DETECTION OF CHROMOSOME INTERACTIONS

Field of the Invention

The invention relates to detecting chromosome interactions.

Background of the Invention

Health care costs are spiralling and so there is a need to treat people more effectively using existing drugs.

Summary of the Invention

The inventors have investigated the use of epigenetic chromosome interactions as the basis of or for use in conjunction with companion diagnostics, and in particular in the detection of epigenetic states to determine responsiveness to therapy (e.g. pharmaceutical therapy), predisposition to disease / conditions, and/or monitoring residual disease. The inventors' work shows the role played by epigenetic interactions in a diverse set of conditions and provides methods for identifying the relevant chromosomal interactions. The invention includes a method of identifying relevant chromosomal interactions based on looking at the chromosome interactions present in subgroups of individuals. The invention also includes using the identified chromosome interactions as the basis for companion diagnostic tests.

Accordingly a **first aspect** of the invention provides a method of determining the epigenetic chromosome interactions which are relevant to a companion diagnostic that distinguishes between subgroups, comprising contacting a first set of nucleic acids from the subgroups with a second set of nucleic acids representing an index population of chromosome interactions, and allowing complementary sequences to hybridise, wherein the nucleic acids in the first and second sets of nucleic acids represent a ligated product comprising sequences from both of the chromosome regions that have come together in the epigenetic chromosome interaction, and wherein the pattern of hybridisation between the first and second set of nucleic acids allows a determination of which epigenetic chromosome interactions are specific to subgroups in the population, wherein the subgroups differ in a characteristic relevant to a companion diagnostic.

Preferably, in the first aspect (and/or any other aspect) of the invention:

- the subgroups are subgroups in a or the animal (e.g. mammal or nematode worm) population, most preferably subgroups in a or the human population; and/or

- the first set of nucleic acids is from at least 8 individuals; and/or

- the first set of nucleic acids is from at least 4 individuals from a first subgroup and at least 4 individuals from a second subgroup which is preferably non-overlapping with the first subgroup, and/or

- the second set of nucleic acids represents an unselected group of chromosome interactions; and/or

- the second set of nucleic acids is bound to an array at defined locations; and/or

- the second set of nucleic acids represents chromosome interactions in least 100 different genes or loci; and/or

- the second set of nucleic acids comprises at least 1000 different nucleic acids representing at least 1000 different epigenetic chromosome interactions; and/or

- the first set of nucleic acids and the second set of nucleic acids comprise nucleic acid sequences of length 10 to 100 nucleotide bases; and/or

- the method is carried out to determine which locus or gene is relevant to said characteristic relevant to a companion diagnostic;

and/or

- the subgroups differ in respect to:

(i) responding to a specific treatment and/or prophylaxis (in particular to a specific pharmaceutical treatment and/or prophylaxis), and/or

(ii) predisposition to a specific condition, and/or

(iii) the presence of residual disease which may lead to relapse;

and/or

- the first set of nucleic acids is generated in a method comprising the steps of:

(i) *in vitro* cross-linking of chromosome regions which have come together in a chromosome interaction;

(ii) subjecting said cross-linked DNA to restriction digestion cleavage with an enzyme; and

(iii) ligating said cross-linked cleaved DNA ends to form the first set of nucleic acids (in particular comprising ligated DNA);

and/or

- said characteristic relevant to a companion diagnostic is:

(i) responsiveness to methotrexate (or to another rheumatoid arthritis drug) in rheumatoid arthritis patients, and/or

(ii) responsiveness to therapy for acute myeloid leukaemia, and/or

(iii) likelihood of relapse in melanoma.

Preferably, in the first and/or other aspects of the invention, the feature "…. the nucleic acids in the first and second sets of nucleic acids represent a ligated product comprising sequences from both of the chromosome regions that have come together in the epigenetic chromosome interaction …" can comprise or be: "… the nucleic acids in the first and second sets of nucleic acids are in the form of a ligated product(s) (preferably a ligated nucleic acid(s), more preferably ligated DNA) comprising sequences from both of the chromosome regions that have come together in the epigenetic chromosome interaction".

A **second aspect** of the invention provides a companion diagnostic assay method which selects a subgroup having a characteristic relevant to treatment and/or prophylaxis (in particular pharmaceutical treatment and/or prophylaxis), which method comprises:

(a) typing a locus which has been identified by the above method as having an epigenetic interaction characteristic to the subgroup, and/or

(b) detecting the presence or absence of at least 5 epigenetic chromosome interactions, preferably at at least 5 different loci, which are characteristic for:

i. responding to a specific treatment and/or prophylaxis (in particular a specific pharmaceutical treatment and/or prophylaxis), and/or
ii. predisposition to a specific condition, and/or
iii. the presence of residual disease which may lead to relapse.

Preferably, in the second aspect (and/or any other aspect) of the invention:

- the method comprises step (a) as defined in the second aspect of the invention, wherein:

(1) said locus is a gene, and/or

(2) a single nucleotide polymorphism (SNP) is typed, and/or

(3) a microRNA (miRNA) is expressed from the locus, and/or

(4) a non-coding RNA (ncRNA) is expressed from the locus, and/or

(5) the locus expresses a nucleic acid sequence encoding at least 10 contiguous amino acid residues, and/or

(6) the locus expresses a regulating element, and/or

(7) said typing comprises sequencing or determining the level of expression from the locus;

and/or

- the method comprises step (b) as defined in the second aspect of the invention, wherein:
- 5 to 500, preferably 20 to 300, more preferably 50 to 100, epigenetic chromosome interactions are typed, preferably at at least 5 different loci; and/or
- the presence or absence of 5 to 500, preferably 20 to 300, more preferably 50 to 100, epigenetic chromosome interactions, preferably at at least 5 different loci, are detected.

Other preferred or particular features of or in the second aspect (and/or any other aspect) of the invention include the following:

The companion diagnostic assay method of the second aspect of the invention can particularly be used to detect the presence of any of the specific conditions or characteristics mentioned herein.

Preferably, the companion diagnostic method of the second aspect of the invention is used to detect:
- responsiveness to methotrexate (or another rheumatoid arthritis drug) in rheumatoid arthritis patients,
- responsiveness to therapy for acute myeloid leukaemia (AML) patients,
- likelihood of relapse in melanoma,
- likelihood of developing prostate cancer and/ or aggressive prostate cancer, and/or
- likelihood of developing and/or having a predisposition to a neurodegenerative disease or condition, preferably a dementia such as Alzheimer's disease, mild cognitive impairment, vascular dementia, dementia with Lewy bodies, frontotemporal dementia, or more preferably Alzheimer's disease, most preferably beta-amyloid aggregate induced Alzheimer's disease, and/or

- a comparison(s) between dementia patients (preferably Alzheimer's disease patients, more preferably Alzheimer's disease patients with beta-amyloid aggregates) and cognitively-impaired patients without Alzheimer's disease, in particular with respect to memory and/or cognition;

in all cases preferably in a human.

Preferably, in the second aspect and in all other aspects of the invention, the disease or condition (in particular in a human) comprises:
- an inflammatory disease, preferably rheumatoid arthritis; in particular in a human;
- a blood cancer, preferably acute myeloid leukaemia (AML); in particular in a human;

- a solid cancer / solid tumour, preferably melanoma, prostate cancer and/ or aggressive prostate cancer; in particular in a human; and/or
- a neurodegenerative disease or condition, preferably a dementia such as Alzheimer's disease, mild cognitive impairment, vascular dementia, dementia with Lewy bodies, frontotemporal dementia, or more preferably Alzheimer's disease such as beta-amyloid aggregate induced Alzheimer's disease; in particular in a human, and/or
- responsiveness to immunotherapy, such as antibody therapy, preferably anti-PD1 therapy.

In one embodiment responsiveness to therapy, preferably anti-PD1 therapy, is detected in any of the following cancers, preferably of the stage or class which is indicated and/or preferably with other indicated characteristics such as viral infection:

- DLBCL_ABC: Diffuse large B-cell lymphoma subtype activated B-cells
- DLBCL_GBC: Diffuse large B-cell lymphoma subtype germinal center B-cells
- HCC: hepatocellular carcinoma
- HCC_HEPB: hepatocellular carcinoma with hepatitis B virus
- HCC_HEPC: hepatocellular carcinoma with hepatitis C virus
- HEPB+R: Hepatitis B in remission
- Pca_Class3: Prostate cancer stage 3
- Pca_Class2: Prostate cancer stage 2
- Pca_Class1: Prostate cancer stage 1
- BrCa_Stg4: Breast cancer stage 4
- BrCa_Stg3B: Breast cancer stage 3B
- BrCa_Stg2A: Breast cancer stage 2A
- BrCa_Stg2B: Breast cancer stage 2B
- BrCa_Stg1A: Breast cancer stage 1A
- BrCa_Stg1: Breast cancer stage 1.

The condition or characteristic may be:
- responsiveness to IFN-B (IFN-beta) treatment in multiple sclerosis patients, and/or
- predisposition to relapsing-remitting multiple sclerosis, and/or
- likelihood of primary progressive multiple sclerosis, and/or
- predisposition to amyotrophic lateral sclerosis (ALS) disease state (in particular in humans), and/or
- predisposition to fast progressing amyotrophic lateral sclerosis (ALS) disease state, and/or
- predisposition to aggressive type 2 diabetes disease state, and/or

- predisposition to type 2 diabetes disease state, and/or
- predisposition to a pre-type 2 diabetes state, and/or
- predisposition to type 1 diabetes disease state, and/or
- predisposition to systemic lupus erythematosus (SLE) disease state, and/or
- predisposition to ulcerative colitis disease state, and/or
- likelihood of relapse of colorectal cancer for ulcerative colitis patients, and/or
- likelihood of malignant peripheral nerve sheath tumours for neurofibromatosis patients, and/or
- likelihood of developing prostate cancer and/or aggressive prostate cancer.

A **third aspect** of the present invention provides a therapeutic agent (in particular a pharmaceutical therapeutic agent) for use in the treatment and/or prophylaxis of a condition in an individual (in particular in a human individual), wherein said individual has been identified as being in need of said therapeutic agent by the method of the second aspect of the invention. The third aspect of the invention also provides the use of a therapeutic agent (e.g. pharmaceutical therapeutic agent) in the manufacture of a medicament (in particular a pharmaceutical composition comprising the therapeutic agent) for use in the treatment and/or prophylaxis of a condition in an individual (in particular in a human individual), wherein said individual has been identified as being in need of said therapeutic agent by the method of the second aspect of the invention. The third aspect of the present invention also provides a method of treatment and/or prophylaxis of a condition in an individual (in particular in a human individual and/or an individual in need thereof), comprising administering a therapeutic agent (e.g. pharmaceutical therapeutic agent and/or an effective amount of a therapeutic agent) to the individual, wherein said individual has been identified as being in need of said therapeutic agent by the method of the second aspect of the invention.

Preferably, in the third aspect (and/or other aspects) of the invention, the therapeutic agent (in particular pharmaceutical therapeutic agent) comprises:

- a pharmaceutically active agent (e.g. compound or biologic / biological agent such as a protein or antibody) suitable for use in the treatment and/or prophylaxis of an inflammatory disease; in particular in a human;
- preferably a pharmaceutically active agent (e.g. compound or biologic / biological agent such as a protein or antibody) suitable for use in the treatment and/or prophylaxis of rheumatoid arthritis (RA); in particular in a human; wherein preferably the pharmaceutically active agent comprises methotrexate; hydroxychloroquine; sulfasalazine; leflunomide; a TNF-alpha (tumor necrosis factor alpha) inhibitor, in particular a monoclonal antibody TNF-alpha inhibitor such as infliximab,

adalimumab, certolizumab pegol or golimumab, or a circulating receptor fusion protein TNF-alpha inhibitor such as etanercept; or a T cell costimulation inhibitor such as abatacept; or an interleukin 1 (IL-1) inhibitor such as anakinra; or a monoclonal antibody against B cells such as rituximab or tocilizumab;

or

- a pharmaceutically active agent (e.g. compound or biologic / biological agent such as a protein or antibody) suitable for use in the treatment and/or prophylaxis of a blood cancer, preferably acute myeloid leukaemia (AML); in particular in a human; or

- a pharmaceutically active agent (e.g. compound or biologic / biological agent such as a protein or antibody) suitable for use in the treatment and/or prophylaxis of a solid cancer / solid tumour, preferably melanoma, prostate cancer and/ or aggressive prostate cancer; in particular in a human; or

- a pharmaceutically active agent (e.g. compound or biologic / biological agent such as a protein or antibody) suitable for use in the treatment and/or prophylaxis of a neurodegenerative disease or condition, preferably a dementia such as Alzheimer's disease, mild cognitive impairment, vascular dementia, dementia with Lewy bodies, frontotemporal dementia, or more preferably Alzheimer's disease such as beta-amyloid aggregate induced Alzheimer's disease; in particular in a human.

A **fourth aspect** of the invention provides a method of identifying an agent which is capable of changing the disease state of an individual from a first state to a second state comprising determining whether a candidate agent is capable of changing the chromosomal interactions from those corresponding with the first state to chromosomal interactions which correspond to the second state, wherein preferably the first and second state correspond to presence or absence of:

(i) responsiveness to a specific treatment and/or prophylaxis (in particular a specific pharmaceutical treatment and/or prophylaxis), and/or

(ii) predisposition to a specific condition, and/or

(iii) a residual disease which may lead to relapse.

A **fifth aspect** of the invention provides a method of determining the effect of a drug comprising detecting the change in epigenetic chromosome interactions caused by the drug, wherein said effect

is preferably the mechanism of action of the drug or are the pharmacodynamics properties of the drug, and wherein said the chromosome interactions are preferably specific to:

(i) responsiveness to a specific treatment and/or prophylaxis (in particular to a specific pharmaceutical treatment and/or prophylaxis), and/or

(ii) predisposition to a specific condition, and/or

(iii) a residual disease which may lead to relapse.

Additionally or alternatively, according to a preferred embodiment of all aspects of the present invention, the present invention does **not** relate to a method of determining responsiveness to a specific therapy (in particular a specific pharmaceutical therapy) for rheumatoid arthritis in a subject (e.g. a mammalian such as human subject), comprising detecting the presence or absence of 5 or more (in particular 7 or more, or 10 or more, or 15 or more, or 20 or more) chromosomal interactions; wherein said chromosomal interactions are in particular at 5 or more (for example 5) different loci; and/or wherein said detecting in particular comprises determining for each interaction whether or not the regions of a chromosome which are part of the interaction have been brought together.

Brief Description of the Drawings

Figure 1 is a figure comprising pie-charts and graphs relating to: Chromosome Conformation Signature EpiSwitch™ Markers discriminate MTX responders (R) from non-responders (NR). A discovery cohort of responder (R) and non-responder (NR) RA patients were selected based on DAS28 (Disease Activity Score of 28 joints) EULAR (The European League Against Rheumatism) response criteria (see methods). (A) Pie charts show the clinical interpretation of CDAI scores for both R and NR patients at baseline and 6 months. (B) CDAI scores of R and NR patients at baseline and 6 months. (C) EpiSwitch™ array analysis of peripheral blood mononuclear cells taken at diagnosis from R and NR, and healthy controls (HC) identified 922 statistically significant stratifying marker candidates. Further analysis revealed that 420 were specific for NR, 210 to R and 159 to HC. Pie charts show the proportion in relation to the 13,322 conditional chromosome conformations screened. All markers showed adjusted $p<0.2$. (D) Hierarchical clustering using Manhattan distance measure with complete linkage agglomeration is shown by the heatmaps. Marker selection using binary pattering across the 3 groups (R, NR and HC) initially reduced the 922 EpiSwitch™ Markers to 65 and then the top 30 markers.

Figure 2 is a figure comprising pie-charts and graphs relating to: Refinement and validation of the Chromosome Conformation Signature EpiSwitch™ Markers. The validation cohort of responder (R) and non-responder (NR) RA patients were selected based on DAS28 (Disease Activity Score of 28

joints) EULAR (The European League Against Rheumatism) response criteria (see methods). (A) Pie charts show the clinical interpretation of CDAI scores for both R and NR patients at baseline and 6 months. (B) CDAI scores of R and NR patients at baseline and 6 months. ****P<0.0001 by Kruskal–Wallis test with Dunn's multiple comparison post-test (C) Correlation plot of the classifying 5 EpiSwitch™ markers. The red box indicates the markers that define NR whilst the orange box indicated markers that define R. (D) Principle Component Analysis (PCA) for a 60 patient cohort based on their binary scores for the classifying 5 EpiSwitch™ markers.

Figure 3 is a figure comprising graphs relating to: Prognostic stratification and model validation for response to methotrexate (MTX) treatment. (A) Representative examples of 5 selected Receiver Operating Characteristics (ROC) curves from 150 randomisations of the data using the 5 CCS marker logistic regression classifiers. (B) Factor Analysis for responder (R) and non-responder (NR) RA patients vs healthy controls (HC) using EpiSwitch™ CCS markers selected for discerning MTX responders from MTX non-responders.

Figure 4 is a Schematic diagram of the 3C extraction process. 3C means chromatin conformation capture, or chromosome conformation capture.

Figure 5 is a Scheme illustrating the Design for Discovery and Validation of Epigenetic Stratifying Biomarker Signature for DMARDS Naïve ERA patients, who were confirmed within 6 months of MTX treatment as responders (N) or non-responders (NR). Epigenetic stratification was based on conditional chromosome confirmations screened and monitored by EpiSwitch™ Array and PCR (polymerase chain reaction) platforms. Disease specific epigenetic nature of the identified biomarkers was confirmed by stratification against healthy controls (HC). Validation was performed on 60 RA patients (30 responders and 30 non-responders) and 30 HC.

Detailed Description of the Invention

The invention has several different aspects:

- a method of identifying chromosome interactions (in particular epigenetic) relevant to a companion diagnostic, in particular that distinguishes between subgroups;
- a companion diagnostic method;
- a therapeutic agent for use in treatment and/or prophylaxis of an individual (e.g. treatment and/or prophylaxis of a condition in an individual, e.g. human individual), wherein said individual has been identified as being in need of the therapeutic agent in particular by the companion diagnostic method of the invention;

- a method of screening for (identifying) an agent, in particular a therapeutic agent, which is capable of changing the disease state in or of an individual, comprising determining whether a candidate agent is capable of changing chromosomal interactions, in particular chromosomal interactions relevant to or associated with the disease state;
- a method of determining the effect of a drug comprising detecting the change in epigenetic chromosome interactions caused by the drug.

Epigenetic Interactions

As used herein, the term 'epigenetic' interactions typically refers to interactions between distal regions of a locus on a chromosome, said interactions being dynamic and altering, forming or breaking depending upon the status of the region of the chromosome.

In particular methods of the invention, chromosome interactions are detected by first generating a ligated nucleic acid that comprises sequence(s) from both regions of the chromosomes that are part of the chromosome interactions. In such methods the regions can be cross-linked by any suitable means. In a preferred embodiment, the interactions are cross-linked using formaldehyde, but may also be cross-linked by any aldehyde, or D-Biotinoyl-e- aminocaproic acid-N-hydroxysuccinimide ester or Digoxigenin-3-O-methylcarbonyl- e-aminocaproic acid-N-hydroxysuccinimide ester. Para-formaldehyde can cross link DNA chains which are 4 Angstroms apart.

The chromosome interaction may reflect the status of the region of the chromosome, for example, if it is being transcribed or repressed in response to change of the physiological conditions. Chromosome interactions which are specific to subgroups as defined herein have been found to be stable, thus providing a reliable means of measuring the differences between the two subgroups.

In addition, chromosome interactions specific to a disease condition will normally occur early in the disease process, for example compared to other epigenetic markers such as methylation or changes to binding of histone proteins. Thus the companion diagnostic method of the invention is able to detect early stages of a disease state. This allows early treatment which may as a consequence be more effective. Another advantage of the invention is that no prior knowledge is needed about which loci are relevant for identification of relevant chromosome interactions. Furthermore there is little variation in the relevant chromosome interactions between individuals within the same subgroup. Detecting chromosome interactions is highly informative with up to 50 different possible interactions per gene, and so methods of the invention can interrogate 500,000 different interactions.

Location and Causes of Epigenetic Interactions

Epigenetic chromosomal interactions may overlap and include the regions of chromosomes shown to encode relevant or undescribed genes, but equally may be in intergenic regions. It should further be noted that the inventors have discovered that epigenetic interactions in all regions are equally important in determining the status of the chromosomal locus. These interactions are not necessarily in the coding region of a particular gene located at the locus and may be in intergenic regions.

The chromosome interactions which are detected in the invention could be caused by changes to the underlying DNA sequence, by environmental factors, DNA methylation, non-coding antisense RNA transcripts, non-mutagenic carcinogens, histone modifications, chromatin remodelling and specific local DNA interactions. The changes which lead to the chromosome interactions may be caused by changes to the underlying nucleic acid sequence, which themselves do not directly affect a gene product or the mode of gene expression. Such changes may be for example, SNP's within and/or outside of the genes, gene fusions and/or deletions of intergenic DNA, microRNA, and non-coding RNA. For example, it is known that roughly 20% SNPs are in non-coding regions, and therefore the method as described is also informative in non-coding situation. In one embodiment the regions of the chromosome which come together to form the interaction are less than 5 kb, 3 kb, 1 kb, 500 base pairs or 200 base pairs apart.

The chromosome interaction which is detected in the companion diagnostic method is preferably one which is within any of the genes mentioned in the Tables herein. However it may also be upstream or downstream of the genes, for example up to 50,000, 30,000, 20,000, 10,000 or 5000 bases upstream or downstream from the gene or from the coding sequence.

The chromosome interaction which is detected may or may not be one which occurs between a gene (including coding sequence) and its regulatory region, such as a promoter. The chromosome interaction which is typed may or may not be one which is inherited, for example an inherited imprinted characteristic of a gene region.

Types of Clinical Situation

The specific case of RA (Rheumatoid Arthritis) illustrates the general principles. There are currently no tests that clinicians can use *a priori* to determine if patients will respond to methotrexate (MTX) when the patients are first given the drug. Since a significant number (about 30%) of patients do not respond to MTX, being able to predict whether a patient is a responder or non-responder will increase the chances of successfully treating RA, as well as saving time and money.

This is one example of how the inventors visualise the present invention to be used. More broadly speaking, the aim of the present invention is to permit detection and monitoring of disease. In more detail, this technology allows stratification based on biomarkers for specific phenotypes relating to medical conditions, i.e. by recognising a particular chromosome confirmation signature and/or a change in that particular signature.

The methods of the invention are preferably used in the context of specific characteristics relating to disease, such as responsiveness to treatments and/or prophylaxes, identification of the most effective therapy/drug, monitoring the course of disease, identifying predisposition to disease, and/or identifying the presence of residual disease and/or the likelihood of relapse. Therefore the methods may or may not be used for diagnosis of the presence of a specific condition. The methods of the invention can be used to type loci where the mechanisms of disease are unknown, unclear or complex. Detection of chromosome interactions provides an efficient way of following changes at the different levels of regulation, some of which are complex. For example in some cases around 37,000 non-coding RNAs can be activated by a single impulse.

Subgroups and Personalised Treatment

As used herein, a "subgroup" preferably refers to a population subgroup (a subgroup in a population), more preferably a subgroup in a or the population of a particular animal such as a particular mammal (e.g. human, non-human primate, or rodent e.g. mouse or rat) or a particular nematode worm (e.g. *C. elegans*). Most preferably, a "subgroup" refers to a subgroup in a or the human population.

Particular populations, e.g. human populations, of interest include: the human population overall, a or the human population suffering from a specific condition / disease (in particular inflammatory disease e.g. RA, blood cancer eg AML, solid cancer eg melanoma or prostate cancer (PC), or neurodegenerative disease / condition e.g. Alzheimer's disease (AD)), the human healthy population (healthy controls), the human population which is healthy in the sense of not suffering from the specific condition / disease of interest or of study (eg RA, AML, melanoma, PC or AD), the human population (e.g. either healthy and/or with a specific condition / disease e.g. RA, AML, melanoma, PC or AD) who are responders to a particular drug / therapy, or the human population (e.g. either healthy and/or with a specific condition / disease e.g. RA, AML, melanoma, PC or AD) who are non-responders to a particular drug / therapy.

The invention relates to detecting and treating particular subgroups in a population, preferably in a or the human population. Within such subgroups the characteristics discussed herein (such as responsiveness to treatment and/or prophylaxis; in particular responsiveness to a specific treatment

and/or prophylaxis of one or more conditions or diseases, and/or responsiveness to a specific medicine or therapeutically active substance / therapeutic agent, in particular in the treatment and/or prophylaxis of one or more conditions or diseases) will be present or absent. Epigenetic interaction differences on a chromosome are, generally speaking, structural differences which exist at a genomic level. The inventors have discovered that these differ between subsets (for example two, or two or more subsets) in a given population. Identifying these differences will allow physicians to categorize their patients as a part of one subset of the population as described in the method. The invention therefore provides physicians with a method of personalizing medicine for the patient based on their epigenetic chromosome interactions, and provide an alternative more effective treatment and/or prophylaxis regime.

In another embodiment, threshold levels for determining to what extent a subject is defined as belonging to one subgroup and not to a or the other subgroup of the population are applied. In one preferable embodiment wherein the subgroups comprise responders versus non-responders of a therapy for the treatment and/or prophylaxis of a particular disease, said threshold may be measured by change in DAS28 (Disease Activity Score of 28 joints) score, in particular for rheumatoid arthritis. In one embodiment, a score above 1.2 units indicates a subject falls into the responder subgroup, whilst a score below 1.2 units indicates a subject is defined as a non-responder.

Typically a subgroup will be at least 10%, at least 30%, at least 50% or at least 80% of the general population.

Generating Ligated Nucleic Acids

Certain embodiments of the invention utilise ligated nucleic acids, in particular ligated DNA. These comprise sequences from both of the regions that come together in a chromosome interaction and therefore provide information about the interaction. The EpiSwitch™ method, described herein, uses generation of such ligated nucleic acids to detect chromosome interactions.

One such method, in particular one particular method of detecting chromosome interactions and/or one particular method of determining epigenetic chromosome interactions and/or one particular method of generating ligated nucleic acids (e.g. DNA), comprises the steps of:

(i) *in vitro* crosslinking of said epigenetic chromosomal interactions present at the chromosomal locus;

(ii) optionally isolating the cross-linked DNA from said chromosomal locus;

(iii) subjecting said cross-linked DNA to restriction digestion with an enzyme that cuts it at least once (in particular an enzyme that cuts at least once within said chromosomal locus);

(iv) ligating said cross-linked cleaved DNA ends (in particular to form DNA loops); and

(v) identifying the presence of said ligated DNA and/or said DNA loops, in particular using techniques such as PCR (polymerase chain reaction), to identify the presence of a specific chromosomal interaction.

One particularly preferable method of detecting, determining and/or monitoring chromosome interactions and/or epigenetic changes, involving *inter alia* the above-mentioned steps of crosslinking, restriction digestion, ligating, and identifying, is disclosed in WO 2009/147386 A1 (Oxford Biodynamics Ltd), the entire disclosure of which (in particular claims 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20 or 21 of which) are incorporated herein by reference as though fully set forth. Claim 1 of WO 2009/147386 A1, which can be used in those methods of the present invention which involve a ligated product(s) and/or a ligated nucleic acid(s), discloses a method of monitoring epigenetic changes comprising monitoring changes in conditional long range chromosomal interactions at at least one chromosomal locus where the spectrum of long range interaction is associated with a specific physiological condition, said method comprising the steps of:-

(i) *in vitro* crosslinking of said long range chromosomal interactions present at the at least one chromosomal locus;
(ii) isolating the cross linked DNA from said chromosomal locus;
(iii) subjecting said cross linked DNA to restriction digestion with an enzyme that cuts at least once within the at least one chromosomal locus;
(iv) ligating said cross linked cleaved DNA ends to form DNA loops; and
(v) identifying the presence of said DNA loops;

wherein the presence of DNA loops indicates the presence of a specific long range chromosomal interaction.

PCR (polymerase chain reaction) may be used to detect or identify the ligated nucleic acid, for example the size of the PCR product produced may be indicative of the specific chromosome interaction which is present, and may therefore be used to identify the status of the locus. The skilled person will be aware of numerous restriction enzymes which can be used to cut the DNA within the chromosomal locus of interest. It will be apparent that the particular enzyme used will depend upon the locus

studied and the sequence of the DNA located therein. A non-limiting example of a restriction enzyme which can be used to cut the DNA as described in the present invention is Taq I polymerase.

Embodiments such as EpiSwitch™ Technology

The EpiSwitch™ Technology relates to the use of microarray EpiSwitch™ marker data in the detection of epigenetic chromosome conformation signatures specific for phenotypes. The present inventors describe herein how the EpiSwitch™ Array Platform has been used for discovery of chromosome signature pool of potential biomarkers specific for particular disadvantageous phenotypes subgroups versus healthy controls. The inventors also provide examples of validated use and translation of chromosome conformation signatures from microarray into PCR platform with examples of several markers specific between subgroups from the cohorts tested on the array.

Embodiments such as EpiSwitch™ which utilise ligated nucleic acids in the manner described herein (for identifying relevant chromosome interactions and in companion diagnostic methods) have several advantages. They have a low level of stochastic noise, for example because the nucleic acid sequences from the first set of nucleic acids of the present invention either hybridise or fail to hybridise with the second set of nucleic acids. This provides a binary result permitting a relatively simple way to measure a complex mechanism at the epigenetic level. EpiSwitch™ technology also has fast processing time and low cost. In one embodiment the processing time is 3 hours to 6 hours.

Samples and Sample Treatment

The sample will contain DNA from the individual. It will normally contain cells. In one embodiment a sample is obtained by minimally invasive means, and may for example be blood. DNA may be extracted and cut up with standard restriction enzymes. This can pre-determine which chromosome conformations are retained and will be detected with the EpiSwitch™ platforms. In one embodiment wherein the sample is a blood sample previously obtained from the patient, the described method is advantageous because the procedure is minimally invasive. Due to the synchronisation of chromosome interactions between tissues and blood, including horizontal transfer, a blood sample can be used to detect the chromosome interactions in tissues, such as tissues relevant to disease. For certain conditions, such as cancer, genetic noise due to mutations can affect the chromosome interaction 'signal' in the relevant tissues and therefore using blood is advantageous.

Properties of Nucleic acids of the invention

The disclosure herein mentions first and second nucleic acids. In addition the nucleic acids are used in the companion diagnostic method and in other embodiments to detect the presence or absence of chromosome interactions (for example by binding to ligated nucleic acids generated from samples). The nucleic acids of the invention typically comprise two portions each comprising sequence from one of the two regions of the chromosome which come together in the chromosome interaction. Typically each portion is at least 8, 10, 15, 20, 30 or 40 nucleotides in length. Preferred nucleic acids comprise sequence from any of the genes mentioned in the tables, in particular where the nucleic acid is used in an embodiments relevant to the condition relevant for that table. Preferred nucleic acids comprise the specific probe sequences mentioned in the tables for specific conditions or fragments or homologues of such sequences. Preferably the nucleic acids are DNA. It is understood that where a specific sequence is provided the invention may use the complementary as required in the particular embodiment.

The Second Set of Nucleic Acids – the 'Index' Sequences

The second set of nucleic acid sequences has the function of being an index, and is essentially a set of nuclei acid sequences which are suitable for identifying subgroup specific sequence. They can represent the 'background' chromosomal interactions and might be selected in some way or be unselected. They are in general a subset of all possible chromosomal interactions.

The second set of nucleic acids may be derived by any suitable method. They can be derived computationally or they may be based on chromosome interaction in individuals. They typically represent a larger population group than the first set of nucleic acids. In one particular embodiment, the second set of nucleic acids represents all possible epigenetic chromosomal interactions in a specific set of genes. In another particular embodiment, the second set of nucleic acids represents a large proportion of all possible epigenetic chromosomal interactions present in a population described herein. In one particular embodiment, the second set of nucleic acids represent at least 50% or at least 80% of epigenetic chromosomal interactions in at least 20, 50, 100 or 500 genes.

The second set of nucleic acids typically represents at least 100 possible epigenetic chromosome interactions which modify, regulate or in any way mediate a disease state/ phenotype in population. The second set of nucleic acids may represent chromosome interactions that affect a diseases state in a species, for example comprising nucleic acids sequences which encode cytokines, kinases, or regulators associated with any disease state, predisposition to a disease or a disease phenotype. The

second set of nucleic acids comprises sequences representing epigenetic interactions relevant and not relevant to the companion diagnostic method.

In one particular embodiment the second set of nucleic acids derive at least partially from a naturally occurring sequences in a population, and are typically obtained by *in silico* methods. Said nucleic acids may further comprise single or multiple mutations in comparison to a corresponding portion of nucleic acids present in the naturally occurring nucleic acids. Mutations include deletions, substitutions and/ or additions of one or more nucleotide base pairs. In one particular embodiment, the second set of nucleic acids may comprise sequence representing a homologue and/or orthologue with at least 70% sequence identity to the corresponding portion of nucleic acids present in the naturally occurring species. In another particular embodiment, at least 80% sequence identity or at least 90% sequence identity to the corresponding portion of nucleic acids present in the naturally occurring species is provided.

Properties of the Second Set of Nucleic Acids

In one particular embodiment, there are at least 100 different nucleic acid sequences in the second set of nucleic acids, preferably at least 1000, 2000 or 5000 different nucleic acids sequences, with up to 100,000, 1,000,000 or 10,000,000 different nucleic acid sequences. A typical number would be 100 to 1,000,000, such as 1,000 to 100,000 different nucleic acids sequences. All or at least 90% or at least 50% or these would correspond to different chromosomal interactions.

In one particular embodiment, the second set of nucleic acids represent chromosome interactions in at least 20 different loci or genes, preferably at least 40 different loci or genes, and more preferably at least 100, at least 500, at least 1000 or at least 5000 different loci or genes, such as 100 to 10,000 different loci or genes.

The lengths of the second set of nucleic acids are suitable for them to specifically hybridise according to Watson Crick base pairing to the first set of nucleic acids to allow identification of chromosome interactions specific to subgroups. Typically the second set of nucleic acids will comprise two portions corresponding in sequence to the two chromosome regions which come together in the chromosome interaction. The second set of nucleic acids typically comprise nucleic acid sequences which are at least 10, preferably 20, and preferably still 30 bases (nucleotides) in length. In another embodiment, the nucleic acid sequences may be at the most 500, preferably at most 100, and preferably still at most 50 base pairs in length. In a preferred embodiment, the second set of nucleic acids comprise nucleic acid sequences of between 17 and 25 base pairs. In one embodiment at least 100, 80% or 50%

of the second set of nucleic acid sequences have lengths as described above. Preferably the different nucleic acids do not have any overlapping sequences, for example at least 100%, 90%, 80% or 50% of the nucleic acids do not have the same sequence over at least 5 contiguous nucleotides.

Given that the second set of nucleic acids acts as an 'index' then the same set of second nucleic acids may be used with different sets of first nucleic acids which represent subgroups for different characteristics, i.e. the second set of nucleic acids may represent a 'universal' collection of nucleic acids which can be used to identify chromosome interactions relevant to different disease characteristics.

The first set of nucleic acids

The first set of nucleic acids are normally from individuals known to be in two or more distinct subgroups defined by presence or absence of a characteristic relevant to a companion diagnostic, such as any such characteristic mentioned herein. The first nucleic acids may have any of the characteristics and properties of the second set of nucleic acids mentioned herein. The first set of nucleic acids is normally derived from a sample from the individual which has undergone treatment and processing as described herein, particularly the EpiSwitch™ cross-linking and cleaving steps. Typically the first set of nucleic acids represent all or at least 80% or 50% of the chromosome interactions present in the samples taken from the individuals.

Typically, the first set of nucleic acids represents a smaller population of chromosome interactions across the loci or genes represented by the second set of nucleic acids in comparison to the chromosome interactions represented by second set of nucleic acids, i.e. the second set of nucleic acids is representing a background or index set of interactions in a defined set of loci or genes.

