.989449741	0.280024885
200615_s_at	AP2B1	0.000481603	0.004726659	0.989449741	0.308163531
203104_at	CSF1R	0.000481603	0.006746971	0.989449741	0.389448679
217179_x_at	LOC96610	0.000481603	0.007048137	0.989449741	0.375568002
201214_s_at	PPP1R7	0.000483398	0.004412192	0.989449741	0.270884223
221666_s_at	PYCARD	0.000485769	0.006739032	0.989449741	0.288863922
200703_at	DYNLL1	0.000492836	0.004306658	0.989449741	0.323659455
217157_x_at	0	0.000499201	0.001679791	0.989449741	0.300769926
201954_at	ARPC1B	0.000499201	0.01354814	0.989449741	0.214105409
209824_s_at	ARNTL	0.000512016	0.009096479	0.989449741	-0.252731918
211458_s_at	GABARAPL1	0.000512016	0.004749386	0.989449741	-0.337349799

AFFYMETRIX HG-U133A Probe set ID	Gene	FDR Exacer'n v Quiet, N = 64	FDR Exacer'n v Quiet, N = 51	FDR Exacer'n v Follow-up, N = 51	Mean $\Delta \log_2$ Exacer'n v Quiet
201762_s_at	PSME2	0.000536775	0.003894405	0.989449741	0.275608632
200684_s_at	UBE2L3	0.000536775	0.007624822	0.989449741	0.388182939
218201_at	NDUFB2	0.000537945	0.002525693	0.989449741	0.279688772
203079_s_at	CUL2	0.000544377	0.002930881	0.989449741	-0.293647521
201903_at	UQCRC1	0.000544814	0.00511929	0.989449741	0.270111589
202013_s_at	EXT2	0.000556834	0.012460713	0.989449741	0.221371121
211048_s_at	PDIA4	0.000565589	0.002746411	0.989449741	0.273878867
210971_s_at	ARNTL	0.000565656	0.003114079	0.989449741	-0.31915569
216105_x_at	PPP2R4	0.000574375	0.002249	0.989449741	0.320742428
219594_at	NINJ2	0.000575274	0.011688155	0.989449741	0.231783025
220964_s_at	RAB1B	0.000575274	0.006930342	0.989449741	0.241663222
212514_x_at	DDX3X	0.000587289	0.00706957	0.989449741	-0.25519555
220485_s_at	SIRPG	0.000587289	0.00331601	0.989449741	0.285246281
218268_at	TBC1D15	0.000599965	0.005225298	0.989449741	-0.281136062
202539_s_at	HMGCR	0.000636419	0.00331601	0.989449741	-0.284457554
214617_at	PRF1	0.000636419	0.001415219	0.999170597	0.47924031
200851_s_at	KIAA0174	0.000647237	0.009929511	0.989449741	-0.233420403
207088_s_at	SLC25A11	0.000649551	0.004374833	0.990401573	0.290426005
208868_s_at	GABARAPL1	0.000650709	0.006968826	0.989449741	-0.34883537
202944_at	NAGA	0.000653612	0.007402147	0.989449741	0.324428948
221763_at	JMJD1C	0.000665011	0.004622991	0.989449741	-0.262994291
204858_s_at	ECGF1	0.000680268	0.014138091	0.989449741	0.274391085
215273_s_at	TADA3L	0.000680268	0.014655112	0.989449741	0.431022902
214224_s_at	PIN4	0.000682813	0.005768649	0.989449741	0.250168816
202297_s_at	RER1	0.000682813	0.004749386	0.992633412	0.3028154
214437_s_at	SHMT2	0.000684445	0.009369724	0.989449741	0.270877435
212203_x_at	IFITM3	0.000685694	0.002727981	0.989449741	0.304891056
217143_s_at	TRA@	0.00069156	0.004726659	0.989449741	0.320170922
218256_s_at	NUP54	0.000700841	0.008087703	0.989449741	-0.290309592
213720_s_at	SMARCA4	0.000702585	0.014810987	0.999875537	0.226058265
206978_at	CCR2	0.000707287	0.016490882	0.989449741	0.240810193
201543_s_at	SAR1A	0.000707287	0.011710089	0.989449741	-0.2625788
214768_x_at	0	0.000712203	0.004306658	0.989449741	0.343460208
206383_s_at	G3BP2	0.000712203	0.002748357	0.989449741	-0.313723775
215176_x_at	NTN2L	0.000727566	0.004726659	0.989449741	0.339751138
209177_at	C3ORF60	0.000727566	0.008506404	0.989449741	0.257293634
204618_s_at	GABPB2	0.000727566	0.006148992	0.989449741	-0.367502426
218773_s_at	MSRB2	0.000727566	0.005418639	0.989449741	0.357615708
221918_at	PCTK2	0.000728806	0.021079092	0.989449741	-0.237531914
204821_at	BTN3A3	0.000739347	0.002155997	0.989449741	0.399235041
212135_s_at	ATP2B4	0.000762738	0.003518947	0.989449741	0.318713047
219343_at	CDC37L1	0.000762738	0.007309057	0.999860944	-0.29606778
207945_s_at	CSNK1D	0.000762738	0.016364469	0.990463252	-0.290788077
204091_at	PDE6D	0.000762738	0.004374833	0.999775135	0.617568961
212632_at	STX7	0.000762738	0.004756217	0.989449741	0.324204972
201100_s_at	USP9X	0.000782045	0.007048137	0.989449741	-0.248495758

AFFYMETRIX HG-U133A Probe set ID	Gene	FDR Exacer'n v Quiet, N = 64	FDR Exacer'n v Quiet, N = 51	FDR Exacer'n v Follow-up, N = 51	Mean $\Delta \log_2$ Exacer'n v Quiet
200765_x_at	CTNNA1	0.000787612	0.00555987	0.989449741	0.246901887
214669_x_at	IGKC	0.000818503	0.006608275	0.989449741	0.338664468
213475_s_at	ITGAL	0.000818503	0.001775858	0.992633412	0.319906726
202447_at	DECR1	0.000822295	0.00331601	0.999875537	0.269322531
200762_at	DPYSL2	0.000822295	0.012331531	0.989449741	0.359599434
215121_x_at	IGL@	0.000822295	0.00724686	0.989449741	0.449199148
200658_s_at	PHB (includes EG:5245)	0.000822295	0.011178107	0.989449741	0.271153703
217148_x_at	0	0.000824507	0.004728268	0.989449741	0.33805833
200812_at	CCT7	0.000824507	0.016482999	0.989449741	0.219696813
207224_s_at	SIGLEC7	0.000824507	0.013385865	0.989449741	0.305830409
219403_s_at	HPSE	0.000830105	0.009732612	0.999875537	0.265302417
221532_s_at	WDR61	0.00084731	0.008087703	0.989449741	0.235336728
202502_at	ACADM	0.000864933	0.002979665	0.989449741	0.401564746
213698_at	ZMYM6	0.000864933	0.01021407	0.989449741	0.270123556
204071_s_at	TOPORS	0.000940098	0.001999151	0.989449741	-0.321902977
218130_at	C17ORF62	0.000959138	0.019509876	0.989449741	0.441340283
220477_s_at	C20ORF30	0.000959138	0.008590251	0.999875537	0.245868211
204759_at	RCBTB2	0.000959138	0.011688155	0.989449741	0.268283287
205671_s_at	HLA-DOB	0.000983379	0.006596765	0.989449741	0.332615313
219679_s_at	WAC	0.00099235	0.00390025	0.989449741	-0.265005602
205996_s_at	AK2	0.000994104	0.014655112	0.989449741	0.240184345
204205_at	APOBEC3G	0.000995041	0.001601914	0.992633412	0.304346622
204369_at	PIK3CA	0.001002085	0.009244488	0.989449741	-0.306938779
213888_s_at	TRAF3IP3	0.00101061	0.002748357	0.989449741	0.298506161
203350_at	AP1G1	0.001012017	0.01779807	0.989449741	-0.290224501
206666_at	GZMK	0.001032512	0.006148992	0.989449741	0.381124515
217973_at	DCXR	0.001041384	0.005901401	0.989449741	0.256480374
202034_x_at	RB1CC1	0.001060851	0.008506404	0.989449741	-0.330899098
203645_s_at	CD163	0.001069412	0.011620845	0.996310208	0.400019376
205552_s_at	OAS1	0.001076471	0.00789891	0.989449741	0.488844142
207831_x_at	DHPS	0.001091307	0.005361731	0.989449741	0.475729022
207655_s_at	BLNK	0.001106608	0.010317256	0.989449741	0.349842564
205001_s_at	DDX3Y (includes EG:8653)	0.001120007	0.001930541	0.989449741	-0.666861961
218571_s_at	CHMP4A	0.00114921	0.001458279	0.989449741	0.318205226
200678_x_at	GRN	0.001185216	0.015004176	0.989449741	0.235273089
202352_s_at	PSMD12	0.001185216	0.005848736	0.989449741	-0.266721911
202589_at	TYMS	0.001199952	0.006148992	0.999875537	0.375833885
203148_s_at	TRIM14	0.001202227	0.010834794	0.989449741	0.392683893
206748_s_at	SPAG9	0.001221534	0.008326908	0.989449741	-0.323085644
216260_at	DICER1	0.001224234	0.005411025	0.989449741	-0.312582444
209171_at	ITPA	0.001224234	0.005361731	0.989449741	0.26696903
215512_at	MARCH6	0.001225556	0.007137669	0.989449741	-0.391768817
203685_at	BCL2	0.001241664	0.014752724	0.989449741	0.316753201
202727_s_at	IFNGR1	0.001244945	0.00511929	0.992633412	-0.304448541

AFFYMETRIX HG-U133A Probe set ID	Gene	FDR Exacer'n v Quiet, N = 64	FDR Exacer'n v Quiet, N = 51	FDR Exacer'n v Follow-up, N = 51	Mean $\Delta \log_2$ Exacer'n v Quiet
215118_s_at	IGHG1	0.001252379	0.002727981	0.989449741	0.342881272
221044_s_at	TRIM34	0.00125746	0.01779807	0.989449741	0.298921393
211595_s_at	MRPS11	0.001301438	0.005411025	0.989449741	0.327142963
217752_s_at	CNDP2	0.001344373	0.009379981	0.989449741	0.281082748
222217_s_at	SLC27A3	0.001344798	0.006968826	0.999170597	0.288456759
205251_at	PER2	0.001364923	0.014531661	0.989449741	-0.273999133
201688_s_at	TPD52	0.001403687	0.009425377	0.9946638	0.253835591
204891_s_at	LCK	0.001419862	0.003894405	0.992633412	0.280545008
218487_at	ALAD	0.001439968	0.006968826	0.989449741	0.326607698
201301_s_at	ANXA4	0.00144365	0.007639163	0.989449741	0.746644814
202201_at	BLVRB	0.001573278	0.01584915	0.994317186	0.288007441
201195_s_at	SLC7A5	0.001573278	0.007106724	0.989449741	-0.361964776
205260_s_at	ACYP1	0.001594725	0.014138091	0.999170597	0.486885421
39318_at	TCL1A	0.001625883	0.015894187	0.989449741	0.292387585
218102_at	DERA	0.001649114	0.011523846	0.989449741	0.248811393
216933_x_at	APC	0.001673247	0.01779807	0.989449741	-0.328628065
215535_s_at	AGPAT1	0.001690954	0.013903896	0.989449741	0.244873423
210793_s_at	NUP98	0.001706911	0.016373934	0.989449741	-0.265306242
210875_s_at	ZEB1	0.001731676	0.006454233	0.999860944	-0.536203945
203720_s_at	ERCC1	0.001744503	0.013206152	0.989449741	0.293891701
200660_at	S100A11	0.001744503	0.037352667	0.989449741	0.279874352
200900_s_at	M6PR	0.00175887	0.009379981	0.989449741	0.355503452
215946_x_at	CTA-246H3.1	0.001776637	0.00325328	0.989449741	0.341566401
201989_s_at	CREBL2	0.001778721	0.016222394	0.989449741	0.239353485
210222_s_at	RTN1	0.001778721	0.014655112	0.989449741	0.4388518
221511_x_at	CCPG1	0.001837478	0.026823359	0.989449741	0.27677713
202503_s_at	KIAA0101	0.001837478	0.005361731	0.989449741	0.344399133
209422_at	PHF20	0.001890809	0.014996942	0.992633412	-0.260712578
213370_s_at	SFMBT1	0.001925515	0.016250748	0.999875537	-0.252680392
216041_x_at	GRN	0.001937213	0.018875106	0.989449741	0.254505572
201990_s_at	CREBL2	0.001947681	0.016435548	0.989449741	0.27904165
216191_s_at	TRA@	0.001947681	0.011133735	0.999875537	0.381662453
211138_s_at	KMO	0.001954903	0.013214901	0.989449741	0.261798831
201711_x_at	RANBP2	0.001954903	0.006608275	0.989449741	-0.359000131
209268_at	VPS45	0.001954903	0.01867368	0.989449741	0.28924038
211684_s_at	DYNC1I2	0.001957198	0.014096459	0.989449741	0.268152837
219666_at	MS4A6A	0.00202555	0.024230535	0.989449741	0.298775239
209123_at	QDPR	0.00202555	0.007624822	0.989449741	0.291374348
210981_s_at	GRK6	0.002108686	0.008590251	0.989449741	0.322221965
218248_at	FAM111A	0.002177781	0.011757556	0.989449741	0.256785004
205639_at	AOAH	0.002200811	0.018063019	0.989449741	0.233983537
218432_at	FBXO3	0.002271966	0.019841242	0.989449741	-0.243052502
217893_s_at	C1ORF108	0.002327952	0.010968324	0.989449741	-0.283241076
211052_s_at	TBCD	0.002327952	0.029443759	0.989449741	0.458961294
204552_at	0	0.0023375	0.010703847	0.999860944	0.259989457
214230_at	CDC42	0.00235967	0.007366046	0.989449741	-0.28391366

AFFYMETRIX HG-U133A Probe set ID	Gene	FDR Exacer'n v Quiet, N = 64	FDR Exacer'n v Quiet, N = 51	FDR Exacer'n v Follow-up, N = 51	Mean $\Delta \log_2$ Exacer'n v Quiet
217957_at	C16ORF80	0.002360504	0.014531661	0.989449741	-0.323672759
208923_at	CYFIP1	0.002403669	0.053507143	0.999860944	0.20010478
204960_at	PTPRCAP	0.002439639	0.014324902	0.989449741	0.259927296
203741_s_at	ADCY7	0.002441506	0.007348671	0.999875537	0.301320352
204222_s_at	GLIPR1	0.002441506	0.0182804	0.989449741	0.372323325
203814_s_at	NQO2	0.002467859	0.020807539	0.989449741	0.309002396
202857_at	TMEM4	0.002467859	0.016111032	0.989449741	0.262027938
206697_s_at	HP	0.002480813	0.033802633	0.989449741	0.318610166
217234_s_at	VIL2	0.002480813	0.008087703	0.999875537	-0.323455207
220068_at	VPREB3	0.002508189	0.008087703	0.989449741	0.36430699
212239_at	PIK3R1	0.002512151	0.008240887	0.989449741	-0.351698742
211430_s_at	IGHM	0.002515933	0.011946681	0.989449741	0.502359564
212890_at	MGC15523	0.002544105	0.019765771	0.989449741	0.4407365
201830_s_at	NET1	0.00255705	0.02191709	0.989449741	-0.365628151
204258_at	CHD1	0.00259005	0.020697692	0.989449741	-0.263374998
222309_at	C6ORF62	0.002613143	0.020025632	0.989449741	-0.309369764
204950_at	CARD8	0.002613143	0.025474368	0.989449741	0.244398697
209555_s_at	CD36	0.002664317	0.027150542	0.989449741	0.313914898
203334_at	DHX8	0.002739188	0.031758827	0.989449741	-0.242178793
221210_s_at	NPL	0.002757438	0.027569971	0.989449741	0.334476885
208930_s_at	ILF3	0.002778072	0.014379033	0.999875537	-0.731713347
214700_x_at	RIF1	0.002804775	0.022785018	0.999170597	-0.245875298
204512_at	HIVEP1	0.002808884	0.048702813	0.999875537	-0.208486404
214836_x_at	IGKC	0.0028273	0.007361396	0.989449741	0.307170528
202869_at	OAS1	0.002836989	0.061278571	0.989449741	0.355521465
202411_at	IFI27	0.002867417	0.005765311	0.999860944	0.827033954
219061_s_at	LAGE3	0.002889493	0.008673311	0.989449741	0.351213669
217118_s_at	C22ORF9	0.002895987	0.015722075	0.989449741	0.252802103
209341_s_at	IKBKB	0.002895987	0.013059559	0.989449741	0.275617947
212647_at	RRAS	0.002956805	0.020254751	0.989449741	0.437888582
207540_s_at	SYK	0.003080047	0.043081212	0.999875537	0.51488359
201878_at	ARIH1	0.003149179	0.024529617	0.999875537	-0.247120857
211798_x_at	IGLJ3	0.003180983	0.015772918	0.989449741	0.284322069
210438_x_at	TROVE2	0.003183382	0.017675986	0.989449741	-0.270741307
220104_at	ZC3HAV1	0.003215554	0.019097439	0.989449741	-0.242782025
209681_at	SLC19A2	0.003218487	0.00724686	0.999875537	-0.340654718
204435_at	NUPL1	0.003225429	0.01847557	0.999860944	-0.278092387
204236_at	FLI1	0.003235464	0.027092973	0.989449741	0.291791808
206011_at	CASP1	0.003252713	0.02180297	0.989449741	0.257280453
209930_s_at	NFE2	0.003252713	0.036706981	0.989449741	0.252075493
201679_at	ARS2	0.003269014	0.006695499	0.989449741	-0.342030018
219529_at	CLIC3	0.003309914	0.026541622	0.999875537	0.501837283
201798_s_at	FER1L3	0.003374801	0.010834794	0.989449741	0.32575619
211865_s_at	FZR1	0.003416575	0.008537732	0.992633412	-0.402156995
200796_s_at	MCL1	0.00343314	0.004367608	0.989449741	-0.379899638
212368_at	ZNF292	0.003471202	0.015153914	0.989449741	-0.326664906