Library of Nucleic Acids

The nucleic acids described herein may be in the form of a library which comprises at least 200, at least 500, at least 1000, at least 5000 or at least 10000 different nucleic acids from the second set of nucleic acids. The invention provides a particular library of nucleic acids which typically comprises at least 200 different nucleic acids. The library of nucleic acids may have any of the characteristics or properties of the second set of nucleic acids mentioned herein. The library may be in the form of nucleic acids bound to an array.

Hybridisation

The invention requires a means for allowing wholly or partially complementary nucleic acid sequences from the first set of nucleic acids and the second set of nucleic acids to hybridise. In one embodiment all of the first set of nucleic acids is contacted with all of the second set of nucleic acids in a single assay, i.e. in a single hybridisation step. However any suitable assay can be used.

Labelled Nucleic Acids and Pattern of Hybridisation

The nucleic acids mentioned herein may be labelled, preferably using an independent label such as a fluorophore (fluorescent molecule) or radioactive label which assists detection of successful hybridisation. Certain labels can be detected under UV light.

The pattern of hybridisation, for example on an array described herein, represents differences in epigenetic chromosome interactions between the two subgroups, and thus provides a method of comparing epigenetic chromosome interactions and determination of which epigenetic chromosome interactions are specific to a subgroup in the population of the present invention.

The term 'pattern of hybridisation' broadly covers the presence and absence of hybridisation between the first and second set of nucleic acids, i.e. which specific nucleic acids from the first set hybridise to which specific nucleic acids from the second set, and so it is not limited to any particular assay or technique, or the need to have a surface or array on which a 'pattern' can be detected.

Companion Diagnostic Method

The invention provides a companion diagnostic method based on information provided by chromosome interactions. Two distinct companion diagnostic methods are provided which identify whether an individual has a particular characteristic relevant to a companion diagnostic. One method is based on typing a locus in any suitable way and the other is based on detecting the presence or absence of chromosome interactions. The characteristic may be any one of the characteristics mentioned herein relating to a condition. The companion diagnostic method can be carried out at more than one time point, for example where monitoring of an individual is required.

Companion Diagnostic Method Based on Typing a Locus

The method of the invention which identified chromosome interactions that are specific to subgroups can be used to identify a locus, which may be a gene that can be typed as the basis of companion

diagnostic test. Many different gene-related effects can lead to the same chromosome interaction occurring. In this embodiment any characteristic of the locus may be typed, such as presence of a polymorphism in the locus or in an expressed nucleic acid or protein, the level of expression from the locus, the physical structure of the locus or the chromosome interactions present in the locus. In one particular embodiment the locus may be any of the genes mentioned herein in the tables, in particular in Tables 1, 3, 5, 6c, 6E, 18a, 18b, 18c, 18d, 18e, 18f, 22, 23, 24 or 25 (in particular Tables 1, 3 and/or 5), or any property of a locus which is in the vicinity of a chromosome interaction found to be linked to the relevant condition.

Companion Diagnostic Method Based on Detecting Chromosome Interactions

The invention provides a companion diagnostic method which comprises detecting the presence or absence of chromosome interactions, typically 5 to 20 or 5 to 500 such interactions, preferably 20 to 300 or 50 to 100 interactions, in order to determine the presence or absence of a characteristic in an individual. Preferably the chromosome interactions are those in any of the genes mentioned herein. In one particular embodiment the chromosome interactions which are typed are those represented by the nucleic acids disclosed in the tables herein, in particular in Tables 6b, 6D, 18b, 18e, 18f, 22, 23, 24 or 25 herein, for example when the method is for the purpose of determining the presence or absence of characteristics defined in those tables.

Specific Conditions

The companion diagnostic method can be used to detect the presence of any of the specific conditions or characteristics mentioned herein. The companion diagnostic method can be used to detect responsiveness to methotrexate (or another rheumatoid arthritis drug) in rheumatoid arthritis patients, responsiveness to therapy for acute myeloid leukaemia (AML) patients, likelihood of relapse in melanoma, likelihood of developing prostate cancer and/ or aggressive prostate cancer, and/or likelihood of developing beta-amyloid aggregate induced Alzheimer's disease.

In one embodiment the method of the invention detects responsiveness to immunotherapy, such as antibody therapy. Preferably the responsiveness to antibody therapy of cancer is detected, for example in immunotherapy using anti-PD-1 or anti-PD-L1 or a combined anti-PD-1/anti-PD-L1 therapy. Preferably the cancer is melanoma, breast cancer, prostate cancer, acute myeloid leukaemia (AML), diffuse large B-cell lymphoma (DLBCL), pancreatic cancer, thyroid cancer, nasal cancer, liver cancer or lung cancer. In such embodiments detection of chromosome interactions in STAT5B and/or IL15 are preferred, such as described in the Examples. The work in the Examples is consistent with the fact that

response to immunotherapy is a feature of the immune system epigenetic set up rather than cancer identity. ['Anti-PD-1' is an antibody or antibody derivative or fragment that binds specifically to PD-1 (programmed cell death protein 1). 'Anti-PD-L1' is an antibody or antibody derivative or fragment that binds specifically to PD-L1 protein which is a ligand of PD-1.]

The method(s) and/or companion diagnostic method of the invention can be used to:

- responsiveness to IFN-B (IFN-beta) treatment in multiple sclerosis patients (in particular in humans), and/or
- predisposition to relapsing-remitting multiple sclerosis (in particular in humans), and/or
- likelihood of primary progressive multiple sclerosis (in particular in humans), and/or
- predisposition to amyotrophic lateral sclerosis (ALS) disease state (in particular in humans), and/or,
- predisposition to fast progressing amyotrophic lateral sclerosis (ALS) disease state (in particular in humans), and/or
- predisposition to aggressive type 2 diabetes disease state (in particular in humans), and/or
- predisposition to type 2 diabetes disease state (in particular in humans), and/or
- predisposition to a pre-type 2 diabetes state (in particular in humans), and/or
- predisposition to type 1 diabetes disease state (in particular in humans), and/or
- predisposition to systemic lupus erythematosus (SLE) disease state (in particular in humans), and/or
- predisposition to ulcerative colitis disease state (in particular in humans), and/or
- likelihood of relapse of colorectal cancer for ulcerative colitis patients (in particular in humans), and/or
- likelihood of malignant peripheral nerve sheath tumours for neurofibromatosis patients (in particular in humans), and/or
- likelihood of developing prostate cancer and/or aggressive prostate cancer (in particular in humans), and/or
- likelihood of developing and/or predisposition to a neurodegenerative disease or condition, preferably a dementia such as Alzheimer's disease, mild cognitive impairment, vascular dementia, dementia with Lewy bodies, frontotemporal dementia, or more preferably Alzheimer's disease, most preferably beta-amyloid aggregate induced Alzheimer's disease; in particular in a human; and/or
- a comparison between dementia patients (preferably Alzheimer's disease patients, more preferably Alzheimer's disease patients with beta-amyloid aggregates) and cognitively-

impaired patients without Alzheimer's disease, in particular with respect to memory and/or cognition; in particular in humans.

Preferably the presence or absence of any of the chromosome interactions within any of the relevant genes mentioned in the tables are detected. For example in at least 1, 3, 10, 20, 50 of the genes mentioned in any one of the tables. Preferably the presence or absence of chromosome interactions represented by the probes sequences in the Tables is determined in the method. For example at least 1, 3, 10, 20, 50, or 100 of the relevant chromosome interactions from any one of the tables. These numbers of genes or chromosome interactions can be used in any of the different embodiments mentioned herein.

The Individual Tested Using the Companion Diagnostic Method

The individual to be tested may or may not have any symptoms of any disease condition or characteristic mentioned herein. The individual may be at risk of any such condition or characteristic. The individual may have recovered or be in the process of recovering from the condition or characteristic. The individual is preferably a mammal, such as a non-human primate, human or rodent. The individual may be male or female. The individual may be 30 years old or older. The individual may be 29 years old or younger.

Screening Method

The invention provides a method of identifying an agent which is capable of changing the disease state of an individual from a first state to a second state comprising determining whether a candidate agent is capable of changing the chromosomal interactions from those corresponding with the first state to chromosomal interactions which correspond to the second state, wherein preferably the first and second state correspond to presence or absence of:

- responsiveness to a specific treatment and/or prophylaxis, and/or
- predisposition to a specific condition, and/or
- a residual disease which may lead to relapse.

In one embodiment the method determines whether a candidate agent is capable of changing any chromosomal interaction mentioned herein.

The method may be carried out in vitro (inside or outside a cell) or in vivo (upon a non-human organism). In one embodiment the method is carried out on a cell, cell culture, cell extract, tissue,

organ or organism, such as one which comprises the relevant chromosome interaction(s). The cell is The method is typically carried out by contacting (or administering) the candidate agent with the gene, cell, cell culture, cell extract, tissue, organ or organism.

Suitable candidate substances which tested in the above screening methods include antibody agents (for example, monoclonal and polyclonal antibodies, single chain antibodies, chimeric antibodies and CDR-grafted antibodies). Furthermore, combinatorial libraries, defined chemical identities, peptide and peptide mimetics, oligonucleotides and natural agent libraries, such as display libraries (e.g. phage display libraries) may also be tested. The candidate substances may be chemical compounds, which are typically derived from synthesis around small molecules which may have any of the properties of the agent mentioned herein.

Preferred Loci, Genes and Chromosome Interactions

For all aspects of the invention preferred loci, genes and chromosome interactions are mentioned in the tables. For all aspects of the invention preferred loci, genes and chromosome interactions are provided in the tables. Typically the methods chromosome interactions are detected from at least 1, 3, 10, 20, 30 or 50 of the relevant genes listed in the table. Preferably the presence or absence of at least 1, 3, 10, 20, 30 or 50 of the relevant specific chromosome interactions represented by the probe sequences in any one table is detected.

The loci may be upstream or downstream of any of the genes mentioned herein, for example 50 kb upstream or 20 kb downstream.

In one embodiment for each condition the presence or absence of at least 1, 3, 5, 10, 20 of the relevant specific chromosome interactions represented by the top range of p-values or adjusted p-values shown in Table 48 are detected. In another embodiment for each condition the presence or absence of at least 1, 3, 5, 10, 20, 30 or 50 of the relevant specific chromosome interactions represented by the mid range of p-values or adjusted p-values shown in Table 48 are detected. In yet another embodiment for each condition the presence or absence of at least 1, 3, 5, 10, 20, 30 or 50 of the relevant specific chromosome interactions represented by the bottom range of p-values or adjusted p-values shown in Table 48 are detected. In another embodiment for each condition the presence or absence of at least 1, 2, 3, 5 or 10 of the relevant specific chromosome interactions from each of the top, mid and bottom ranges of p-values or adjusted p-values shown in Table 48 are detected, i.e. at least 3, 6, 9, 18 or 30 in total.

Particular combinations of chromosome interactions can be detected (i.e. determining the presence of absence of), which typically represent all of the interactions disclosed in a table herein or a selection

from a table. As mentioned herein particular numbers of interactions can be selected from individual tables. In one embodiment at least 10%, 20%, 30%, 50%, 70% or 90% of the interactions disclosed in any table, or disclosed in relation to any condition, are detected.

The interactions which are detected may correspond to presence or absence of a particular characteristic, for example as defined herein, such as in any table herein. If a combination of interactions are detected then they may all correspond with presence of the characteristic or they may all correspond to absence of the characteristic. In one embodiment the combination of interactions which is detected corresponds to at least 2, 5 or 10 interactions which relate to presence of the characteristic and at least 2, 5 or 10 other interactions that relate to absence of the characteristic.

The probe shown in table 49 may be part of or combined with any of the selections mentioned herein, particularly for conditions relating to cancer, and responsiveness to therapy, such as anti-PD1 therapy.

Embodiments Concerning Genetic Modifications

In certain embodiments the methods of the invention can be carried out to detect chromosome interactions relevant to or impacted by a genetic modification, i.e. the subgroups may differ in respect to the genetic modification. Clearly the modification might be of entire (non-human) organisms or parts of organisms, such as cells. In the method of determining which chromosomal interactions are relevant to a biological system state the first set of nucleic acids may be from at least two subgroups, one of which has a defined genetic modification and one which does not have the genetic modification, and the method may determine which chromosomal interactions are relevant to, and/or affected by, the genetic modification. The modification may be achieved by any suitable means, including CRISPR technology.

The invention includes a method of determining whether a genetic modification to the sequence at a first locus of a genome affects other loci of the genome comprising detecting chromosome signatures at one or more other loci after the genetic modification is made, wherein preferably the genetic modification changes system characteristics, wherein said system is preferably the metabolic system, the immune system, the endocrine system, the digestive system, integumentary system, the skeletal system, the muscular system, the lymphatic system, the respiratory system, the nervous system, or the reproductive system. Said detecting chromosome signatures optionally comprises detecting the presence or absence of 5 or more (e.g. 5) different chromosomal interactions, preferably at 5 or more (e.g. 5) different loci, preferably as defined in any of the Tables. Preferably the chromosomal signatures or interactions are identified by any suitable method mentioned herein.

In one embodiment the genetic modification is achieved by a method comprising introducing into a cell (a) two or more RNA-guided endonucleases or nucleic acid encoding two or more RNA-guided endonucleases and (b) two or more guiding RNAs or DNA encoding two or more guiding RNAs, wherein each guiding RNA guides one of the RNA-guided endonucleases to a targeted site in the chromosomal sequence and the RNA-guided endonuclease cleaves at least one strand of the chromosomal sequence at the targeted site.

In another embodiment the modification is achieved by a method of altering expression of at least one gene product comprising introducing into a eukaryotic cell containing and expressing a DNA molecule having a target sequence and encoding the gene product an engineered, non-naturally occurring Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR)—CRISPR associated (Cas) (CRISPR-Cas) system comprising one or more vectors comprising:

a) a first regulatory element operable in a eukaryotic cell operably linked to at least one nucleotide sequence encoding a CRISPR-Cas system guide RNA that hybridizes with the target sequence, and

b) a second regulatory element operable in a eukaryotic cell operably linked to a nucleotide sequence encoding a Type-II Cas9 protein,

wherein components (a) and (b) are located on same or different vectors of the system, whereby the guide RNA targets the target sequence and the Cas9 protein cleaves the DNA molecule, whereby expression of the at least one gene product is altered; and, wherein the Cas9 protein and the guide RNA do not naturally occur together, wherein preferably each RNA-guided endonuclease is derived from a Cas9 protein and comprises at least two nuclease domains, and optionally wherein one of the nuclease domains of each of the two RNA-guided endonucleases is modified such that each RNA-guided endonuclease cleaves one strand of a double-stranded sequence, and wherein the two RNA-guided endonucleases together introduce a double-stranded break in the chromosomal sequence that is repaired by a DNA repair process such that the chromosomal sequence is modified.

Typically the modification comprised a deletion, insertion or substitution of at least 5, 20, 50, 100 or 1000 bases, preferably up 10,000 or 1000,000 bases.

The modification may be at any of the loci mentioned herein, for example in any of the regions or genes mentioned in any of the tables. The chromosomal interactions which are detected at other (non-modified) loci may also be in any of the loci mentioned herein, for example in any of the regions or genes mentioned in any of the tables.

Embodiments relating to genetic modifications many be performed on any organism, including eukaryotes, chordates, mammals, plants, agricultural animals and plants, and non-human organisms.

Methods and Uses of the Invention

The method of the invention can be described in different ways. It can be described as a method of making a ligated nucleic acid comprising (i) *in vitro* cross-linking of chromosome regions which have come together in a chromosome interaction; (ii) subjecting said cross-linked DNA to cutting or restriction digestion cleavage; and (iii) ligating said cross-linked cleaved DNA ends to form a ligated nucleic acid, wherein detection of the ligated nucleic acid may be used to determine the chromosome state at a locus, and wherein preferably :

- the locus may be any of the loci, regions or genes mentioned herein,

- and/or wherein the chromosomal interaction may be any of the chromosome interactions mentioned herein or corresponding to any of the probes disclosed in the tables, and/or

- wherein the ligated product may have or comprise (i) sequence which is the same as or homologous to any of the probe sequences disclosed herein; or (ii) sequence which is complementary to (ii).

The method of the invention can be described as a method for detecting chromosome states which represent different subgroups in a population comprising determining whether a chromosome interaction is present or absent within a defined region of the genome, wherein preferably:

- the subgroup is defined by presence or absence of a characteristic mentioned herein, and/or
- the chromosome state may be at any locus, region or gene mentioned herein; and/or
- the chromosome interaction may be any of those mentioned herein or corresponding to any of the probes or primer pairs disclosed herein.

The invention includes detecting chromosome interactions at any locus, gene or regions mentioned herein. The invention includes use of the nucleic acids and probes (or primers) mentioned herein to detect chromosome interactions, for example use of at least 10, 50, 100 or 500 such nucleic acids or probes to detect chromosome interactions in at least 10, 20, 100 or 500 different loci or genes.

Tables Provided Herein

Tables herein either show probe (Episwitch™ marker) data or gene data representing chromosome interactions present in a condition (the first mentioned group) and absent in a control group, typically but not necessarily healthy individuals (the second mentioned group). The probe sequences show sequence which can be used to detect a ligated product generated from both sites of gene regions

that have come together in chromosome interactions, i.e. the probe will comprise sequence which is complementary to sequence in the ligated product. The first two sets of Start-End positions show probe positions, and the second two sets of Start-End positions show the relevant 4kb region. The following information is provided in the probe data table:

- HyperG_Stats: p-value for the probability of finding that number of significant EpiSwitch™ markers in the locus based on the parameters of hypergeometric enrichment
- Probe Count Total: Total number of EpiSwitch™ Conformations tested at the locus
- Probe Count Sig: Number of EpiSwitch™ Conformations found to be statistical significant at the locus
- FDR HyperG: Multi-test (False Discovery Rate) corrected hypergeometric p-value
- Percent Sig: Percentage of significant EpiSwitch™ markers relative the number of markers tested at the locus
- logFC: logarithm base 2 of Epigenetic Ratio (FC)
- AveExpr: average log2-expression for the probe over all arrays and channels
- T: moderated t-statistic
- p-value: raw p-value
- adj. p-value: adjusted p-value or q-value
- B - B-statistic (lods or B) is the log-odds that that gene is differentially expressed.
- FC - non-log Fold Change
- FC_1 - non-log Fold Change centred around zero
- LS – Binary value this relates to FC_1 values. FC_1 value below -1.1 it is set to -1 and if the FC_1 value is above 1.1 it is set to 1. Between those values the value is 0

The gene table data shows genes where a relevant chromosome interaction has been found to occur. The p-value in the loci table is the same as the HyperG_Stats (p-value for the probability of finding that number of significant EpiSwitch™ markers in the locus based on the parameters of hypergeometric enrichment).

The probes are designed to be 30bp away from the Taq1 site. In case of PCR, PCR primers are also designed to detect ligated product but their locations from the Taq1 site vary.

Probe locations:

Start 1 - 30 bases upstream of TaqI site on fragment 1

End 1 - TaqI restriction site on fragment 1

Start 2 - TaqI restriction site on fragment 2

End 2 - 30 bases downstream of TaqI site on fragment 2

4kb Sequence Location:

Start 1 - 4000 bases upstream of TaqI site on fragment 1

End 1 - TaqI restriction site on fragment 1

Start 2 - TaqI restriction site on fragment 2

End 2 - 4000 bases downstream of TaqI site on fragment 2

The following information is also provided in the tables:

- GLMNET - procedures for fitting the entire lasso or elastic-net regularization. Lambda set to 0.5 (elastic-net)
- GLMNET_1 - lambda set to 1 (lasso)
- Fishers P-value - Exact Fishers Test P-value
- Coef - Logistic Regression Coefficient, if you raise e (e^X) to power of the coefficient you get the odds ratio for the variable
- S.E. - Standard Error
- Wald - Wald Equation Statistic. Wald statistics are part of a Wald test that the maximum likelihood estimate of a model coefficient is equal to 0. The test assumes that the difference between the maximum likelihood estimate and 0 is asymptotically normally distributed
- Pr(>|Z|) - P-value for the marker within the logistic model. Values below <0.05 are statistically significant and should be used in the logistic model.

Preferred Embodiments for Sample Preparation and Chromosome Interaction Detection

Methods of preparing samples and detecting chromosome conformations are described herein. Optimised (non-conventional) versions of these methods can be used, for example as described in this section.

Typically the sample will contain at least 2 $x10^5$ cells. The sample may contain up to 5 $x10^5$ cells. In one embodiment, the sample will contain 2 $x10^5$ to 5.5 $x10^5$ cells

Crosslinking of epigenetic chromosomal interactions present at the chromosomal locus is described herein. This may be performed before cell lysis takes place. Cell lysis may be performed for 3 to 7 minutes, such as 4 to 6 or about 5 minutes. In some embodiments, cell lysis is performed for at least 5 minutes and for less than 10 minutes.

Digesting DNA with a restriction enzyme is described herein. Typically, DNA restriction is performed at about 55°C to about 70°C, such as for about 65°C, for a period of about 10 to 30 minutes, such as about 20 minutes.

Preferably a frequent cutter restriction enzyme is used which results in fragments of ligated DNA with an average fragment size up to 4000 base pair. Optionally the restriction enzyme results in fragments of ligated DNA have an average fragment size of about 200 to 300 base pairs, such as

about 256 base pairs. In one embodiment, the typical fragment size is from 200 base pairs to 4,000 base pairs, such as 400 to 2,000 or 500 to 1,000 base pairs.

In one embodiment of the EpiSwitch method a DNA precipitation step is not performed between the DNA restriction digest step and the DNA ligation step.

DNA ligation is described herein. Typically the DNA ligation is performed for 5 to 30 minutes, such as about 10 minutes.

The protein in the sample may be digested enzymatically, for example using a proteinase, optionally Proteinase K. The protein may be enzymatically digested for a period of about 30 minutes to 1 hour, for example for about 45 minutes. In one embodiment after digestion of the protein, for example Proteinase K digestion, there is no cross-link reversal or phenol DNA extraction step.

In one embodiment PCR detection is capable of detecting a single copy of the ligated nucleic acid, preferably with a binary read-out for presence/absence of the ligated nucleic acid.

Homologues

Homologues of polynucleotide / nucleic acid (e.g. DNA) sequences are referred to herein. Such homologues typically have at least 70% homology, preferably at least 80%, at least 85%, at least 90%, at least 95%, at least 97%, at least 98% or at least 99% homology, for example over a region of at least 10, 15, 20, 30, 100 or more contiguous nucleotides, or across the portion of the nucleic acid which is from the region of the chromosome involved in the chromosome interaction. The homology may be calculated on the basis of nucleotide identity (sometimes referred to as "hard homology").

Therefore, in a particular embodiment, homologues of polynucleotide / nucleic acid (e.g. DNA) sequences are referred to herein by reference to % sequence identity. Typically such homologues have at least 70% sequence identity, preferably at least 80%, at least 85%, at least 90%, at least 95%, at least 97%, at least 98% or at least 99% sequence identity, for example over a region of at least 10, 15, 20, 30, 100 or more contiguous nucleotides, or across the portion of the nucleic acid which is from the region of the chromosome involved in the chromosome interaction.

For example the UWGCG Package provides the BESTFIT program which can be used to calculate homology and/or % sequence identity (for example used on its default settings) (Devereux et al (1984) Nucleic Acids Research 12, p387-395). The PILEUP and BLAST algorithms can be used to calculate homology and/or % sequence identity and/or line up sequences (such as identifying equivalent or corresponding sequences (typically on their default settings), for example as described in Altschul S. F. (1993) J Mol Evol 36:290-300; Altschul, S, F et al (1990) J Mol Biol 215:403-10.

Software for performing BLAST analyses is publicly available through the National Center for Biotechnology Information. This algorithm involves first identifying high scoring sequence pair (HSPs) by identifying short words of length W in the query sequence that 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 neighbourhood word score threshold (Altschul et al, supra). These initial neighbourhood word hits act as seeds for initiating searches to find HSPs containing them. The word hits are extended in both directions along each sequence for as far as the cumulative alignment score can be increased. Extensions for the word hits in each direction are halted when: the cumulative alignment score falls off by the quantity X from its maximum achieved value; the cumulative score goes to zero or below, due to the accumulation of one or more negative-scoring residue alignments; or the end of either sequence is reached. The BLAST algorithm parameters W5 T and X determine the sensitivity and speed of the alignment. The BLAST program uses as defaults a word length (W) of 11 , the BLOSUM62 scoring matrix (see Henikoff and Henikoff (1992) Proc. Natl. Acad. Sci. USA 89: 10915-10919) alignments (B) oi 50, expectation (E) of 10, M=5, N=4, and a comparison of both strands.

The BLAST algorithm performs a statistical analysis of the similarity between two sequences; see e.g., Karlin and Altschul (1993) Proc. Natl. Acad. Sci. USA 90: 5873-5787. One measure of similarity provided by the BLAST algorithm is the smallest sum probability (P(N)), which provides an indication of the probability by which a match between two polynucleotide sequences would occur by chance. For example, a sequence is considered similar to another sequence if the smallest sum probability in comparison of the first sequence to the second sequence is less than about 1, preferably less than about 0.1, more preferably less than about 0.01, and most preferably less than about 0.001.

The homologous sequence typically differs by 1, 2, 3, 4 or more bases, such as less than 10, 15 or 20 bases (which may be substitutions, deletions or insertions of nucleotides). These changes may be measured across any of the regions mentioned above in relation to calculating homology and/or % sequence identity.

Arrays

The second set of nucleic acids may be bound to an array, and in one embodiment there are at least 15,000, 45,000, 100,000 or 250,000 different second nucleic acids bound to the array, which preferably represent at least 300, 900, 2000 or 5000 loci. In one embodiment one, or more, or all of the different populations of second nucleic acids are bound to more than one distinct region of the array, in effect repeated on the array allowing for error detection. The array be based on an Agilent

SurePrint G3 Custom CGH microarray platform. Detection of binding of first nucleic acids to the array may be performed by a dual colour system.

Therapeutic Agents

Therapeutic agents are mentioned herein. The invention provides such agents for use in preventing or treating the relevant condition. This may comprise administering to an individual in need a therapeutically effective amount of the agent. The invention provides use of the agent in the manufacture of a medicament to prevent or treat the disease. The methods of the invention may be used to select an individual for treatment. The methods of the invention, and in particular the companion diagnostic assay method, may include a treatment step where a person identified by the method may then be administered with an agent that prevents or treats the relevant condition.

The formulation of the agent will depend upon the nature of the agent. The agent will be provided in the form of a pharmaceutical composition containing the agent and a pharmaceutically acceptable carrier or diluent. Suitable carriers and diluents include isotonic saline solutions, for example phosphate-buffered saline. Typical oral dosage compositions include tablets, capsules, liquid solutions and liquid suspensions. The agent may be formulated for parenteral, intravenous, intramuscular, subcutaneous, transdermal or oral administration.

The dose of agent may be determined according to various parameters, especially according to the substance used; the age, weight and condition of the individual to be treated; the route of administration; and the required regimen. A physician will be able to determine the required route of administration and dosage for any particular agent. A suitable dose may however be from 0.1 to 100 mg/kg body weight such as 1 to 40 mg/kg body weight, for example, to be taken from 1 to 3 times daily.

Forms of the Substance Mentioned Herein

Any of the substances, such as nucleic acids or therapeutic agents, mentioned herein may be in purified or isolated form. The may be in a form which is different from that found in nature, for example they may be present in combination with other substance with which they do not occur in nature. The nucleic acids (including portions of sequences defined herein) may have sequences which are different to those found in nature, for example having at least 1, 2, 3, 4 or more nucleotide changes in the sequence as described in the section on homology. The nucleic acids may have heterologous

sequence at the 5' or 3' end. The nucleic acids may be chemically different from those found in nature, for example they may be modified in some way, but preferably are still capable of Watson-Crick base pairing. Where appropriate the nucleic acids will be provided in double stranded or single stranded form. The invention provides all the of specific nucleic acid sequences mentioned herein in single or double stranded form, and thus includes the complementary strand to any sequence which is disclosed.

The invention also provides a kit for carrying out any method of the invention, including detection of a chromosomal interaction associated with a particular subgroup. Such a kit can include a specific binding agent capable of detecting the relevant chromosomal interaction, such as agents capable of detecting a ligated nucleic acid generated by processes of the invention. Preferred agents present in the kit include probes capable of hybridising to the ligated nucleic acid or primer pairs, for example as described herein, capable of amplifying the ligated nucleic acid in a PCR reaction.

The invention also provides a device that is capable of detecting the relevant chromosome interactions. The device preferably comprises any specific binding agents, probe or primer pair capable of detecting the chromosome interaction, such as any such agent, probe or primer pair described herein.

Preferred therapeutic agents for use in the invention for specific stated condition

A. Predisposition to Relapsing-Remitting Multiple Sclerosis (RRMS)

- **Drugs used to treat the condition:**

  - **Disease modifying therapies (DMT):**

- Injectable medications
  - Avonex (interferon beta-1a)
  - Betaseron (interferon beta-1b)
  - Copaxone (glatiramer acetate)
  - Extavia (interferon beta-1b)
  - Glatopa (glatiramer acetate)
  - Plegridy (peginterferon beta-1a)
  - Rebif (interferon beta-1a)
- Oral medications
  - Aubagio (teriflunomide)
  - Gilenya (fingolimod)
  - Tecfidera (dimethyl fumarate)
- Infused medications
  - Lemtrada (alemtuzumab)
  - Novantrone (mitoxantrone)
  - Tysabri (natalizumab)

- **Managing relapses:**
  - High-dose intravenous Solu-Medrol® (methylprednisolone)
  - High-dose oral Deltasone® (prednisone)
  - H.P. Acthar Gel (ACTH)

- **Steriods:**
  - Methylprednisolone

B. Likelihood of Primary Progressive Multiple Sclerosis (PPMS)

- **Drugs used to treat the condition:**

  - Steroids
  - Immunosuppressive therapies such as total lymphoid radiation, cyclosporine, methotrexate, 2-chlorodeoxyadenosine, cyclophosphamide, mitoxantrone, azathioprine, interferon, steroids, and immune globulin.
  - Copaxone
  - Ocrelizumab (Genetech).

C. Predisposition to fast progressing amyotrophic lateral sclerosis (ALS) disease state

- **Drugs used to treat the condition:**

  - Riluzole
  - Baclofen.

D. Predisposition to type 2 diabetes disease state

- **Drugs used to treat the condition:**
  - Metformin
  - Sulphonylureas such as:
    - glibenclamide
    - gliclazide
    - glimepiride
    - glipizide
    - gliquidone
  - Glitazones (thiazolidinediones, TZDs)
  - Gliptins (DPP-4 inhibitors) such as:
    - Linagliptin
    - Saxagliptin
    - Sitagliptin
    - Vildagliptin
  - GLP-1 agonists such as:
    - Exenatide
    - Liraglutide
  - Acarbose
  - Nateglinide and Repaglinide
  - Insulin treatment.

E. **Predisposition to type 1 diabetes disease state**

- **Drugs used to treat the condition:**

- Lantus subcutaneous
- Lantus Solostar subcutaneous
- Levemir subcutaneous
- Novolog Flexpen subcutaneous
- Novolog subcutaneous
- Humalog subcutaneous
- Novolog Mix 70-30 FlexPen subcutaneous
- SymlinPen 60 subcutaneous
- Humalog KwikPen subcutaneous
- SymlinPen 120 subcutaneous
- Novolin R injection
- Toujeo SoloStar subcutaneous
- Apidra subcutaneous
- Humalog Mix 75-25 subcutaneous
- Humulin 70/30 subcutaneous
- Humalog Mix 75-25 KwikPen subcutaneous
- Novolin N subcutaneous
- Humulin R injection
- Novolin 70/30 subcutaneous
- insulin detemir subcutaneous
- Levemir FlexTouch subcutaneous
- Humulin N subcutaneous
- insulin glargine subcutaneous
- Apidra SoloStar subcutaneous
- insulin lispro subcutaneous
- insulin regular human injection
- insulin regular human inhalation
- Humalog Mix 50-50 KwikPen subcutaneous
- insulin aspart subcutaneous
- Novolog Mix 70-30 subcutaneous
- Humalog Mix 50-50 subcutaneous
- Afrezza inhalation
- insulin NPH human recomb subcutaneous
- insulin NPH and regular human subcutaneous
- insulin aspart protamine-insulin aspart subcutaneous
- Humulin 70/30 KwikPen subcutaneous
- Humulin N KwikPen subcutaneous
- Tresiba FlexTouch U-100 subcutaneous
- Tresiba FlexTouch U-200 subcutaneous
- insulin lispro protamine and lispro subcutaneous
- pramlintide subcutaneous
- insulin glulisine subcutaneous
- Novolog PenFill subcutaneous
- insulin degludec subcutaneous

F. **Predisposition to systemic lupus erythematosus (SLE) disease state**

- **Drugs used to treat the condition:**

  - Non-steroidal anti-inflammatory drugs (NSAIDS): ibuprofen, naproxen and diclofenac.
  - Hydroxychloroquine
  - Corticosteriods
  - Immunosuppressants: azathioprine, methotrexate, mycophenolate mofetil and cyclophosphamide.
  - Rituximab
  - Belimumab.
  - Corticosteroids: prednisone, cortisone and hydrocortisone
  - NSAIDs: indomethacin (Indocin), nabumetone (Relafen), and celecoxib (Celebrex)
  - Anti-inflammatories: aspirin and acetaminophen (Tylenol)
  - Disease-Modifying Anti-Rheumatic Drugs (DMARDs): hydroxychloroquine (Plaqenil), cyclosporine (Gengraf, Neoral, Sandimmune), and azathioprine (Azasan, Imuran).
  - Antimalarials: chloroquine (Aralen) and hydroxychloroquine (Plaquenil).
  - BLyS-specific Inhibitors or Monoclonal Antibodies (MAbS): Belimumab (Benlysta).
  - Immunosuppressive Agents/Immune Modulators: azathioprine (Imuran), methotrexate (Rheumatrex), and cyclophosphamide (Cytoxan).
  - Anticoagulants: low-dose aspirin, heparin (Calciparine, Liquaemin), and warfarin (Coumadin).

G. **Predisposition to ulcerative colitis disease state**

- **Drugs used to treat the condition:**

  - Anti-inflammatory drugs: Aminosalicylates - sulfasalazine (Azulfidine), as well as certain 5-aminosalicylates, including mesalamine (Asacol, Lialda, Rowasa, Canasa, others), balsalazide (Colazal) and olsalazine (Dipentum) and Corticosteroids – prednisone and hydrocortisone.
  - Immune system supressors: azathioprine (Azasan, Imuran), mercaptopurine (Purinethol, Purixam), cyclosporine (Gengraf, Neoral, Sandimmune), infliximab (Remicade), adalimumab (Humira), golimumab (Simponi) and vedolizumab (Entyvio).
  - Other medications to manage specific symptoms of ulcerative colitis:
    - Antibiotics
    - Anti-diarrheal medication
    - Pain relievers
    - Iron supplements.

H. **Likelihood of relapse of colorectal cancer for ulcerative colitis patients**

- **Drugs used to treat the condition:**

  Aminosalicylates
  UC steroids
  Azathioprine

I. Likelihood of malignant peripheral nerve sheath tumours for neurofibromatosis patients

- Treatment

Treatments for MPNST include surgery, radiotherapy and chemotherapy.

J. Likelihood of developing prostate cancer and/or aggressive prostate cancer

- Drugs used to treat the condition:
    - luteinising hormone-releasing hormone (LHRH) agonists
    - anti-androgen treatment
    - combined LHRH and anti-androgen treatment
  - Steroids
  - Other medical treatments:
    - Abiraterone
    - Enzalutamide
    - docetaxel (Taxotere®)
    - carboplatin or cisplatin chemotherapy

K. Alzheimer's disease:

- Drugs used to treat the condition:

◦ Donepezil

◦Rivastigmine

◦Galantamine

•Memantine

Publications

The contents of all publications mentioned herein are incorporated by reference into the present specification and may be used to further define the features relevant to the invention.