AFFYMETRIX HG-U133A Probe set ID	Gene	FDR Exacer'n v Quiet, N = 64	FDR Exacer'n v Quiet, N = 51	FDR Exacer'n v Follow-up, N = 51	Mean $\Delta \log_2$ Exacer'n v Quiet
208898_at	ATP6V1D	0.003659949	0.03422722	0.989449741	0.226487959
206934_at	SIRPB1	0.00366028	0.043217608	0.999875537	0.343668306
213024_at	TMF1	0.003682604	0.009369724	0.989449741	-0.283458269
221136_at	GDF2	0.003730435	0.026915366	0.999860944	0.41393192
206398_s_at	CD19	0.003756272	0.009014956	0.989449741	0.267618155
220386_s_at	EML4	0.003756272	0.027580386	0.989449741	-0.249592455
219191_s_at	BIN2	0.003812976	0.008087703	0.998443527	0.28972134
201369_s_at	ZFP36L2	0.00382513	0.008087703	0.989449741	-0.396936859
209674_at	CRY1	0.00383637	0.04338212	0.989449741	-0.294783202
212631_at	STX7	0.003894289	0.010518011	0.999875537	0.284992549
213300_at	ATG2A	0.003971598	0.042915787	0.989449741	-0.291057792
210837_s_at	PDE4D	0.003992387	0.030850293	0.989449741	-0.238971281
201459_at	RUVBL2	0.003997839	0.020048456	0.996310208	0.420997172
200849_s_at	AHCYL1	0.004152031	0.026336476	0.989449741	0.239521439
216510_x_at	IGHM	0.004152031	0.022115542	0.989449741	0.267384564
218673_s_at	ATG7	0.004181766	0.031980345	0.990401573	0.242400077
209448_at	HTATIP2	0.004294431	0.016998728	0.989449741	0.289392365
209657_s_at	HSF2	0.004295648	0.038492458	0.989449741	-0.250387579
210104_at	MED6	0.004362687	0.059705599	0.989449741	-0.206476793
209199_s_at	MEF2C	0.004366742	0.033848804	0.989449741	0.277362016
208901_s_at	TOP1	0.004371954	0.01845181	0.989449741	-0.244197725
212420_at	ELF1	0.004409498	0.011736904	0.989449741	-0.421075125
207001_x_at	TSC22D3	0.00441375	0.008087703	0.989449741	-0.385669354
204565_at	THEM2	0.004447673	0.034175352	0.989449741	0.261898479
201713_s_at	RANBP2	0.004486641	0.025862737	0.989449741	-0.290946919
201101_s_at	BCLAF1	0.004493632	0.015623198	0.989449741	-0.33563532
209773_s_at	RRM2	0.004538428	0.009062127	0.989449741	0.317141015
204244_s_at	DBF4	0.004667713	0.018925816	0.989449741	-0.276178697
218562_s_at	TMEM57	0.004667713	0.02031709	0.992633412	-0.337272049
206743_s_at	ASGR1	0.0047202	0.048329949	0.989449741	0.262995524
211368_s_at	CASP1	0.004724575	0.029689301	0.989449741	0.248072171
215049_x_at	CD163	0.004724575	0.029653891	0.989449741	0.343903258
214777_at	0	0.00474319	0.030851645	0.999875537	0.470253868
213853_at	DPH4	0.00474319	0.032504947	0.989449741	0.284103318
202684_s_at	RNMT	0.004827006	0.020195849	0.989449741	-0.339233164
212189_s_at	COG4	0.004915846	0.021664295	0.989449741	0.304605563
214766_s_at	AHCTF1	0.005045322	0.031035179	0.989449741	-0.2389356
202643_s_at	TNFAIP3	0.005049625	0.026107956	0.989449741	-0.256706151
204520_x_at	BRD1	0.005056176	0.037489214	0.989449741	-0.236422395
218160_at	NDUFA8	0.005104732	0.02725912	0.989449741	0.265540404
41577_at	PPP1R16B	0.005114154	0.03758103	0.989449741	-0.266716491
202802_at	DHPS	0.005153729	0.012341023	0.989449741	0.411326347
212579_at	SMCHD1	0.005242671	0.020195849	0.989449741	-0.270301779
213138_at	ARID5A	0.005374749	0.025862737	0.999875537	-0.257003315
205202_at	PCMT1	0.005419642	0.031014488	0.989449741	0.274242936
206474_at	PCTK2	0.005420029	0.009425377	0.989449741	-0.280266936

AFFYMETRIX HG-U133A Probe set ID	Gene	FDR Exacer'n v Quiet, N = 64	FDR Exacer'n v Quiet, N = 51	FDR Exacer'n v Follow-up, N = 51	Mean $\Delta \log_2$ Exacer'n v Quiet
222142_at	CYLD	0.005433797	0.056829739	0.989449741	-0.221781393
208325_s_at	AKAP13	0.005479037	0.015178539	0.989449741	-0.338103785
204354_at	POT1	0.005501641	0.007361396	0.989449741	0.291545231
207686_s_at	CASP8	0.005510098	0.022693611	0.992633412	-0.262343036
207791_s_at	RAB1A	0.005532348	0.016970375	0.989449741	-0.260040425
205819_at	MARCO	0.0055492	0.022798957	0.989449741	0.556337817
210776_x_at	TCF3	0.005580048	0.005135308	0.999860944	0.343587607
201448_at	TIA1	0.005592773	0.008753175	0.989449741	0.384888382
210314_x_at	TNFSF13	0.005631239	0.030050096	0.989449741	0.251922246
213830_at	TRA@	0.005631239	0.061278571	0.999875537	0.313025901
202771_at	FAM38A	0.005764725	0.019176407	0.999860944	0.277325037
218232_at	C1QA	0.005843574	0.022998906	0.989449741	0.294564228
211634_x_at	IGHM	0.005874475	0.003209262	0.989449741	0.401747885
211676_s_at	IFNGR1	0.005895325	0.017278892	0.992633412	-0.26708949
211658_at	PRDX2	0.00592062	0.046710505	0.989449741	0.300257179
218660_at	DYSF	0.005988683	0.038845427	0.989449741	0.26516736
210321_at	GZMH	0.00599779	0.014324902	0.989449741	0.385606971
212842_x_at	RGPD5	0.006040184	0.029375171	0.989449741	-0.256742246
213238_at	ATP10D	0.006148056	0.014752724	0.989449741	0.396761691
218598_at	RINT-1	0.006309451	0.031494602	0.989449741	-0.23835499
208130_s_at	TBXAS1	0.006360222	0.048745041	0.989449741	0.238746065
207630_s_at	CREM	0.006433074	0.02936887	0.989449741	-0.346620151
206761_at	CD96	0.006452047	0.010509546	0.999875537	0.305052027
209581_at	HRASLS3	0.006522732	0.037537936	0.989449741	0.273100246
209099_x_at	JAG1	0.0065548	0.043881101	0.989449741	-0.237884195
218321_x_at	STYXL1	0.006594919	0.014655112	0.989449741	0.377829635
220560_at	C11ORF21	0.006888885	0.006785178	0.999875537	0.310692295
218400_at	OAS3	0.006916555	0.033848804	0.999875537	0.291024811
204630_s_at	GOSR1	0.007048224	0.055725696	0.989449741	-0.370355173
209480_at	HLA-DQB1	0.007072014	0.012627228	0.989449741	0.583368519
208810_at	DNAJB6	0.007115524	0.026083865	0.989449741	-0.248474131
213674_x_at	IGHD	0.007117464	0.042140113	0.989449741	0.314831791
218504_at	FAHD2A	0.007261903	0.027569971	0.989449741	0.275918665
201218_at	0	0.007297492	0.027150542	0.989449741	0.319848628
217236_x_at	IGHG1	0.007312652	0.01466556	0.989449741	0.277945656
207190_at	ZZEF1	0.007312652	0.061503008	0.989449741	-0.231303663
200683_s_at	UBE2L3	0.007490607	0.06144415	0.989449741	0.318072482
212070_at	GPR56	0.007499462	0.016998728	0.989449741	0.352222843
208499_s_at	DNAJC3	0.00794364	0.026676031	0.989449741	-0.377832728
203454_s_at	ATOX1	0.007964188	0.05950856	0.989449741	0.228088671
210660_at	LILRA1	0.008046967	0.038992611	0.989449741	0.293688016
45714_at	HCFC1R1	0.008346281	0.016208342	0.989449741	0.321583436
218628_at	CCDC53	0.008370392	0.026336476	0.989449741	0.308291932
207104_x_at	LILRB1	0.008370392	0.028390504	0.989449741	0.276273653
202906_s_at	NBN	0.008412904	0.061710728	0.989449741	-0.228774539
212841_s_at	PPFIBP2	0.008431717	0.070499722	0.999875537	-0.308356194

AFFYMETRIX HG-U133A Probe set ID	Gene	FDR Exacer'n v Quiet, N = 64	FDR Exacer'n v Quiet, N = 51	FDR Exacer'n v Follow-up, N = 51	Mean $\Delta \log_2$ Exacer'n v Quiet
202820_at	AHR	0.008543591	0.023346042	0.989449741	-0.333964081
218793_s_at	SCML1	0.008724804	0.019699152	0.989449741	-0.302915244
211644_x_at	IGKC	0.008836995	0.04251771	0.989449741	0.368362779
215460_x_at	BRD1	0.008856719	0.043881101	0.989449741	-0.240914782
216100_s_at	TOR1AIP1	0.008935905	0.067754828	0.989449741	-0.251357762
201841_s_at	HSPB1	0.008945424	0.026676031	0.989449741	0.322182392
201906_s_at	CTDSPL	0.008949709	0.115094717	0.989449741	0.229704349
205483_s_at	ISG15	0.009046991	0.030070903	0.999775135	0.3301337
209771_x_at	CD24	0.009174971	0.068140197	0.989449741	0.401443846
219184_x_at	TIMM22	0.009174971	0.006968826	0.989449741	-0.626545634
211133_x_at	LILRB2	0.009264483	0.031360675	0.989449741	0.246592831
208621_s_at	VIL2	0.009378043	0.015178539	0.989449741	-0.292897213
218968_s_at	ZFP64	0.009405491	0.02878907	0.989449741	0.278043195
203542_s_at	KLF9	0.009421114	0.014138091	0.989449741	-0.303213811
213844_at	HOXA5	0.009456431	0.019884878	0.989449741	-0.336925595
220532_s_at	TMEM176B	0.009456431	0.072462443	0.989449741	0.253768337
203197_s_at	C1ORF123	0.009475056	0.025967346	0.989449741	0.316251039
220646_s_at	KLRF1	0.009842474	0.026676031	0.998443527	0.307337492
202932_at	YES1	0.009845258	0.063320125	0.989449741	-0.260259979
212240_s_at	PIK3R1	0.010102748	0.044571978	0.989449741	-0.280321363
214719_at	SLC46A3	0.010385639	0.08498821	0.989449741	0.234249392
203227_s_at	TSPAN31	0.010385639	0.081869754	0.989449741	0.269839505
217230_at	VIL2	0.010484209	0.030850293	0.999875537	-0.606267812
212830_at	MEGF9	0.010642378	0.05302726	0.989449741	0.310775116
207840_at	CD160	0.010813258	0.03869558	0.999875537	0.248985995
205239_at	AREG	0.010892256	0.046710505	0.992633412	-0.447684123
203485_at	RTN1	0.011091972	0.079062359	0.989449741	0.352208833
215925_s_at	CD72	0.011114129	0.045839519	0.989449741	0.426533268
218877_s_at	TRMT11	0.011114129	0.052857992	0.989449741	-0.243831432
209184_s_at	IRS2	0.011377086	0.025854059	0.989449741	-0.370878022
206770_s_at	SLC35A3	0.01152795	0.081874529	0.989449741	-0.210129814
202275_at	G6PD	0.011571849	0.076810207	0.989449741	0.223272707
220370_s_at	USP36	0.011657632	0.017396935	0.989449741	-0.316048827
219854_at	ZNF14	0.011657632	0.071210572	0.989449741	-0.216348273
207983_s_at	STAG2	0.011784294	0.029443759	0.989449741	-0.283436906
209460_at	ABAT	0.011814732	0.077338625	0.989449741	0.332456127
202729_s_at	LTBP1	0.012045807	0.060192971	0.989449741	0.259651211
215716_s_at	ATP2B1	0.012329558	0.087788247	0.999775135	-0.234367527
202382_s_at	GNPDA1	0.012329558	0.074482324	0.999875537	0.226427543
211135_x_at	LILRB2	0.012329558	0.04720123	0.989449741	0.290183832
217022_s_at	IGHA1	0.012330644	0.071279406	0.989449741	0.37940291
204771_s_at	TTF1	0.012349011	0.026541622	0.992633412	-0.612140469
206881_s_at	LILRA3	0.012382773	0.146996117	0.989449741	0.205018265
208993_s_at	PPIG	0.012478202	0.046710505	0.989449741	-0.495377578
209385_s_at	PROSC	0.012685741	0.086929712	0.989449741	0.281793793
213241_at	PLXNC1	0.012797271	0.06201157	0.989449741	0.245225098

AFFYMETRIX HG-U133A Probe set ID	Gene	FDR Exacer'n v Quiet, N = 64	FDR Exacer'n v Quiet, N = 51	FDR Exacer'n v Follow-up, N = 51	Mean $\Delta \log_2$ Exacer'n v Quiet
209417_s_at	IFI35	0.01288426	0.052543489	0.989449741	0.245500095
202996_at	POLD4	0.01288426	0.013904233	0.989449741	0.504213833
208661_s_at	TTC3	0.013577437	0.020067307	0.998443527	-0.558621455
203504_s_at	ABCA1	0.013691899	0.064956405	0.999875537	-0.270427783
202723_s_at	FOXO1	0.013812872	0.111956122	0.989449741	-0.219524825
211199_s_at	ICOSLG	0.013899311	0.084773153	0.989449741	-0.418583364
211576_s_at	SLC19A1	0.013947132	0.052781693	0.989449741	0.282972566
203791_at	DMXL1	0.013982542	0.102658371	0.999875537	0.254810714
215379_x_at	IGL@	0.014228373	0.029729359	0.989449741	0.299774111
202027_at	TMEM184B	0.01463017	0.15080112	0.989449741	-0.238216082
214995_s_at	APOBEC3F	0.015429877	0.023623476	0.989449741	0.30052076
216379_x_at	CD24	0.01546115	0.10927203	0.989449741	0.337940524
211840_s_at	PDE4D	0.015530692	0.077171886	0.989449741	-0.315843621
212764_at	0	0.015730425	0.093235833	0.999875537	-0.302079268
208983_s_at	PECAM1	0.015730425	0.058827879	0.989449741	0.222235435
214508_x_at	CREM	0.015876726	0.046275245	0.989449741	-0.276762529
214273_x_at	C16ORF35	0.016155203	0.029776129	0.989449741	0.274342013
206829_x_at	ZNF430	0.01628046	0.031084112	0.999875537	-0.334510066
219228_at	ZNF331	0.016758668	0.038989413	0.989449741	-0.265651975
209281_s_at	ATP2B1	0.016778489	0.094912682	0.999875537	-0.216021467
219210_s_at	RAB8B	0.016810155	0.080902359	0.999860944	-0.249121329
210154_at	ME2	0.016929959	0.058473604	0.989449741	0.231317327
206707_x_at	C6ORF32	0.017069796	0.061278571	0.989449741	0.245248804
210784_x_at	LILRB2	0.017430703	0.074383254	0.999875537	0.234595745
204181_s_at	ZBTB43	0.018118096	0.038102953	0.989449741	-0.359978259
208450_at	LGALS2	0.018840047	0.151080324	0.999875537	0.231199005
213397_x_at	RNASE4	0.018840047	0.050336409	0.989449741	0.246937949
208541_x_at	TFAM	0.01888466	0.043301094	0.999875537	-0.36578751
220363_s_at	ELMO2	0.019035865	0.04251771	0.989449741	-0.336672576
209127_s_at	SART3	0.019084727	0.01867368	0.989449741	-0.579425607
211423_s_at	SC5DL	0.019738942	0.054658281	0.999170597	-0.26933491
203203_s_at	KRR1	0.019761987	0.081365496	0.989449741	-0.273574762
217977_at	SEPX1	0.019798679	0.095742497	0.989449741	0.30918947
204833_at	ATG12	0.020092997	0.060143693	0.999860944	-0.29732725
216576_x_at	0	0.020504101	0.033500356	0.989449741	0.356263226
215621_s_at	IGHD	0.020537251	0.049535517	0.989449741	0.469561382
205936_s_at	HK3	0.020626319	0.077265558	0.989449741	0.370492283
219497_s_at	BCL11A	0.020630202	0.031084112	0.989449741	0.277512558
218856_at	TNFRSF21	0.020646727	0.258615288	0.989449741	-0.365340192
212229_s_at	FBXO21	0.020966502	0.048891302	0.999875537	-0.27937857
212531_at	LCN2	0.021154912	0.094912682	0.989449741	0.299904534
213672_at	MARS (includes EG:4141)	0.022676752	0.16378389	0.989449741	-0.190080228
216915_s_at	PTPN12	0.023085786	0.028802905	0.989449741	-0.322773907
208991_at	STAT3	0.023105118	0.04251771	0.989449741	-0.429258343
207808_s_at	PROS1	0.024454572	0.097813067	0.989449741	0.277242815