Specific Embodiments

The EpiSwitch™ platform technology detects epigenetic regulatory signatures of regulatory changes between normal and abnormal conditions at loci. The EpiSwitch™ platform identifies and monitors the fundamental epigenetic level of gene regulation associated with regulatory high order structures of human chromosomes also known as chromosome conformation signatures. Chromosome signatures are a distinct primary step in a cascade of gene deregulation. They are high order

biomarkers with a unique set of advantages against biomarker platforms that utilize late epigenetic and gene expression biomarkers, such as DNA methylation and RNA profiling.

EpiSwitch™ Array Assay

The custom EpiSwitch™ array-screening platforms come in 4 densities of, 15K, 45K, 100K, and 250K unique chromosome conformations, each chimeric fragment is repeated on the arrays 4 times, making the effective densities 60K, 180K, 400K and 1 Million respectively.

Custom Designed EpiSwitch™ Arrays

The 15K EpiSwitch™ array can screen the whole genome including around 300 loci interrogated with the EpiSwitch™ Biomarker discovery technology. The EpiSwitch™ array is built on the Agilent SurePrint G3 Custom CGH microarray platform; this technology offers 4 densities, 60K, 180K, 400K and 1 Million probes. The density per array is reduced to 15K, 45K, 100K and 250K as each EpiSwitch™ probe is presented as a quadruplicate, thus allowing for statistical evaluation of the reproducibility. The average number of potential EpiSwitch™ markers interrogated per genetic loci is 50; as such the numbers of loci that can be investigated are 300, 900, 2000, and 5000.

EpiSwitch™ Custom Array Pipeline

The EpiSwitch™ array is a dual colour system with one set of samples, after EpiSwitch™ library generation, labelled in Cy5 and the other of sample (controls) to be compared/ analyzed labelled in Cy3. The arrays are scanned using the Agilent SureScan Scanner and the resultant features extracted using the Agilent Feature Extraction software. The data is then processed using the EpiSwitch™ array processing scripts in R. The arrays are processed using standard dual colour packages in Bioconductor in R: Limma *. The normalisation of the arrays is done using the normalised within Arrays function in Limma * and this is done to the on chip Agilent positive controls and EpiSwitch™ positive controls. The data is filtered based on the Agilent Flag calls, the Agilent control probes are removed and the technical replicate probes are averaged, in order for them to be analysed using Limma *. The probes are modelled based on their difference between the 2 scenarios being compared and then corrected by using False Discovery Rate. Probes with Coefficient of Variation (CV) <=30% that are <=-1.1 or =>1.1 and pass the p<=0.1 FDR p-value are used for further screening. To reduce the probe set further Multiple Factor Analysis is performed using the FactorMineR package in R.

* Note: LIMMA is Linear Models and Empirical Bayes Methods for Assessing Differential Expression in Microarray Experiments. Limma is a R package for the analysis of gene expression data arising from microarray or RNA-Seq.

The pool of probes is initially selected based on adjusted p-value, FC and CV <30% (arbitrary cut off point) parameters for final picking. Further analyses and the final list are drawn based only on the first two parameters (adj p-value; FC).

Examples

The invention is illustrated by the following non-limiting Examples.

Statistical Pipeline

EpiSwitch™ screening arrays are processed using the EpiSwitch™ Analytical Package in R in order to select high value EpiSwitch™ markers for translation on to the EpiSwitch™ PCR platform.

Step 1

Probes are selected based on their corrected p-value (False Discovery Rate, FDR), which is the product of a modified linear regression model. Probes below p-value

<= 0.1 are selected and then further reduced by their Epigenetic ratio (ER), probes ER have to be <=-1.1 or =>1.1 in order to be selected for further analysis. The last filter is a coefficient of variation (CV), probes have to be below <=0.3.

Step 2

The top 40 markers from the statistical lists are selected based on their ER for selection as markers for PCR translation. The top 20 markers with the highest negative ER load and the top 20 markers with the highest positive ER load form the list.

Step 3

The resultant markers from step 1, the statistically significant probes form the bases of enrichment analysis using hypergeometric enrichment (HE). This analysis enables marker reduction from the significant probe list, and along with the markers from step 2 forms the list of probes translated on to the EpiSwitch™ PCR platform.

The statistical probes are processed by HE to determine which genetic locations have an enrichment of statistically significant probes, indicating which genetic locations are hubs of epigenetic difference.

The most significant enriched loci based on a corrected p-value are selected for probe list generation. Genetic locations below p-value of 0.3 or 0.2 are selected. The statistical probes mapping to these genetic locations, with the markers from step2, form the high value markers for EpiSwitch™ PCR translation.

Array design and processing

Array Design

1. Genetic loci are processed using the SII software (currently v3.2) to:
    a. Pull out the sequence of the genome at these specific genetic loci (gene sequence with 50kb upstream and 20kb downstream)
    b. Define the probability that a sequence within this region is involved in CC's
    c. Cut the sequence using a specific RE
    d. Determine which restriction fragments are likely to interact in a certain orientation
    e. Rank the likelihood of different CC's interacting together.
2. Determine array size and therefore number of probe positions available (x)
3. Pull out x/4 interactions.
4. For each interaction define sequence of 30bp to restriction site from part 1 and 30bp to restriction site of part 2. Check those regions aren't repeats, if so exclude and take next interaction down on the list. Join both 30bp to define probe.
5. Create list of x/4 probes plus defined control probes and replicate 4 times to create list to be created on array
6. Upload list of probes onto Agilent Sure design website for custom CGH array.
7. Use probe group to design Agilent custom CGH array.

Array Processing

1. Process samples using EpiSwitch™ SOP for template production.
2. Clean up with ethanol precipitation by array processing laboratory.
3. Process samples as per Agilent SureTag complete DNA labelling kit - Agilent Oligonucleotide Array-based CGH for Genomic DNA Analysis Enzymatic labelling for Blood, Cells or Tissues
4. Scan using Agilent C Scanner using Agilent feature extraction software.

Example 1: A method of determining the chromosome interactions which are relevant to a companion diagnostic that distinguishes between non-responders and responders of methotrexate for the treatment of Rheumatoid Arthritis.

Source: Glasgow Scottish Educational Research Association (SERA) cohort.

Introduction to and Brief Summary of Example 1

Stable epigenetic profiles of individual patients modulate sensitivity of signalling pathways, regulate gene expression, influence the paths of disease development, and can render ineffective the regulatory controls responsible for effective action of the drug and response to treatment. Here we analysed epigenetic profiles of rheumatoid arthritis (RA) patients in order to evaluate its role in defining the non-responders to Methotrexate (MTX) treatment.

Reliable clinical prediction of response to first-line disease modifying anti-rheumatic drugs (DMARDs, usually methotrexate (MTX)) in rheumatoid arthritis is not currently possible. Currently the ability to determine response to first line DMARDs (in particular, methotrexate (MTX)) is dependent on empiric clinical measures after the therapy.

In early rheumatoid arthritis (ERA), it has not been possible to predict response to first line DMARDs (in particular, methotrexate (MTX)) and as such treatment decisions rely primarily on clinical algorithms. The capacity to classify drug naïve patients into those that will not respond to first line DMARDs would be an invaluable tool for patient stratification. Here we report that chromosome conformational signatures (highly informative and stable epigenetic modifications that have not previously been described in RA) in blood leukocytes of early RA patients can predict non-responsiveness to MTX treatment.

Methods:

Peripheral blood mononuclear cells (PBMCs) were obtained from DMARD naïve ERA patients recruited in the Scottish early rheumatoid arthritis (SERA) inception cohort. Inclusion in this study was based on diagnosis of RA (fulfilling the 2010 ACR/EULAR Criteria) with moderate to high disease activity (DAS28 ≥ 3.2) and subsequent monotherapy with methotrexate (MTX). DAS28 = Disease Activity Score of 28 joints. EULAR = The European League Against Rheumatism. ACR = American College of Rheumatology. MTX responsiveness was defined at 6 months using the following criteria: Responders – DAS28 remission (DAS28 <2.6) or a good response (DAS28 improvement of >1.2 and DAS28 3.2). Non-responders - no improvement in DAS28 (≤0.6). Initial analysis of chromosome conformational signatures (CCS) in 4 MTX responders, 4 MTX non-responders and 4 healthy controls was undertaken

using an EpiSwitch™ array containing 13,322 unique probes covering 309 RA-related genetic loci. Differentiating CCS were defined by LIMMA * linear modeling, subsequent binary filtering and cluster analysis. A validation cohort of 30 MTX responders and 30 non-responders were screened for the differentiating CCS using the EpiSwitch™ PCR platform. The differentiating signature was further refined using binary scores and logistical regression modeling, and the accuracy and robustness of the model determined by ROC analysis **.

* Note: LIMMA is Linear Models and Empirical Bayes Methods for Assessing Differential Expression in Microarray Experiments. Limma is a R package for the analysis of gene expression data arising from microarray or RNA-Seq.

** Note: ROC means Receiver Operating Characteristic and refers to ROC curves. An ROC curve is a graphical plot that illustrates the performance of a binary classifier system as its discrimination threshold is varied. The curve is created by plotting the true positive rate against the false positive rate at various threshold settings.

CCS EpiSwitch™ array analysis identified a 30-marker stratifying profile differentiating responder and non-responder ERA patients. Subsequent evaluation of this signature in our validation cohort refined this to a 5-marker CCS signature that was able to discriminate responders and non-responders. Prediction modeling provided a probability score for responders and non-responders, ranging from 0.0098 to 0.99 (0 = responder, 1 = non-responder). There was a true positive rate of 92% (95% confidence interval [95% CI] 75-99%) for responders and a true negative rate of 93% (95% CI 76-99%) for non-responders. Importantly, ROC analysis to validate this stratification model demonstrated that the signature had a predictive power of sensitivity at 92% for NR to MTX.

We have identified a highly informative systemic epigenetic state in the peripheral blood of DMARD naïve ERA patients that has the power to stratify patients at the time of diagnosis. The capacity to differentiate patients *a priori* into non-responders, using a blood-based clinical test, would be an invaluable clinical tool; paving the way towards stratified medicine and justifying more aggressive treatment regimes in ERA clinics.

Detailed Version of Example 1

The capacity to differentiate patients *a priori* into responders (R) and non-responders (NR) would be an invaluable tool for patient stratification leading to earlier introduction of effective treatment. We have used the EpiSwitch™ biomarker discovery platform to identify Chromosome Conformation Signatures (CCS) in blood-derived leukocytes, which are indicative of disease state and MTX

responsiveness. Thereby we identified an epigenetic signature contained in the CXCL13, IFNAR1, IL-17A, IL-21R and IL-23 loci that provide the first prognostic molecular signature that enables the stratification of treatment naïve early RA (ERA) patients into MTX R and NR. Importantly, this stratification model had a predictive power of sensitivity at 92% for NR to MTX. This epigenetic RA biomarker signature can distinguish between ERA and healthy controls (HC). This combinatorial, predictive peripheral blood signature can support earlier introduction of more aggressive therapeutics in the clinic, paving the way towards personalized medicine in RA.

RA is a chronic autoimmune disease affecting up to 1% of the global population. Pathogenesis is multifactorial and characterized by primarily immune host gene loci interacting with environmental factors, particularly smoking and other pulmonary stimuli. The exposure of a genetically susceptible individual to such environmental factors suggests an epigenetic context for disease onset and progression. Recent studies of chromatin markers (e.g. methylation status of the genome) provide the first evidence of epigenetic differences associated with RA. However, to date neither genetic associations, nor epigenetic changes, have provided a validated predictive marker for response to a given therapy. Moreover, clinical presentation only weakly predicts the efficacy and toxicity of conventional DMARDs. MTX[8], the commonest first-choice medication recommended by EULAR (The European League Against Rheumatism) and ACR (American College of Rheumatology) management guidelines, delivers clinically meaningful response rates ranging from 50 to 65% after 6 months of treatment. Such responses, and especially the rather smaller proportion that exhibits high hurdle responses, cannot currently be predicted in an individual patient. This begets a 'trial and error' based approach to therapeutic regimen choice (mono or combinatorial therapeutics). The ability to predict drug responsiveness in an individual patient would be an invaluable clinical tool, given that response to first-line treatment is the most significant predictor of long-term outcome.

Herein we focused on epigenetic profiling of DMARD-naïve, ERA patients from the Scottish Early Rheumatoid Arthritis (SERA) inception cohort in order to ascertain if there is a stable blood-based epigenetic profile that indicates NR to MTX treatment and thus enables *a priori* identification and stratification of such patients to an alternate therapeutic. The source Epigenetic modulation can strongly influence cellular activation and transcriptional profiles. Conceivably, the mode of action for a drug could be affected by epigenetically modified loci. We have focused on CCS, also known as long-range chromatin interactions, because they reflect highly informative and stable high-order epigenetic status which have significant implications for transcriptional regulation. They also offer significant advantages[15] and early functional links to phenotypic differences[16], and have been reported as

informative biomarkers candidates in oncology and other disease areas.

We used early RA (ERA) patients provided by the Scottish early rheumatoid arthritis (SERA) inception cohort. Demographic, clinical and immunological factors were obtained at diagnosis and 6 months. Inclusion in this study was based on a diagnosis of RA (fulfilling the 2010 ACR/EULAR Criteria) with moderate to high disease activity (DAS28 ≥ 3.2) and subsequent monotherapy with MTX. Responders were defined as patients who upon receiving MTX achieved DAS28 remission (DAS28 <2.6) or a good response (DAS28 improvement of >1.2 and DAS28 ≤3.2) at 6 months. Non-responders were defined as patients who upon receiving MTX had no improvement in DAS28 (≤0.6) at 6 months. Blood samples for epigenetic analysis were collected at diagnosis. (DAS28 = Disease Activity Score of 28 joints.)

We used a binary epigenetic biomarker profiling by analysing over 13,322 chromosome conformation signatures (CCS) (13,322 unique probes) across 309 genetic loci functionally linked to RA. CCS, as a highly informative class of epigenetic biomarkers (1), were read, monitored and evaluated on EpiSwitch™ platform which has been already successfully utilized in blood based stratifications of Mayo Clinic cohort with early melanoma (2) and is currently used for predictive stratification of responses to immunotherapies with PD-1/PD-L1.

Identified epigenetic profiles of naïve RA patients were subject to statistical analysis using GraphPad Prism, WEKA and R Statistical language. By using EpiSwitch™ platform and extended cohort of 90 clinical samples we have identified a pool of over 922 epigenetic lead biomarkers, statistically significant for responders, non-responders, RA patients and healthy controls.

To identify a pre-treatment circulating CCS status in ERA patients, 123 genetic loci (Table 1) associated with RA pathogenesis were selected and annotated with chromosome conformations interactions predicted using the EpiSwitch™ *in silico* prediction package. The EpiSwitch™ *in silico* prediction generated 13,322 high-confidence CCS marker candidates (Table 1). These candidates were used to generate a bespoke discovery EpiSwitch™ array (Figure 5) to screen peripheral blood mononuclear cells isolated at the time of diagnosis (DMARD-naïve) from 4 MTX responders (R) and 4 MTX NR, all clinically defined after 6 months therapy (Figure 1A, B and Table 2), and 4 healthy controls (HC). To identify the CCS that differentiated R, NR and HC, a LIMMA * linear model of the normalized epigenetic load was employed. A total of 922 statistically significant stratifying markers (significance assessed on the basis of adjusted p value and EpiSwitch™ Ratio) were identified. Of the 922 lead markers, 420 were associated with NR, 210 with R and 159 with HC (Fig. 1C). Binary filtering and cluster analysis was applied to the EpiSwitch™ markers to assess the significance of CCS identified. A stepwise hierarchical

clustering approach (using Manhattan distance measure with complete linkage agglomeration and taking into account R vs NR, HC vs R & HC vs NR) reduced the number of significant markers from 922 to 65 and finally resulted in a 30-marker stratifying profile (Figure 1D and Table 3).

* Note: LIMMA is Linear Models and Empirical Bayes Methods for Assessing Differential Expression in Microarray Experiments. Limma is a R package for the analysis of gene expression data arising from microarray or RNA-Seq.

To refine and validate the CCS signature, the 30 identified markers were screened in a second ERA patient cohort of R and NR (Figure 2A, B and Table 4) in a stepwise approach, using the EpiSwitch™ PCR platform (Figure 5). In the first instance, the entire 30 CCS markers were run in 12 ERA patients (6 R and 6 NR). The best differentiating CCS markers were identified by applying a Chi-squared test for independence with Yate's continuity correction on the binary scores, revealing a 12-marker CCS profile (Table 5). These 12 CCS markers were run on an additional 12 ERA patients (6 R and 6 NR) and the data combined with the previous 12 ERA. Combining the 24 patient samples (12 R and 12 NR) a logistic regression Model in the WEKA classification platform (using 5-fold cross validation to score the discerning power of each marker) was built and run 10 times by random data re-sampling of the initial data set to generate 10 different start points for model generation. The markers with the highest average scores were selected, thus reducing the profile to the 10 best discerning CCS markers (Table 5). The 10 CCS markers were used to probe a further 36 ERA samples (18 R and 18 NR). Combining all data (30 R and 30 NR), and using the same logistical regression and score calculation analysis, revealed a 5 CCS marker signature (IFNAR1, IL-21R, IL-23, IL-17A and CXCL13) that distinguished MTX R from NR (Figure 2C, Table 5). CCS in the CXCL13 and IL-17A loci were associated with non-responders whilst CCS in the IFNAR1, IL-23 and IL-21R loci were associated with responders. This was an intriguing profile given the central role postulated for the IL-17 axis in human autoimmunity.

Importantly, the composition of the stratifying signature identifies the location of chromosomal conformations that potentially control genetic locations of primary importance for determining MTX response. Principal component analysis (PCA) of the binary scores for the classifying 5 EpiSwitch™ CCS markers provided clear separation of ERA patients based on their MTX response (Figure 2D). The model provided a prediction probability score for responders and non-responders, ranging from 0.0098 to 0.99 (0 = responder, 1 = non-responder). The cut-off values were set at ≤0.30 for responders and ≥0.70 for non-responders. The score of ≤0.30 had a true positive rate of 92% (95% confidence interval [95% CI] 75-99%) whilst a score of ≥0.70 had a true negative response rate of 93% (95% CI 76-

99%). The number of observed and predicted patients per response category (R or NR to MTX) is shown in Table 6. With the EpiSwitch™ CCS marker model, 53 patients (88%) were classified as either responder or non-responder.

Table 6. Observed and predicted number of R and NR to MTX monotherapy at 6 months using the EpiSwitch™ CCS model

	Predicted response		
Observed response	Non-responder	Undefined	Responder
Non-responder	25	3	2
Responder	2	4	24

Notes to Table 6: Cut off levels were chosen based on the probability of response to MTX of (approximately) >0.70 for NR and <0.3 for R. NR and R were defined as described in the methods.

In order to test the 'accuracy' and 'robustness of performance' of the logistic classifying model that determined the 5 EpiSwitch™ CSS markers, 150 ROC ** curves (with unique start points) were generated by random data re-sampling of the R and NR data (Figure 3A). This resulted in the data being split into training (66%, equivalent to 6000 known class samples) and test (34%, equivalent to 3000 unknown class samples) groups; importantly the same split is never seen in the data for cross validation. The average discriminative ability (AUC) of the model was 89.9% (95% CI 87-100%), with an average sensitivity (adjusted for response prevalence) for NR of 92% and an average specificity for R of 84%. To determine the predictive capability of the model, the average model accuracy statistics were adjusted for population R/NR to MTX using Bayes prevalence theorem[21]. Using a 55% MTX response rate, the positive predictive value (PPV) was 90.3% whilst the negative predictive value (NPV) was 86.5%. If the response rate was adjusted to 60%, this decreased the PPV to 87% whilst increasing the NPV to 89%.

** Note: ROC means Receiver Operating Characteristic and refers to ROC curves. An ROC curve is a graphical plot that illustrates the performance of a binary classifier system as its discrimination threshold is varied. The curve is created by plotting the true positive rate against the false positive rate at various threshold settings.

As an independent evaluation of the discerning powers of the selected 5 EpiSwitch™ CCS markers, factor analysis of mixed data (FAMD) incorporating 30 HC was performed. This illustrated that the

signature not only has the power to differentiate between MTX R and NR but also retains sufficient disease-specific features to differentiate between healthy individuals and RA patients (Figure 3B).

Example 1 - Table 6D and 6E - Stratifying between RA-MTX responders and non-responders

Table 6D, and continuation Table 6E, presented hereinafter **after** Tables 6b+6c from Example 1A, show *inter alia* a list of about 54 DNA probes (60mers) and their DNA sequences. These probes represent some of the probes used in Example 1. Without being bound, most of the probes illustrated in Table 6D+6E are thought likely to be significant to / useful in stratifying between RA-MTX responders and RA-MTX non-responders. The shown probes were investigated further by PCR. P Value = Probability value; adj. = adjusted.

Example 1 - Conclusion

In conclusion, our study of the epigenetic profile classification of DMARD naïve ERA patients on the basis of prospective clinical assessment for R/NR has identified a consistent epigenetic signature, which discriminates an epigenetic state that is conducive and non-conducive to MTX response. This is to our knowledge, the first example of a stable and selectively differentiating blood based epigenetic biomarker in early RA patients that appears disease related (versus healthy controls) and that can predict non-responsiveness to first-line MTX therapy. This model offers direct and practical benefits with a validated classifier based on 5 conditional CCS and their detection by the industrial ISO-13485 EpiSwitch™ platform, which has the potential to be routinely available in the near future within clinical practice. Importantly, by adopting this predictive signature it should be possible to stratify MTX naïve ERA patients into R and NR cohorts. This offers the potential to accelerate patient progression through the currently approved treatment strategy for ERA seeking earlier use of effective therapeutics, hence leading to a 'personalised' treatment regime. Furthermore, it is conceivable that alternative CCS signatures are present in RA patients (and patients with other autoimmune diseases) that could be used to justify fast-tracked biological treatment regimes in the clinic. This would have far reaching socio-economic implications, providing more cost effective and robust therapeutic approaches.

Example 1 - Material and Methods

Example 1 - RA patient population

ERA patients in this study are part of the Scottish early rheumatoid arthritis (SERA) inception cohort. Demographic, clinical and immunological factors were obtained at diagnosis and 6 months (Table 1). Inclusion in the inception cohort was based on clinical diagnosis of undifferentiated polyarthritis or RA (≥1 swollen joint) at a secondary care rheumatology unit in Scotland. Exclusion criteria were previous

or current DMARD/biological therapy and/or established alternative diagnosis (i.e. psoriatic arthritis, reactive arthritis). Inclusion in this study was based on a diagnosis of RA (fulfilled the 2010 ACR/EULAR criteria for RA) with moderate to high disease activity (DAS28 ≥ 3.2) and subsequent monotherapy with MTX. [DAS28 = Disease Activity Score of 28 joints. EULAR = European League Against Rheumatism. ACR = American College of Rheumatology.] Responders were defined as patients who upon receiving MTX achieved DAS28 remission (DAS28 <2.6) or a good response (DAS28 improvement of >1.2 and DAS28 ≤3.2) at 6 months. Non-responders were defined as patients who upon receiving MTX had no improvement in DAS28 (≤0.6) at 6 months. Blood samples were collected at diagnosis (Baseline) in EDTA tubes and centrifuged to generate a buffy layer containing PBMCs, which was harvested and stored at -80°C. Local ethics committees approved the study protocol and all patients gave informed consent before enrolment into the study.

Example 1 - EpiSwitch™ processing, array and PCR detection. Probe design and locations for EpiSwitch™ assays

Pattern recognition methodology was used to analyse human genome data in relation to the transcriptional units in the human genome. The proprietary EpiSwitch™ pattern recognition software[18, 20] provides a probabilistic score that a region is involved in chromatin interaction. Sequences from 123 gene loci were downloaded and processed to generate a list of the 13,322 most probable chromosomal interactions. 60mer probes were designed to interrogate these potential interactions and uploaded as a custom array to the Agilent SureDesign website. Sequence-specific oligonucleotides were designed using Primer3[23], at the chosen sites for screening potential markers by nested PCR. Oligonucleotides were tested for specificity using oligonucleotide specific BLAST.

Example 1 - Chromatin Conformation signature analysis from patient PBMC's

Template preparation: Chromatin from 50 µl of each PBMC sample was extracted using the EpiSwitch™ assay following the manufacturer's instructions (Oxford BioDynamics Ltd). Briefly, the higher order structures are fixed with formaldehyde, the chromatin extracted, digested with TaqI, dilution and ligation in conditions to maximize intramolecular ligation, and subsequent proteinase K treatment. *EpiSwitch™ microarray:* EpiSwitch™ microarray hybridization was performed using the custom Agilent 8x60k array using the Agilent system, following the manufacturer's instructions (Agilent). Each array contains 55088 probes spots, representing 13,322 potential chromosomal interactions predicted by the EpiSwitch™ pattern recognition software quadruplicated, plus EpiSwitch™ and Agilent controls. Briefly, 1 µg of EpiSwitch™ template was labelled using the Agilent

SureTag labelling kit. Processing of labelled DNA was performed. Array analysis was performed immediately after washing using the Agilent scanner and software. In order to compare all the experiments the data was background corrected and normalized. Since each spot in the array is present in quadruplicate, the median of the four spots of each probe in the array was calculated and its log2 transformed value was used for further analysis. The coefficient of variation and *p*-value was calculated for each probe replicate. *EpiSwitch™ PCR detection:* Oligonucleotides were tested on template to confirm that each primer set was working correctly. To accommodate for technical and replicate variations, each sample was processed four times. All the extracts from these four replicates were pooled and the final nested PCR was performed on each sample. This procedure permitted the detection of limited copy-number templates with higher accuracy. All PCR amplified samples were visualised by electrophoresis in the LabChip® GX from Perkin Elmer, using the LabChip DNA 1K Version2 kit (Perkin Elmer) and internal DNA marker was loaded on the DNA chip according to the manufacturer's protocol using fluorescent dyes. Fluorescence was detected by laser and electropherogram read-outs translated into a simulated band on gel picture using the instrument software. The threshold we set for a band to be deemed positive was 30 fluorescence units and above.

Example 1 - Statistical Methods and Packages.

GraphPad Prism and SPSS were used for all statistical analyses of clinical data. The chi-square test and Fisher's exact test (for categorical variables), the t-test for independent samples (for continuous normally distributed variables), and the Mann-Whitney U test (for continuous variables without normal distribution) were used to identify differences. The level of statistical significance was set at 0.05, and all tests were 2-sided. R (and appropriate packages) were used for evaluation of EpiSwitch™ data. This included Stats package for Chi-square test and GLM (logit), ROCR package for ROC curves from WEKA odds probabilities, gplot & stats package in R for Heatmaps. FactorMiner package was used for PCA and Factor plots. Weka was used for Attribute Reduction, data randomisation and re-sampling, Logistic Model Classifier, AUC calculations and model accuracy calculations.

Example 1 - Table 1. Selected genes for EpiSwitch™ Array

GENE	Description	Comments	Number of identified EpiSwitch™ sites
ABCB1	ATP-binding cassette, sub-family B (MDR/TAP), member 1	MTX related genes	56
ABCG2	ATP-binding cassette, sub-family G (WHITE), member 2	MTX related genes	84
ADORA2A	Adenosine A2a receptor	MTX related genes	72
AFF3	AF4/FMR2 family, member 3	RA SNP association	140
AMPD1	Adenosine monophosphate deaminase 1	MTX related genes	24
ApoE	Apolipoprotein E	Apolipoproteins	96
ATIC	5-aminoimidazole-4-carboxamide ribonucleotide formyltransferase/IMP cyclohydrolase	MTX related genes	32
BLK	B lymphoid tyrosine kinase	RA SNP association	196
BTNL2	Butyrophilin-like 2 (MHC class II associated)	Associated with RA via exome sequencing	44
C5orf30	Chromosome 5 open reading frame 30	RA SNP association	96
CCL2	Chemokine (C-C motif) ligand 2	Cytokines & Chemokines	404
CCL21	Chemokine (C-C motif) ligand 21	Cytokines & Chemokines	28
CCL3	Chemokine (C-C motif) ligand 3	Cytokines & Chemokines	52
CCL5	Chemokine (C-C motif) ligand 5	Cytokines & Chemokines	52
CCR1	Chemokine (C-C motif) receptor 1	Cytokines & Chemokines receptors	172
CCR2	Chemokine (C-C motif) receptor 2	Cytokines & Chemokines receptors	164
CCR6	Chemokine (C-C motif) receptor 6	Cytokines & Chemokines receptors	56
CD28	Cluster of Differentiation 28	RA SNP association	132
CD40	Cluster of Differentiation 40	RA SNP association	148
CD80	Cluster of Differentiation 80	Cell surface	76
CHI3L1	Chitinase 3-like 1 (cartilage glycoprotein-39)	Extracellular	64

Example 1 - Table 1. Selected genes for EpiSwitch™ Array

GENE	Description	Comments	Number of identified EpiSwitch™ sites
CHUK	Conserved helix-loop-helix ubiquitous kinase	NFKB	92
CIITA	Class II, major histocompatibility complex, transactivator	NLR pathway	80
CLEC12A	C-type lectin domain family 12, member A	Other	52
CLEC16A	C-type lectin domain family 16, member A	Other	108
COL2A1	Collagen, type II, alpha 1	Collagens	100
CTLA4	Cytotoxic T-lymphocyte-associated protein 4	RA SNP association	68
CX3CL1	Chemokine (C-X3-C motif) ligand 1	Cytokines & Chemokines	92
CXCL12	Chemokine (C-X-C motif) ligand 12	Cytokines & Chemokines	80
CXCL13	Chemokine (C-X-C motif) ligand 13	Cytokines & Chemokines	80
CXCL8	Chemokine (C-X-C motif) ligand 8	Cytokines & Chemokines	48
CXCR3	Chemokine (C-X-C motif) receptor 3	Cytokines & Chemokines receptors	72
CXCR4	Chemokine (C-X-C motif) receptor 4	Cytokines & Chemokines receptors	56
DHFR	Dihydrofolate reductase	MTX related genes	72
ESR1	Oestrogen receptor 1	FLS MTX responsive genes	140
FCGR2A	Fc fragment of IgG, low affinity IIa, receptor (CD32)	RA SNP association	100
FCGR3B	Fc fragment of IgG, low affinity IIIb, receptor (CD16b)	RA SNP association	192
FCRL3	Fc receptor-like 3	Other	68
FPGS	Folylpolyglutamate synthase	MTX related genes	56
HTR2A	5-hydroxytryptamine (serotonin) receptor 2A, G protein-coupled	Other	80
ICAM1	Intercellular adhesion molecule 1	FLS MTX responsive genes	132
ICOS	Inducible T-cell co-stimulator	RA SNP association	200

Example 1 - Table 1. Selected genes for EpiSwitch™ Array

GENE	Description	Comments	Number of identified EpiSwitch™ sites
IFNAR1	Interferon (alpha, beta and omega) receptor 1	Cytokines & Chemokines receptors	80
IFNg	Interferon, gamma	Cytokines & Chemokines	52
IKBKB	Inhibitor of kappa light polypeptide gene enhancer in B-cells, kinase beta	NFKB	128
IL-10	Interleukin 10	Cytokines & Chemokines	48
IL-15	Interleukin 15	Cytokines & Chemokines	76
IL-17A	Interleukin 17A	Cytokines & Chemokines	32
IL-18	Interleukin 18	Cytokines & Chemokines	64
IL-1a	Interleukin 1 alpha	Cytokines & Chemokines	196
IL-2	Interleukin 2	Cytokines & Chemokines	44
IL-21R	Interleukin 21 receptor	Cytokines & Chemokines receptors	60
IL-23	Interleukin 23	Cytokines & Chemokines	56
IL-23R	Interleukin 23 receptor	Cytokines & Chemokines receptors	104
IL-2RA	Interleukin 2 receptor, alpha	Cytokines & Chemokines receptors	100
IL-2RB	Interleukin 2 receptor, beta	Cytokines & Chemokines receptors	72
IL-32	Interleukin 32	Cytokines & Chemokines	44
IL-4	Interleukin 4	Cytokines & Chemokines	32
IL-4R	Interleukin 4 receptor	Cytokines & Chemokines receptors	76
IL-6	Interleukin 6	Cytokines & Chemokines	48
IL-6ST	Interleukin 6 signal transducer (gp130, oncostatin M receptor)	Cytokines & Chemokines receptors	72

Example 1 - Table 1. Selected genes for EpiSwitch™ Array

GENE	Description	Comments	Number of identified EPISwitch sites
IL-7	Interleukin 7	Cytokines & Chemokines	72
IL1RN	Interleukin 1 receptor antagonist	MTX related genes	28
IRAK3	Interleukin-1 receptor-associated kinase 3	Signalling	80
IRF5	Interferon regulatory factor 5	Signalling	76
ITGA4	Integrin, alpha 4 (antigen CD49D, alpha 4 subunit of VLA-4 receptor)	Cell surface	100
ITPA	Inosine triphosphatase (nucleoside triphosphate pyrophosphatase)	MTX related genes	56
JAG1	Jagged 1	FLS MTX responsive genes	84
M-CSF	Colony stimulating factor 1	Cytokines & Chemokines	96
MafB	V-maf musculoaponeurotic fibrosarcoma oncogene homolog B	Transcription factors	52
MAL	Mal, T-cell differentiation protein	TLR pathway	68
MEFV	Mediterranean fever	Other	76
MMP14	Matrix metallopeptidase 14	Matrix Metalloprotineases	92
MMP2	Matrix metallopeptidase 2	Matrix Metalloprotineases	212
MMP9	Matrix metallopeptidase 9	Matrix Metalloprotineases	68
MTHFD1	Methylenetetrahydrofolate dehydrogenase (NADP+ dependent) 1, methenyltetrahydrofolate cyclohydrolase, formyltetrahydrofolate synthetase	MTX related genes	80
MTHFR	Methylenetetrahydrofolate reductase (NAD(P)H)	MTX related genes	52
MyD88	Myeloid differentiation primary response gene 88	TLR pathway	80
NFAT	Nuclear factor of activated T cells	Transcription factors	204
NFATC2IP	Nuclear factor of activated T-cells, cytoplasmic, calcineurin-dependent 2 interacting protein	RA SNP association	84
NFKB1	Nuclear factor of kappa light polypeptide gene enhancer in B-cells 1	NFKB	96
NFKB2	Nuclear factor of kappa light polypeptide gene enhancer in B-cells 2 (p49/p100)	NFKB	64

Example 1 - Table 1. Selected genes for EpiSwitch™ Array

GENE	Description	Comments	Number of identified EpiSwitch™ sites
NFKBIB	Nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor, beta	NFKB	120
NFKBIA	Nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor, alpha	NFKB	88
NLRP1	NLR family, pyrin domain containing 1	NLR pathway	108
NLRP3	NLR family, pyrin domain containing 3	NLR pathway	128
PADI4	Peptidyl arginine deiminase, type IV	RA SNP association	168
PRDM1	PR domain containing 1, with ZNF domain	RA SNP association	120
PRKCQ	Protein kinase C, theta	RA SNP association	216
PRKCZ	Protein kinase C, zeta	Other	184
PSTPIP1	Proline-serine-threonine phosphatase interacting protein 1	Cytoskeletal	96
PTGS2	Prostaglandin-endoperoxide synthase 2 (prostaglandin G/H synthase and cyclooxygenase)	Signalling	52
PTPN22	Protein tyrosine phosphatase, non-receptor type 22	RA SNP association	196
PXK	PX domain containing serine/threonine kinase	RA SNP association	296
RBPJ	Recombination signal binding protein for immunoglobulin kappa J region	RA SNP association	296
REL	V-rel reticuloendotheliosis viral oncogene homolog A	NFKB	92
RFC-1	Replication factor C (activator 1) 1, 145kDa	MTX related genes	52
RGMB	RGM domain family, member B	FLS MTX responsive genes	80
RUNX1	Runt-related transcription factor 1	RA SNP association	212
SH2B3	SH2B adaptor protein 3	RA SNP association	124
SHMT	Serine hydroxymethyltransferase 1 (soluble)	MTX related genes	68
SLC19A1	Solute carrier family 19 (folate transporter), member 1	MTX related genes	76
SPRED2	Sprouty-related, EVH1 domain containing 2	RA SNP association	336
STAT4	Signal transducer and activator of transcription 4	Signalling	128