AFFYMETRIX HG-U133A Probe set ID	Gene	FDR Exacer'n v Quiet, N = 64	FDR Exacer'n v Quiet, N = 51	FDR Exacer'n v Follow-up, N = 51	Mean $\Delta \log_2$ Exacer'n v Quiet
213979_s_at	0	0.02446421	0.057863327	0.989449741	0.265547674
204619_s_at	VCAN	0.024551356	0.154020939	0.989449741	0.189540592
201367_s_at	ZFP36L2	0.024691689	0.042874833	0.999875537	-0.499101398
220330_s_at	SAMSN1	0.025070537	0.062360925	0.999775135	-0.263647206
216491_x_at	IGHM	0.0254179	0.04328448	0.989449741	0.501481085
201110_s_at	THBS1	0.025706246	0.039755163	0.989449741	-0.554321888
207269_at	DEFA4	0.025927783	0.143378347	0.989449741	0.328951536
207978_s_at	NR4A3	0.025927783	0.136476074	0.989449741	-0.289082826
202208_s_at	ARL4C	0.026525797	0.117920787	0.989449741	-0.250545565
202988_s_at	RGS1	0.0275444	0.072842185	0.989449741	-0.386389145
201939_at	PLK2	0.027574591	0.07697782	0.989449741	-0.318660078
202458_at	PRSS23	0.027728103	0.162974212	0.999875537	0.262008375
209829_at	C6ORF32	0.028448903	0.083382181	0.989449741	0.242964416
202933_s_at	YES1	0.028448903	0.110632076	0.989449741	-0.302993319
210367_s_at	PTGES	0.02861839	0.09725281	0.999875537	-0.231156235
208772_at	ANKHD1	0.028686587	0.112218548	0.989449741	-0.44588397
207735_at	RNF125	0.028919122	0.098198128	0.989449741	-0.306157663
214091_s_at	GPX3	0.029127031	0.076316804	0.989449741	-0.251707391
204959_at	MNDA	0.029463273	0.162352719	0.989449741	0.217286616
210139_s_at	PMP22	0.030423473	0.039148997	0.989449741	-0.439210039
209967_s_at	CREM	0.03081361	0.128158563	0.989449741	-0.398455681
220001_at	PADI4	0.030881449	0.11007471	0.989449741	0.248581247
208651_x_at	CD24	0.031022644	0.101596709	0.989449741	0.380097925
212720_at	PAPOLA	0.031022644	0.159495805	0.999875537	0.209683615
204006_s_at	FCGR3A	0.031040754	0.044398381	0.999170597	0.376554
204198_s_at	RUNX3	0.031235279	0.11007471	0.989449741	-0.263762479
201631_s_at	IER3	0.031367646	0.040272223	0.989449741	-0.332792024
201534_s_at	UBL3	0.031682917	0.054438594	0.989449741	-0.267888461
211635_x_at	0	0.03230983	0.015674081	0.989449741	0.340412689
200895_s_at	FKBP4	0.03273201	0.11357739	0.989449741	0.217516851
209153_s_at	TCF3	0.033314149	0.051510117	0.999170597	0.281960028
208960_s_at	KLF6	0.033465179	0.091784194	0.989449741	-0.691636254
206488_s_at	CD36	0.033527437	0.129528475	0.989449741	0.221187201
210178_x_at	FUSIP1	0.033527437	0.074158718	0.989449741	-0.415118743
209504_s_at	PLEKHB1	0.033661797	0.031758827	0.989449741	0.318126329
203913_s_at	HPGD	0.033684873	0.008087703	0.989449741	-0.458826569
205033_s_at	DEFA1	0.033802918	0.20812861	0.989449741	0.338694932
218723_s_at	C13ORF15	0.033903606	0.07876279	0.989449741	-0.249750457
205070_at	ING3	0.034660832	0.079120731	0.999875537	-0.310353631
220751_s_at	C5ORF4	0.034700433	0.172103477	0.999860944	0.202019036
208987_s_at	FBXL11	0.034788285	0.048580539	0.989449741	-0.447799698
208992_s_at	STAT3	0.034896789	0.031994065	0.989449741	-0.338569068
208942_s_at	TLOC1	0.034896789	0.104374493	0.989449741	-0.386927768
209604_s_at	GATA3	0.034927254	0.098912567	0.989449741	-0.253801443
202871_at	TRAF4	0.03542462	0.08416156	0.989449741	-0.274481617
219392_x_at	PRR11	0.035621799	0.075234284	0.989449741	-0.402711374

AFFYMETRIX HG-U133A Probe set ID	Gene	FDR Exacer'n v Quiet, N = 64	FDR Exacer'n v Quiet, N = 51	FDR Exacer'n v Follow-up, N = 51	Mean $\Delta \log_2$ Exacer'n v Quiet
205027_s_at	MAP3K8	0.035676625	0.062623254	0.989449741	-0.265793388
204567_s_at	ABCG1	0.035736869	0.092341417	0.996080789	-0.251947095
218449_at	C4ORF20	0.035948991	0.127321099	0.999875537	0.225420003
203505_at	ABCA1	0.036437022	0.132615325	0.992633412	-0.278556795
211560_s_at	ALAS2	0.036875551	0.051998922	0.999860944	0.531623369
214446_at	ELL2	0.037411336	0.051163635	0.989449741	-0.527512602
212954_at	DYRK4	0.03744809	0.245711527	0.989449741	0.184060875
202927_at	PIN1	0.037481626	0.076508004	0.999875537	0.263650358
212592_at	IGJ	0.037485741	0.058827879	0.989449741	0.331582846
218401_s_at	ZNF281	0.037632567	0.061278571	0.989449741	-0.289322273
214786_at	MAP3K1	0.039034036	0.04512331	0.989449741	-0.348471489
210653_s_at	BCKDHB	0.039877111	0.067715814	0.999875537	0.286175627
200878_at	EPAS1	0.039920199	0.101126257	0.989449741	-0.305545648
220319_s_at	MYLIP	0.040709639	0.130484533	0.989449741	-0.272540562
209959_at	NR4A3	0.04271719	0.146996117	0.989449741	-0.384959402
207414_s_at	PCSK6	0.042954608	0.130824771	0.989449741	0.266397191
210244_at	CAMP	0.043058783	0.15724045	0.989449741	0.370996496
201109_s_at	THBS1	0.043727365	0.076171233	0.989449741	-0.468029423
211285_s_at	UBE3A	0.04463363	0.158570058	0.999775135	-0.262984362
204961_s_at	NCF1	0.046220251	0.180186992	0.989449741	0.218415324
209023_s_at	STAG2	0.04635073	0.043778052	0.989449741	-0.334015439
213653_at	METTL3	0.047100971	0.043065116	0.999860944	0.304049124
218237_s_at	SLC38A1	0.047158302	0.077497989	0.989449741	-0.332756015
206871_at	ELA2	0.047306295	0.151483987	0.989449741	0.375756567
211506_s_at	IL8	0.047319227	0.110267486	0.989449741	-0.422779419
212224_at	ALDH1A1	0.04837586	0.168321646	0.989449741	0.231824985
212005_at	0	0.049589112	0.051163635	0.992633412	-0.367774805

Table 6: Subgroup X - IL-15 Regulated Genes and Metrics

Gene Name	Gene Description	Log Ratio	False Discovery Rate	Entrez Gene ID for Human	Entrez Gene ID for Mouse	Entrez Gene ID for Rat	Exemplar SEQ ID NO.
BCL2	B-cell CLL/lymphoma 2	0.336331	0.0076092	596	12043	24224	1
CALM1	calmodulin 1 (phosphorylase kinase, delta)	0.317008	2.80E-05	801	12313	24242	2
CCL2	chemokine (C-C motif) ligand 2	-3.197736	7.90E-12	6347	20293	287562	3
CCR1	chemokine (C-C motif) receptor 1	-1.080562	3.03E-04	1230	12768	57301	4
CCR2	chemokine (C-C motif) receptor 2	-0.327232	0.0080358	1231	12772	60463	5
CD40	CD40 molecule, TNF receptor superfamily member 5	-0.500496	4.45E-04	958	21939	171369	6
CD44	CD44 molecule (Indian blood group)	0.390189	5.38E-04	960	12505	25406	7
CD53	CD53 molecule	-0.324923	8.30E-05	963	12508	24251	8
CD86	CD86 molecule	-0.375037	1.94E-04	942	12524	56822	9
CD8B	CD8b molecule	0.529394	0.0041036	926	12526	24931	10
CEACAM1 (includes EG:634)	carcinoembryonic antigen-related cell adhesion molecule 1 (biliary glycoprotein)	-0.332004	0.0126034	634	26365	81613	11
CKS1B	CDC28 protein kinase regulatory subunit 1B	-0.272981	0.0053558	1163	54124	499655	12
CX3CR1	chemokine (C-X3-C motif) receptor 1	-0.921081	4.55E-04	1524	13051	171056	13
CXCR4	chemokine (C-X-C motif) receptor 4	0.435521	8.49E-05	7852	12767	60628	14
DUSP11	dual specificity phosphatase 11 (RNA/RNP complex 1-interacting)	0.263793	0.0052424	8446	72102	297412	15
FAS	Fas (TNF receptor superfamily, member 6)	-0.452922	5.24E-05	355	14102	246097	16
GABPB2	GA binding protein transcription factor, beta subunit 2	0.359036	0.0375917	2553	14391	364738	17
GDI2 (includes EG:2665)	GDP dissociation inhibitor 2	0.316008	4.30E-05	2665	14569	29662	18
GNAS (includes EG:2778)	GNAS complex locus	0.281187	0.0067831	2778	14683	24896	19
GZMB	granzyme B (granzyme 2, cytotoxic T-lymphocyte-associated serine esterase 1)	-0.353436	0.0469344	3002	14939	171528	20
HIST2H2AA3	histone cluster 2, H2aa3	-0.491629	6.69E-06	8337	15267	690131, 365877	21
HNRPA2B1	heterogeneous nuclear ribonucleoprotein A2/B1	-0.31297	0.0199395	3181	53379	362361	22
ICAM2	intercellular adhesion molecule 2	-0.411062	1.03E-04	3384	15896	360647	23
IFI35	interferon-induced protein 35	-1.539826	1.00E-14	3430	70110	287719	24
IFIT1	interferon-induced protein with tetratricopeptide repeats 1	-3.348328	1.00E-14	3434	112419	294090	25
IFITM1	interferon induced transmembrane protein 1 (9-27)	-1.137174	1.00E-14	8519	68713	293618	26
IL15	interleukin 15	-0.721076	3.65E-08	3600	16168	25670	27

Gene Name	Gene Description	Log Ratio	False Discovery Rate	Entrez Gene ID for Human	Entrez Gene ID for Mouse	Entrez Gene ID for Rat	Exemplar SEQ ID NO.
IL2RG	interleukin 2 receptor, gamma (severe combined immunodeficiency)	-0.345266	0.0395431	3561	16186	140924	28
KLRK1	killer cell lectin-like receptor subfamily K, member 1	0.309414	0.0062409	22914	27007	24934	29
LEF1	lymphoid enhancer-binding factor 1	0.382174	0.0058507	51176	16842	161452	30
LYN	v-src-1 Yamaguchi sarcoma viral related oncogene homolog	-0.286898	0.0067434	4067	17096	81515	31
MT1G	metallothionein 1G	-0.486602	6.25E-05	4495			32
MT1H	metallothionein 1H	-0.703151	4.92E-04	4496			33
MX1	myxovirus (influenza virus) resistance 1, interferon-inducible protein p78 (mouse)	-2.060167	1.00E-14	4599	17858	286918	34
MYD88	myeloid differentiation primary response gene (88)	-0.405963	2.54E-09	4615	17874	301059	35
NAGA	N-acetylgalactosaminidase, alpha-	-0.278443	0.0181778	4668	17939	315165	36
NP	nucleoside phosphorylase	-0.283364	0.0153042	4860	18950	290029	37
PIM1	pim-1 oncogene	-0.436049	1.78E-08	5292	18712	24649	38
PLEK	pleckstrin	-0.538329	4.27E-04	5341	56193	364206	39
PSMB10	proteasome (prosome, macropain) subunit, beta type, 10	-0.673245	1.32E-09	5699	19171	291983	40
PSMB9	proteasome (prosome, macropain) subunit, beta type, 9 (large multifunctional peptidase 2)	-0.859797	5.56E-10	5698	16912	24967	41
RAB8A	RAB8A, member RAS oncogene family	-0.364174	3.01E-06	4218	17274	117103	42
RAC2	ras-related C3 botulinum toxin substrate 2 (rho family, small GTP binding protein Rac2)	-0.313038	0.012755	5880	19354	366957	43
S100A11	S100 calcium binding protein A11	-0.854907	6.19E-08	6282	277089	445415	44
SELL	selectin L (lymphocyte adhesion molecule 1)	-0.574007	8.36E-07	6402	20343	29259	45
SFRS7	splicing factor, arginine/serine-rich 7, 35kDa	0.277934	0.042304	6432	225027	362687	46
SP100	SP100 nuclear antigen	-0.433437	4.59E-11	6672	20684	363269	47
TFDP2	transcription factor Dp-2 (E2F dimerization partner 2)	0.282919	0.0456667	7029	211586	300947	48
TJP2	tight junction protein 2 (zona occludens 2)	-0.341516	0.0078942	9414	21873	115769	49
TLR2	toll-like receptor 2	-0.523644	7.64E-04	7097	24088	310553	50
HLX	Homeobox-like gene	-0.301298	0.0105950	3142	15284	364069	61
IL15RA	interleukin 15 receptor, alpha			3601	16169	364775	62
PDIA4	protein disulfide isomerase family A, member 4	-0.3346159	0.00237448	9601	12304	116598	63
SORL1	sortilin-related receptor, L(DLR class) A repeats-containing	0.3383286	9.76E-05	6653	20660	300652	64
TNFSF10	tumor necrosis factor (ligand) superfamily, member 10	-1.3477080	3.11E-10	8743	22035	246775	65

TABLE 7: Stringency Conditions

Stringency Condition	Polynucleotide Hybrid	Hybrid Length (bp) ¹	Hybridization Temperature and Buffer ^H	Wash Temp. and Buffer ^H
A	DNA:DNA	>50	65°C; 1xSSC -or- 42°C; 1xSSC, 50% formamide	65°C; 0.3xSSC
B	DNA:DNA	<50	T _B [*] ; 1xSSC	T _B [*] ; 1xSSC
C	DNA:RNA	>50	67°C; 1xSSC -or- 45°C; 1xSSC, 50% formamide	67°C; 0.3xSSC
D	DNA:RNA	<50	T _D [*] ; 1xSSC	T _D [*] ; 1xSSC
E	RNA:RNA	>50	70°C; 1xSSC -or- 50°C; 1xSSC, 50% formamide	70°C; 0.3xSSC
F	RNA:RNA	<50	T _F [*] ; 1xSSC	T _F [*] ; 1xSSC
G	DNA:DNA	>50	65°C; 4xSSC -or- 42°C; 4xSSC, 50% formamide	65°C; 1xSSC
H	DNA:DNA	<50	T _H [*] ; 4xSSC	T _H [*] ; 4xSSC
I	DNA:RNA	>50	67°C; 4xSSC -or- 45°C; 4xSSC, 50% formamide	67°C; 1xSSC
J	DNA:RNA	<50	T _J [*] ; 4xSSC	T _J [*] ; 4xSSC
K	RNA:RNA	>50	70°C; 4xSSC -or- 50°C; 4xSSC, 50% formamide	67°C; 1xSSC
L	RNA:RNA	<50	T _L [*] ; 2xSSC	T _L [*] ; 2xSSC

¹: The hybrid length is that anticipated for the hybridized region(s) of the hybridizing polynucleotides. When hybridizing a polynucleotide to a target polynucleotide of unknown sequence, the hybrid length is assumed to be that of the hybridizing polynucleotide. When polynucleotides of known sequence are hybridized, the hybrid length can be determined by aligning the sequences of the polynucleotides and identifying the region or regions of optimal sequence complementarity.

^H: SSPE (1x SSPE is 0.15M NaCl, 10 mM NaH₂PO₄, and 1.25 mM EDTA, pH 7.4) can be substituted for SSC (1x SSC is 0.15M NaCl and 15 mM sodium citrate) in the hybridization and wash buffers.

- 10** T_B^{*} - T_R^{*}: The hybridization temperature for hybrids anticipated to be less than 50 base pairs in length should be 5-10°C less than the melting temperature (T_m) of the hybrid, where T_m is determined according to the following equations. For hybrids less than 18 base pairs in length, T_m(°C) = 2(# of A + T bases) + 4(# of G + C bases). For hybrids between 18 and 49 base pairs in length, T_m(°C) = 81.5 + 16.6(log₁₀[Na⁺]) + 0.41(%G + C) - (600/N), where N is the number of bases in the hybrid, and [Na⁺]
- 15** is the molar concentration of sodium ions in the hybridization buffer ([Na⁺] for 1x SSC = 0.165 M).

TABLE 8: Serum Markers of Exacerbation

Serum Biomarker	P value: Exacerb v Quiet	P value: Asthma v Healthy	P value: Quiet v Healthy	Mean pg/ml Exacerb	Mean pg/ml Quiet	Mean pg/ml Healthy	N Exacerb	N Quiet	N Healthy
ST2	0.017	0.006	0.152	90.2	61.1	55.4	69	85	43
CHI3L1 (YKL-40)		0.003		*64,750		43,800	*82		52
IL5	0.028	0.001	0.018	0.5	0.4	0.1	37	37	45
Eotaxin	0.803	0.188	0.098	578.2	525.1	626.4	37	37	45
TNF α	0.017	0.200	0.953	1.7	1.4	1.4	37	37	45
IL8	0.110	0.140	0.502	6.0	4.1	3.5	37	37	45
IL13	0.711	0.126	0.140	5.0	5.6	3.0	13	13	7
MCP-1	0.096	0.139	0.753	240.8	201.4	196.8	37	37	45
TARC	0.690	0.583	0.486	42.2	44.9	40.6	37	37	45

* Represents total asthma (quiet and exacerbation)