Example 1 - Table 1. Selected genes for EpiSwitch™ Array

GENE	Description	Comments	Number of identified EpiSwitch™ sites
SUMO1	SMT3 suppressor of mif two 3 homolog 1	SUMO	132
TAGAP	T-cell activation RhoGTPase activating protein	RA SNP association	92
TLR1	Toll-like receptor 1	TLR pathway	204
TLR2	Toll-like receptor 2	TLR pathway	52
TLR4	Toll-like receptor 4	TLR pathway	52
TNF	Tumour necrosis factor	Cytokines & Chemokines	68
TNFAIP3	Tumour necrosis factor, alpha-induced protein 3	RA SNP association	180
TNFRSF11B	Tumour necrosis factor receptor superfamily, member 11b	Cytokines & Chemokines receptors	80
TNFRSF13C	Tumour necrosis factor receptor superfamily, member 13C	Cytokines & Chemokines receptors	52
TNFRSF14	Tumour necrosis factor receptor superfamily, member 14	RA SNP association	112
TNFRSF17	Tumour necrosis factor receptor superfamily, member 17	Cytokines & Chemokines receptors	44
TNFRSF1A	Tumour necrosis factor receptor superfamily, member 1A	Cytokines & Chemokines receptors	72
TNFRSF1B	Tumour necrosis factor receptor superfamily, member 1B	Cytokines & Chemokines receptors	72
TNFSF11	Tumour necrosis factor (ligand) superfamily, member 11	Cytokines & Chemokines	52
TNFSF13	Tumour necrosis factor (ligand) superfamily, member 13	Cytokines & Chemokines	48
TRAF1	TNF receptor-associated factor 1	RA SNP association	120
TRAF6	TNF receptor-associated factor 6	RA SNP association	72
TYMS	Thymidylate synthetase	MTX related genes	48
WISP3	WNT1 inducible Signalling pathway protein 3	Signalling	88

Example 1 - Table 2. Patient Characteristics – Discovery Cohort

	Baseline			6 months			Healthy control
	Non-responder	Responder	*P* value	Non-responder	Responder	*P* value	
Age – years	55± 6.1	55±19.7	>0.99	-	-	-	52±13.3
Males – no. (%)	1 (25)	1 (25)	1	-	-	-	3 (38)
Caucasian – no. (%)	4 (100)	4 (100)	-	-	-	-	8 (100)
Body mass index – kg/m^2	29.5± 0.96$^{\$}$	25.0± 4.88	0.19	-	-	-	-
Patient global assessment (VAS, 0-100 mm)	54.3±33.5	39.3±30.2	0.53	54.5±20.0	9.3±6.2	0.029	-
Physician global assessment (VAS, 0-100 mm)	55±29.7	38.5±17.8	0.38	32.5±20.2	8.8±7.0	0.068	-
Number of swollen joints (0-28)	11.3±5.3	4.8±3.9	0.09	15±10.7	2.0±2.8	0.057	-
Number of tender joints (0-28)	10.5±7.7	4.8±6.4	0.2	11.25±10.6	0.5±1.0	0.029	-
CDAI	32.7±5.2	17.3±9.6	0.03	35.0±21.2	4.3±3.7	0.03	-
DAS28-CRP	5.1±0.2	4.2±0.77	0.06	-	-	-	-
DAS28-ESR	5.5±0.5$^{\$}$	4.6±0.9$^{\$}$	0.4	5.3±1.3	2.8±0.7	0.016	-
RF (IU/ml)	35.4±25.6	321±140$^{\$}$	0.06	-	-	-	-
CCP (U/ml)	10.3±7.2	340±0$^{\$}$	0.06	-	-	-	-
Current smoker – no. (%)	2 (50)	1 (25)	-	-	-	-	-
Previous smoker – no. (%)	1 (25)	1 (25)	-	-	-	-	-
Non-smoker – no. (%)	1 (25)	2 (50)	-	-	-	-	-

The Fisher exact unconditional test is used to assess differences in proportions between the two groups. To examine differences in continuous variables between the two groups, the independent samples t-test or the Mann-Whitney U-test (depending on distribution of data) is used. $^{\$}$ n=3

Example 1 - Table 3. 65 Selected genes from EpiSwitch™ Array analysis

Gene	Probes*	adj. p value	EpiSwitch™ ratio	HC_NR_MTX	HC_R_MTX	NR_R_MTX	Association
19_55449062_55451429_55484960_50_55486708_RF	19_55449062_55451429_55484960_55486708_RF	0.079228864	-1.43395525	0	-1	-1	R
C5orf30	C5orf30_Site5_Site2_FF	0.079228864	-1.24257534	1	-1	-1	R
CHUK	CHUK_Site7_Site2_RF	0.079228864	-1.32868581	1	-1	-1	R
CXCL13	CXCL13_Site1_Site3_RR	0.079228864	-1.29833859	0	-1	-1	R
TLR1	TLR1_Site4_Site7_FR	0.079228864	-1.43064593	1	-1	-1	R
11_47175706_47180170_47251505_47252468_FR	11_47175706_47180170_47251505_47252468_FR	0.083312472	-1.20859706	1	-1	-1	R
C5orf30	C5orf30_Site4_Site2_FF	0.084204721	-1.20024867	1	-1	-1	R
TLR1	TLR1_Site9_Site2_FF	0.086622849	-1.37554182	1	-1	-1	R
FCRL3	FCRL3_Site9_Site7_FF	0.090200643	-1.25121814	1	-1	-1	R
SH2B3	SH2B3_Site6_Site5_FF	0.090200643	-1.32868581	1	-1	-1	R
12_69705360_69711928_69799162_69800678_RF	12_69705360_69711928_69799162_69800678_RF	0.097224197	-1.20580783	1	-1	-1	R
IL-23R	IL-23R_Site5_Site8_FF	0.108787769	-1.26868449	1	-1	-1	R
CLEC12A	CLEC12A_Site6_Site1_FR	0.112869007	-1.22264028	0	-1	-1	R
IL-17A	IL-17A_Site3_Site1_RR	0.115042065	-1.16473359	0	-1	-1	R
CXCL8	CXCL8_Site7_Site6_FR	0.118123176	-1.13288389	0	-1	-1	R
MyD88	MyD88_Site5_Site1_FR	0.129904996	-1.18372449	1	0	-1	R
PRDM1	PRDM1_Site6_Site2_RR	0.144057138	-1.19195794	1	-1	-1	R
MMP2	MMP2_Site8_Site9_FF	0.146105678	-1.20859706	1	-1	-1	R
SPRED2	SPRED2_Site4_Site8_RF	0.149371667	-1.38510947	1	-1	-1	R

Gene	Probes*	adj. p value	EpiSwitch™ ratio	HC_NR_MTX	HC_R_MTX	NR_R_MTX	Association
C5orf30	C5orf30_Site4_Site8_RF	0.150085134	-1.17826714	1	-1	-1	R
19_10294661_10295285_10370560_0_10371551_RR	19_10294661_10295285_10370560_1_0371551_RR	0.153140631	-1.20859706	1	-1	-1	R
TNFRSF13C	TNFRSF13C_Site3_Site6_FF	0.15333898	-1.20580783	1	-1	-1	R
IL-23	IL-23_Site4_Site5_FR	0.160960834	-1.18099266	0	-1	-1	R
NFKBIB	NFKBIB_Site8_Site9_FR	0.168381727	-1.23114441	1	-1	-1	R
TNFRSF13C	TNFRSF13C_Site1_Site6_FF	0.16921449	-1.1198716	1	-1	-1	R
CD28	CD28_Site5_Site9_RR	0.171723501	-1.14340249	1	-1	-1	R
NFKB1	NFKB1_Site4_Site8_RR	0.185725586	-1.20024867	1	-1	-1	R
CHUK	CHUK_Site3_Site5_RF	0.188137111	-1.13026939	1	-1	-1	R
TLR1	TLR1_Site9_Site3_FR	0.188137111	-1.19747871	1	-1	-1	R
M-CSF	M-CSF_Site5_Site6_FF	0.191292635	-1.20859706	1	-1	-1	R
NFKBIB	NFKBIB_Site1_Site8_FF	0.191922112	-1.12766093	1	-1	-1	R
11_47175706_47180170_47202910_0_47204016_FF	11_47175706_47180170_47202910_4_7204016_FF	0.192002056	-1.20580783	1	-1	-1	R
PRDM1	PRDM1_Site6_Site1_RR	0.194604588	-1.18920712	1	-1	-1	R
TNFRSF14	TNFRSF14_Site4_Site1_RR	0.082014717	1.526259209	0	1	1	NR
SH2B3	SH2B3_Site3_Site2_FF	0.083312472	1.228303149	-1	1	1	NR
MyD88	MyD88_Site2_Site4_FR	0.086246871	1.211392737	0	1	1	NR
MafB	MafB_Site2_Site4_FF	0.090511832	1.170128253	-1	1	1	NR
PRKCZ	PRKCZ_Site6_Site3_RF	0.093763087	1.316462719	0	1	1	NR
IFNAR1	IFNAR1_Site2_Site4_RR	0.093849223	1.228303149	-1	1	1	NR
NFAT	NFAT_Site2_Site10_FR	0.093849223	1.208597056	-1	1	1	NR

Gene	Probes*	adj. p value	EpiSwitch™ ratio	HC_NR_MTX	HC_R_MTX	NR_R_MTX	Association
NFAT	NFAT_Site5_Site10_RR	0.094393734	1.25411241	-1	1	1	NR
MAL	MAL_Site2_Site6_RF	0.095094028	1.274560627	0	1	1	NR
FCGR2A	FCGR2A_Site3_Site6_RR	0.096581892	1.170128253	-1	1	1	NR
IL-32	IL-32_Site5_Site4_RF	0.097224197	1.205807828	0	1	1	NR
MTHFD1	MTHFD1_Site1_Site7_RF	0.114751424	1.175547906	-1	1	1	NR
TLR2	TLR2_Site1_Site5_RR	0.120590183	1.217003514	-1	1	1	NR
NFAT	NFAT_Site6_Site10_RR	0.129631525	1.211392737	-1	1	1	NR
ICAM1	ICAM1_Site4_Site9_FR	0.131386096	1.180992661	-1	1	1	NR
NFAT	NFAT_Site5_Site10_FR	0.133034069	1.170128253	-1	1	1	NR
MTHFD1	MTHFD1_Site5_Site7_RF	0.144559523	1.156688184	-1	1	1	NR
MTHFR	MTHFR_Site6_Site4_RR	0.150085134	1.170128253	-1	1	1	NR
ICAM1	ICAM1_Site4_Site1_FF	0.151103565	1.140763716	-1	1	1	NR
MTHFD1	MTHFD1_Site1_Site7_RF	0.114751424	1.175547906	-1	1	1	NR
NFAT	NFAT_Site11_Site10_RR	0.158903523	1.197478705	-1	1	1	NR
NFAT	NFAT_Site10_Site9_RF	0.160614052	1.197478705	-1	1	1	NR
MafB	MafB_Site5_Site2_RF	0.167291268	1.164733586	-1	1	1	NR
NFAT	NFAT_Site7_Site10_RR	0.169766598	1.189207115	-1	1	1	NR
FCGR2A	FCGR2A_Site3_Site7_RR	0.180386617	1.125058485	-1	1	1	NR
MafB	MafB_Site6_Site2_RF	0.186948332	1.107008782	-1	1	1	NR
ADORA2A	ADORA2A_Site1_Site7_FR	0.191209559	1.138131035	-1	1	1	NR
MMP9	MMP9_Site2_Site3_FR	0.192328613	1.132883885	-1	1	1	NR
COL2A1	COL2A1_Site7_Site2_FF	0.193661549	1.112136086	-1	1	1	NR
TNFRSF1B	TNFRSF1B_Site1_Site7_FR	0.19556991	1.154018752	-1	1	1	NR
FCGR2A	FCGR2A_Site3_Site2_RR	0.197822331	1.117287138	-1	1	1	NR
IL-21R	IL-21R_Site5_Site2_RR	0.199109911	1.125058485	0	1	1	NR

Example 1 - Table 4. Patient characteristics – Validation Cohort

	Baseline			6 months			
	Non-Responder	responder	*P* value	Non-Responder	responder	*P* value	Healthy control
Age – years	58±14.5	54±13.2	0.26	-	-	-	45±15.4
Males – no. (%)	10 (33)	13 (43)	0.6	-	-	-	11 (37)
Caucasian – no. (%)	30 (100)	28 (97) [$]	-	-	-	-	-
Body mass index – kg/m^2	28.3± 5.4	27.4± 4.6[$$]	0.48	-	-	-	-
Patient global assessment (VAS, 0-100 mm)	48±30.2	62±23.0	0.05	64±23.2	11±12.9	<0.0001	-
[€]Physician global assessment (VAS, 0-100 mm)	46±22.7	54±21.0	0.19	39±6.4	6.4±6.1	<0.0001	-
Number of swollen joints (0-28)	5.8±3.7	8.3±4.3	0.006	6.0±5.2	0.2±0.48	<0.0001	-
Number of tender joints (0-28)	8.4±6.2	7.9±5.2	0.97	11.6±7.7	0.4±0.72	<0.0001	-
[€]CDAI	23.6±10.9	27.8±9.8	0.13	27.9±12.6	2.3±2.2	<0.0001	-
[#]DAS28-CRP	4.8±1.0	5.1±0.9	0.27	5.0±0.8	1.8±0.44	<0.0001	-
[§]DAS28-ESR	5.2±0.8	5.2±1.0	0.98	5.3±0.8	1.8±0.45	<0.0001	-
[¢]RF (IU/ml)	196±244	138±155	0.48	-	-	-	-
[∞]CCP (U/ml)	244±201	314±798	0.25	-	-	-	-
[#]C-reactive protein (mg/liter)	25.8±33.7	23.4±30.0	0.40	12.7±12.2	5.5±5.6	0.005	-

	Baseline			6 months			
	Non-Responder	responder	*P* value	Non-Responder	responder	*P* value	Healthy control
[$]Erythrocyte sedimentation rate (mm/hour)	35±19.8	22.6±16.2	0.02	23±18.6	8.5±5.6	0.0004	-
[¶]Whole Blood cell count	8.4±2.2	7.5±1.7	0.09	7.6±2.4	6.5±1.7	0.07	-
[¶]Lymphocytes	1.9±0.59	1.7±0.78	0.09	1.8±0.76	1.7±0.95	0.31	-
[¶]Monocytes	0.63±0.16	0.59±0.22	0.50	0.59±0.45	0.52±0.13	0.38	-
[¶]Eosinophil	0.18±0.14	0.19±0.13	0.55	0.19±0.15	0.17±0.12	0.89	-
[¶]Platelets	332±107	307±86	0.34	299±103	270±79	0.25	-
Current smoker – no. (%)	10 (33)	4 (14)	-	-	-	-	-
Previous smoker – no. (%)	10 (33)	9 (31)	-	-	-	-	-
Non-smoker – no. (%)	10 (33)	16 (55)	-	-	-	-	-

The Fisher exact unconditional test is used to assess differences in proportions between the two groups. To examine differences in continuous variables between the two groups, we used the independent samples t-test or the Mann-Whitney U-test (depending on distribution of data).

[$] One patient "other" (non-white, non-South East Asian, non-Indian Sub-Continent, Non-Afro-Caribbean), one patient did not give an answer.

[$$] n= 25 in responders for BMI

[€] Baseline - n = 29 non-R, n= 30 R; 6m - n = 30 non-R, n= 29

[#] Baseline - n = 26 non-R, n= 29 R; 6m - n = 21 non-R, n= 29

[§] Baseline - n = 19 non-R, n= 23 R; 6m - n = 19 non-R, n= 22

[ç] Baseline - n = 13 non-R, n= 23 R

[^^] Baseline - n = 26 non-R, n= 29 R

[¶] Baseline - n = 29 non-R, n= 27 R; 6m - n = 28 non-R, n= 25

Example 1 - Table 5. 12 Selected genes from EpiSwitch™ PCR

Gene	EpiSwitch Marker	adjusted.p.value	EpiSwitch™ ratio	HC_NR_MTX	HC_R_MTX	NR_R_MTX	Association
C5orf30	C5orf30_Site5_Site2_FF	0.079228864	-1.242575344	1	-1	-1	R
IFNAR1	IFNAR1_Site2_Site4_RR	0.093849223	1.228303149	-1	1	1	NR
IL-17A	IL-17A_Site3_Site1_RR	0.115042065	-1.164733586	0	-1	-1	R
CXCL13	CXCL13_Site1_Site3_RR	0.079228864	-1.298338588	0	-1	-1	R
IL-21R	IL-21R_Site5_Site2_RR	0.199109911	1.125058485	0	1	1	NR
IL-23	IL-23_Site4_Site5_FR	0.160960834	-1.180992661	0	-1	-1	R
MafB	MafB_Site6_Site2_RF	0.186948332	1.107008782	-1	1	1	NR
FCGR2A	FCGR2A_Site3_Site2_RR	0.197822331	1.117287138	-1	1	1	NR
CLEC12A	CLEC12A_Site6_Site1_FR	0.112869007	-1.222640278	0	-1	-1	R
PRKCZ	PRKCZ_Site6_Site3_RF	0.093763087	1.316462719	0	1	1	NR
MafB	MafB_Site2_Site4_FF	0.090511832	1.170128253	-1	1	1	NR
C5orf30	C5orf30_Site4_Site2_FF	0.084204721	-1.200248667	1	-1	-1	R

Example 1 - Table 6. Observed and predicted number of R and NR to MTX monotherapy at 6 months using the EpiSwitch™ CCS model.

	Predicted response		
Observed response	Non-responder	Undefined	Responder
Non-responder	25	3	2
Responder	2	4	24

Notes to Table 6: Cut off levels were chosen based on the probability of response to MTX of (approximately) >0.70 for NR and <0.3 for R. NR and R were defined as described in the methods.

Example 1A – RA analysis: MTX responders vs non-responders: Work subsequent to Example 1

Following on after Example 1, in Example 1A, a biostatistical hypergeometric analysis was carried out, using the "Statistical Pipeline" method(s) at the beginning of the Examples section in the present specification, to generate further refined DNA probes stratifying between MTX responders vs MTX non-responders, for RA patients on MTX monotherapy.

Example 1A Results: Table 6b (and continuation part Table 6c) hereinafter discloses Probe and Loci data for RA-MTX – DNA probes stratifying between responders (R) and non-responders (NR). B = B-statistic (lods or B), which is the log-odds that that gene is differentially expressed. FC is the non-log Fold Change. FC_1 is the non-log Fold Change centred around zero. It is seen that Table 6b+6c includes the sequences of 25 refined preferable DNA probes (60mers) for identifying MTX responders (MTX-R), and of 24 refined preferable DNA probes (60mers) for identifying MTX responders (MTX-NR), from the hypergeometric analysis.

Example 1A - Table 6b. Probe and Loci data for RA-MTX - probes stratifying between responders and non-responders.

FC	FC_1	LS	Loop detected	**60 mer**
0.5774097	-1.7318725	-1	MTX-R	TGTTTTTTGGCTGCATAAATGTCTTCTTTCGAAATAATCATCAAAATATTTTTCATTGAC
0.6052669	-1.6521636	-1	MTX-R	CACCCCCATCTCCCTTTGCTGACTCTCTTCGATGAATCCATTTTTTTGGAAATAGATGAT
0.6567507	-1.5226477	-1	MTX-R	CACCCCCATCTCCCTTTGCTGACTCTCTTCGAACTGTGGCAATTTTAACTTTTCAAATTG
0.6624775	-1.5094851	-1	MTX-R	CACCCCCATCTCCCTTTGCTGACTCTCTTCGAGGCATGATTTGAGTCTTGACAGAAGTTC
0.6628804	-1.5085678	-1	MTX-R	TGCCAGTATTTTATTGAGGATTTTTGCATCGAGATTGGGTTGCATCATGTTGGCCAGGCT
0.6850588	-1.4597286	-1	MTX-R	TGTTTTTTGGCTGCATAAATGTCTTCTTTCGAACTCATGGGCACAAGCAATCCTCCCACC
0.6868153	-1.4559955	-1	MTX-R	TGCCAGTATTTTATTGAGGATTTTTGCATCGAACAGATGGAGGGAAGAGGGGATAGCTCC
0.6890053	-1.4513676	-1	MTX-R	TGCCCTAGAGATCTGTGGAACTTTGAACTCGAGTCAAAGAGATATCAAGAGCTTCTATCA
0.6943398	-1.4402171	-1	MTX-R	CACCCCCATCTCCCTTTGCTGACTCTCTTCGAGGGCAGAATGAGCCTCAGACATCTCCAG
0.6963019	-1.4361587	-1	MTX-R	TCTCCTGCCTGATTGCCCTGCCAGAACTTCGATTTGGGCTATAGTGTTGTTCCAGTCTAA
0.7008036	-1.4269334	-1	MTX-R	CACCCCCATCTCCCTTTGCTGACTCTCTTCGATCTTGAAGAGATCTCTTCTTAGCAAAGC
0.7132593	-1.4020146	-1	MTX-R	CACCCCCATCTCCCTTTGCTGACTCTCTTCGAAATATTTTTGCTTGAGCTCCTGTCTCAT
0.7141705	-1.4002258	-1	MTX-R	TAGGCGCACATGCACACAGCTCGCCTCTTCGACCCAGGAAGATCCAAAGGAGGAACTGAG

FC	FC_1	LS	Loop detected	60 mer
0.7156204	-1.397389	-1	MTX-R	CCCCCACCCCCATCCCAGGAAATTGGTTTCGATGAGAGAAGGCAAGAGAACATGGGGTCT
0.7183721	-1.3920362	-1	MTX-R	TGCCAGTATTTTATTGAGGATTTTTGCATCGAGTTCAAAGTTCCACAGATCTCTAGGGCA
0.7189408	-1.390935	-1	MTX-R	CTAAAAATTACATCCAGGAAATGAGATATCGAAAGAAGACATTTATGCAGCCAAAAAACA
0.722487	-1.384108	-1	MTX-R	TAGGCGCACATGCACACAGCTCGCCTCTTCGATGTACAAGCTGCCTATTGATAGACTTTC
0.7254458	-1.3784627	-1	MTX-R	AAAGTTGTGCAATCAGGCAAGTCAAGATTCGAAAGAAGACATTTATGCAGCCAAAAAACA
0.7374119	-1.3560941	-1	MTX-R	CACCCCCATCTCCCTTTGCTGACTCTCTTCGAGTGGTGAGCAGCCAAACCAGGGTTCACT
0.7374768	-1.3559748	-1	MTX-R	GGGTCTTGCTATGTTGCCCAGGCTGGCCTCGAGATCAGCCTGGGCAACACGGTGAAAACC
0.738555	-1.3539954	-1	MTX-R	CTGGTTTAGTCTTGGGAGAGTGTATGTGTCGAGTTAAGCCATCTGCAAATAGCAAGAGAG
0.7415639	-1.3485014	-1	MTX-R	AGCCTTGCATCCCAGGGATGAAGCCCACTCGAGATATAGATTGAGCCCCAGTTTTTGGAG
0.7422652	-1.3472274	-1	MTX-R	ATCGTGTGGGCTGTGTGTGGCAGACTGTTCGAAATCGGAAGCCTCTCTGAAGGTCCAAGG
0.7430431	-1.3458169	-1	MTX-R	TGCCAGTATTTTATTGAGGATTTTTGCATCGAATTCCTGGGTTTATATCCCAATCATTGT
0.7432273	-1.3454835	-1	MTX-R	CACCCCCATCTCCCTTTGCTGACTCTCTTCGATATTGGTGTATATTCAAAGGGTACTTGA
1.6553355	1.65533547	1	MTX-NR	TGATCACTGTTTCCTATGAGGATACAGCTCGAGGGGCAGGGGCGGTCCTGGGCCAGGCG
1.4321012	1.43210121	1	MTX-NR	AACTTATGATTCTAATCTTGAATGTCTGTCGATCTATGAGGAAATGCCCCCAGCCTCCCA
1.4179763	1.41797626	1	MTX-NR	CATAATGCATGTGCATGAAAACTAATCTTCGATCTATGAGGAAATGCCCCCAGCCTCCCA
1.4150017	1.41500165	1	MTX-NR	ATCAGTAAGCTGGTCAGCTACCCATGAATCGATCTATGAGGAAATGCCCCCCAGCCTCCCA
1.3755396	1.37553964	1	MTX-NR	GTGTCCCAATTTCTAGTGCACTGTGAACTCGACCTCGCGGGAGGGGGTGCCAGGCCGCATC
1.366009	1.36600904	1	MTX-NR	CCGGGGCTTCTCGTTTAAGAATTCTTTGTCGATCTATGAGGAAATGCCCCCCAGCCTCCCA
1.3611955	1.36119553	1	MTX-NR	GTCTTTGAAGAAGGACTAAATGCTTAGTATCGAGTGCAGCGCCGGTGGGCCAGCACTGCTG
1.3408009	1.34080092	1	MTX-NR	GTTCATTTAAACATTTTATTATGTATATTCGAGGGGCCAGGCTTTTATACCCCCATCTGA
1.3350815	1.33508153	1	MTX-NR	TTCTCCACAGCCGGCCGGTCCTTGGCAGTCGAGGGGCAGGGGCGGTCCTGGGCCAGGCG
1.3191431	1.31914307	1	MTX-NR	GCAACACATACAACGACTAATCTTCTTTTCGACGCCGAGGAGCTCTGCAGTGGGGGGCGTA
1.3183444	1.31834441	1	MTX-NR	GTAGGTGCTGAGTAAGTGAGCACTTGCCTCGAGGGGCAGGGGGCGGTCCTGGGCCAGGCG
1.3164851	1.31648512	1	MTX-NR	CAGAAAGACCTTGCAATCATACGGTGCTTCGACGCCGAGGAGCTCTGCAGTGGGGGGCGTA
1.3056925	1.3056925	1	MTX-NR	TACTGTGCTGTGCTCGTCAAAGAGTATGTCGATCTATGAGGAAATGCCCCCAGCCTCCCA
1.2876529	1.2876529	1	MTX-NR	CAGAAATTAATCAAATGCAAGTGCACCCTCGACCACCCAAGGGCTGAGGAGTGCGGGCAC

FC	FC_1	LS	Loop detected	60 mer
1.2777853	1.27778527	1	MTX-NR	AAGGGACCTAGTCCCCTATTAAGATTTCTCGAGGGGCCAGGCTTTTATACCCCCATCTGA
1.2773474	1.2773474	1	MTX-NR	CCTGCCGAGACACGGGACGTGGGATTGCTCGATCTATGAGGAAATGCCCCCCAGCCTCCCA
1.2754233	1.2754233	1	MTX-NR	CCAAAGCTCGCTTTCTTAACCACTATGCTCGAGGGGCCAGGCTTTTATACCCCCATCTGA
1.2747737	1.27477371	1	MTX-NR	TGAATTGTGTAGCGTAAGAATTTATATCTCGAAGTTTGTGAACTGGCAGGTGGACGGGGA
1.2710171	1.2710171	1	MTX-NR	ACCTGATCTGGGGAAGATTAGGAATTGTTCGAAACCAATTTCCTGGGATGGGGGTGGGGG
1.2689263	1.26892631	1	MTX-NR	GCAAGAGGATCTCTTGAGGCCCAGGAGTTCGAGGGGCCAGGCTTTTATACCCCCATCTGA
1.2665372	1.2665372	1	MTX-NR	TATCAAGTGATCCAAAAGGCTGCCAGTGTCGAGGGGCAGGGGGCGGTCCTGGGCCAGGCG
1.2648953	1.26489531	1	MTX-NR	AAGGGACCTAGTCCCCTATTAAGATTTCTCGAAACCAATTTCCTGGGATGGGGGTGGGGG
1.2592485	1.25924848	1	MTX-NR	TATGGACTTTGTAGTCTCATATCAAAGCTCGAAACCAATTTCCTGGGATGGGGGTGGGGG
1.2559537	1.25595366	1	MTX-NR	AAAAATAATCTGGCTCTACACTTAGGATTCGAAACCAATTTCCTGGGATGGGGGTGGGGG

Example 1A - Table 6c. Probe And Loci data for RA-MTX

		Probe Location					4 kb Sequence Location				
FC	FC_1	Chr	Start1	End1	Start2	End2	Chr	Start1	End1	Start2	End2
0.5774097	-1.7318725	12	69702274	69702303	69759619	69759648	12	69702274	69706273	69759619	69763618
0.6052669	-1.6521636	7	22743265	22743294	22801876	22801905	7	22739295	22743294	22797906	22801905
0.6567507	-1.5226477	7	22743265	22743294	22769055	22769084	7	22739295	22743294	22769055	22773054
0.6624775	-1.5094851	7	22743265	22743294	22757576	22757605	7	22739295	22743294	22757576	22761575
0.6628804	-1.5085678	1	67644699	67644728	67729398	67729427	1	67640729	67644728	67725428	67729427
0.6850588	-1.4597286	12	69702274	69702303	69805129	69805158	12	69702274	69706273	69805129	69809128
0.6868153	-1.4559955	1	67644699	67644728	67672222	67672251	1	67640729	67644728	67672222	67676221
0.6890053	-1.4513676	1	67673763	67673792	67752422	67752451	1	67669793	67673792	67748452	67752451
0.6943398	-1.4402171	7	22743265	22743294	22766800	22766829	7	22739295	22743294	22762830	22766829
0.6963019	-1.4361587	4	123383001	123383030	123399247	123399276	4	123379031	123383030	123399247	123403246
0.7008036	-1.4269334	7	22743265	22743294	22765456	22765485	7	22739295	22743294	22765456	22769455
0.7132593	-1.4020146	7	22718635	22718664	22743265	22743294	7	22718635	22722634	22739295	22743294
0.7141705	-1.4002258	12	48397660	48397689	48423816	48423845	12	48397660	48401659	48423816	48427815

Example 1A - Table 6c. Probe And Loci data for RA-MTX (continued)

		Probe location					4 kb Sequence location				
FC	FC_1	Chr	Start1	End1	Start2	End2	Chr	Start1	End1	Start2	End2
0.7156204	-1.397389	17	32738857	32738886	32777305	32777334	17	32738857	32742856	32777305	32781304
0.7183721	-1.3920362	1	67644699	67644728	67673763	67673792	1	67640729	67644728	67669793	67673792
0.7189408	-1.390935	12	69702274	69702303	69766052	69766081	12	69702274	69706273	69762082	69766081
0.722487	-1.384108	12	48397660	48397689	48412400	48412429	12	48397660	48401659	48412400	48416399
0.7254458	-1.3784627	12	69702274	69702303	69806507	69806536	12	69702274	69706273	69802537	69806536
0.7374119	-1.3560941	7	22743265	22743294	22773903	22773932	7	22739295	22743294	22769933	22773932
0.7374768	-1.3559748	19	55449063	55449092	55486679	55486708	19	55449063	55453062	55482709	55486708
0.738555	-1.3539954	17	32622187	32622216	32745745	32745774	17	32618217	32622216	32745745	32749744
0.7415639	-1.3485014	13	43129388	43129417	43181041	43181070	13	43125418	43129417	43181041	43185040
		10	104130466	104130495	104156468	104156497	10	104126496	104130495	104152498	104156497
0.7430431	-1.3458169	1	67614064	67614093	67644699	67644728	1	67614064	67618063	67640729	67644728
0.7432273	-1.3454835	7	22743265	22743294	22798802	22798831	7	22739295	22743294	22798802	22802801
1.6553355	1.6553354	1	2460436	2460465	2486982	2487011	1	2456466	2460465	2486982	2490981
1.4321012	1.4321012	10	6391740	6391769	6577853	6577882	10	6391740	6395739	6577853	6581852
1.4179763	1.4179762	10	6520005	6520034	6577853	6577882	10	6516035	6520034	6577853	6581852

Example 1A - Table 6c. Probe And Loci data for RA-MTX (continued)

		Probe location					4 kb Sequence location				
FC	FC_1	Chr	Start1	End1	Start2	End2	Chr	Start1	End1	Start2	End2
1.415001	1.4150016										
7	5	10	6427823	6427852	6577853	6577882	10	6427823	6431822	6577853	6581852
1.375539	1.3755396										
6	4	18	74845065	74845094	74866978	74867007	18	74845065	74849064	74863008	74867007
	1.3660090										
1.366009	4	10	6470268	6470297	6577853	6577882	10	6466298	6470297	6577853	6581852
1.361195	1.3611955										
5	3	20	44704386	44704415	44720665	44720694	20	44700416	44704415	44716695	44720694
1.340800	1.3408009										
9	2	17	32551069	32551098	32617664	32617693	17	32551069	32555068	32617664	32621663
1.335081	1.3350815										
5	3	1	2486982	2487011	2540813	2540842	1	2486982	2490981	2536843	2540842
1.319143	1.3191430										
1	7	12	66647072	66647101	66696510	66696539	12	66647072	66651071	66696510	66700509
1.318344	1.3183444										
4	1	1	2476023	2476052	2486982	2487011	1	2472053	2476052	2486982	2490981
1.316485	1.3164851										
1	2	12	66663907	66663936	66696510	66696539	12	66663907	66667906	66696510	66700509
1.305692											
5	1.3056925	10	6556987	6557016	6577853	6577882	10	6556987	6560986	6577853	6581852
1.287652											
9	1.2876529	12	6268999	6269028	6304632	6304661	12	6268999	6272998	6300662	6304661
1.277785	1.2777852										
3	7	17	32617664	32617693	32708031	32708060	17	32617664	32621663	32704061	32708060
1.277347											
4	1.2773474	10	6442502	6442531	6577853	6577882	10	6442502	6446501	6577853	6581852

Example 1A - Table 6c. Probe And Loci data for RA-MTX (continued)

		Probe location					4 kb Sequence location				
FC	FC_1	Chr	Start1	End1	Start2	End2	Chr	Start1	End1	Start2	End2
1.275423 3	1.2754233	17	32529051	32529080	32617664	32617693	17	32525081	32529080	32617664	32621663
1.274773 7	1.2747737 1	19	45364170	45364199	45397229	45397258	19	45360200	45364199	45397229	45401228
1.271017 1	1.2710171	17	32689356	32689385	32738857	32738886	17	32685386	32689385	32738857	32742856
1.266537 2	1.2665372	1	2486982	2487011	2556784	2556813	1	2486982	2490981	2552814	2556813
1.264895 3	1.2648953 1	17	32708031	32708060	32738857	32738886	17	32704061	32708060	32738857	32742856
1.259338 2	1.2593381 8	1	11042009 7	11042012 6	11047238 6	11047241 5	1	11041612 7	11042012 6	11047238 6	11047638 5
1.259248 5	1.2592484 8	17	32553720	32553749	32738857	32738886	17	32549750	32553749	32738857	32742856
1.255953 7	1.2559536 6	17	32522613	32522642	32738857	32738886	17	32522613	32526612	32738857	32742856