TABLE 9: Cluster X Biomarkers Having Low Intra-subject Variability

Gene Name	GenBank No.	AOS v HVOS FDR all visits	Quiet v. Exacerb FDR	Q v. E followup 1 FDR
interferon induced transmembrane protein 1 (IFITM1)	NM_003641.1	0	0	0.932963506
transcriptional coactivator Sp110b (SP110)	AF280094.1	0	7.81859E-11	0.838299238
tumor necrosis factor (ligand) superfamily, member 10 (TNFSF10)	NM_003810.1	0	1.72681E-10	0.971768475
interferon-induced protein 41, 30kD (IFI41)	NM_004509.1	0	6.0713E-10	0.663534687
interferon induced transmembrane protein 1 (IFITM1)	AA749101	6.87162E-15	0	0.977627636
interferon induced transmembrane protein pseudogene (SEQ ID NO:58)	AL121994	5.45762E-12	0	0.764947366
Homo sapiens hypothetical protein (LOC51316) (SEQ ID NO:59)	NM_016619.1	2.67267E-11	0	0.547460786
ubiquitin-conjugating enzyme E2L 6 (UBE2L6)	NM_004223.1	2.80205E-11	0	0.804966785
interferon induced transmembrane protein 3 (IFITM3)	BF338947	4.70201E-11	0	0.804966785
Fc-gamma receptor I B1 (FCGR1A)	L03419.1	1.45092E-09	1.03296E-09	0.713883189
myxovirus (influenza) resistance 2, homolog of murine (MX2)	NM_002463.1	7.20437E-09	0	0.823670503
2-5oligoadenylate synthetase 2 (OAS2)	NM_016817.1	1.39899E-08	1.23025E-13	0.994302012
high affinity Fc receptor (FcRI) b form (FCGR1A)	X14355.1	2.84849E-08	4.37509E-11	0.543105461
signal transducer and activator of transcription 1, 91kD (STAT1)	NM_007315.1	7.50544E-08	8.19311E-10	0.806943262
myxovirus (influenza) resistance 1 (interferon-inducible protein p78) (MX1)	NM_002462.1	1.25342E-06	0	0.92335789
interferon, alpha-inducible protein (clone IFI-6-16) (G1P3) (IFI6)	NM_022873.1	2.7602E-06	0	0.911573276
bone marrow stromal cell antigen 2 (BST2)	NM_004335.2	1.61277E-05	3.80484E-11	0.947786651
hypothetical protein FLJ22693 (FLJ22693) (PARP12)	NM_022750.1	2.68573E-05	0	0.906722412
similar to interferon-induced protein 35, clone MGC:2935 (IFI35)	BC001356.1	4.13047E-05	0	0.844024603
proteasome (prosome, macropain) activator subunit 2 (PA28 beta) (PSME2)	NM_002818.1	5.5437E-05	4.12266E-12	0.576624724

TABLE 10: Cluster Y Biomarkers Having Low Intra-subject Variability

Gene Name	GenBank No.	AOS v HVOS FDR all visits	Quiet v. Exacerb FDR	Q v. E followup FDR
CDC28 protein kinase 1 (CKS1)	NM_001826.1	0.000741	0.00039	0.999876
defender against cell death 1 (DAD1)	NM_001344.1	0.000526	0.000469	0.98945
hypothetical protein FLJ10143 (FLJ10143) (TAPBPL)	NM_018009.1	0.000144	0.000269	0.98945
immunoglobulin (mAb59) light chain V region (IGL2)	D84143.1	9.65E-05	0.000466	0.98945
intercellular adhesion molecule 2 (ICAM2)	AA126728	6.25E-05	0.000308	0.98945
ELAV (embryonic lethal, abnormal vision, Drosophila)-like 1 (Hu antigen R)	BC003376.1	5.9E-05	0.000298	0.98945
interleukin 2 receptor, gamma (severe combined immunodeficiency) (IL2RG)	NM_000206.1	5.64E-05	0.000206	0.98945
vesicle-associated membrane protein 8 (endobrevin) (VAMP8)	NM_003761.1	1.28E-07	0.000469	0.98945
annexin A2 (ANXA2)	BC001388.1	6.08E-08	0.000938	0.98945
intercellular adhesion molecule 2 (ICAM2)	NM_000873.2	1.45E-08	0.000298	0.98945
cat eye syndrome chromosome region, candidate 1 (CECR1)	NM_017424.1	7.13E-09	0.000714	0.98945
natural killer cell transcript 4 (NK4) (IL32)	NM_004221.1	2.02E-09	0.000635	0.98945
leukocyte-associated Ig-like receptor 1b (LAIR1)	AF109683.1	8.04E-10	0.000689	0.98945
arginine-rich, mutated in early stage tumors (ARMET)	NM_006010.1	6.4E-10	0.000486	0.98945
adenylate kinase 2 (AK2)	AL513611	1.33E-11	0.000469	0.98945
natural killer cell enhancing factor (NKEFA) (PRDX1)	L19184.1	4.38E-14	0.00039	0.98945
KIAA0102 gene product (KIAA0102) (SPCS2)	NM_014752.1	6.87E-15	0.000228	0.98945
HSPC022 protein (RAC2)	BE138888	0	0.000269	0.98945
Hs.11774 protein (peptidyl-prolyl cistrans isomerase) NIMA-interacting, 4 (parvulin) (PIN4)	BE797213	0	0.000269	0.98945
ribonuclease, RNase A family, 2 (liver, eosinophil-derived neurotoxin) (RNASE2)	NM_002934.1	0	0.000931	0.98945

TABLE 11: Exacerbation plus Infection Sample Biomarkers

Gene	FDR: Exacer only v. Quiet	$\Delta\log_2$: Exacer only v. Quiet	FDR: Exacer/Infec v. Quiet	FDR: All Exacer v. Quiet	FDR Quiet asthma v. Healthy non- asthma	SEQ ID NO
IFITM3	0.001	-0.333	0.003	5.17094E-06	4.70201E-11	
G1P2	0.027	-0.408	0.001	7.23786E-05	0.000782438	
IFI27	0.025	-0.731	0.002	8.16669E-05	#N/A	
TCN2	0.022	-0.209	0.010	0.000100698	1.11604E-05	
G1P3	0.022	-0.365	0.016	0.000146777	2.7602E-06	
SN	0.027	-0.324	0.007	0.000165414	0.391303978	
IFI44	0.045	-0.333	0.002	0.000165414	0.129278459	
EIF4B	0.025	0.142	0.023	0.000253558	0.007556601	
SERPING1	0.091	-0.420	0.003	0.000539881	0.003395405	
APOBEC3A	0.045	-0.287	0.023	0.000587634	0.002173562	
LY6E	0.067	-0.357	0.018	0.000762438	0.235837992	
RPL22	0.067	0.119	0.035	0.001291265	0.058418958	
MX1	0.171	-0.281	0.007	0.001557619	1.25342E-06	
OASL	0.175	-0.246	0.012	0.002382976	0.869662043	
IFIT3	0.151	-0.344	0.028	0.002974539	0.226938617	
PPGB	0.370	-0.114	0.002	0.002974539	2.09308E-06	
UNK_AF06361 2	0.154	-0.225	0.041	0.004087944	0.495985855	
OAS3	0.265	-0.277	0.050	0.009513928	0.000250457	
PSME2	0.293	-0.174	0.041	0.009513928	5.5437E-05	
CD44	0.492	0.071	0.011	0.015400702	0.1315576	
IFITM2	0.445	-0.164	0.032	0.017938992	2.59456E-14	
ECGF1	0.531	-0.170	0.012	0.020179897	0.058038605	
OAS1	0.445	-0.311	0.042	0.022950993	0.002188974	
PLAC8	0.492	-0.137	0.028	0.02429545	2.67267E-11	
IRF7	0.492	-0.202	0.034	0.026794854	0.174138096	
IFI35	0.506	-0.200	0.032	0.027466143	4.13047E-05	
TYMS	0.514	-0.172	0.030	0.027466143	2.20758E-07	
RNASE2	0.706	-0.142	0.002	0.027466143	0	
FLJ38348	0.561	-0.129	0.041	0.042413043	0.039377722	
KIAA0101	0.572	-0.147	0.036	0.043812874	4.44916E-07	
UBE2L6	0.579	-0.133	0.032	0.043812874	2.80205E-11	
PIAS2	0.560	0.088	0.050	0.045371225	6.69202E-05	
IFIT1	0.588	-0.438	0.035	0.046057322	0.001371158	
FCGR1A	0.570	-0.141	0.048	0.046330608	2.84849E-08	
PSMA6	0.562	-0.074	0.042	0.047062283	0	
PSMB3	0.644	-0.068	0.022	0.050202891	0	
RRM2	0.591	-0.142	0.038	0.050259485	7.24762E-05	
FCER1G	0.638	-0.109	0.030	0.055052737	6.78321E-11	
S100A11	0.616	-0.162	0.042	0.063397546	0	
DYSF	0.773	-0.120	0.028	0.12030689	2.2082E-06	
PSMD8	0.856	-0.046	0.041	0.217968184	2.75751E-12	
CECR1	0.899	-0.071	0.022	0.232280881	7.13012E-09	
BLVRA	0.886	-0.043	0.030	0.232506885	0	

Gene	FDR: Exacer only v. Quiet	$\Delta\log_2$: Exacer only v. Quiet	FDR: Exacer/Infec v. Quiet	FDR: All Exacer v. Quiet	FDR Quiet asthma v. Healthy non- asthma	SEQ ID NO
HP	0.898	-0.083	0.030	0.244441709	2.18019E-05	
BLVRA	0.886	-0.065	0.036	0.255095135	0	
PSMB2	0.930	-0.030	0.023	0.283759498	2.0947E-11	
UNK_AW5142 67	0.925	0.052	0.042	0.304446425	8.82495E-08	
SEPHS1	0.959	0.018	0.022	0.336856388	0.293094414	
FLJ10726	0.957	0.017	0.038	0.367468887	0.9215285	
PDXK	0.974	-0.017	0.023	0.385945685	2.17167E-05	
TSPYL5	0.982	0.014	0.041	0.45192057	0.016253975	
ARIH2	0.983	0.007	0.042	0.474810162	0.008139129	
TRIM10	0.990	-0.012	0.007	0.484966296	0.690008027	
SMARCB1	0.966	-0.023	0.050	0.718001203	0.869116514	