Example 1A - Table 6cc. Continuation of Tables 6b and 6c (RA-MTX)

probe	Gene Locus	Probe_Count_Total	Probe_Count_Sig	HyperG_Stats	FDR_HyperG	Per-cent_Sig	logFC	Ave Expr	t	P. Value	Adj. P. Value	B	FC	FC_1	LS	Loop detected
12_69702273_69705360_69759618_69766081_RR	12_69702273_69705360_69759618_69766081	4	2	0.034576041	0.518640615	50	-0.792332744	-0.792332744	-6.352796842	0.001540038	0.236236361	-0.525734091	0.577409703	-1.731872526	-1	MTX-R
IL-6_Site4_Site5_FF	IL-6	48	13	7.18E-05	0.014530844	27.08	-0.724356533	-0.724356533	-4.707112783	0.005590201	0.249035946	-1.652257403	0.605266944	-1.652163579	-1	MTX-R
IL-6_Site4_Site2_FR	IL-6	48	13	7.18E-05	0.014530844	27.08	-0.606582168	-0.606582168	-6.460394591	0.001429141	0.236236361	-0.464821575	0.656750743	-1.522647688	-1	MTX-R
IL-6_Site4_Site3_FR	IL-6	48	13	7.18E-05	0.014530844	27.08	-0.594056548	-0.594056548	-8.583674236	0.000391843	0.236236361	-0.497776542	0.662477542	-1.509485133	-1	MTX-R
IL-23R_Site4_Site2_FF	IL-23R	104	19	0.000550011	0.054890393	18.27	-0.593179555	-0.593179555	-4.111539379	0.009661387	0.255484712	-2.165608129	0.662880374	-1.508567818	-1	MTX-R
12_69702273_69705360_69805128_69806536_RR	12_69702273_69705360_69805128_69806536	4	2	0.034576041	0.518640615	50	-0.545700188	-0.545700188	-11.32682228	0.000106595	0.236236361	-1.272674673	0.685055884	-1.459728628	-1	MTX-R
IL-23R_Site4_Site3_FR	IL-23R	104	19	0.000550011	0.054890393	18.27	-0.542005944	-0.542005944	-5.428609826	0.003062642	0.238248996	-1.109864705	0.686815287	-1.455995548	-1	MTX-R
IL-23R_Site3_Site7_FF	IL-23R	104	19	0.000550011	0.054890393	18.27	-0.537412982	-0.537412982	-5.114255946	0.003905047	0.245648426	-1.336115162	0.689005315	-1.451367613	-1	MTX-R

IL-6_Site4_Site1_FF	IL-6	48	13	7.18E-05	0.0145308	27.08	-0.526286321	-0.526286321	-9.186377243	0.0002857662	0.2362361	0.7041720	0.6943397	-1.440217119	-1	MTX-R
IL-2_Site2_Site4_FR	IL-2	44	7	0.0591442	0.7726915	15.91	-0.522215223	-0.522215223	-5.718310426	0.0024461	0.2362361	0.9143854	0.6963018	-1.436158743	-1	MTX-R
IL-6_Site4_Site1_FR	IL-6	48	13	7.18E-05	0.0145308	27.08	-0.512918	-0.512918	-7.365051101	0.0007919	0.2362361	0.0032634	0.7008035	-1.426933	-1	MTX-R
IL-6_Site6_Site4_RF	IL-6	48	13	7.18E-05	0.0145308	27.08	-0.487501401	-0.487501401	-10.39123759	0.0001602650	0.2362361	1.0516479	0.7132593	-1.402014627	-1	MTX-R
COL2A1_Site2_Site5_RR	COL2A1	100	15	0.0132660	0.4884323	15	-0.485659509	-0.485659509	-5.378633994	0.0031869	0.2382489	1.1448880	0.7141705	-1.400225814	-1	MTX-R
CCL2_Site6_Site14_RR	CCL2	404	58	9.15E-06	0.0037050	14.36	-0.482733674	-0.482733674	-8.467642183	0.0004173	0.2362361	0.4551617	0.7156203	-1.397388986	-1	MTX-R
IL-23R_Site4_Site3_FF	IL-23R	104	19	0.0005500	0.0548903	18.27	-0.477196734	-0.477196734	-4.678820538	0.0057311	0.2490359	1.6752449	0.7183721	-1.392036205	-1	MTX-R
12_69702273_69705360_69759618_69766081_RF	12_69702273_69705360_69759618_69766081	4	2	0.0345760	0.5186406	50	-0.476055026	-0.476055026	-6.933158571	0.0010412	0.2362361	0.2128359	0.7189408	-1.390935016	-1	MTX-R
COL2A1_Site2_Site4_RR	COL2A1	100	15	0.0132660	0.4884323	15	-0.468956553	-0.468956553	-4.969850387	0.0044576	0.2473367	1.4451611	0.7224869	-1.384108032	-1	MTX-R
12_69702273_69705360_69805128_69806536_RF	12_69702273_69705360_69805128_69806536	4	2	0.0345760	0.5186406	50	-0.463060243	-0.463060243	-8.264131154	0.0004670277	0.2362361	0.3780309	0.7254811	-1.378462712	-1	MTX-R
IL-6_Site4_Site2_FF	IL-6	48	13	7.18E-05	0.0145308	27.08	-0.439457343	-0.439457343	-9.296613034	0.0002270277	0.2362361	0.7393759	0.7374119	-1.356094149	-1	MTX-R

19_55449062_55451429_55484960_554 86708_RF	19_55449062_55451429_55484960_554 86708	4	2	0.0345 76041	0.5186 40615	50	0.4393 30382	- 0.4393 30382	- 3.3433 80062	0.0211 28841	0.2949 434	- 2.9239 26031	0.7374 76825	- 1.3559 74814	1	MTX -R
CCL2_Site10_Site13_FR	CCL2	404	58	9.15E-06	0.0037 05017	14. 36	0.4372 22819	- 0.4372 22819	- 6.9610 47822	0.0010 22576	0.2362 361	- 0.1987 30934	0.7385 54956	- 1.3539 95383	1	MTX -R
TNFSF11_Site4_Site2_FR	TNFSF11	52	12	0.0006 77659	0.0548 90393	23. 08	0.4313 57024	- 0.4313 57024	- 3.6909 11039	0.0146 6314	0.2777 2544	- 2.5671 90834	0.7415 63929	- 1.3485 01404	1	MTX -R
NFKB2_Site5_Site2_FF	NFKB2	54	9	0.0266 86973	0.5186 40615	16. 67	0.4299 9336	- 0.4299 9336	- 7.2809 58467	0.0008 34343	0.2362 361	- 0.0426 2056	0.7422 65202	- 1.3472 27376	1	MTX -R
IL-23R_Site5_Site4_RF	IL-23R	104	19	0.0005 50011	0.0548 90393	18. 27	0.4284 82185	- 0.4284 82185	- 5.6230 09709	0.0026 31353	0.2362 361	- 0.9773 92524	0.7430 43107	- 1.3458 16939	1	MTX -R
IL-6_Site4_Site5_FR	IL-6	48	13	7.18E-05	0.0145 30844	27. 08	0.4281 24668	- 0.4281 24668	- 7.9572 32876	0.0005 55975	0.2362 361	- 0.2555 68458	0.7432 27265	- 1.3454 83471	1	MTX -R
TNFRSF14_Site4_Site1_FR	TNFRSF14	112	14	0.0638 86514	0.7840 61767	12. 5	0.7271 23624	0.7271 23624	3.4991 9083	0.0178 94673	0.2866 24284	- 2.7611 97677	1.6553 35471	1.6553 35471	1	MTX -NR
PRKCQ_Site11_Site4_RR	PRKCQ	213	31	0.0008 52984	0.0575 76386	14. 55	0.5181 33451	0.5181 33451	3.4418 02618	0.0190 15331	0.2891 91715	- 2.8206 09109	1.4321 01206	1.4321 01206	1	MTX -NR
PRKCQ_Site7_Site4_FR	PRKCQ	213	31	0.0008 52984	0.0575 76386	14. 55	0.5038 33375	0.5038 33375	3.5630 03996	0.0167 36154	0.2829 50401	- 2.6958 57596	1.4179 76256	1.4179 76256	1	MTX -NR
PRKCQ_Site9_Site4_RR	PRKCQ	213	31	0.0008 52984	0.0575 76386	14. 55	0.5008 0374	0.5008 0374	3.9015 43743	0.0118 59009	0.2663 7802	- 2.3620 04516	1.4150 01654	1.4150 01654	1	MTX -NR
18_74845064_74846657_74864995_748 67007_RF	18_74845064_74846657_74864995_748 67007	4	2	0.0345 76041	0.5186 40615	50	0.4599 97712	0.4599 97712	3.6256 2346	0.0156 82006	0.2829 50401	- 2.6324 82122	1.3755 39636	1.3755 39636	1	MTX -NR

PRKCQ_Site2_Site4_FR	PRKCQ	213	31	0.0008 52984	0.0575 76386	14.55	0.4499 6703	0.4499 6703	3.4940 64593	0.0179 91649	0.2866 24284	-2.7664 7964	1.3660 09039	1.3660 09039	1	MTX -NR
CD40_Site10_Site9_FF	CD40	142	17	0.0622 22744	0.7840 61767	11.97	0.4448 74319	0.4448 74319	3.5963 60937	0.0161 64851	0.2829 50401	-2.6620 06295	1.3611 9553	1.3611 9553	1	MTX -NR
CCL2_Site11_Site10_RR	CCL2	404	58	9.15E-06	0.0037 05017	14.36	0.4230 95044	0.4230 95044	4.0374 30853	0.0103 78328	0.2564 91595	-2.2340 32001	1.3408 0092	1.3408 0092	1	MTX -NR
TNFRSF14_Site1_Site8_RF	TNFRSF14	112	14	0.0638 86514	0.7840 61767	12.5	0.4169 2785	0.4169 2785	3.3953 81579	0.0199 80609	0.2894 83909	-2.8691 15138	1.3350 81534	1.3350 81534	1	MTX -NR
IRAK3_Site2_Site5_RR	IRAK3	75	11	0.0360 66824	0.5216 80846	14.67	0.3996 01038	0.3996 01038	4.7783 21582	0.0052 52968	0.2490 35946	-1.5949 97683	1.3191 43065	1.3191 43065	1	MTX -NR
TNFRSF14_Site6_Site1_FR	TNFRSF14	112	14	0.0638 86514	0.7840 61767	12.5	0.3987 27315	0.3987 27315	3.5466 17882	0.0170 25241	0.2839 12444	-2.7125 63011	1.3183 44409	1.3183 44409	1	MTX -NR
IRAK3_Site4_Site5_RR	IRAK3	75	11	0.0360 66824	0.5216 80846	14.67	0.3966 91209	0.3966 91209	6.1294 28964	0.0018 04535	0.2362 361	-0.6566 68121	1.3164 85115	1.3164 85115	1	MTX -NR
PRKCQ_Site3_Site4_RR	PRKCQ	213	31	0.0008 52984	0.0575 76386	14.55	0.3848 15172	0.3848 15172	4.1304 30098	0.0094 87914	0.2554 84712	-2.1484 19919	1.3056 925	1.3056 925	1	MTX -NR
12_6268998_6272753_6301795_6304661_RF	12_6268998_6272753_6301795_6304661	2	2	0.0064 28387	0.2892 77402	10 0	0.3647 43757	0.3647 43757	3.5905 166	0.0162 63314	0.2829 50401	-2.6679 22157	1.2876 52904	1.2876 52904	1	MTX -NR
CCL2_Site10_Site5_RF	CCL2	404	58	9.15E-06	0.0037 05017	14.36	0.3536 45409	0.3536 45409	4.3788 84995	0.0075 11833	0.2554 84712	-1.9274 3217	1.2777 85266	1.2777 85266	1	MTX -NR
PRKCQ_Site8_Site4_RR	PRKCQ	213	31	0.0008 52984	0.0575 76386	14.55	0.3531 50952	0.3531 50952	4.9818 96454	0.0044 1255	0.2473 36967	-1.4359 37375	1.2773 47404	1.2773 47404	1	MTX -NR

CCL2_Site12_Site10_FR	CCL2	404	58	9.15E-06	0.0037 05017	14.36	0.3509 76141	0.3509 76141	4.5280 90618	0.0065 55946	0.2510 96737	- 1.8000 21979	1.2754 23299	1.2754 23299	1	MTX-NR
ApoE_Site3_Site6_FR	ApoE	96	17	0.0015 08547	0.0816 21699	17.71	0.3502 41172	0.3502 41172	5.5579 40873	0.0027 67294	0.2362 361	- 1.0211 47938	1.2747 7371	1.2747 7371	1	MTX-NR
CCL2_Site7_Site6_FR	CCL2	404	58	9.15E-06	0.0037 05017	14.36	0.3459 83436	0.3459 83436	3.5563 42165	0.0168 53001	0.2836 24894	- 2.7026 43166	1.2710 17097	1.2710 17097	1	MTX-NR
CCL2_Site2_Site10_FR	CCL2	404	58	9.15E-06	0.0037 05017	14.36	0.3436 08292	0.3436 08292	4.8095 44682	0.0051 12639	0.2490 35946	- 1.5701 58657	1.2689 26312	1.2689 26312	1	MTX-NR
TNFRSF14_Site1_Site9_RF	TNFRSF14	112	14	0.0638 86514	0.7840 61767	12.5	0.3408 89449	0.3408 89449	3.7341 22588	0.0140 30572	0.2766 82133	- 2.5244 17542	1.2665 37198	1.2665 37198	1	MTX-NR
CCL2_Site5_Site6_FR	CCL2	404	58	9.15E-06	0.0037 05017	14.36	0.3390 17988	0.3390 17988	4.1920 80779	0.0089 46373	0.2554 84712	- 2.0925 41211	1.2648 95314	1.2648 95314	1	MTX-NR
M-CSF_Site8_Site3_FR	M-CSF	96	13	0.0426 13318	0.5951 17032	13.54	0.3326 65749	0.3326 65749	4.6055 04441	0.0061 16205	0.2490 35946	- 1.7354 49183	1.2593 38177	1.2593 38177	1	MTX-NR
CCL2_Site11_Site6_FR	CCL2	404	58	9.15E-06	0.0037 05017	14.36	0.3325 62994	0.3325 62994	3.9356 74905	0.0114 65355	0.2629 59895	- 2.3295 38136	1.2592 48484	1.2592 48484	1	MTX-NR
CCL2_Site12_Site6_RR	CCL2	404	58	9.15E-06	0.0037 05017	14.36	0.3287 83229	0.3287 83229	3.8761 62824	0.0121 61863	0.2672 29746	- 2.3862 88494	1.2559 53655	1.2559 53655	1	MTX-NR

Example 1 - Table 6D - Stratifying between RA-MTX responders and non-responders

Table 6D			Probe sequence
Probes	NR_R_P.Value	NR_R_adj.P.Val	60 mer
TNFRSF14_Site4_Site1_FR	0.001232118	0.079419805	TGATCACTGTTTCCTATGAGGATACAGCTCGAGGGGCAGGGGGCGGTCCTGGGCCAGGCG
TNFRSF14_Site4_Site1_RR	0.002061691	0.082014717	AACCTGGAGAACGCCAAGCGCTTCGCCATCGAGGGGCAGGGGGCGGTCCTGGGCCAGGCG
TNFRSF1A_Site2_Site5_FR	0.004469941	0.093849223	CTACCTTTGTGGCACTTGGTACAGCAAATCGACGGGCCCCGTGAGGCGGGGGCGGGACCC
TNFRSF1A_Site1_Site5_FR	0.005468033	0.09532964	CATCAATTATAACTCACCTTACAGATCATCGACGGGCCCCGTGAGGCGGGGGCGGGACCC
TNFRSF14_Site4_Site8_FR	0.005244102	0.094393734	TGATCACTGTTTCCTATGAGGATACAGCTCGAAGATTAGGTAAAGGTGGGGACGCGGAGA
RUNX1_Site7_Site2_RR	0.001313112	0.079419805	GAAAGGTAATTGCCCCCAATATTTATTTTCGAAACAGATCGGGCGGCTCGGGTTACACAC
TNFRSF14_Site1_Site8_RF	0.003725772	0.090200643	TTCTCCACAGCCGGCCGGTCCTTGGCAGTCGAGGGGCAGGGGGCGGTCCTGGGCCAGGCG
18_74845064_74846657_74864995_74867007_RF	0.001604249	0.079419805	CGTGTCCCAATTTCTAGTGCACTGTGAACTCGACCTCGCGGGAGGGGTGCCAGGCCGCAT
PRKCZ_Site8_Site6_FR	1.26726E-05	0.079228864	CCTCTCTTCTAAAAGGTCTCAACATCACTCGACTGGAGAGCCCGGGGGCCTCGCGCCGCTT
RUNX1_Site5_Site2_RR	0.000540863	0.079228864	GTTTCCCCTTGATGCTCAGAGAAAGGCCTCGAAACAGATCGGCGCCTCGGGTTACACAC
PRKCQ_Site7_Site4_FR	0.003958472	0.090816122	CATAATGCATGTGCATGAAAACTAATCTTCGATCTATGAGGAAATGCCCCCAGCCTCCCA
18_74756101_74757557_74845064_74846657_RR	0.003489147	0.089578901	AGATGTGTAAGTCACCAGGGAGTGCATTCGCGACCTCGCGGGAGGGGGTGCCAGGCCGCAT
PRKCQ_Site10_Site4_FR	0.004639159	0.093849223	GTAATGGTGCCATCATAGCTCCAAGCTCCTCGATCTATGAGGAAATGCCCCCAGCCTCCCA
PRKCQ_Site10_Site4_RR	0.007812066	0.108064059	AATACAAAGGATGGTATATTTTGCATATTCGATCTATGAGGAAATGCCCCCAGCCTCCCA
PRKCZ_Site8_Site9_FR	0.000560117	0.079228864	CCTCTCTTCTAAAAGGTCTCAACATCACTCGATGGTGCCGGGAGGTGGCCGGCAGGGTTGG
MTHFD1_Site5_Site1_RF	0.000404338	0.079228864	ATAATTCTTCCTGGCACATAATAAGTATTCGAATCGGGCGGGTTCCGGCGTGGGTTTCAG
NFAT_Site6_Site1_FF	0.000514351	0.079228864	TCTAAAGGGATTTCCACTATATGTAGATTCGAGGGGCGTGTGCGCGCGTGGCGGGGCCCG

Table 6D			Probe sequence
Probes	NR_R_P.Value	NR_R_adj.P.Val	60 mer
PRKCQ_Site11_Site4_RR	0.006796573	0.102494645	AACTTATGATTCTAATCTTGAATGTCTGTCGATCTATGAGGAAATGCCCCCCAGCCTCCCA
TNFRSF1A_Site5_Site6_FF	0.011987094	0.126537326	GAGGTGGGCAGATCACGGGGTCAGGGTATCGAGGCCCATCACTGGCGGGGAGACGGGAGG
18_74845064_74846657_74864266_74864995_RF	0.008686097	0.111746517	ACTGAATATGAAAAAAAAATGTAAAAATTATCGACCTCGCGGGAGAGGGTGCCAGGCCGCAT
PRKCQ_Site7_Site4_RR	0.011239245	0.123381356	GATTTTATAGCAAATTTACAAAAATGAGTCGATCTATGAGGAAATGCCCCCAGCCTCCCA
PRKCZ_Site5_Site9_RR	0.002885944	0.086622849	ACCAAGAGTTGGACCCCCTTTTTGATGTTCGATGGTGCGGGAGGTGGCCGGCAGGGTTGG
MAL_Site4_Site2_FR	0.000818457	0.079228864	TATATTGCTATCTACTAGCAAAGGATAATCGAAGAGGTTCAGGGCGGTGCCCGCGGCGCT
PRKCQ_Site9_Site4_RR	0.003669785	0.090200643	ATCAGTAAGCTGGTCAGCTACCCATGAATCGATCTATGAGGAAATGCCCCCAGCCTCCCA
TNFRSF14_Site3_Site8_FR	0.000995361	0.079228864	TGAAAACAGTTCATCCTGAGTTTCAGTCTCGAAGATTAGGTAAAGGTGGGGACGCGGAGA
IFNAR1_Site2_Site4_RR	0.004801376	0.093849223	GTGCAGAGCGAGAGCGGGGCAGAGGCGGTCGAAACTGGGAGAATTCATCTGAAATGATTA
IL-21R_Site5_Site2_RR	0.034533931	0.199109911	GAGGCAGGCAGATCATGAGGTCAGGAGTTCGAGCCCTGGACCCCAGGCCAGCTAATGAGG
19_10326358_10327821_10368389_10370560_RR	0.000174676	0.079228864	GCTCACTGCAACCTCCACCTCCCAGGTTCGCGAACCTCCTGATAACTTCAGCATTAACAG
19_55449062_55451429_55484960_55486708_RF	7.78E-05	0.079228864	AGGGTCTTGCTATGTTGCCCAGGCTGGCCTCGAGATCAGCCTGGGCAACACGGTGAAAAC
TLR1_Site4_Site7_FR	0.000969535	0.079228864	TGTAATATAAGCATAGCTCACTGCAGCCTCGAAGCATTTGTACGACATTCTCATCTTCTT
IRF5_Site8_Site2_FF	0.000148986	0.079228864	ACAGAGGAGCGAGGCCCGATCCTTACTTTCGAACTCCTGACCTCGTGATCTGCCCACCTC
SPRED2_Site4_Site8_RF	0.018236449	0.149371667	GGGTTTCACCATGTTAGCCAGGATGGTCTCGATCTCCTGACCTCATGATCCGCCTGCCTC
IKBKB_Site5_Site8_FR	0.013123191	0.130076121	GCATTTCACCATGTTGGTGAGGCTGGTCTCGAAGAGTTCACACGTGTCCAAATTTGGTGG
TLR1_Site9_Site2_FF	0.002914123	0.086622849	CTGGGATCACAGGCATGTGCCACCATGCTCGACAAGAATAGTCTCCTTGTTTCTGAACAT
CD28_Site1_Site9_RR	0.003257956	0.088621062	GTATTTCTGGTTCTAGATCCTTGAGGAATCGAGCAGAAGGAGTCTCTCCCTGAGGCCACC
12_10289678_10290500_10350455_10351677_RF	0.001491578	0.079419805	CGAGGCGGGCGGATCACGAGGTCAGGAGATCGACCCCCACGTTCTCACCACCTGTTTCTT

Table 6D			Probe sequence
Probes	NR_R_P.Value	NR_R_adj.P.Val	60 mer
CD28_Site1_Site8_RR	0.007644106	0.107723492	GTATTTCTGGTTCTAGATCCTTGAGGAATCGACCTCCTGGGCTCAACCTATCCTCCCACC
CXCL8_Site2_Site6_RF	0.002891692	0.086622849	GGGTTTCACTGTGTTAGCCAGGATGGTCTCGACCTCCCTGGCTCAAGTGATCTTCCCACC
IL-23R_Site4_Site3_RF	0.001588257	0.079419805	TGCCCTAGAGATCTGTGGAACTTTGAACTCGATATATGAAAATAGTTTTTTAATTATAAA
RBPJ_Site14_Site13_FF	0.010539749	0.118804917	GGTGGGGGGAATCACTTGAGGTCAGAAGTTCGAGACCATCCTGGGCAACATGGTAAAACCC
CHUK_Site7_Site2_RF	0.000132328	0.079228864	AATGGCACGATCACGGCTCACTGCAGCCTCGAATGTTACTGACAGTGGACACAGTAAGAA
SH2B3_Site6_Site5_FF	0.003743845	0.090200643	GAGTTTTGCCATGTTGCCCAGGCTGGTCTCGAGAACAGCCTGGCCAACATGGTGAAACCC
IRAK3_Site7_Site5_FR	0.00056928	0.079228864	AGGTCTCACTATGTTGCCCGGGCTGGTCTCGACGCCGAGGAGCTCTGCAGTGGGGGCGTA
CD28_Site4_Site2_RF	0.014801185	0.136839161	GGGTTTCACCATGTTGGCGAGGCTGGTCTCGAACTCCTGACCTCAGGTGATCCGCCTGCC
CD28_Site5_Site6_FR	0.007402719	0.106291976	GGTGGGTGGATCACCTGAGGTCAGGAGTTCGACCTAAGGGTGGTCATAATTCTGCTGCTG
19_39424583_39425930_39445791_39449626_FF	0.001743055	0.079577656	GGGTCTCACAGCCTTCAGAGCTGAGAGCCTAGGCTTCAGTGAGCCATAATCACGCCACTA
IL-1a_and_IL-1b_Site1_Site7_RF	0.002815998	0.086622849	CTTTGGGAGGCCAAGGTGAGTGGATTGCTCGACATCTCATTTGATAGGATTAAGTCAACG
IRAK3_Site7_Site1_FF	0.00166033	0.079419805	AGGTCTCACTATGTTGCCCGGGCTGGTCTCGAACAGCAGCGTGTGCGCCGACAGCGCGCC
C5orf30_Site2_Site8_FR	0.00524841	0.094393734	TCTGTCGCCCAGGTTGGAGTACAGTGGCTCGAGGATGTCCTATTTTGCCACCTTATCTAA
CXCL13_Site1_Site3_RR	6.56394E-05	0.079228864	TTATATCTCCTACCTCCAAGCCTGGCAGTCGATTCCAAAGTGAAGCAAAAAAAAAACTTC
14_55507409_55508411_55583475_55586339_RF	0.003368236	0.088703855	AAAGACCCTGTCTCTAAATAAATAGAACATCGAGATCATGCCACTGCACTCCAGCCTGGG
14_91450408_91451505_91524833_91527062_FF	0.004287708	0.093190996	GGGGTTTTTCCATGTTAGTCAGGCTGGTCTAATGGCTCCCTTACCTTGCTGGCTGTGGGC
IL-23_Site4_Site5_FR	0.021765214	0.160960834	AGTGGCATGATCACAGCTCACTGCCACCTCGAAACCAAACCCTGTGACTTCAACACCCAA
IL-17A_Site3_Site1_RR	0.009698852	0.115042065	CCCTCCCTCAACATGCAGGGATTACAATTCGAAGGATGGTCTGAAGGAAGCAATTGGGAAA

Example 1 - Table 6E. Stratifying between RA-MTX responders and non-responders

Probe Location					4 kb Sequence Location				
Chr	Start1	End1	Start2	End2	Chr	Start1	End1	Start2	End2
1	2460436	2460465	2486982	2487011	1	2456466	2460465	2486982	2490981
1	2457910	2457939	2486982	2487011	1	2457910	2461909	2486982	2490981
12	6443253	6443282	6472689	6472718	12	6439283	6443282	6472689	6476688
12	6452140	6452169	6472689	6472718	12	6448170	6452169	6472689	6476688
1	2460436	2460465	2539015	2539044	1	2456466	2460465	2539015	2543014
21	36117642	36117671	36260589	36260618	21	36117642	36121641	36260589	36264588
1	2486982	2487011	2540813	2540842	1	2486982	2490981	2536843	2540842
18	74845065	74845094	74866978	74867007	18	74845065	74849064	74863008	74867007
1	1977899	1977928	2066129	2066158	1	1973929	1977928	2066129	2070128
21	36206580	36206609	36260589	36260618	21	36206580	36210579	36260589	36264588
10	6520005	6520034	6577853	6577882	10	6516035	6520034	6577853	6581852
18	74756102	74756131	74845065	74845094	18	74756102	74760101	74845065	74849064
10	6454073	6454102	6577853	6577882	10	6450103	6454102	6577853	6581852
10	6448929	6448958	6577853	6577882	10	6448929	6452928	6577853	6581852
1	1977899	1977928	2125692	2125721	1	1973929	1977928	2125692	2129691
14	64856944	64856973	64805460	64805493	14	64852973	64856973	64805460	64801460
18	77135881	77135910	77156058	77156087	18	77131911	77135910	77152088	77156087

Example 1 - Table 6E continued. Stratifying between RA-MTX responders and non-responders

Chr	Start1	End1	Start2	End2	Chr	Start1	End1	Start2	End2
10	6391740	6391769	6577853	6577882	10	6391740	6395739	6577853	6581852
12	6473688	6473717	6494374	6494403	12	6469718	6473717	6490404	6494403
18	74845065	74845094	74864966	74864995	18	74845065	74849064	74860996	74864995
10	6515356	6515385	6577853	6577882	10	6515356	6519355	6577853	6581852
1	2035712	2035741	2125692	2125721	1	2035712	2039711	2125692	2129691
2	95655674	95655703	95691307	95691336	2	95651704	95655703	95691307	95695306
10	6427823	6427852	6577853	6577882	10	6427823	6431822	6577853	6581852
1	2483531	2483560	2539015	2539044	1	2479561	2483560	2539015	2543014
21	34696685	34696714	34746263	34746292	21	34696685	34700684	34746263	34750262
16	27367634	27367663	27460580	27460609	16	27367634	27371633	27460580	27464579
19	10326359	10326388	10368390	10368419	19	10326359	10330358	10368390	10372389
19	55449063	55449092	55486679	55486708	19	55449063	55453062	55482709	55486708
4	38794092	38794121	38904213	38904242	4	38790122	38794121	38904213	38908212
7	128578517	128578546	128592079	128592108	7	128574547	128578546	128588109	128592108
2	65604070	65604099	65634253	65634282	2	65604070	65608069	65630283	65634282
8	42092338	42092367	42202562	42202591	8	42088368	42092367	42202562	42206561
4	38788263	38788292	38859677	38859706	4	38784293	38788292	38855707	38859706
2	204566973	204567002	204624489	204624518	2	204566973	204570972	204624489	204628488

Example 1 - Table 6E continued. Stratifying between RA-MTX responders and non-responders

Chr	Start1	End1	Start2	End2	Chr	Start1	End1	Start2	End2
12	10289679	10289708	10351648	10351677	12	10289679	10293678	10347678	10351677
2	204566973	204567002	204645538	204645567	2	204566973	204570972	204645538	204649537
4	74601393	74601422	74662726	74662755	4	74601393	74605392	74658756	74662755
1	67639374	67639403	67673763	67673792	1	67639374	67643373	67669793	67673792
4	26109288	26109317	26147759	26147788	4	26105318	26109317	26143789	26147788
10	101933094	101933123	101989686	101989715	10	101933094	101937093	101985716	101989715
12	111834072	111834101	111901271	111901300	12	111830102	111834101	111897301	111901300
12	66544383	66544412	66696510	66696539	12	66540413	66544412	66696510	66700509
2	204522870	204522899	204607547	204607576	2	204522870	204526869	204603577	204607576
2	204541606	204541635	204582161	204582190	2	204537636	204541635	204582161	204586160
19	39425901	39425930	39449597	39449626	19	39421931	39425930	39445627	39449626
2	113627760	113627789	113530289	113530318	2	113623789	113627789	113530289	113526289
12	66544383	66544412	66583104	66583133	12	66540413	66544412	66579134	66583133
5	102618306	102618335	102629447	102629476	5	102614336	102618335	102629447	102633446
4	78431568	78431597	78523781	78523810	4	78431568	78435567	78523781	78527780
14	55507410	55507439	55586310	55586339	14	55507410	55511409	55582340	55586339
14	91451476	91451505	91527033	91527062	14	91447506	91451505	91523063	91527062
12	56741028	56741057	56754855	56754884	12	56737058	56741057	56754855	56758854
6	52026497	52026526	52049432	52049461	6	52026497	52030496	52049432	52053431

Example 2: A method of determining the chromosome interactions relevant to a companion diagnostic as pharmacodynamic biomarker during the inhibition of LSD1 in the treatment of AML (acute myeloid leukemia)

Source: Institute of Cancer Research UK.

Pharmacodynamic Biomarkers

Pharmacodynamic (PD) biomarkers are molecular indicators of drug effect on the target in an organism. A PD biomarker can be used to examine the link between drug regimen, target effect, and biological tumour response. Coupling new drug development with focused PD biomarker measurements provides critical data to make informed, early go/no-go decisions, to select rational combinations of targeted agents, and to optimise schedules of combination drug regimens. Use of PD endpoints also enhances the rationality and hypothesis-testing power throughout drug development, from selection of lead compounds in preclinical models to first-in-human trials (National Cancer Institute).

The inventors have discovered that chromosome signatures could be used as pharmacodynamic biomarkers to monitor response to a number of drugs at time points consistent with phenotypic changes observed.

EpiSwitch™ Markers - Ideal Pharmacodynamic Biomarkers

Work on BET (bromodomain and extra-terminal) inhibitors on MV4-11 cell lines has shown that BET inhibition causes the transcriptional repression of key oncogenes BCL2, CDK6, and C-MYC BET inhibitors like LSD1 inhibitors are epigenetic therapies, targeting the acetylated and methylation states of histones. As topological changes at loci precede any regulatory changes, the findings at the MYC locus with EpiSwitch™ show evidence of regulatory change with LSD1 inhibition. MV4-11 cell line harbours translocations that express MLL-AF4 and FLT3-ITD whereas THP-1 only expresses MLL-AF9.

EpiSwitch™ LSD1 Inhibition Biomarker Study for AML (acute myeloid leukemia)

Epigenetic biomarkers identified by EpiSwitchTM platform are well suited for delineating epigenetic mechanisms of LSD1 demethylase and for stratification of different specificities of LSD1 inhibitors within and between cell lines. This work demonstrates that chromosome conformation signatures could be used

as mechanism-linked predictive biomarkers in LSD1 inhibition. A standard LSD1 inhibitor is investigated in this study, tranylcypromine (TCP).

EpiSwitch™ LSD1 Pharmacodynamic Biomarker Discovery

The cells were treated with 1uM of tranylcypromine (TCP). Two AML (acute myeloid leukemia) cell lines THP-1 and MV4-11 were tested with the above compound. Chromosome signatures identified in the vicinity of MYD88 gene in THP-1 cells are shown in Table 7. Chromosome signatures identified in the vicinity of MYD88 gene in MV4-11 cells are shown in Table 8. Each number combination, points to individual chromosome interaction. The positions across the gene have been created and selected based on restriction sites and other features of detection and primer efficiency and were then analysed for interactions. The result in tables 7 and 8 represent no signature detection. A signature detection is represented with the number 1. Below are the PCR EpiSwitch™ marker results for the MyD88 locus for cell lines THP-1 and MV4-11. FACS analysis was used to sort for the expression of CD11b± cells, as an indicator of differentiation. MyD88 and MYC loci were selected on the basis of previously published studies, as key genetic drivers of treatment changes at 72 hrs.

LSD1 Inhibitor (TCP) Experiments - Discovery Findings

The conformations that change at the later time point (72hrs) relative to the untreated cells show the most consistency between the 2 cell types. These are the markers above the bold double line shown in the THP-1 data, and highlighted by the shaded cells in the MV4-11 data.

LSD1 inhibition removes a long range interaction with 5' upstream to the ORF of MYD88, changing the regulatory landscape for the locus.

LSD1 Inhibition Analysis versus Gene Expression Data - Temporal and Structural Correlation of MYC Locus Conformations with Gene Expression (GEX)

MYC is the target gene that drives the AML (acute myeloid leukemia) pathology, but at 72hrs treatment, the fold change is too small to be significant for a marker. The changes seen in Table 9 at the MYC locus at 72hrs for GEX data correlates to the conformation changes identified at 72hrs. The negative GEX change at MYC relative to the untreated cells is in keeping with the requirement to perturb MYC proliferation effect. The change is small also in keeping with the tight control elicited on this locus by numerous signal cascades.

Unlike GEX data above, the EpiSwitch™ biomarkers clearly detect changes in chromosome conformation signatures at 72hr treatments correspondent with cells differentiation and their death by apoptosis (phenotypic change).

LSD1 Inhibition Analysis versus Gene Expression Data - Temporal and Structural Correlation of MyD88 Locus Conformations with Gene Expression (GEX)

The changes seen at MyD88 at 72hrs for the GEX data correlate to the conformation changes identified at 72hrs. The GEX change is positive relative to untreated cells, which is in keeping with the differential seen in these AML (acute myeloid leukemia) cells after treatment with the LSD1 inhibitor.

Only 1.5 fold change observed at 72hr treatment with TCP at MYD88 locus identified both by GEX and EpiSwitch™. This level of change is too affected by noise in microarray gene expression analysis. However, epigenetic changes observed for chromosome signatures are clean to follow a binary format of 0 or 1. The data shows distinct pattern of changes. Both MYC and MYD88 are epigenetic drivers that, as shown in the GEX data, may not present with the strong response in gene expression, but can be identified as key epigenetic changes are visible through chromosome signatures. These two genetic drivers define phenotypic changes required for successful therapy treatment. At 72hrs cells differentiate and undergo apoptosis.