TABLE 12: Exacerbation with Infection Biomarkers

Gene	FDR: Exacer only v. Quiet	$\Delta\log_2$: Exacer only v. Quiet	FDR: Exacer/Infec v. Quiet	FDR: All Exacer v. Quiet	FDR Quiet asthma v. Healthy non- asthma	SEQ ID NO
SMARCB1	0.966	-0.023	0.050	0.718001203	0.869116514	63
TRIM10	0.990	-0.012	0.007	0.484966296	0.690008027	64
ARIH2	0.983	0.007	0.042	0.474810162	0.008139129	65
TSPYL5	0.982	0.014	0.041	0.45192057	0.016253975	66
PDXK	0.974	-0.017	0.023	0.385945685	2.17167E-05	67
FLJ10726	0.957	0.017	0.038	0.367468887	0.9215285	68
SEPHS1	0.959	0.018	0.022	0.336856388	0.293094414	69
UNK_AW514267	0.925	0.052	0.042	0.304446425	8.82495E-08	70
PSMB2	0.930	-0.030	0.023	0.283759498	2.0947E-11	71
BLVRA	0.886	-0.065	0.036	0.255095135	0	72
HP	0.898	-0.083	0.030	0.244441709	2.18019E-05	73
BLVRA	0.886	-0.043	0.030	0.232506885	0	74
CECR1	0.899	-0.071	0.022	0.232280881	7.13012E-09	75
PSMD8	0.856	-0.046	0.041	0.217968184	2.75751E-12	76
DYSF	0.773	-0.120	0.028	0.12030689	2.2082E-06	77
S100A11	0.616	-0.162	0.042	0.063397546	0	44

WHAT IS CLAIMED IS:

1. A method of determining a molecular signature of asthma exacerbation of a patient with asthma, comprising:

(a) obtaining a sample from the patient;

5 (b) measuring the levels of two or more products in a sample obtained from the patient, wherein each product is produced from a gene which is differentially expressed during asthma exacerbation; and

(c) comparing said levels of step (b) to reference levels of said two or more products, wherein a difference between said levels of step (b) and the reference levels indicates the
10 molecular signature of asthma exacerbation for the individual, wherein the molecular signature indicates a type of asthma exacerbation selected from the group comprising exacerbation associated with innate immunity, exacerbation associated with cognate immunity, exacerbation associated with concomitant airway infection and exacerbation associated with no airway infection.

15 2. The method of claim 1, wherein the reference level is the level of said product in a sample obtained from the individual during an asthma quiet period.

3. The method of claim 1, wherein the reference level is the average of the level of said product in samples obtained from individuals who are not undergoing an asthma attack or asthma exacerbation.

20 4. The method of any one of claims 1-3, wherein the sample comprises peripheral blood mononuclear cells.

5. The method of any one of claims 1-4, wherein the type of asthma exacerbation comprises exacerbation associated with innate immunity and the gene is selected from the group comprising genes set forth in Table 4, Table 6 and Table 9.

25 6. The method of any one of claims 1-5, wherein the gene is selected from the group consisting of IFI35, IFIT1, IFITM1, MX1, CCL2, SP100, PSMB9, PSMB10, MYD88 chemokine C-C motif receptor 1 (CCR1), chemokine C-X3-C motif receptor 1 (CX3CR1), S100 calcium binding protein A11 (S100A11), interleukin 15 (IL15) and PIM1.

7. The method of any one of claims 1-4, wherein the type of asthma exacerbation comprises
30 exacerbation associated with cognate immunity and the gene is selected from the group comprising genes set forth in Table 5 and Table 10.

8. The method of any one of claims 1-4, wherein the type of asthma exacerbation comprises exacerbation associated with concomitant airway infection and the gene is selected from the group comprising genes set forth in Table 11 and Table 12.
9. The method of any one of claims 1-4, wherein the type of asthma exacerbation comprises
5 exacerbation not associated with airway infection and the gene is selected from the group
group comprising interferon induced with helicase C domain 1 (IFIH1), leukotriene A4
hydrolase (LTA4H) and open reading frame number 25 of human chromosome 6
(C6ORF25).
10. The method of any one of claims 1-9, wherein the product is a protein.
- 10 11. The method of any one of more of claims 1-9, wherein the product is a mRNA.
12. A method for assessing the effectiveness of a therapy, comprising:
(a) administering a therapy to a patient;
(b) measuring the level of at least one product in a sample obtained from the
individual, wherein the product is produced from a gene which is differentially expressed
15 during asthma exacerbation;
(c) comparing said level of step (a) to a reference level of said product, wherein a
difference between said level of step (a) and the reference level indicates that the therapy is
effective,
wherein the therapy is either an asthma therapy or an investigational asthma therapy.
- 20 13. The method of claim 12, wherein the reference level is the level of said product in a
sample obtained from the individual prior to the administration of the therapy.
14. The method of claim 12, wherein the reference level is an average of the level of said
product in samples obtained from individuals who are undergoing an asthma attack or
asthma exacerbation.
- 25 15. The method of any one of claims 12-14, wherein the sample comprises peripheral blood
mononuclear cells.
16. The method of any one of claims 12-15, wherein said gene is selected from the group
consisting the genes set forth in Table 2, Table 3, Table 4, Table 5, Table 6, Table 8, Table
9, Table 10, Table 11 and Table 12.
- 30 17. The method of any one of claims 12-16, wherein the gene is selected from the group
consisting of interferon-induced protein 35 (IFI35), interferon-induced protein with
tetratricopeptide repeats 1 (IFIT1), interferon-induced protein 44-like (IFI44L), interferon-

induced protein 27 (IFI27), interferon-stimulated gene 15 (ISG15), serpin peptidase inhibitor clade G member 1 (SERPING1), interferon-induced protein with tetratricopeptide repeats 3 (IFIT3), interferon-induced protein 44 (IFI44), lymphocyte antigen 6 complex locus E (LY6E), interferon induced transmembrane protein 1 (IFITM1), interferon-inducible protein p78 (MX1), chemokine C-C motif ligand 2 (CCL2), SP100 nuclear antigen (SP100), proteasome subunit beta type 9 (PSMB9), chemokine C-C motif receptor 1 (CCR1), chemokine C-X3-C motif receptor 1 (CX3CR1), proteasome subunit beta type 10 (PSMB10), myeloid differentiation primary response gene 88 (MYD88), interleukin 15 (IL15), calcium binding protein A11 (S100A11) and pim-1 oncogene (PIM1).

10 18. The method of any one of claims 12-17, wherein the product is a protein.

19. The method of any one of more of claims 12-17, wherein the product is an mRNA.

20. A method of identifying a compound that is effective for treating asthma exacerbation, comprising: providing a candidate compound to a cell and determining whether said compound inhibits IL-15 activity in the cell, wherein inhibition of IL-15 activity indicates that
15 said compound is effective for treating acute exacerbation of asthma.

21. The method according to claim 20, wherein said IL-15 activity is (a) binding of IL-15 to a cognate receptor, (b) a downstream IL-15 signaling event, or (c) both.

22. The method according to claim 20, wherein the cell is a peripheral blood mononuclear cell (PBMC).

20 23. An array for use in diagnosing asthma exacerbation in a patient, comprising a plurality of discrete regions on a substrate, each of which comprises a probe disposed thereon, wherein at least 15% of the plurality of discrete regions has disposed thereon probes that specifically detect a marker of asthma exacerbation in PBMCs or other tissues.

24. The array of claim 23, wherein the marker of asthma exacerbation comprises at least
25 one marker selected from the group consisting of the markers set forth in Tables 2, 3, 4, 5, 6, 8, 9, 10, 11 and 12.

25. The array of claim 23 or 24, wherein the marker of asthma exacerbation comprises at least one marker selected from the group consisting of the markers set forth in Tables 2, 3, 4, 5, 6, 8, 9, 10, 11 and 12 having an FDR for exacerbation versus quiet of less than or equal
30 to 10⁻⁵.

26. The array of any one of claims 23-25, wherein the probe is a polynucleotide.

27. The array of any one of claims 23-25, wherein the probe is an antibody or fragment thereof.

28. The array of any one of claims 23-25, wherein the probe is an aptamer.

29. An array for use in diagnosing asthma exacerbation in a patient comprising an IFIT1
5 polynucleotide, an MX1 polynucleotide, and a CCL2 polynucleotide; and optionally
comprising any one or more of a polynucleotide selected from the group consisting of IFI35,
IFITM1, SP100, PSMB9, PSMB10, MYD88, PIM1, CCR1, CX3CR1, S100A11, IL15, IFI27,
ISG15 SERPING1, IFIT3, IFI44 and LY6E polynucleotide; wherein each of said
10 polynucleotide is a single-stranded polynucleotide comprising at least 22 contiguous
nucleotides.

30. A kit comprising a detection reagent which binds to the gene product of any one of a
plurality of genes that are differentially expressed in a sample obtained from an individual
having an asthma exacerbation versus a sample obtained from an individual having an
asthma quiet period.

15 31. The kit of claim 30, wherein the plurality of genes is selected from the group consisting
of the genes set forth in Tables 1-6 and 8-12.

32. The kit of claim 30 or 31, wherein the gene product comprises a polypeptide and the
detection reagent comprises an antibody, a fragment of an antibody, or an aptamer,.

33. The kit of any one of claims 30 or 31, wherein the gene product comprises a
20 polynucleotide and the detection reagent comprises an oligonucleotide that hybridizes to the
polynucleotide.