Table 7 THP cells - LSD1 Inhibitor (TCP) treated and untreated at 48hrs and 72hrs

THP-1	Untreated	TCP treatment 48hr	TCP Treatment 72 hr
MYD88 1/29	1	1	0
MYD88 7/27	1	1	0
MYD88 9/17	1	1	0
MYD88 3/27	1	1	0
MYD881/13	1	1	0
MYD88 17/29	1	1	0
MYD88 3/19	1	1	0
MYD88 5/21	1	1	0
MYD88 5/29	1	1	0
MYD88 3/31	1	1	0
MYD88 7/23	1	1	1
MYD88 3/7	1	1	1
MYD88 1/25	0	0	1
MYD88 3/25	0	1	1
MYD88 1/27	0	1	1
MYD88 3/11	0	1	1
MYD88 11/27	0	1	1
MYD88 9/25	0	1	0

MYD88 13/25	0	1	1
MYD88 3/15	0	1	0
MYD88 13/29	0	1	0
MYD88 7/11	0	1	0
MYD88 7/31	0	1	0

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Table 8. MV4-11 cells - LSD1 Inhibitor (TCP) treated and untreated at 48hrs and 72hrs

MV4-11	Untreated	TCP treatment 48hr	TCP Treatment 72 hr
MYD88 3/27	0	0	0
MYD88 7/11	0	0	0
MYD88 7/27	0	1	0
MYD88 7/31	0	0	0
MYD88 1/13	1	1	0
MYD88 11/27	1	1	0
MYD88 1/25	1	1	0
MYD88 13/29	1	1	0
MYD88 1/17	1	1	1
MYD88 13/25	1	1	0
MYD88 1/29	1	1	0
MYD88 17/29	1	1	0
MYD88 5/21	1	1	1
MYD88 3/11	1	1	1
MYD88 3/15	1	1	0
MYD88 3/19	1	1	0
MYD88 3/31	1	1	1
MYD88 3/7	1	1	0
MYD88 5/25	1	1	1
MYD88 5/29	1	1	0
MYD88 7/23	1	1	0
MYD88 9/17	1	1	0
MYD88 9/25	1	1	0

10 Table 9. Illumina Human HT-12 V4.0 expression beadchip GEX Data for MYC

HUGO_SYN	TCP/un 3h	TCP/un 12h	TCP/un 72h
MYC	0.99	0.81	-1.27

Table 10. Treatment with TCP

MYC			
MV4-11	Untreated	TCP treatment 48hr	TCP Treatment 72hr
MYCUS 1/ MYCUS 23	1	1	0
MYCUS 3/ MYCUS 13	1	1	0
MYCUS 5/ MYCUS 21	1	1	0
MYCUS 9/ MYC 5	1	1	0

Table 11. Illumina Human HT-12 V4.0 expression beadchip GEX Data for MYD88

HUGO_SYN	TCP/un 3h	TCP/un 12h	TCP/un 72h
MyD88	1.07	1.13	1.53

Table 12. Treatment with TCP

MyD88			
MV4-11	Untreated	TCP treatment 48hr	TCP Treatment 72hr
1/13	1	1	0
11/27	1	1	0
1/25	1	1	0
13/29	1	1	0
5/29	1	1	0
7/23	1	1	0
9/17	1	1	0
9/25	1	1	0

Example 3: A method of determining the chromosome interactions which are relevant to a companion diagnostic for prognosis of melanoma relapse in treated patients (PCR data).

Source: Mayo Clinic metastatic melanoma cohort, USA

A prognostic biomarker predicts the course or outcome (e.g. end, stabilisation or progression) of disease. This study discovers and validates chromosome signatures that could act as prognostic biomarkers for relapse to identify clear epigenetic chromosome conformation differences in monitored melanoma patients, who undergone surgery treatment, for signs of relapse or recovery, and to validate such biomarkers for potential to be prognostic biomarkers for monitoring relapse of melanoma. Here we want to present our example of validated prognostic use of chromosome conformation signatures in application to confirmed melanoma patients who have undergone treatment by the resection of the original growth in order to identify the candidates who are likely to relapse within 2 years of treatment.

224 melanoma patients were treated with surgery to remove their cancer. They were then observed for a period of two years with blood being drawn for analysis at >100 days after the surgery.

EpiSwitch™ Prognostic Biomarker Discovery

Chromosome signatures of 44 genes associated with melanoma and the rest of the genome for any disease-specific long range interaction by Next Generation Sequencing NGS were tested. Non-biased assessment of chromosome signatures associated with melanoma through deep sequencing provided initial pool of 2500 candidate markers. Further analysis by EpiSwitch™ platform on expanding sets of blood

samples from melanoma patients and patients with non-melanoma skin cancers (NMSC) as control, reduced the initial pool of candidate markers to 150. With further expansion on sample numbers it has been reduced to 32, as shown in Table13.

Table 13. Number of EpiSwitch™ Markers screened and patients used.

EpiSwitch™ Markers Screened	Melanoma Patients Used	NMSC Patients Used
150	4	4
94	14	14
55	21	20
32	74	33

Prognosis of Relapse

Top 15 markers previously identified for stratification of melanoma from non-melanoma skin cancers comprise TBx2 7/15, TYR 1/9, TYR 13/17, TYR 3/11, TYR 3/23, P16 11/19, P16 7/23, P16 9/29, MITF 35/51, MITF 43/61, MITF 49/55, BRAF 5/11, BRAF 27/31, BRAF 21/31, BRAF 13/21, which were taken from a total of 8 genes: TBx2; TYR; BRAF; MiTF; p16; BRN2; p21; TBx3

3C analysis of melanoma patients' epigenetic profiles revealed 150 chromosome signatures with a potential to be prognostic biomarkers, reduced to three in expanding sets of testing sample cohorts. The three chromosome signatures which show the switches in chromosome conformational signature highly consistent with treatment and 2 year outcome for relapse, and this are the best potential prognostic melanoma markers are: BRAF 5/11, p16-11/19 and TYR 13/17. Finally, three chromosome signatures were carried out to the validation stage as prognostic biomarkers.

Table 14. EpiSwitch™ Prognostic signature for patients who relapsed 2 years after treatment (0 = No chromosome conformation detected, 1 = chromosome conformation detected) – Group A

Sample ID	BRAF 5/11	P16 11/19	TYR 13/17	Mel_gone
AZ250439M-2	1	1	1	No
AZ250439M-1	1	1	1	No
JB220262F-2	1	1	1	No
JS150868F	1	1	1	No
KB200873F-2	1	1	1	No
SW14101951F-1	1	1	1	No
VW250929M-1	1	1	1	No
AC130954F-1	1	1	1	No
AC130954F-2	1	1	1	No
GM271147M-2	1	1	1	No
LW191048F-2	1	1	1	No
LG040535M-2	1	0	1	No
JB220262F-1	1	0	1	No
RH070234F-2	1	0	1	No
RH070234F-4	1	0	1	No

Sample ID	BRAF 5/11	P16 11/19	TYR 13/17	Mel_gone
GM271147M-1	1	0	1	No
LW191048F-1	1	0	1	No
BB08111957F-2	1	1	0	No
RH070234F-1	1	1	0	No
RH070234F-1	1	1	0	No
RD200666M-2	1	1	0	No
RD200666M-1	1	1	0	No
KB200873F-1	1	1	0	No
VW250928M-2	1	1	0	No

Table 14 shows that relapse has been observed within two years after the treatment among the above patients. Through completely non-biased analysis of chromosome signatures these disease-specific three markers remained present and unchanged after treatment in majority of patients who relapsed after treatment.

Table 15 provides evidence that chromosome signatures change as a result of treatment to reflect more healthy profile. Through completely non-biased analysis of chromosome signatures the same disease-specific three markers have changed and were absent in majority of patients after treatment, with no signs of relapse for 2 years.

Table 16 shows that the same three prognostic biomarkers show a strong tendency to be absent in healthy population. From all melanoma specific biomarkers identified in initial discovery stage, only these three markers carried prognostic value due to their change after treatment, in that they were different from diagnostic markers.

These results confirm that the three identified chromosome signatures exemplify the evidence for chromosome signatures acting as valid and robust prognostic biomarkers.

Table 15. EpiSwitch™ Prognostic Signature for Successful Treatment in Melanoma Patients who did not relapse after 2 years (0 = No chromosome conformation detected, 1 = chromosome conformation detected) – Group B

Sample ID	BRAF 5/11	P16 11/19	TYR 13/17	Mel_gone
DG04081968M-2	0	0	0	Yes
DG04081968M-1	0	0	0	Yes
JR08061937F-2	0	0	0	Yes
EM110366F-4	0	0	0	Yes
FS17051942M-2	0	0	0	Yes
GS18081951M-1	0	0	0	Yes
DB24021936M-1	0	0	0	Yes
DB24021936M-2	0	0	0	Yes

Sample ID	BRAF 5/11	P16 11/19	TYR 13/17	Mel_gone
ML23131937M-2	0	0	0	Yes
ML23131937M-1	0	0	0	Yes
DM210555M-2	0	0	0	Yes
DM210555M-1	0	0	0	Yes
JS121060F-2	0	0	0	Yes
JH280944M-2	0	0	0	Yes
JH280944M-1	0	0	0	Yes
RF15091934M-2	0	0	0	Yes
GC23051957M-2	0	0	0	Yes
PA24011941M-2	0	0	0	Yes
PA24011941M-1	0	0	0	Yes
MH12031946M-2	0	0	0	Yes
MH12031946M-1	0	0	0	Yes
AC17071938M-2	0	0	0	Yes
AC17071938M-1	0	0	0	Yes
TR080147M-2	0	0	0	Yes

Table 16. EpiSwitch™ Reference Epigenetic Profile in Healthy Controls (HC = Healthy Controls, 0 = No chromosome conformation detected, 1 = chromosome conformation detected) – Group C

Sample ID	BRAF 5/11	P16 11/19	TYR 13/17	Condition
JP74(5) -1	0	0	0	HC
JG80 (6) -1	0	0	0	HC
JG80 (6) -2	0	0	0	HC
MS80 (7) -1	0	0	0	HC
MS80 (7) -2	0	0	0	HC
RS86 (8) -1	0	0	0	HC
ES86 (9) -1	0	0	0	HC
DL (10) -1	0	0	0	HC
RM81 (11) -1	0	0	0	HC
CS (12) -1	0	0	0	HC
CL84 (13) -1	0	0	0	HC
ER83 (14) -1	0	0	0	HC
AP57 (15) -1	0	0	0	HC
AP57 (15) -2	0	0	0	HC
SR86 (17) -1	0	0	0	HC
YD80 (18) -1	0	0	0	HC
KK69 (19) -1	0	0	0	HC
KK69 (19) -2	0	0	0	HC
RS84 (20) -1	0	0	0	HC
AA85 (21) -1	0	0	0	HC
AA85 (21) -2	0	0	0	HC
AD75 (22) -1	0	0	0	HC
JJ84 (23) -1	0	0	0	HC
SP71 (24) -1	0	0	0	HC

Prognosis for Relapse (Residual Disease Monitoring in Treated Melanoma Patients)

Cross-validation for the 224 melanoma patients, observed for 2 years after the treatment for a relapse, on the basis of stratification with the three prognostic chromosome signatures from post-operational blood test. Table 17 shows the relevant confusion table.

Table 16b.

Classification	Result	95% Confidence Interval (CI)
Sensitivity	82.1%	70.1%-89.4%
Specificity	87.8%	81.9%-92.1%
PPV	71.0%	59.4%-80.4%
NPV	92.9%	87.7%-96.1%

Table 17. Confusion table

Group	A	B	Classified as
A	49	11	Still has melanoma
B	20	144	Re-categorised

Predictive/Pharmacodynamic Biomarkers for Drug Response: anti-PD-1 in Metastatic Melanoma Patients (array data)

Melanoma

Malignant melanoma is the least common, but most aggressive form of skin cancer. It occurs in melanocytes, cells responsible for synthesis of the dark pigment melanin. The majority of malignant melanomas are caused by heavy UV exposure from the sun. Most of the new melanoma cases are believed to be linked to behavioural changes towards UV exposure from sunlight and sunbeds. Globally, in 2012, melanoma occurred in 232,000 people and resulted in 55,000 deaths. Incidence rates are highest in Australia and New Zealand. The worldwide incidence has been increasing more rapidly amongst men than any other cancer type and has the second fastest incidence increase amongst women over the last decade. The survival rates are very good for individuals with stage 1 and 2 melanomas. However, only 7 – 19% of melanoma patients whose cancer has spread to distant lymph nodes or other parts of the body will live for more than 5 years. Currently, the only way to accurately diagnose melanoma is to perform an excision biopsy on the suspicious mole. The treatment includes surgical removal of the tumour. There is no melanoma screening programme in the UK, but educational programmes have been created to raise awareness of risks and symptoms of melanoma. There is a high demand for screening programmes in countries where melanoma incidence is very high e.g. in Australia. This work concerns biomarkers for diagnosis, prognosis, residual disease monitoring and companion diagnostics for melanoma immunotherapies.

Study Background

The major issue with all immunomodulators currently tested in the treatment of cancers is their low response rates. In the case of late melanoma, for anti-PD-1 or anti-PD-L1 monoclonal antibodies, the

objective response rate is only 30-40%. Such therapy is in strong need of biomarkers predicting responders vs. non-responders. The PD-1 locus is regulated by cytokines epigenetically through resetting of long range chromosome conformation signatures.

OBD technology

EpiSwitch™ platform technology is ideally suited for stratification of PD-1 epigenetic states prior to and in response to immunotherapy. An EpiSwitch™ array has been designed for analysis of >332 loci implicated in controls and modulation of response to anti-PD-1 treatment in melanoma patients.

Methods

Biomarker identification using EpiSwitch™ array analysis:

1. Chromosome conformations for 332 gene locations determined by EpiSwitch™ pattern recognition.
2. 14,000 EpiSwitch™ markers on PD1 screening array.

Samples

All patients have been previously treated with chemotherapy and anti-CTLA-4 therapy. Two time points considered pre-treatment (baseline samples) and post-treatment (12 week samples)

Discovery Cohort

- 4 responders vs. 4 non-responders at baseline
- 4 responders vs. 4 responders at 12 weeks (Matched)

Hypergeometric Analysis

As the last step of the array data analysis, the hypergeometric analysis was carried out in order to identify regulatory hubs i.e. most densely regulated genes as being potential causative targets and preferred loci for stratification. The data is ranked by the Epigenetic Ratio for R vs R 12W (12W_FC_1), 1 in BL Binary indicates the loop is present in Responders vs Non-Responders, but when Responders baseline are compared to Responders at 12 weeks. The epigenetic ratio indicates that the presence of the loop is more abundant in the 12 week Responder patient samples. This indicates that there has been an expansion of this signature.

Summary

This epigenetic screen of anti-PD1 therapy for potential predictive and pharmacodynamic biomarkers provides a wealth of new regulatory knowledge, consistent with prior biological evidence. The work provides a rich pool of predictive and pharmacodynamic/response EpiSwitch™ markers to use in

validation analysis. The results show presence of a defined epigenetic profile permissive for anti- PD-1 therapy. The epigenetic profile permissive for anti-PD1 therapy is present in naïve patients at baseline and is strengthened with treatment over 12 weeks period.

Further Information

This work concerns EpiSwitch™ as the basis for a diagnostic test to address the issue of poor melanoma diagnosis by general practitioners. 15 lead EpiSwitch™ biomarkers were screened and identified from an initial set of 86 patient samples representing true clinical setting. The biomarkers were then trained and validated in 2 independent patient cohorts: one from Australia (395 patients) and one from the Mayo Clinic (119 patients):

- 119 independently and retrospectively annotated blood samples
- 59 Melanoma Samples
- 60 Controls (20 NMSC, 20 Benign Conditions, 20 Healthy Patients))
- 2 Clinic collection in the USA

		95% Confidence Interval (CI)
Sensitivity	90.0%	79.9%-95.3%
Specificity	78.3%	66.4%-86.9%
PPV	88.7%	77.4%-94.7%
NPV	80.6%	69.6%-88.3%

68 EpiSwitch™ Markers identified by statistical processing as predictive biomarkers at baseline for anti-PD-1 therapy. (PD1-R vs NR BL). R is Responder, and NR is Non-Responder. 63 EpiSwitch™ Markers identified by statistical processing as response biomarkers for anti-PD-1 therapy. (PD1 R-BL v R-12W). 10 Markers are both good candidates for predictive and response markers.

Fisher-Exact test results: top 8 predictive EpiSwitch™ Array Markers validated with the EpiSwitch™ PCR platform on the independent patient cohort (see Table 37). See Table 38 for the discerning markers from the Fisher-Exact analysis for PCR analysis between Responders at Baseline and Responders at 12 weeks. 1 is Conformation Present. 0 is Conformation Absent/ Array: R12_W indicates that the conformation was present in the Responders at 12 weeks.

The STAT5B_17_40403935_40406459_40464294_40468456_FR probe was measured in Responder v Non-Responder at Baseline and the conformation is present in the Responder. In this comparison the

marker is in Responders at 12 weeks, this is the case as the concentrating of DNA used to detect the conformation in Responder vs Non Responder is greater than in Responder baseline v Responder at 12 weeks, indicating the Epigenetic Load has increased in the anti-PD-1 responding patients. Markers STAT5B and IL15 are of particular interest and are involved in key personalised medical and regulatory events responsible for the efficacies response to anti-PD1 therapies (see tables 39 to 40, 43 to 47).

The following Tables 36a to 36f, 37a, 37b, 38a, and 38b also pertain to Example 3 and are as follows:

Table 36a. Top Probes – Anti PD1 (Melanoma) – responders

Table 36b. Top Probes – Anti PD1 (Melanoma) – responders - probe sequences

Table 36c. Top Probes – Anti PD1 (Melanoma) – Responders – Loci

Table 36d. Top Probes – Anti PD1 (Melanoma) Non—responders

Table 36e. Top Probes – Anti PD1 (Melanoma) Non—responders

Table 36f. Top Probes – Anti PD1 (Melanoma) Non—responders – probes sequences and loci

Table 37a. Anti-PD1: pharmacodynamic response markers

Table 37b. Anti-PD1: pharmacodynamic response markers

Table 38a. Anti-PD1: pharmacodynamic response markers - No difference in baseline Responders and baseline Non-Responders but show a significant change in 12 week Responder

Table 38b. Probe location - Anti-PD1: pharmacodynamic response markers - No difference in baseline Responders and baseline Non-Responders but shows a significant change in 12 week Responders

Indication Examples

Example 4 - Amyotrophic lateral sclerosis (ALS)

The motor neurone disease Amyotrophic lateral sclerosis (ALS or Lou Gehrig's disease) is a fatal neurodegenerative disease characterised by progressive death of the primary motor neurones in the central nervous system. Symptoms include muscle weakness and muscle wasting, difficulty in swallowing and undertaking everyday tasks. As the disease progresses, the muscles responsible for breathing gradually fail, causing difficulty in breathing, and finally death. ALS has an average prevalence of 2 per 100,000, but is higher in the UK and USA with up to 5 per 100,000. There are estimated to be over 50,000 patients in the USA and 5,000 patients in the UK with the condition. The mortality rate for ALS sufferers is high: the median survival from diagnosis with ALS (i.e. the time when 50% of patients have died) varies in different studies, but in the most reliable (unbiased) population studies it is about 22 months with a range of 18-30 months. With no known cure, treatment of ALS focuses on supportive care. There is only one drug currently approved for treatment, riluzole which provides a modest increase in lifespan for ALS patients but minimal improvement in symptoms. Despite intensive research into the biological basis of ALS, diagnosis and methods of treatment, as well as monitoring of disease progression remains a

challenge. Such prognostic tests would greatly benefit ALS sufferers by allowing sub-stratification of patients according to the biological mediators of clinical heterogeneity, potentially allowing a more precise prognosis and care planning by identifying fast and slow progressors. OBD has been discovering EpiSwitch™ markers to stratify ALS vs. healthy controls, and fast progressing ALS vs. slow progressing ALS, to develop and validate diagnostic, prognostic and predictive EpiSwitch™ biomarkers for ALS.

Source: Northeast Amyotrophic Lateral Sclerosis Consortium (NEALS) – USA.

See Tables 1 , 2, 18, and 42 and hereinafter for ALS Probes - EpiSwitch™ markers to stratify ALS vs. healthy controls. Table 27 shows the gene data for this indication.

Further work was performed to validate the top ALS array markers and identify primers that could study the interactions. Statistical analysis of the array markers informed shortlist selection for PCR based assay development. From the list of the best stratifying ALS array probes, 99 markers were taken to the PCR stage.

Primers were designed using Integrated DNA Technologies (IDT) software (and Primer3web version 4.0.0 software if required) from markers identified from the microarray. Primer testing was carried out on each primer set; each set was tested on a pooled subset of samples to ensure that appropriate primers could study the potential interactions. Presence of an amplified product from PCR was taken to indicate the presence of a ligated product, indicating that a particular chromosome interaction was taking place. If the primer testing was successful then the primer sets were taken through to screening.

The signature set was isolated using a combination of univariate (LIMMA package, R language) and multivariate (GLMNET package, R language) statistics and validated using logistic modelling within WEKA (Machine learning algorithms package). The best 10 stratifying PCR markers were selected for validation on 58 individuals (29 x ALS; 29 x Healthy controls - HC) using data from the Northeast Amyotrophic Lateral Sclerosis Consortium (NEALS). These were selected based on their Exact Fisher's P-value. A consistently good marker from all 3 tests was the EpiSwitch marker in CD36. The first 9 PCR markers shown in Table 41 stratified between ALS and HC with 90% rank discrimination index.

The ALS marker set was analysed against a small independent cohort of samples provided by Oxford University. Even in a small subset of samples stratification of the samples was shown based on the biomarkers. Four markers stratify the subset of 32 (16 ALS, 16 Healthy Control) samples with p-value < 0.3. These core markers are ALS.21.23_2, DNM3.5.7_8, ALS.61.63_4 and NEALS.101.103_32, in genes

EGFR, DNM3, CD36 and GLYCAM1 respectively. The Fisher-Exact test, GLMNET and Bayesian Logistic modelling marked CLIC4 as a valuable addition to the four core markers.

The sequences of the primers for the PCR markers given in Table 41 are provided in Table 42.

Example 5 - Diabetes mellitus (DM) type II (T2DM)

Type 2 diabetes (also known as T2DM) is the most common form of diabetes. Diabetes may occur through either, the pancreas not producing enough hormone insulin which regulates blood sugar levels, or the body not being able to effectively use the hormone it produces due to reduced insulin sensitivity. Until recently, T2DM has only been diagnosed in adults, but it is now occurring in children and young adults. According to World Health Organisation (WHO), diabetes reached pandemic levels with 346 million sufferers worldwide and its incidence is predicted to double by 2030. In 2004 alone, approximately 3.4 million people died as a consequence of diabetes and its complications with the majority of deaths occurring in low- and middle-income countries. The incidence of T2DM is increasing due to an ageing population, changes in lifestyle such as lack of exercise and smoking, as well as diet and obesity. T2DM is not insulin dependent and can be controlled by changes in lifestyle such as diet, exercise and further aided with medication. Individuals treated with insulin are at a higher risk of developing severe hypoglycaemia (low blood glucose levels) and thus their medication and blood glucose levels require routine monitoring. Generally, older individuals with established T2DM are at a higher risk of cardiovascular disease (CVD) and other complications and thus usually require more treatment than younger adults with a recently-recognised disease. It has been estimated that seven million people in the UK are affected by pre-diabetic conditions, which increase the risk of progressing to T2DM. Such individuals are characterised by raised blood glucose levels, but are usually asymptomatic and thus may be overlooked for many years having a gradual impact on their health. Inventors develop prognostic stratifications for pre-diabetic state and T2DM. Presented herein are EpiSwitch™ markers to stratify pre-diabetic state (Pre-T2DM) vs. healthy controls, as well as the discovery of EpiSwitch™ markers to stratify T2DM vs. healthy control, and prognostic markers to stratify aggressive T2DM vs. slow T2DM.

Source: Norfolk and Norwich University Hospitals (NNUH), NHS Foundation Trust - Norwich UK

See Tables 19a, 19b, 19c and 19d hereinafter for Pre-type 2 diabetes mellitus probes - EpiSwitch™ markers to stratify pre-type 2 diabetes vs. healthy controls. Table 28 shows the gene data.

See also Tables 20a, 20b, 20c, 20d hereinafter for Type 2 diabetes mellitus probes – EpiSwitch™ markers to stratify type 2 diabetes mellitus vs. healthy controls. Table 29 shows the gene data.

Example 6 - Diabetes mellitus type I (T1DM)

Diabetes mellitus (DM) type 1 (also known as T1DM; formerly insulin-dependent diabetes or juvenile diabetes) is a form of diabetes that results from the autoimmune destruction of the insulin-producing beta cells in the pancreas. The classical symptoms are polyuria (frequent urination), polydipsia (increased thirst), polyphagia (increased hunger) and weight loss. Although, T1DM accounts for 5% of all diabetes cases, it is one of the most common endocrine and metabolic conditions among children. Its cause is unknown, but it is believed that both genetic factors and environmental triggers are involved. Globally, the number of people with T1DM is unknown, although it is estimated that about 80,000 children develop the disease each year. The development of new cases varies by country and region. The United States and northern Europe fall between 8-17 new cases per 100,000 per year. Treatment of diabetes involves lowering blood glucose and the levels of other known risk factors that damage blood vessels. Administration of insulin is essential for survival. Insulin therapy must be continued indefinitely and does not usually impair normal daily activities. Untreated, diabetes can cause many serious long-term complications such as heart disease, stroke, kidney failure, foot ulcers and damage to the eyes. Acute complications include diabetic ketoacidosis and coma. OBD's diabetes programme is focused on a development of EpiSwitch™ biomarkers for diagnostic and prognostic stratifications of T1DM.

Presented herein are EpiSwitch™ markers to stratify T1DM versus healthy controls.

Source: Caucasian samples collected by Procurement Company Tissue Solutions based in Glasgow (Samples collected in Russia); NEALS consortium controls (USA).

See Tables 21a, 21b, 21c and 21d hereinafter for Type 1 diabetes mellitus (T1DM) probes - EpiSwitch™ markers to stratify T1DM vs. healthy controls. Table 30 shows the gene data.

Example 7 - Ulcerative colitis (UC)

Ulcerative colitis (UC), a chronic inflammatory disease of the gastrointestinal tract, is the most common type of inflammatory disease of the bowel, with an incidence of 10 per 100,000 people annually, and a prevalence of 243 per 100,000. Although, UC can occur in people of any age, it is more likely to develop in people between the ages of 15 and 30 and older than 60. The exact cause of ulcerative colitis is unknown. However, it is believed that an overactive intestinal immune system, family history and environmental factors (e.g. emotional stress) may play a role in causing UC.

It is more prevalent in people of Caucasian and Ashkenazi Jewish origin than in other racial and ethnic subgroups. The most common signs and symptoms of this condition are diarrhoea with blood or pus and abdominal discomfort. It can also cause inflammation in joints, spine, skin, eyes, and the liver and its bile ducts. UC diagnosis is carried out through taking family history, physical exam, lab tests and endoscopy of

large intestine. This lifelong disease is associated with a significant morbidity, and the potential for social and psychological sequelae particularly if poorly controlled. An estimated 30–60% of people with ulcerative colitis will have at least one relapse per year. About 80% of these are mild to moderate and about 20% are severe. Approximately 25% of people with UC will have one or more episodes of acute severe colitis in their lifetime. Of these, 20% will need a surgical removal of all or part of the colon (colectomy) on their first admission and 40% on their next admission. Although mortality rates have improved steadily over the past 30 years, acute severe colitis still has a mortality rate of up to 2%. Mortality is directly influenced by the timing of interventions, including medical therapy and colectomy.

Ulcerative colitis has a well-documented association with the development of colorectal cancer, with greatest risk in longstanding and extensive disease. Treatment of relapse may depend on the clinical severity, extent of disease and patient's preference and may include the use of aminosalicylates, corticosteroids or immunomodulators. The resulting wide choice of agents and dosing regimens has produced widespread heterogeneity in management across the UK, and emphasises the importance of comprehensive guidelines to help healthcare professionals provide consistent high quality care.

Presented herein are EpiSwitch™ markers to stratify UC versus healthy controls for a development of disease-specific signatures for UC.

Source: Caucasian samples collected by Procurement Company Tissue Solutions based in Glasgow (Samples collected in Russia); NEALS consortium controls (USA).

See Tables 22a, 22b, 22c and 22d hereinafter for Ulcerative colitis (UC) probes – EpiSwitch™ markers to stratify UC vs. healthy controls. Table 31 shows the gene data.

Example 8 - Systemic lupus erythematosus (SLE)

Systemic lupus erythematosus (SLE), also known as discoid lupus or disseminated lupus erythematosus, is an autoimmune disease which affects the skin, joints, kidneys, brain, and other organs. Although "lupus" includes a number of different diseases, SLE is the most common type of lupus. SLE is a disease with a wide array of clinical manifestations including rash, photosensitivity, oral ulcers, arthritis, inflammation of the lining surrounding the lungs and heart, kidney problems, seizures and psychosis, and blood cell abnormalities. Symptoms can vary and can change over time and are not disease specific which makes diagnosis difficult. It occurs from infancy to old age, with peak occurrence between ages 15 and 40. The reported prevalence of SLE in the population is 20 to 150 cases per 100,000. In women, prevalence rates vary from 164 (white) to 406 (African American) per 100,000. Due to improved detection of mild disease, the incidence nearly tripled in the last 40 years of the 20th century. Estimated incidence rates are 1 to 25

per 100,000 in North America, South America, Europe and Asia. The exact cause of SLE is not known, but several factors have been associated with the disease. People with lupus often have family members with other autoimmune conditions. There may be environmental triggers like ultraviolet rays, certain medications, a virus, physical or emotional stress, and trauma. There is no cure for SLE and the treatment is to ease the symptoms. These will vary depending on expressed symptoms and may include anti-inflammatory medications, steroids, corticosteroids and anti-malarial drugs. Survival has been improving, suggesting that more or milder cases are being recognised. OBD has been developing prognostic signatures for SLE.

See Tables 23a, 23b, 23c and 23d for SLE probes – EpiSwitch™ markers to stratify SLE vs. healthy controls. Table 32 shows the gene data.

Source: Caucasian samples collected by Procurement Company Tissue Solutions based in Glasgow (Samples collected in USA); NEALS consortium controls.

Example 9 - Multiple sclerosis (MS)

Multiple sclerosis (MS) is an acquired chronic immune-mediated inflammatory condition of the central nervous system (CNS), affecting both the brain and spinal cord. The cause of MS is unknown. It is believed that an abnormal immune response to environmental triggers in people who are genetically predisposed results in immune-mediated acute, and then chronic, inflammation. The initial phase of inflammation is followed by a phase of progressive degeneration of the affected cells in the nervous system. MS is more common among people in Europe, the United States, Canada, New Zealand, and sections of Australia and less common in Asia and the tropics. It affects approximately 100,000 people in the UK. In the US, the number of people with MS is estimated to be about 400,000, with approximately 10,000 new cases diagnosed every year. People with MS typically develop symptoms between the ages 20 and 40, experiencing visual and sensory disturbances, limb weakness, gait problems, and bladder and bowel symptoms. They may initially have partial recovery, but over time develop progressive disability. Although, there is no cure, there are many options for treating and managing MS. They include drug treatments, exercise and physiotherapy, diet and alternative therapies. MS is a potentially highly disabling disorder with considerable personal, social and economic consequences. People with MS live for many years after diagnosis with significant impact on their ability to work, as well as an adverse and often highly debilitating effect on their quality of life and that of their families. OBD's MS programme involves looking at prognostic stratifications between primary progressive and relapsing-remitting MS.

The most common (approx. 90%) pattern of disease is relapsing--remitting MS (MSRR). Most people with this type of MS first experience symptoms in their early 20s. After that, there are periodic attacks

(relapses), followed by partial or complete recovery (remissions).The pattern of nerves affected, severity of attacks, degree of recovery, and time between relapses all vary widely from person to person. Eventually, around two-thirds of people with relapsing-remitting MS enter a secondary progressive phase of MS. This occurs when there is a gradual accumulation of disability unrelated to relapses, which become less frequent or stop completely.

Presented herein are EpiSwitch™ monitoring markers to stratify MS patients who are responders to IFN-B treatment versus non-responders; EpiSwitch™ markers to stratify MSRR versus healthy controls and EpiSwitch™ markers to stratify MSRR (relapsing remitting type of MS) versus MSPP (primary progressive type of MS).

Source: Caucasian samples collected by procurement company Tissue Solutions, based in Glasgow (Samples collected in MS-RR: Russia; MS IFN-B R vs NR: USA); NEALS consortium controls (USA)

See Tables 24a, b, c and d hereinafter for Relapsing-Remitting Multiple Sclerosis (MSRR) probes – EpiSwitch™ markers to stratify MSRR vs. healthy controls. Table 33 shows the gene data.

See also Tables 25a, 25b, 25c and 25d hereinafter for Multiple Sclerosis (MS) probes - EpiSwitch™ monitoring markers to stratify MS patients who are (B) responders to IFN-B (IFN-beta) treatment vs. (A) non-responders. Table 34 shows the gene data.

Example 10 - Neurofibromatosis (NF)

In patients with NF1 mutation transformation into malignant state is difficult to predict, as it is governed by epigenetic context of the patient. In NF2 mutants, prognosis of the disease is very reliable and strongly defined by the genetics itself. Presented herein are EpiSwitch™ markers to stratify Malignant Peripheral Nerve Sheath Tumours (MPNSTs) vs. Benign plexiform showing 329 top probes in enriched data.

Source: Belgium - University of Leuven

See Tables 26a and 26b hereinafter for Neurofibromatosis (NF) probes - EpiSwitch™ markers to stratify Benign plexiform vs. Malignant Peripheral Nerve Sheath Tumours (MPNSTs). Table 35 shows the gene data.

Example 11 - Chromosome Interactions Relevant to Anti-PD1 Responsiveness in Different Cancers

Table 47 shows the pattern of chromosome interactions present in responders to anti-PD1 (unless otherwise stated with NR (non-responder)) in individuals with particular cancers. The terminology used in the table is explained below.

DLBCL_ABC: Diffuse large B-cell lymphoma subtype activated B-cells

DLBCL_GBC: Diffuse large B-cell lymphoma subtype germinal centre B-cells

HCC: hepatocellular carcinoma

HCC_HEPB: hepatocellular carcinoma with hepatitis B virus

HCC_HEPC: hepatocellular carcinoma with hepatitis C virus

HEPB+R: Hepatitis B in remission

Pca_Class3: Prostate cancer stage 3

Pca_Class2: Prostate cancer stage 2

Pca_Class1: Prostate cancer stage 1

BrCa_Stg4: Breast cancer stage 4

BrCa_Stg3B: Breast cancer stage 3B

BrCa_Stg2A: Breast cancer stage 2A

BrCa_Stg2B: Breast cancer stage 2B

BrCa_Stg1A: Breast cancer stage 1A

BrCa_Stg1: Breast cancer stage 1

PD_1_R_Melanoma: Melanoma responder

PD_1_NR_Melanoma: Melanoma non responder

Table 18a ALS Probes - EpiSwitch™ markers to stratify ALS vs healthy controls

Probe	GeneName	Probe_Count_Total	Probe_Count_Sig	HyperG_Stats	FDR_HyperG	Percent_Sig	logFC
11_923549_925733_976127_979142_FR	AP2A2	19	8	0.006668	0.24512	42.11	-0.74197
11_36524913_36530925_36605543_36609927_FR	RAG1	46	16	0.001656	0.127493	34.78	-0.69372
1_161590754_161594100_161627152_161631654_RR	FCGR2B;FCGR3A	106	33	9.75E-05	0.015455	31.13	-0.68658
11_36531355_36534043_36605543_36609927_RR	RAG1	46	16	0.001656	0.127493	34.78	-0.68331
11_36531355_36534043_36605543_36609927_FR	RAG1	46	16	0.001656	0.127493	34.78	-0.66709
11_36588999_36590845_36605543_36609927_FR	RAG2;RAG1	10	4	0.064184	0.80436	40	-0.66598
11_36583119_36588432_36605543_36609927_RR	RAG2;RAG1	10	4	0.064184	0.80436	40	-0.66346
1_172061602_172067357_172083100_172087823_RF	DNM3	1004	200	0.000673	0.069123	19.92	-0.64487
1_171936106_171939290_172083100_172087823_RF	DNM3	1004	200	0.000673	0.069123	19.92	-0.63828
1_171811918_171813464_172083100_172087823_RF	DNM3	1004	200	0.000673	0.069123	19.92	-0.6224
1_172083100_172087823_172151185_172154127_FF	DNM3	1004	200	0.000673	0.069123	19.92	-0.62018
1_171887726_171889817_172083100_172087823_RF	DNM3	1004	200	0.000673	0.069123	19.92	-0.6103
13_111748012_111752622_111942125_111944243_RR	ARHGEF7	71	20	0.007714	0.24512	28.17	-0.59912
1_172083100_172087823_172212232_172223166_FF	DNM3	1004	200	0.000673	0.069123	19.92	-0.58901
11_36489037_36490716_36605543_36609927_FR	RAG1	46	16	0.001656	0.127493	34.78	-0.56054
16_31228760_31230406_31342509_31344379_FR	ITGAM	42	12	0.031165	0.564628	28.57	-0.5409
X_153269405_153271257_153287046_153289165_RR	IRAK1	3	2	0.070512	0.80436	66.67	-0.51331
13_111748012_111752622_111822569_111834523_RR	ARHGEF7	71	20	0.007714	0.24512	28.17	-0.50678
1_172053648_172060321_172083100_172087823_RR	DNM3	1004	200	0.000673	0.069123	19.92	-0.49381
6_112058283_112061400_112189648_112191961_RR	FYN	286	61	0.013161	0.344967	21.33	-0.49133
11_923549_925733_976127_979142_RR	AP2A2	19	8	0.006668	0.24512	42.11	-0.48405
6_111995015_111999450_112042041_112045568_FR	FYN	286	61	0.013161	0.344967	21.33	-0.48326
1_198560813_198564901_198619228_198622003_FF	PTPRC	140	33	0.015074	0.344967	23.57	-0.46857
1_198564901_198567426_198666515_198673906_FF	PTPRC	140	33	0.015074	0.344967	23.57	-0.46848
19_55146487_55148774_55168120_55169250_RR	LILRB4	9	4	0.044033	0.749763	44.44	-0.45415

Probe	GeneName	Probe_Count_Total	Probe_Count_Sig	HyperG_Stats	FDR_HyperG	Percent_Sig	logFC
1_161590754_161594100_161613514_161615341_RR	FCGR2B;FCGR3A	106	33	9.75E-05	0.015455	31.13	-0.45064
10_6639985_6645189_6663527_6669234_RR	PRKCQ	135	28	0.097688	0.81988	20.74	-0.44815
1_161495318_161496726_161576950_161581654_RF	FCGR3A	41	11	0.057992	0.80436	26.83	-0.44617
6_111995015_111999450_112042041_112045568_RR	FYN	286	61	0.013161	0.344967	21.33	-0.44013
16_31342509_31344379_31355595_31363682_RF	ITGAM	42	12	0.031165	0.564628	28.57	-0.43779
6_111968389_111970413_111988059_111992304_RF	FYN	286	61	0.013161	0.344967	21.33	-0.43175
6_112042041_112045568_112210969_112216626_RF	FYN	286	61	0.013161	0.344967	21.33	-0.43125
6_111988059_111992304_112042041_112045568_FR	FYN	286	61	0.013161	0.344967	21.33	-0.4278
6_112008166_112013438_112042041_112045568_RR	FYN	286	61	0.013161	0.344967	21.33	-0.42596
6_112042041_112045568_112061400_112062959_RF	FYN	286	61	0.013161	0.344967	21.33	-0.42515
6_112042041_112045568_112058283_112061400_RF	FYN	286	61	0.013161	0.344967	21.33	-0.42322
6_112042041_112045568_112189648_112191961_RF	FYN	286	61	0.013161	0.344967	21.33	-0.4227
11_923549_925733_976127_979142_RF	AP2A2	19	8	0.006668	0.24512	42.11	-0.41839
1_161496726_161500050_161560557_161562782_FF	FCGR3A	41	11	0.057992	0.80436	26.83	-0.41237
10_6474855_6481197_6530169_6531558_FR	PRKCQ	135	28	0.097688	0.81988	20.74	-0.41233
11_1010876_1013083_964245_969445_FF	AP2A2	19	8	0.006668	0.24512	42.11	-0.41196
8_42121759_42128721_42138740_42142593_FR	IKBKB	13	5	0.046252	0.749763	38.46	-0.40929
6_112042041_112045568_112109707_112111662_RF	FYN	286	61	0.013161	0.344967	21.33	-0.40843
1_172053648_172060321_172094882_172096647_RR	DNM3	1004	200	0.000673	0.069123	19.92	-0.40354
6_111982743_111987540_112042041_112045568_RR	FYN	286	61	0.013161	0.344967	21.33	-0.39579
6_112042041_112045568_112071383_112076102_RF	FYN	286	61	0.013161	0.344967	21.33	-0.39434
11_36507808_36510397_36605543_36609927_RR	RAG1	46	16	0.001656	0.127493	34.78	-0.38968
1_198564901_198567426_198619228_198622003_FF	PTPRC	140	33	0.015074	0.344967	23.57	-0.38595
12_54983093_54985391_55002281_55007763_RR	GLYCAM1	6	3	0.058173	0.80436	50	-0.38567
1_172053648_172060321_172111598_172120521_RR	DNM3	1004	200	0.000673	0.069123	19.92	-0.37565
1_161590754_161594100_161627152_161631654_RR	FCGR2B;FCGR3A	106	33	0.000098	0.015454931	31.13	-0.68658
10_6474855_6481197_6530169_6531558_FR	PRKCQ	135	28	0.097688	0.819879953	20.74	-0.41233
7_55089963_55093430_55294211_55302386_RF	EGFR	199	39	0.116519	0.819879953	19.6	-0.450938

Table 18b. ALS Probes - EpiSwitch™ markers to stratify ALS vs. healthy controls

Probe	AveExpr	t	P.Value	adj.P.Val	B	FC	FC_1	LS	Loop detected
11_923549_925733_976127_979142_FR	-0.74197	-6.35597	0.000138	0.044071	1.465965	0.597922	-1.67246	-1	ALS
11_36524913_36530925_36605543_36609927_FR	-0.69372	-4.70509	0.001143	0.045761	-0.49348	0.618257	-1.61745	-1	ALS
1_161590754_161594100_161627152_161631654_RR	-0.68658	-5.74114	0.00029	0.044071	0.788561	0.621327	-1.60946	-1	ALS
11_36531355_36534043_36605543_36609927_RR	-0.68331	-5.81653	0.000264	0.044071	0.874877	0.622736	-1.60582	-1	ALS
11_36531355_36534043_36605543_36609927_FR	-0.66709	-4.3522	0.001888	0.049346	-0.9712	0.629774	-1.58787	-1	ALS
11_36588999_36590845_36605543_36609927_FR	-0.66598	-4.62622	0.001276	0.046471	-0.59845	0.630261	-1.58664	-1	ALS
11_36583119_36588432_36605543_36609927_RR	-0.66346	-4.90718	0.000864	0.045761	-0.22922	0.631364	-1.58387	-1	ALS
1_172061602_172067357_172083100_172087823_RF	-0.64487	-5.96817	0.000219	0.044071	1.045707	0.639548	-1.5636	-1	ALS
1_171936106_171939290_172083100_172087823_RF	-0.63828	-5.97658	0.000217	0.044071	1.05507	0.642477	-1.55648	-1	ALS
1_171811918_171813464_172083100_172087823_RF	-0.6224	-5.88362	0.000243	0.044071	0.950922	0.649591	-1.53943	-1	ALS
1_172083100_172087823_172151185_172154127_FF	-0.62018	-5.9045	0.000237	0.044071	0.974434	0.650591	-1.53706	-1	ALS
1_171887726_171889817_172083100_172087823_RF	-0.6103	-5.86877	0.000248	0.044071	0.934149	0.655059	-1.52658	-1	ALS
13_111748012_111752622_111942125_111944243_RR	-0.59912	-5.06808	0.000695	0.045348	-0.02376	0.660154	-1.5148	-1	ALS
1_172083100_172087823_172212232_172223166_FF	-0.58901	-6.00417	0.00021	0.044071	1.085715	0.6648	-1.50421	-1	ALS
11_36489037_36490716_36605543_36609927_FR	-0.56054	-4.51138	0.001502	0.046471	-0.75317	0.678046	-1.47483	-1	ALS
16_31228760_31230406_31342509_31344379_FR	-0.5409	-6.15285	0.000175	0.044071	1.248786	0.687343	-1.45488	-1	ALS
X_153269405_153271257_153287046_153289165_RR	-0.51331	-4.49207	0.001544	0.046471	-0.7794	0.700615	-1.42732	-1	ALS
13_111748012_111752622_111822569_111834523_RR	-0.50678	-5.88851	0.000242	0.044071	0.956426	0.703792	-1.42087	-1	ALS

Probe	AveExpr	t	P.Value	adj.P.Val	B	FC	FC_1	LS	Loop detected
1_172053648_172060321_172083100_172087823_RR	-0.49381	-5.07129	0.000692	0.045348	-0.01971	0.710146	-1.40816	-1	ALS
6_112058283_112061400_112189648_112191961_RR	-0.49133	-5.76624	0.000281	0.044071	0.817402	0.71137	-1.40574	-1	ALS
11_923549_925733_976127_979142_RR	-0.48405	-4.33332	0.001941	0.049346	-0.99734	0.714966	-1.39867	-1	ALS
6_111995015_111999450_112042041_112045568_FR	-0.48326	-5.12181	0.000646	0.045348	0.043877	0.715362	-1.39789	-1	ALS
1_198560813_198564901_198619228_198622003_FF	-0.46857	-5.53965	0.000374	0.045348	0.553299	0.722683	-1.38373	-1	ALS
1_198564901_198567426_198666515_198673906_FF	-0.46848	-4.59704	0.00133	0.046471	-0.63757	0.722726	-1.38365	-1	ALS
19_55146487_55148774_55168120_55169250_RR	-0.45415	-3.59971	0.005845	0.066691	-2.05425	0.729942	-1.36997	-1	ALS
1_161590754_161594100_161613514_161615341_RR	-0.45064	-4.47431	0.001584	0.046791	-0.80357	0.73172	-1.36664	-1	ALS
10_6639985_6645189_6663527_6669234_RR	-0.44815	-5.15619	0.000617	0.045348	0.086906	0.732982	-1.36429	-1	ALS
1_161495318_161496726_161576950_161581654_RF	-0.44617	-6.57127	0.000107	0.044071	1.689256	0.733991	-1.36241	-1	ALS
6_111995015_111999450_112042041_112045568_RR	-0.44013	-4.82984	0.000961	0.045761	-0.32954	0.737066	-1.35673	-1	ALS
16_31342509_31344379_31355595_31363682_RF	-0.43779	-5.32335	0.000495	0.045348	0.293243	0.738265	-1.35453	-1	ALS
6_111968389_111970413_111988059_111992304_RF	-0.43175	-6.06363	0.000195	0.044071	1.151353	0.741361	-1.34887	-1	ALS
6_112042041_112045568_112210969_112216626_RF	-0.43125	-4.84006	0.000947	0.045761	-0.31623	0.741621	-1.3484	-1	ALS
6_111988059_111992304_112042041_112045568_FR	-0.4278	-4.61927	0.001289	0.046471	-0.60776	0.743394	-1.34518	-1	ALS
6_112008166_112013438_112042041_112045568_RR	-0.42596	-4.40407	0.001752	0.048299	-0.8997	0.744345	-1.34346	-1	ALS
6_112042041_112045568_112061400_112062959_RF	-0.42515	-4.68527	0.001175	0.045761	-0.51975	0.744764	-1.34271	-1	ALS
6_112042041_112045568_112058283_112061400_RF	-0.42322	-4.26948	0.00213	0.050442	-1.08611	0.745758	-1.34092	-1	ALS
6_112042041_112045568_112189648_112191961_RF	-0.4227	-4.40459	0.001751	0.048299	-0.89898	0.746026	-1.34044	-1	ALS

Probe	AveExpr	t	P.Value	adj.P.Val	B	FC	FC_1	LS	Loop detected
11_923549_925733_976127_979142_RF	-0.41839	-5.24568	0.000548	0.045348	0.197959	0.748257	-1.33644	-1	ALS
1_161496726_161500050_161560557_161562782_FF	-0.41237	-5.11609	0.000651	0.045348	0.036697	0.751389	-1.33087	-1	ALS
10_6474855_6481197_6530169_6531558_FR	-0.41233	-6.13891	0.000178	0.044071	1.233651	0.751408	-1.33084	-1	ALS
11_1010876_1013083_964245_969445_FF	-0.41196	-5.1686	0.000607	0.045348	0.102386	0.751603	-1.33049	-1	ALS
8_42121759_42128721_42138740_42142593_FR	-0.40929	-5.61946	0.000338	0.045348	0.647288	0.752995	-1.32803	-1	ALS
6_112042041_112045568_112109707_112111662_RF	-0.40843	-4.55006	0.001422	0.046471	-0.70081	0.753443	-1.32724	-1	ALS
1_172053648_172060321_172094882_172096647_RR	-0.40354	-3.84586	0.004005	0.059124	-1.6911	0.756	-1.32275	-1	ALS
6_111982743_111987540_112042041_112045568_RR	-0.39579	-4.65594	0.001224	0.045896	-0.55877	0.760075	-1.31566	-1	ALS
6_112042041_112045568_112071383_112076102_RF	-0.39434	-4.24316	0.002213	0.05138	-1.12291	0.760836	-1.31434	-1	ALS
11_36507808_36510397_36605543_36609927_RR	-0.38968	-3.63982	0.005493	0.064718	-1.99454	0.763301	-1.3101	-1	ALS
1_198564901_198567426_198619228_198622003_FF	-0.38595	-4.19734	0.002367	0.05251	-1.18721	0.765274	-1.30672	-1	ALS
12_54983093_54985391_55002281_55007763_RR	-0.38567	-5.1471	0.000625	0.045348	0.075549	0.765425	-1.30646	-1	ALS
1_172053648_172060321_172111598_172120521_RR	-0.37565	-3.78978	0.004362	0.060452	-1.77314	0.77076	-1.29742	-1	ALS
1_161590754_161594100_161627152_161631654_RR	-0.68658	-5.74114	0.000290	0.044071	0.788560	0.621327	-1.60946	-1	ALS
10_6474855_6481197_6530169_6531558_FR	-0.41233	-6.13891	0.000178	0.044071	1.233651	0.751408	-1.33084	-1	ALS
7_55089963_55093430_55294211_55302386_RF	-0.45094	-5.99775	7.84E-05	0.004052	1.891281	0.731567	-1.36693	-1	ALS

Table 18c. ALS Probes - EpiSwitch™ markers to stratify ALS vs. healthy controls

Probe	Probe sequence 60 mer
11_923549_925733_976127_979142_FR	GCCTGCAGGGGGCGCCCCCGCGCCTGCCTCGACCACACATCCACATGGACGCATGGCAGG
11_36524913_36530925_36605543_36609927_FR	TTATCAACCCGGCGTCTGGAACAATCGCTCGATCCACACCACACCAGCAGTGGGGCACAA
1_161590754_161594100_161627152_161631654_RR	AGGACAGAGACCCCTAATTCCACCACCATCGACCCTTCTGCTTTCTCTCCAGGGGATGGC
11_36531355_36534043_36605543_36609927_RR	CCGCCCCTGTCCTCTCGCTTCCCGCTGGTCGATCCACACCACACCAGCAGTGGGGCACAA
11_36531355_36534043_36605543_36609927_FR	AGTTCTTTCTTGAATTCTTTCCTGATACTCGATCCACACCACACCAGCAGTGGGGCACAA
11_36588999_36590845_36605543_36609927_FR	CCTGTAGCTCTGATGTCAGATGGCAATGTCGATCCACACCACACCAGCAGTGGGGCACAA
11_36583119_36588432_36605543_36609927_RR	CCACCTCATAGGGGAGGGCTTTACTCAGTCGATCCACACCACACCAGCAGTGGGGCACAA
1_172061602_172067357_172083100_172087823_RF	TCACCTCTGTCACCCACCCGTTCCACTCTCGATAAAGCACTTAGAACATGGCATATACTC
1_171936106_171939290_172083100_172087823_RF	TCACCTCTGTCACCCACCCGTTCCACTCTCGAATAGCTCCTATTGTTATGGAGTGTAGCA
1_171811918_171813464_172083100_172087823_RF	TCACCTCTGTCACCCACCCGTTCCACTCTCGAATTAGGAATCAGCATTTCTTCCACTGAG
1_172083100_172087823_172151185_172154127_FF	TCACCTCTGTCACCCACCCGTTCCACTCTCGATGCTCTCTTAGTGTTCCAATTCTCAGCT
1_171887726_171889817_172083100_172087823_RF	TCACCTCTGTCACCCACCCGTTCCACTCTCGAAATAGTAAAATTTGATTATCAAAATTTT
13_111748012_111752622_111942125_111944243_RR	TCCGTGACCCCCACAGCCGGTCGCCACATCGATTATCCAGAAGCTTCTTTTTTTTTAACC
1_172083100_172087823_172212232_172223166_FF	TCACCTCTGTCACCCACCCGTTCCACTCTCGAGGCTGCAGTGAATCATAATCATAGCACT
11_36489037_36490716_36605543_36609927_FR	AGTGTTGGTGAGATATTGTCTCTCAGTTTCGATCCACACCACACCAGCAGTGGGGCACAA
16_31228760_31230406_31342509_31344379_FR	GGTGGCATCCCCATCACTTCTCCATGCCTCGAGGTCCCCAACCCCCTGCCGCTCATCGTG
X_153269405_153271257_153287046_153289165_RR	TCCTGCCCACAGCCCCCGCTTTAGCCTCTCGAGAATGCTAACAGCACAGGATACAGTACT
13_111748012_111752622_111822569_111834523_RR	TCCGTGACCCCCACAGCCGGTCGCCACATCGAGTAGCTGAGATTACAGGCATGTACCACC

Probe	Probe sequence 60 mer
1_172053648_172060321_172083100_172087823_RR	CTCCACGTCACCCCATGTCAATTCCAAGTCGATGCCAGACACTCTTCTGGGGGTGGGGTG
6_112058283_112061400_112189648_112191961_RR	CCTCTGTCCACACCATTATTTTAAAGAGTCGACATGCCTTGCTTTACCATTGTTTAATTT
11_923549_925733_976127_979142_RR	AGTGGTACAATCATGAATCACTACAGCCTCGACCACACATCCACATGGACGCATGGCAGG
6_111995015_111999450_112042041_112045568_FR	CTCCCAAGGTAAACTCATTGCCGAAACCTCGAGTTGTTGCCACCCCACCCTCCTCAAACC
1_198560813_198564901_198619228_198622003_FF	TGTTTTTTATTGTTTGATGTCCAATGTATCGAGCCGCCCTTGACATAACACCATCTTTTA
1_198564901_198567426_198666515_198673906_FF	TTGAACCCAAGAGGTCACACCACTGCACTCGACGCCCAGCAAGTAGGCACAGTTCCCAAT
19_55146487_55148774_55168120_55169250_RR	TTGGAGCCCCCTGCCCTGCACACACAGCTCGAGATTTGTCTTTCTGTTCCTGGCTTATTT
1_161590754_161594100_161613514_161615341_RR	AGGACAGAGACCCCTAATTCCACCACCATCGAACAACTGCAAACTCCACTCAACATCTTT
10_6639985_6645189_6663527_6669234_RR	AACCACACAACTGCTACTCACAATTCTTTCGAAACCAGAAGACCCAATATAATATCTAGT
1_161495318_161496726_161576950_161581654_RF	ACCCAGGATAAAACGCAGTGTTGACCGATCGAGGGCGTGGACTTCTACACGTCCATCACT
6_111995015_111999450_112042041_112045568_RR	GGCTTATCCATGCTTAAATTGATTAACGTCGAGTTGTTGCCACCCCACCCTCCTCAAACC
16_31342509_31344379_31355595_31363682_RF	AGTGGTCTCACCATGGCTTTCTTCCAATTCGAGGTCCCCAACCCCCTGCCGCTCATCGTG
6_111968389_111970413_111988059_111992304_RF	GGAACTGCATCCATACTTGTTACACATCTCGAACCGGAGTGGACGTGTGTCCACATGTAA
6_112042041_112045568_112210969_112216626_RF	ATCTAAACACAGTCCATGCTAAAAAGCTTCGAGTTGTTGCCACCCCACCCTCCTCAAACC
6_111988059_111992304_112042041_112045568_FR	GGAACTGCATCCATACTTGTTACACATCTCGAGTTGTTGCCACCCCACCCTCCTCAAACC
6_112008166_112013438_112042041_112045568_RR	CTCAGGAAGAAGTGGATCCCTGTTTCTTTCGAGTTGTTGCCACCCCACCCTCCTCAAACC
6_112042041_112045568_112061400_112062959_RF	AGTGTATTTTTCACTACACTAGTGGTTTTCGAGTTGTTGCCACCCCACCCTCCTCAAACC
6_112042041_112045568_112058283_112061400_RF	TAAATACAGATGAAACCAACTAATAGACTCGAGTTGTTGCCACCCCACCCTCCTCAAACC
6_112042041_112045568_112189648_112191961_RF	AGCTGGGCCCCCAAAGGTTAAAAAGGACTTCGAGTTGTTGCCACCCCACCCTCCTCAAACC

Probe	Probe sequence 60 mer
11_923549_925733_976127_979142_RF	CCACGTGTCGCGGGCCTGAGTGTGCCCCTCGAGGCTGTAGTGATTCATGATTGTACCACT
1_161496726_161500050_161560557_161562782_FF	ACCTAGGATAAAAGGCAGTGTTGACCGATCGACACCCATATGAGCCCCACCCGGCTTCAA
10_6474855_6481197_6530169_6531558_FR	TTCCACCTGTAATACTGTGCCTGTATTCTCGAGCAGGCGCTCAACAAATACAACTTCCTT
11_1010876_1013083_964245_969445_FF	GTGCCCTCCTCGCCCCCTGATGGGTCTGGTCGAGACCAGCCTCAACATGGAGAAACACCAT
8_42121759_42128721_42138740_42142593_FR	CCACCCCCGCCCCGGGGGAGTCGCCCGGTCGAGGGCCTGGCAAGAAGACAGAAGCCGACT
6_112042041_112045568_112109707_112111662_RF	AAGTCCTAAGAACACTGAAAATCTCAGATCGAGTTGTTGCCACCCCACCCTCCTCAAACC
1_172053648_172060321_172094882_172096647_RR	CTCCACGTCACCCCATGTCAATTCCAAGTCGAATACTCAAAACAGAATTTGATATTCAAA
6_111982743_111987540_112042041_112045568_RR	CCAAATCCGAACCTCCTCTGTGAAGCATTCGAGTTGTTGCCACCCCACCCTCCTCAAACC
6_112042041_112045568_112071383_112076102_RF	GTTAACAGTAATACGATGTTAAAAGGACTCGAGTTGTTGCCACCCCACCCTCCTCAAACC
11_36507808_36510397_36605543_36609927_RR	GGCTGGCGGATTACTTGAAGCCAGGAGTTCGATCCACACCACCAGCAGTGGGGCACAA
1_198564901_198567426_198619228_198622003_FF	TTGAACCCAAGAGGTCACACCACTGCACTCGAGCCGCCCTTGACATAACACCATCTTTTA
12_54983093_54985391_55002281_55007763_RR	CCCCTAATTTAGCAAGCAGAAAGAGAACTCGATGCTTCATTTGACTCACACTCACATTTA
1_172053648_172060321_172111598_172120521_RR	CTCCACGTCACCCCATGTCAATTCCAAGTCGAAAATAAGTCGCTAGAGCCACATCAAGCA
1_161590754_161594100_161627152_161631654_RR	AGGACAGAGACCCCTAATTCCACCACCATCGACCCTTCTGCTTTCTCTCCAGGGGATGGC
10_6474855_6481197_6530169_6531558_FR	TTCCACCTGTAATACTGTGCCTGTATTCTCGAGCAGGCGCTCAACAAATACAACTTCCTT
7_55089963_55093430_55294211_55302386_RF	ACCAAACCCAAGGTCCGCTGCTCGCTGCTCGAATTCCCAACTGAGGGAGCTTTGTGGAAA

Table 18d. ALS Probes – EpiSwitch™ markers to stratify ALS v. healthy controls	Probe Location					4 kb Sequence Location				
Probe	Chr	Start1	End1	Start2	End2	Chr	Start1	End1	Start2	End2
11_923549_925733_976127_979142_FR	11	925704	925733	976128	976157	11	921734	925733	976128	980127
11_36524913_36530925_36605543_36609927_FR	11	36530896	36530925	36605544	36605573	11	36526926	36530925	36605544	36609543
1_161590754_161594100_161627152_161631654_RR	1	161590755	161590784	161627153	161627182	1	161590755	161594754	161627153	161631152
11_36531355_36534043_36605543_36609927_RR	11	36531356	36531385	36605544	36605573	11	36531356	36535355	36605544	36609543
11_36531355_36534043_36605543_36609927_FR	11	36534014	36534043	36605544	36605573	11	36530044	36534043	36605544	36609543
11_36588999_36590845_36605543_36609927_FR	11	36590816	36590845	36605544	36605573	11	36586846	36590845	36605544	36609543
11_36583119_36588432_36605543_36609927_RR	11	36583120	36583149	36605544	36605573	11	36583120	36587119	36605544	36609543
1_172061602_172067357_172083100_172087823_RF	1	172061603	172061632	172087794	172087823	1	172061603	172065602	172083824	172087823
1_171936106_171939290_172083100_172087823_RF	1	171936107	171936136	172087794	172087823	1	171936107	171940106	172083824	172087823
1_171811918_171813464_172083100_172087823_RF	1	171811919	171811948	172087794	172087823	1	171811919	171815918	172083824	172087823
1_172083100_172087823_172151185_172154127_FF	1	172087794	172087823	172154098	172154127	1	172083824	172087823	172150128	172154127
1_171887726_171889817_172083100_172087823_RF	1	171887727	171887756	172087794	172087823	1	171887727	171891726	172083824	172087823
13_111748012_111752622_111942125_111944243_RR	13	111748013	111748042	111942126	111942155	13	111748013	111752012	111942126	111946125
1_172083100_172087823_172212232_172223166_FF	1	172087794	172087823	172223137	172223166	1	172083824	172087823	172219167	172223166
11_36489037_36490716_36605543_36609927_FR	11	36490687	36490716	36605544	36605573	11	36486717	36490716	36605544	36609543

Table 18d. ALS Probes – EpiSwitch™ markers to stratify ALS v. healthy controls	Probe Location					4 kb Sequence Location				
Probe	Chr	Start1	End1	Start2	End2	Chr	Start1	End1	Start2	End2
16_31228760_31230406_31342509_31344379_FR	16	31230377	31230406	31342510	31342539	16	31226407	31230406	31342510	31346509
X_153269405_153271257_153287046_153289165_RR	X	153269406	153269435	153287047	153287076	X	153269406	153273405	153287047	153291046
13_111748012_111752622_111822569_111834523_RR	13	111748013	111748042	111822570	111822599	13	111748013	111752012	111822570	111826569
1_172053648_172060321_172083100_172087823_RR	1	172053649	172053678	172083101	172083130	1	172053649	172057648	172083101	172087100
6_112058283_112061400_112189648_112191961_RR	6	112058284	112058313	112189649	112189678	6	112058284	112062283	112189649	112193648
11_923549_925733_976127_979142_RR	11	923550	923579	976128	976157	11	923550	927549	976128	980127
6_111995015_111999450_112042041_112045568_FR	6	111999421	111999450	112042042	112042071	6	111995451	111999450	112042042	112046041
1_198560813_198564901_198619228_198622003_FF	1	198564872	198564901	198621974	198622003	1	198560902	198564901	198618004	198622003
1_198564901_198567426_198666515_198673906_FF	1	198567397	198567426	198673877	198673906	1	198563427	198567426	198669907	198673906
19_55146487_55148774_55168120_55169250_RR	19	55146488	55146517	55168121	55168150	19	55146488	55150487	55168121	55172120
1_161590754_161594100_161613514_161615341_RR	1	161590755	161590784	161613515	161613544	1	161590755	161594754	161613515	161617514
10_6639985_6645189_6663527_6669234_RR	10	6639986	6640015	6663528	6663557	10	6639986	6643985	6663528	6667527
1_161495318_161496726_161576950_161581654_RF	1	161495319	161495348	161581625	161581654	1	161495319	161499318	161577655	161581654
6_111995015_111999450_112042041_112045568_RR	6	111995016	111995045	112042042	112042071	6	111995016	111999015	112042042	112046041
16_31342509_31344379_31355595_31363682_RF	16	31342510	31342539	31363653	31363682	16	31342510	31346509	31359683	31363682

Table 18d. ALS Probes – EpiSwitch™ markers to stratify ALS v. healthy controls	Probe Location					4 kb Sequence Location				
Probe	Chr	Start1	End1	Start2	End2	Chr	Start1	End1	Start2	End2
6_111968389_111970413_111988059_111992304_RF	6	111968390	111968419	111992275	111992304	6	111968390	111972389	111988305	111992304
6_112042041_112045568_112210969_112216626_RF	6	112042042	112042071	112216597	112216626	6	112042042	112046041	112212627	112216626
6_111988059_111992304_112042041_112045568_FR	6	111992275	111992304	112042042	112042071	6	111988305	111992304	112042042	112046041
6_112008166_112013438_112042041_112045568_RR	6	112008167	112008196	112042042	112042071	6	112008167	112012166	112042042	112046041
6_112042041_112045568_112061400_112062959_RF	6	112042042	112042071	112062930	112062959	6	112042042	112046041	112058960	112062959
6_112042041_112045568_112058283_112061400_RF	6	112042042	112042071	112061371	112061400	6	112042042	112046041	112057401	112061400
6_112042041_112045568_112189648_112191961_RF	6	112042042	112042071	112191932	112191961	6	112042042	112046041	112187962	112191961
11_923549_925733_976127_979142_RF	11	923550	923579	979113	979142	11	923550	927549	975143	979142
1_161496726_161500050_161560557_161562782_FF	1	161500021	161500050	161562753	161562782	1	161496051	161500050	161558783	161562782
10_6474855_6481197_6530169_6531558_FR	10	6481168	6481197	6530170	6530199	10	6477198	6481197	6530170	6534169
11_1010876_1013083_964245_969445_FF	11	1013054	1013083	969416	969445	11	1009084	1013083	965446	969445
8_42121759_42128721_42138740_42142593_FR	8	42128692	42128721	42138741	42138770	8	42124722	42128721	42138741	42142740
6_112042041_112045568_112109707_112111662_RF	6	112042042	112042071	112111633	112111662	6	112042042	112046041	112107663	112111662
1_172053648_172060321_172094882_172096647_RR	1	172053649	172053678	172094883	172094912	1	172053649	172057648	172094883	172098882
6_111982743_111987540_112042041_112045568_RR	6	111982744	111982773	112042042	112042071	6	111982744	111986743	112042042	112046041

Table 18d. ALS Probes – EpiSwitch™ markers to stratify ALS v. healthy controls	Probe Location					4 kb Sequence Location				
Probe	Chr	Start1	End1	Start2	End2	Chr	Start1	End1	Start2	End2
6_112042041_112045568_112071383_112076102_RF	6	112042042	112042071	112076073	112076102	6	112042042	112046041	112072103	112076102
11_36507808_36510397_36605543_36609927_RR	11	36507809	36507838	36605544	36605573	11	36507809	36511808	36605544	36609543
1_198564901_198567426_198619228_198622003_FF	1	198567397	198567426	198621974	198622003	1	198563427	198567426	198618004	198622003
12_54983093_54985391_55002281_55007763_RR	12	54983094	54983123	55002282	55002311	12	54983094	54987093	55002282	55006281
1_172053648_172060321_172111598_172120521_RR	1	172053649	172053678	172111599	172111628	1	172053649	172057648	172111599	172115598
1_161590754_161594100_161627152_161631654_RR	1	161590754	161590783	161627152	161627181	1	161590754	161594753	161627152	161631151
10_6474855_6481197_6530169_6531558_FR	10	6481168	6481197	6530169	6530198	10	6477198	6481197	6530169	6534168
7_55089963_55093430_55294211_55302386_RF	7	55089963	55089992	55302357	55302386	7	55089963	55093962	55298387	55302386

Table 19a. Pre-type 2 diabetes mellitus probes - EpiSwitch™ markers to stratify pre-type 2 diabetes vs. healthy controls							
Probe	GeneLocus	Probe_Count_ Total	Probe_Count_ Sig	HyperG_ Stats	FDR_Hyper G	Percent_ Sig	logFC
IGF2_11_2162616_2164979_2210793_2214417_RF	IGF2	20	6	0.013782	0.264753	30	0.477536
ADCY5_3_123037100_123044621_123133741_123143812_RF	ADCY5	90	21	0.000309	0.032153	23.33	0.391689
TASP1_20_13265932_13269301_13507251_13521471_RR	TASP1	172	30	0.003377	0.154079	17.44	0.356789
TNFRSF1B_1_12241967_12245164_12269283_12270518_RR	TNFRSF1B	12	5	0.005227	0.162271	41.67	0.345092
SREBF1_17_17743896_17753157_17777190_17783023_RF	SREBF1	19	8	0.000366	0.032153	42.11	0.340726
TSPAN8_12_71690883_71707188_71850942_71857145_RF	TSPAN8	200	31	0.016203	0.295714	15.5	0.339978
CYB5R4_6_84553857_84562119_84611173_84616879_FF	CYB5R4	39	11	0.001648	0.085942	28.21	0.336289
KCNJ11_11_17401446_17405499_17445199_17452295_RF	KCNJ11	22	9	0.000203	0.032153	40.91	0.325425
PTPRD_9_9058670_9068143_9186543_9197535_FF	PTPRD	171	28	0.010775	0.218484	16.37	0.325058
ICAM1_19_10368390_10370561_10406169_10407761_RF	ICAM1	9	4	0.009728	0.218484	44.44	0.323175
ABCC8_11_17401446_17405499_17445199_17452295_RF	ABCC8	22	7	0.005571	0.162271	31.82	0.322412
CYP2C9_10_96661464_96668745_96741594_96747469_FR	CYP2C9	8	6	3.00E-05	0.010944	75	0.315667
KCNJ11_11_17401446_17405499_17419957_17422762_RF	KCNJ11	22	9	0.000203	0.032153	40.91	0.313372
LEP_7_127838673_127843908_127864269_127868140_RF	LEP	19	6	0.010562	0.218484	31.58	0.308548
CDKN2A_9_21967880_21969373_22029988_22034038_RR	CDKN2A	13	6	0.001156	0.070344	46.15	0.306887
CACNA1C_12_2099248_2111840_2394923_2398377_FR	CACNA1C	197	33	0.004207	0.162271	16.75	0.306732
PIK3R3_1_46633134_46639474_46678880_46685388_RF	PIK3R3	17	6	0.00578	0.162271	35.29	0.305924
ABCC8_11_17445199_17452295_17545007_17546815_RF	ABCC8	22	7	0.005571	0.162271	31.82	0.30417
CDKN2A_9_21967880_21969373_22029988_22034038_RF	CDKN2A	13	6	0.001156	0.070344	46.15	0.30104
KCNJ11_11_17419957_17422762_17445199_17452295_RR	KCNJ11	22	9	0.000203	0.032153	40.91	0.299727
ICAM1_19_10341612_10343024_10406169_10407761_RF	ICAM1	9	4	0.009728	0.218484	44.44	0.298038
SREBF1_17_17722022_17726360_17743896_17753157_RR	SREBF1	19	8	0.000366	0.032153	42.11	0.296794
IGF2_11_2162616_2164979_2191728_2194389_FF	IGF2	20	6	0.013782	0.264753	30	0.293116
ABCC8_11_17419957_17422762_17445199_17452295_RR	ABCC8	22	7	0.005571	0.162271	31.82	0.290947
CACNA1C_12_2099248_2111840_2221145_2224007_FR	CACNA1C	197	33	0.004207	0.162271	16.75	0.280735
INS_11_2191728_2194389_2210793_2214417_RF	INS	17	6	0.00578	0.162271	35.29	0.275842
MAPK10_4_87459424_87462716_87493751_87502639_FF	MAPK10	171	28	0.010775	0.218484	16.37	0.274476
PTPRD_9_8886566_8895563_9186543_9197535_FF	PTPRD	171	28	0.010775	0.218484	16.37	0.273693

Table 19a. Pre-type 2 diabetes mellitus probes - EpiSwitch™ markers to stratify pre-type 2 diabetes vs. healthy controls

Probe	GeneLocus	Probe_Count_Total	Probe_Count_Sig	HyperG_Stats	FDR_HyperG	Percent_Sig	logFC
CDKN2A_9_22005914_22007156_22029988_22034038_RF	CDKN2A	13	6	0.001156	0.070344	46.15	0.273046
LEP_7_127838673_127843908_127903727_127906543_RF	LEP	19	6	0.010562	0.218484	31.58	0.272802
TSPAN8_12_71559221_71564078_71667712_71675824_RR	TSPAN8	200	31	0.016203	0.295714	15.5	0.27188
CYB5R4_6_84533887_84541872_84600402_84604101_RF	CYB5R4	39	11	0.001648	0.085942	28.21	0.271658
CYP2C9_10_96661464_96668745_96755577_96760846_FF	CYP2C9	8	6	3.00E-05	0.010944	75	0.270453
TSPAN8_12_71559221_71564078_71675824_71684278_RF	TSPAN8	200	31	0.016203	0.295714	15.5	0.266085
CYB5R4_6_84533887_84541872_84611173_84616879_FF	CYB5R4	39	11	0.001648	0.085942	28.21	0.265364
TASP1_20_13441063_13442565_13507251_13521471_FR	TASP1	172	30	0.003377	0.154079	17.44	0.255345
KCNJ11_11_17430922_17433660_17445199_17452295_RR	KCNJ11	22	9	0.000203	0.032153	40.91	0.25388
INS_11_2162616_2164979_2191728_2194389_FF	INS	17	6	0.00578	0.162271	35.29	0.253761
PTPRD_9_9551379_9564487_9852099_9857206_RR	PTPRD	171	28	0.010775	0.218484	16.37	0.253043
IGF2_11_2162616_2164979_2191728_2194389_RR	IGF2	20	6	0.013782	0.264753	30	0.251753
TNFRSF1B_1_12241967_12245164_12274102_12277104_RF	TNFRSF1B	12	5	0.005227	0.162271	41.67	0.251298
TSPAN8_12_71667712_71675824_71850942_71857145_RF	TSPAN8	200	31	0.016203	0.295714	15.5	0.248869
CACNA1C_12_2099248_2111840_2200229_2202042_RF	CACNA1C	197	33	0.004207	0.162271	16.75	0.24864
CYP2C9_10_96690028_96694118_96748928_96755577_FR	CYP2C9	8	6	3.00E-05	0.010944	75	0.247789
TSPAN8_12_71559221_71564078_71690883_71707188_RR	TSPAN8	200	31	0.016203	0.295714	15.5	0.24768
ABCC8_11_17445199_17452295_17514252_17516772_RF	ABCC8	22	7	0.005571	0.162271	31.82	0.247675
ADCY5_3_123098260_123106114_123133741_123143812_RF	ADCY5	90	21	0.000309	0.032153	23.33	0.245589
IGF2_11_2191728_2194389_2210793_2214417_RF	IGF2	20	6	0.013782	0.264753	30	0.244894
SREBF1_17_17722022_17726360_17743896_17753157_FR	SREBF1	19	8	0.000366	0.032153	42.11	0.243916
ABCC8_11_17445199_17452295_17538995_17541116_RF	ABCC8	22	7	0.005571	0.162271	31.82	0.243453

Table 19b. Pre-type 2 diabetes mellitus probes - EpiSwitch™ markers to stratify pre-type 2 diabetes vs. healthy controls

Probe	AveExpr	t	P.Value	adj.P.Val	B	FC	FC_1	LS	Loop detected
IGF2_11_2162616_2164979_2210793_2214417_RF	0.477536	3.535151	0.006208	0.083614	-2.156406	1.392363	1.392363	1	pre-T2DM
ADCY5_3_123037100_123044621_123133741_123143812_RF	0.391689	3.616002	0.005464	0.080553	-2.032765	1.311928	1.311928	1	pre-T2DM
TASP1_20_13265932_13269301_13507251_13521471_RR	0.356789	6.963954	6.09E-05	0.036169	2.219697	1.280572	1.280572	1	pre-T2DM
TNFRSF1B_1_12241967_12245164_12269283_12270518_RR	0.345092	5.317703	0.000458	0.047353	0.352959	1.270232	1.270232	1	pre-T2DM
SREBF1_17_17743896_17753157_17777190_17783023_RF	0.340726	5.383925	0.000419	0.046852	0.436391	1.266394	1.266394	1	pre-T2DM
TSPAN8_12_71690883_71707188_71850942_71857145_RF	0.339978	6.894591	6.59E-05	0.036169	2.149351	1.265738	1.265738	1	pre-T2DM
CYB5R4_6_84553857_84562119_84611173_84616879_FF	0.336289	4.684603	0.001097	0.053336	-0.481351	1.262505	1.262505	1	pre-T2DM
KCNJ11_11_17401446_17405499_17445199_17452295_RF	0.325425	5.839875	0.000232	0.042245	0.991283	1.253034	1.253034	1	pre-T2DM
PTPRD_9_9058670_9068143_9186543_9197535_FF	0.325058	6.01299	0.000187	0.04041	1.193155	1.252715	1.252715	1	pre-T2DM
ICAM1_19_10368390_10370561_10406169_10407761_RF	0.323175	4.217282	0.002171	0.060012	-1.139093	1.251081	1.251081	1	pre-T2DM
ABCC8_11_17401446_17405499_17445199_17452295_RF	0.322412	6.516205	0.000102	0.037879	1.753307	1.250419	1.250419	1	pre-T2DM
CYP2C9_10_96661464_96668745_96741594_96747469_FR	0.315667	5.688997	0.000282	0.042245	0.811417	1.244587	1.244587	1	pre-T2DM
KCNJ11_11_17401446_17405499_17419957_17422762_RF	0.313372	6.220593	0.000145	0.039036	1.428992	1.242609	1.242609	1	pre-T2DM
LEP_7_127838673_127843908_127864269_127868140_RF	0.308548	6.038536	0.000181	0.04041	1.22254	1.23846	1.23846	1	pre-T2DM
CDKN2A_9_21967880_21969373_22029988_22034038_RR	0.306887	4.203439	0.002217	0.060605	-1.159095	1.237036	1.237036	1	pre-T2DM
CACNA1C_12_2099248_2111840_2394923_2398377_FR	0.306732	6.600332	9.23E-05	0.037879	1.843184	1.236903	1.236903	1	pre-T2DM
PIK3R3_1_46633134_46639474_46678880_46685388_RF	0.305924	5.715643	0.000272	0.042245	0.843449	1.23621	1.23621	1	pre-T2DM
ABCC8_11_17445199_17452295_17545007_17546815_RF	0.30417	6.346622	0.000125	0.037879	1.568892	1.234708	1.234708	1	pre-T2DM

Table 19b. Pre-type 2 diabetes mellitus probes - EpiSwitch™ markers to stratify pre-type 2 diabetes vs. healthy controls

Probe	AveExpr	t	P.Value	adj.P.Val	B	FC	FC_1	LS	Loop detected
CDKN2A_9_21967880_21969373_22029988_22034038_RF	0.30104	3.555782	0.006008	0.083182	-2.124789	1.232032	1.232032	1	pre-T2DM
KCNJ11_11_17419957_17422762_17445199_17452295_RR	0.299727	6.400185	0.000117	0.037879	1.627611	1.230911	1.230911	1	pre-T2DM
ICAM1_19_10341612_10343024_10406169_10407761_RF	0.298038	3.7795	0.004231	0.076034	-1.785033	1.229471	1.229471	1	pre-T2DM
SREBF1_17_17722022_17726360_17743896_17753157_RR	0.296794	5.555377	0.000335	0.04429	0.649035	1.228411	1.228411	1	pre-T2DM
IGF2_11_2162616_2164979_2191728_2194389_FF	0.293116	4.660277	0.001136	0.053336	-0.514728	1.225284	1.225284	1	pre-T2DM
ABCC8_11_17419957_17422762_17445199_17452295_RR	0.290947	5.099022	0.000615	0.049081	0.072288	1.223443	1.223443	1	pre-T2DM
CACNA1C_12_2099248_2111840_2221145_2224007_FR	0.280735	5.809957	0.000241	0.042245	0.955909	1.214814	1.214814	1	pre-T2DM
INS_11_2191728_2194389_2210793_2214417_RF	0.275842	4.673253	0.001115	0.053336	-0.496912	1.210701	1.210701	1	pre-T2DM
MAPK10_4_87459424_87462716_87493751_87502639_FF	0.274476	4.833587	0.000889	0.053336	-0.279053	1.209554	1.209554	1	pre-T2DM
PTPRD_9_8886566_8895563_9186543_9197535_FF	0.273693	4.733721	0.001023	0.053336	-0.414255	1.208898	1.208898	1	pre-T2DM
CDKN2A_9_22005914_22007156_22029988_22034038_RF	0.273046	6.139505	0.00016	0.039221	1.337681	1.208357	1.208357	1	pre-T2DM
LEP_7_127838673_127843908_127903727_127906543_RF	0.272802	6.193991	0.00015	0.039186	1.399149	1.208152	1.208152	1	pre-T2DM
TSPAN8_12_71559221_71564078_71667712_71675824_RR	0.27188	4.533782	0.001363	0.055293	-0.689833	1.207381	1.207381	1	pre-T2DM
CYB5R4_6_84533887_84541872_84600402_84604101_RF	0.271658	4.921912	0.000785	0.053336	-0.160847	1.207194	1.207194	1	pre-T2DM
CYP2C9_10_96661464_96668745_96755577_96760846_FF	0.270453	4.918804	0.000789	0.053336	-0.164985	1.206187	1.206187	1	pre-T2DM
TSPAN8_12_71559221_71564078_71675824_71684278_RF	0.266085	4.741123	0.001013	0.053336	-0.404177	1.20254	1.20254	1	pre-T2DM
CYB5R4_6_84533887_84541872_84611173_84616879_FF	0.265364	3.734665	0.004537	0.076978	-1.852645	1.20194	1.20194	1	pre-T2DM
TASP1_20_13441063_13442565_13507251_13521471_FR	0.255345	4.438612	0.001565	0.055431	-0.823269	1.193621	1.193621	1	pre-T2DM

Table 19b. Pre-type 2 diabetes mellitus probes - EpiSwitch™ markers to stratify pre-type 2 diabetes vs. healthy controls

Probe	AveExpr	t	P.Value	adj.P.Val	B	FC	FC_1	LS	Loop detected
KCNJ11_11_17430922_17433660_17445199_17452295_RR	0.25388	5.45502	0.000382	0.046163	0.525154	1.192409	1.192409	1	pre-T2DM
INS_11_2162616_2164979_2191728_2194389_FF	0.253761	4.302499	0.001913	0.058469	-1.016596	1.192311	1.192311	1	pre-T2DM
PTPRD_9_9551379_9564487_9852099_9857206_RR	0.253043	5.604223	0.000314	0.044166	0.708733	1.191718	1.191718	1	pre-T2DM
IGF2_11_2162616_2164979_2191728_2194389_RR	0.251753	4.52036	0.00139	0.055424	-0.708564	1.190653	1.190653	1	pre-T2DM
TNFRSF1B_1_12241967_12245164_12274102_12277104_RF	0.251298	5.26762	0.00049	0.048568	0.28938	1.190277	1.190277	1	pre-T2DM
TSPAN8_12_71667712_71675824_71850942_71857145_RF	0.248869	5.506825	0.000357	0.045219	0.589309	1.188275	1.188275	1	pre-T2DM
CACNA1C_12_2099248_2111840_2200229_2202042_RF	0.24864	4.853482	0.000864	0.053336	-0.252315	1.188087	1.188087	1	pre-T2DM
CYP2C9_10_96690028_96694118_96748928_96755577_FR	0.247789	4.674106	0.001114	0.053336	-0.495742	1.187386	1.187386	1	pre-T2DM
TSPAN8_12_71559221_71564078_71690883_71707188_RR	0.24768	4.287891	0.001955	0.058885	-1.037516	1.187296	1.187296	1	pre-T2DM
ABCC8_11_17445199_17452295_17514252_17516772_RF	0.247675	5.217723	0.000524	0.048568	0.225622	1.187292	1.187292	1	pre-T2DM
ADCY5_3_123098260_123106114_123133741_123143812_RF	0.245589	4.056041	0.002768	0.065995	-1.37385	1.185577	1.185577	1	pre-T2DM
IGF2_11_2191728_2194389_2210793_2214417_RF	0.244894	3.926099	0.003374	0.070388	-1.565763	1.185005	1.185005	1	pre-T2DM
SREBF1_17_17722022_17726360_17743896_17753157_FR	0.243916	3.351811	0.008314	0.09188	-2.439215	1.184203	1.184203	1	pre-T2DM
ABCC8_11_17445199_17452295_17538995_17541116_RF	0.243453	4.73022	0.001028	0.053336	-0.419024	1.183822	1.183822	1	pre-T2DM

Table 19c. Pre-type 2 DM Probes - EpiSwitch™ markers to stratify Pre-type 2 DM vs. healthy controls

Probe	60 mer	Probe sequence
IGF2_11_2162616_2164979_2210793_2214417_RF	CTCCTCAAAAAAAAGAGGAGGCCCAGGCTCGAGACTCCAGAAAAATAGATTACAGGTTTG	
ADCY5_3_123037100_123044621_123133741_123143812_RF	TTTAGCCAAAAAGAAAAAAAAGGTTCATTTCGAGAACCAGAGTCAAACTTAGACCCCAGGA	
TASP1_20_13265932_13269301_13507251_13521471_RR	TCCTTTCTTTTTTATTTTTTAAGCTGTTTCGATTCAACATTAATTCATTTTAGACTTCTC	
TNFRSF1B_1_12241967_12245164_12269283_12270518_RR	ACCAGCCCTGGGTTCTTAAGGATGGGTGTCGACCCCTGGCTCTGCCTGGGGTCTGGGCTT	
SREBF1_17_17743896_17753157_17777190_17783023_RF	ACATCTCAGACATGACTTTTGTGTTTCCTCGAGCCTTTTCGGGCAGGCGTCCAGCACGGG	
TSPAN8_12_71690883_71707188_71850942_71857145_RF	CTCAGACTGTATATTCTCTTAGCTTCAGTCGAGCTGTTTCTTTATATGGTCTCTGCTATC	
CYB5R4_6_84553857_84562119_84611173_84616879_FF	ATTATAACATTTATATATCATCTTTTCCTCGAGGTTGCAGTAAGCTGATCATGCCACTAC	
KCNJ11_11_17401446_17405499_17445199_17452295_RF	GACCAAACAGCTGTGGTTTGGCCATCACTCGAGAGAGAGCCTGTGTGAGGAGTGCAGTCA	
PTPRD_9_9058670_9068143_9186543_9197535_FF	CTTTTAGCTTTTACTTAGCATAATTTTCTCGAGAGGGTGGGGCAGGAGAATCTCTTGAAC	
ICAM1_19_10368390_10370561_10406169_10407761_RF	GGAAGGCCGAGGCGGCCAGATCACGAGGTCGAACCTCCTGATAACTTCAGCATTAACAGC	
ABCC8_11_17401446_17405499_17445199_17452295_RF	GACCAAACAGCTGTGGTTTGGCCATCACTCGAGAGAGAGCCTGTGTGAGGAGTGCAGTCA	
CYP2C9_10_96661464_96668745_96741594_96747469_FR	GAGTAGGTAAACAAAGCAGTCAGGAAGCTCGAGTCTTTGGTTTTCCCTAGATAATTAATA	
KCNJ11_11_17401446_17405499_17419957_17422762_RF	CTTAGAGCAAAGGCTAGGCTCAGTAATGTCGAGAGAGAGCCTGTGTGAGGAGTGCAGTCA	
LEP_7_127838673_127843908_127864269_127868140_RF	AGATCAAATCCAGTTTAAGGCTACTCCTTCGATTCATACACCATTCAGGGTATACAATAG	
CDKN2A_9_21967880_21969373_22029988_22034038_RR	TTGCGAGCCTCGCAGCCTCCGGAAGCTGTCGATTTTAAGTCTATTTTGTTAGATCTAAAG	
CACNA1C_12_2099248_2111840_2394923_2398377_FR	ACTGACAGTTTCTTGGGATTCTCCAGACTCGAGAGAGGCTGGTGCGCACCTACCCAGCGG	
PIK3R3_1_46633134_46639474_46678880_46685388_RF	CCACTCCCCCAGGCTTACCTGCGAGCCATCGAGGTGGGCCTGGGTTCTCGTGGAGGGAGA	
ABCC8_11_17445199_17452295_17545007_17546815_RF	CCATCCTGGACGCAGAATGTAGTCCCGTTCGAACAGAGCTGGGAGCTGGGGCCTAGGCTA	

Table 19c. Pre-type 2 DM Probes - EpiSwitch™ markers to stratify Pre-type 2 DM vs. healthy controls	Probe sequence
Probe	60 mer
CDKN2A_9_21967880_21969373_22029988_22034038_RF	TGCTTTTTAAAAAATCAAAGGTGTAACTTCGACAGCTTCCGGAGGCTGCGAGGCTCGCAA
KCNJ11_11_17419957_17422762_17445199_17452295_RR	TATGAGGCCCGGTTCCAGCAGAAGCTTCTCGAACAGAGCTGGGAGCTGGGGCCTAGGCTA
ICAM1_19_10341612_10343024_10406169_10407761_RF	GGAAGGCCGAGGCGGCCAGATCACGAGGTCGAAAGCGCTCGGATTCAGCCTTCTCCCCGG
SREBF1_17_17722022_17726360_17743896_17753157_RR	ATGGACAGTAGGCAGGATGAATAAGTGCTCGAGCCTTTTCGGGCAGGCGTCCAGCACGGG
IGF2_11_2162616_2164979_2191728_2194389_FF	TAACGTCCAAGAAAATTATTGTGACCCGTCGAGAAGTCAGGGAGCGTCTAGGGCTTCTGG
ABCC8_11_17419957_17422762_17445199_17452295_RR	TATGAGGCCCGGTTCCAGCAGAAGCTTCTCGAACAGAGCTGGGAGCTGGGGCCTAGGCTA
CACNA1C_12_2099248_2111840_2221145_2224007_FR	ACTGACAGTTTCTTGGGATTCTCCAGACTCGAGGCCTGGAGAAGCCCAGGAGGAGGCGTG
INS_11_2191728_2194389_2210793_2214417_RF	CTCCTCAAAAAAAAGAGGAGGCCCAGGCTCGATCCCAGAGCCGTCCCAGGCCTGGACAGA
MAPK10_4_87459424_87462716_87493751_87502639_FF	AGGCTGAACTTCAAATGTGATAATAACCTCGACTTAATTTTATTACAGCACTAATATAAT
PTPRD_9_8886566_8895563_9186543_9197535_FF	GACTTCAACTCACTATGAATAAATAAAATCGAGAGGGTGGGGCAGGAGAATCTCTTGAAC
CDKN2A_9_22005914_22007156_22029988_22034038_RF	TGCTTTTTAAAAAATCAAAGGTGTAACTTCGAATTAGGTGGGTGGGGGTGGGAAATTGGG
LEP_7_127838673_127843908_127903727_127906543_RF	ATAAGAAACTGAATTTAAATGCTCTCTTTCGATTCATACACCATTCAGGGTATACAATAG
TSPAN8_12_71559221_71564078_71667712_71675824_RR	AAGGTCTTCAGCTTCACTCCTGAAGCCATCGAGTTCTGTACTTAAGCAAACATTATCCTT
CYB5R4_6_84533887_84541872_84600402_84604101_RF	CCATGTTGTAATATTGGATTTTTATCATTCGATATAGTGGTTTCTAGGTATCATGGTAAA
CYP2C9_10_96661464_96668745_96755577_96760846_FF	GAGTAGGTAAACAAAGCAGTCAGGAAGCTCGATCCAGTGTGCTTTTCACTTCAGACCTTG
TSPAN8_12_71559221_71564078_71675824_71684278_RF	AATATCTTTTCATTTTTTGGTGAAGTCTTCGATGGCTTCAGGAGTGAAGCTGAAGACCTT
CYB5R4_6_84533887_84541872_84611173_84616879_FF	TGTTCAATCAAAGGAAGGGATAACACTATCGAGGTTGCAGTAAGCTGATCATGCCACTAC
TASP1_20_13441063_13442565_13507251_13521471_FR	GATGTTTATACAAGATTCATTCTTTCCATCGATTCAACATTAATTCATTTTAGACTTCTC

Table 19c. Pre-type 2 DM Probes - EpiSwitch™ markers to stratify Pre-type 2 DM vs. healthy controls

Probe	Probe sequence
	60 mer
KCNJ11_11_17430922_17433660_17445199_17452295_RR	TTCCTTGAGGAATCAGTGATCAGGACTCTCGAACAGAGCTGGGAGCTGGGGCCTAGGCTA
INS_11_2162616_2164979_2191728_2194389_FF	TAACGTCCAAGAAAATTATTGTGACCCGTCGAGAAGTCAGGGAGCGTCTAGGGCTTCTGG
PTPRD_9_9551379_9564487_9852099_9857206_RR	TAGTACTACCACTGGAAAGCTAGAATATTCGATGCATTAAAATGTTCTCGGAAAGAGATA
IGF2_11_2162616_2164979_2191728_2194389_RR	CAAACCTGTAATCTATTTTTCTGGAGTCTCGATCCCAGAGCCGTCCCAGGCCTGGACAGA
TNFRSF1B_1_12241967_12245164_12274102_12277104_RF	GTTGAGGCTGCAATAAACCGTGATCAAGTCGACACCCATCCTTAAGAACCCAGGGCTGGT
TSPAN8_12_71667712_71675824_71850942_71857145_RF	CTCAGACTGTATATTCTCTTAGCTTCAGTCGAGTTCTGTACTTAAGCAAACATTATCCTT
CACNA1C_12_2099248_2111840_2200229_2202042_RF	GGAAATGAGTCTCATGTCTAATTAAATGTCGAAGTTAAGGTTTCTTGGTTCAAGTGGTGT
CYP2C9_10_96690028_96694118_96748928_96755577_FR	TGAGGTAGGCAGATCACAGGTCAGGAGATCGACCTCCATTACGGAGAGTTTCCTATGTTT
TSPAN8_12_71559221_71564078_71690883_71707188_RR	AAGGTCTTCAGCTTCACTCCTGAAGCCATCGAGCTGTTTCTTTATATGGTCTCTGCTATC
ABCC8_11_17445199_17452295_17514252_17516772_RF	TGGGCTCCTTCAGCCCCACATGCCTGGTTCGAACAGAGCTGGGAGCTGGGGCCTAGGCTA
ADCY5_3_123098260_123106114_123133741_123143812_RF	TTTAGCCAAAAAGAAAAAAAAGGTTCATTTCGAGGAATGTTTCCAAGCAATTCTCTCTGCT
IGF2_11_2191728_2194389_2210793_2214417_RF	CTCCTCAAAAAAAAGAGGAGGCCCAGGCTCGATCCCAGAGCCGTCCCAGGCCTGGACAGA
SREBF1_17_17722022_17726360_17743896_17753157_FR	CCCTTTACCCCAGTCCGTGTGAGCCTCTTCGAGCCTTTTCGGGCAGGCGTCCAGCACGGG
ABCC8_11_17445199_17452295_17538995_17541116_RF	GGATTACTTCCATGAGAAGCAATTAAAATCGAACAGAGCTGGGAGCTGGGGCCTAGGCTA

Table 19d. Pre-type 2 diabetes mellitus probes - EpiSwitch™ markers to stratify pre-type 2 diabetes vs. healthy controls	Probe Location					4 kb Sequence Location				
Probe	Chr	Start1	End1	Start2	End2	Chr	Start1	End1	Start2	End2
IGF2_11_2162616_2164979_2210793_2214417_RF	11	2162617	2162646	2214388	2214417	11	2162617	2166616	2210418	2214417
ADCY5_3_123037100_123044621_123133741_123143812_RF	3	123037101	123037130	123143783	123143812	3	123037101	123041100	123139813	123143812
TASP1_20_13265932_13269301_13507251_13521471_RR	20	13265933	13265962	13507252	13507281	20	13265933	13269932	13507252	13511251
TNFRSF1B_1_12241967_12245164_12269283_12270518_RR	1	12241968	12241997	12269284	12269313	1	12241968	12245967	12269284	12273283
SREBF1_17_17743896_17753157_17777190_17783023_RF	17	17743897	17743926	17782994	17783023	17	17743897	17747896	17779024	17783023
TSPAN8_12_71690883_71707188_71850942_71857145_RF	12	71690884	71690913	71857116	71857145	12	71690884	71694883	71853146	71857145
CYB5R4_6_84553857_84562119_84611173_84616879_FF	6	84562090	84562119	84616850	84616879	6	84558120	84562119	84612880	84616879
KCNJ11_11_17401446_17405499_17445199_17452295_RF	11	17401447	17401476	17452266	17452295	11	17401447	17405446	17448296	17452295
PTPRD_9_9058670_9068143_9186543_9197535_FF	9	9068114	9068143	9197506	9197535	9	9064144	9068143	9193536	9197535
ICAM1_19_10368390_10370561_10406169_10407761_RF	19	10368391	10368420	10407732	10407761	19	10368391	10372390	10403762	10407761
ABCC8_11_17401446_17405499_17445199_17452295_RF	11	17401447	17401476	17452266	17452295	11	17401447	17405446	17448296	17452295
CYP2C9_10_96661464_96668745_96741594_96747469_FR	10	96668716	96668745	96741595	96741624	10	96664746	96668745	96741595	96745594
KCNJ11_11_17401446_17405499_17419957_17422762_RF	11	17401447	17401476	17422733	17422762	11	17401447	17405446	17418763	17422762
LEP_7_127838673_127843908_127864269_127868140_RF	7	127838674	127838703	127868111	127868140	7	127838674	127842673	127864141	127868140

Table 19d. Pre-type 2 diabetes mellitus probes - EpiSwitch™ markers to stratify pre-type 2 diabetes vs. healthy controls	Probe Location					4 kb Sequence Location				
Probe	Chr	Start1	End1	Start2	End2	Chr	Start1	End1	Start2	End2
CDKN2A_9_21967880_21969373_22029988_22034038_RR	9	21967881	21967910	22029989	22030018	9	21967881	21971880	22029989	22033988
CACNA1C_12_2099248_2111840_2394923_2398377_FR	12	2111811	2111840	2394924	2394953	12	2107841	2111840	2394924	2398923
PIK3R3_1_46633134_46639474_46678880_46685388_RF	1	46633135	46633164	46685359	46685388	1	46633135	46637134	46681389	46685388
ABCC8_11_17445199_17452295_17545007_17546815_RF	11	17445200	17445229	17546786	17546815	11	17445200	17449199	17542816	17546815
CDKN2A_9_21967880_21969373_22029988_22034038_RF	9	21967881	21967910	22034009	22034038	9	21967881	21971880	22030039	22034038
KCNJ11_11_17419957_17422762_17445199_17452295_RR	11	17419958	17419987	17445200	17445229	11	17419958	17423957	17445200	17449199
ICAM1_19_10341612_10343024_10406169_10407761_RF	19	10341613	10341642	10407732	10407761	19	10341613	10345612	10403762	10407761
SREBF1_17_17722022_17726360_17743896_17753157_RR	17	17722023	17722052	17743897	17743926	17	17722023	17726022	17743897	17747896
IGF2_11_2162616_2164979_2191728_2194389_FF	11	2164950	2164979	2194360	2194389	11	2160980	2164979	2190390	2194389
ABCC8_11_17419957_17422762_17445199_17452295_RR	11	17419958	17419987	17445200	17445229	11	17419958	17423957	17445200	17449199
CACNA1C_12_2099248_2111840_2221145_2224007_FR	12	2111811	2111840	2221146	2221175	12	2107841	2111840	2221146	2225145
INS_11_2191728_2194389_2210793_2214417_RF	11	2191729	2191758	2214388	2214417	11	2191729	2195728	2210418	2214417
MAPK10_4_87459424_87462716_87493751_87502639_FF	4	87462687	87462716	87502610	87502639	4	87458717	87462716	87498640	87502639
PTPRD_9_8886566_8895563_9186543_9197535_FF	9	8895534	8895563	9197506	9197535	9	8891564	8895563	9193536	9197535

Table 19d. Pre-type 2 diabetes mellitus probes - EpiSwitch™ markers to stratify pre-type 2 diabetes vs. healthy controls	Probe Location					4 kb Sequence Location				
Probe	Chr	Start1	End1	Start2	End2	Chr	Start1	End1	Start2	End2
CDKN2A_9_22005914_22007156_22029988_22034038_RF	9	22005915	22005944	22034009	22034038	9	22005915	22009914	22030039	22034038
LEP_7_127838673_127843908_127903727_127906543_RF	7	127838674	127838703	127906514	127906543	7	127838674	127842673	127902544	127906543
TSPAN8_12_71559221_71564078_71667712_71675824_RR	12	71559222	71559251	71667713	71667742	12	71559222	71563221	71667713	71671712
CYB5R4_6_84533887_84541872_84600402_84604101_RF	6	84533888	84533917	84604072	84604101	6	84533888	84537887	84600102	84604101
CYP2C9_10_96661464_96668745_96755577_96760846_FF	10	96668716	96668745	96760817	96760846	10	96664746	96668745	96756847	96760846
TSPAN8_12_71559221_71564078_71675824_71684278_RF	12	71559222	71559251	71684249	71684278	12	71559222	71563221	71680279	71684278
CYB5R4_6_84533887_84541872_84611173_84616879_FF	6	84541843	84541872	84616850	84616879	6	84537873	84541872	84612880	84616879
TASP1_20_13441063_13442565_13507251_13521471_FR	20	13442536	13442565	13507252	13507281	20	13438566	13442565	13507252	13511251
KCNJ11_11_17430922_17433660_17445199_17452295_RR	11	17430923	17430952	17445200	17445229	11	17430923	17434922	17445200	17449199
INS_11_2162616_2164979_2191728_2194389_FF	11	2164950	2164979	2194360	2194389	11	2160980	2164979	2190390	2194389
PTPRD_9_9551379_9564487_9852099_9857206_RR	9	9551380	9551409	9852100	9852129	9	9551380	9555379	9852100	9856099
IGF2_11_2162616_2164979_2191728_2194389_RR	11	2162617	2162646	2191729	2191758	11	2162617	2166616	2191729	2195728
TNFRSF1B_1_12241967_12245164_12274102_12277104_RF	1	12241968	12241997	12277075	12277104	1	12241968	12245967	12273105	12277104
TSPAN8_12_71667712_71675824_71850942_71857145_RF	12	71667713	71667742	71857116	71857145	12	71667713	71671712	71853146	71857145

Table 19d. Pre-type 2 diabetes mellitus probes - EpiSwitch™ markers to stratify pre-type 2 diabetes vs. healthy controls	Probe Location					4 kb Sequence Location				
Probe	Chr	Start1	End1	Start2	End2	Chr	Start1	End1	Start2	End2
CACNA1C_12_2099248_2111840_2200229_2202042_RF	12	2099249	2099278	2202013	2202042	12	2099249	2103248	2198043	2202042
CYP2C9_10_96690028_96694118_96748928_96755577_FR	10	96694089	96694118	96748929	96748958	10	96690119	96694118	96748929	96752928
TSPAN8_12_71559221_71564078_71690883_71707188_RR	12	71559222	71559251	71690884	71690913	12	71559222	71563221	71690884	71694883
ABCC8_11_17445199_17452295_17514252_17516772_RF	11	17445200	17445229	17516743	17516772	11	17445200	17449199	17512773	17516772
ADCY5_3_123098260_123106114_123133741_123143812_RF	3	123098261	123098290	123143783	123143812	3	123098261	123102260	123139813	123143812
IGF2_11_2191728_2194389_2210793_2214417_RF	11	2191729	2191758	2214388	2214417	11	2191729	2195728	2210418	2214417
SREBF1_17_17722022_17726360_17743896_17753157_FR	17	17726331	17726360	17743897	17743926	17	17722361	17726360	17743897	17747896
ABCC8_11_17445199_17452295_17538995_17541116_RF	11	17445200	17445229	17541087	17541116	11	17445200	17449199	17537117	17541116

Table 20a. Type 2 diabetes mellitus probes – EpiSwitch™ markers to stratify type 2 diabetes mellitus vs. healthy controls							
Probe	GeneLocus	Probe_Count_Total	Probe_Count_Sig	HyperG_Stats	FDR_HyperG	Percent_Sig	logFC
ICAM1_19_10368390_10370561_10406169_10407761_RF	ICAM1	9	5	0.001732	0.070257	55.56	0.454102
SREBF1_17_17743896_17753157_17777190_17783023_RF	SREBF1	19	9	0.000113	0.013705	47.37	0.405312
CAMK1D_10_12558950_12568337_12770482_12771684_FR	CAMK1D	115	24	0.002791	0.092599	20.87	0.389359
SLC2A2_3_170700264_170710807_170738889_170750047_RF	SLC2A2	5	4	0.000809	0.038824	80	0.37933
ICAM1_19_10341612_10343024_10406169_10407761_RF	ICAM1	9	5	0.001732	0.070257	55.56	0.374366
SREBF1_17_17722022_17726360_17743896_17753157_RR	SREBF1	19	9	0.000113	0.013705	47.37	0.370578
IDE_10_94207972_94216393_94322805_94330672_RR	IDE	7	6	1.49E-05	0.004309	85.71	0.335806
CACNA1C_12_2099248_2111840_2394923_2398377_FR	CACNA1C	197	35	0.006212	0.174409	17.77	0.335327
KCNJ11_11_17401446_17405499_17419957_17422762_RF	KCNJ11	22	8	0.002252	0.082207	36.36	0.334267
SREBF1_17_17754197_17760488_17777190_17783023_RF	SREBF1	19	9	0.000113	0.013705	47.37	0.305866
CACNA1C_12_2099248_2111840_2221145_2224007_FR	CACNA1C	197	35	0.006212	0.174409	17.77	0.304928
CYB5R4_6_84553857_84562119_84611173_84616879_FF	CYB5R4	39	10	0.011329	0.217632	25.64	0.304406
SLC2A2_3_170700264_170710807_170767515_170774153_RF	SLC2A2	5	4	0.000809	0.038824	80	0.304351
KCNJ11_11_17419957_17422762_17452295_17453614_FR	KCNJ11	22	8	0.002252	0.082207	36.36	0.30432
CAMK1D_10_12425560_12430245_12558950_12568337_RF	CAMK1D	115	24	0.002791	0.092599	20.87	0.29721
KCNJ11_11_17401446_17405499_17445199_17452295_RF	KCNJ11	22	8	0.002252	0.082207	36.36	0.294294
CAMK1D_10_12558950_12568337_12609856_12611356_FR	CAMK1D	115	24	0.002791	0.092599	20.87	0.293636
CAMK1D_10_12509013_12511923_12558950_12568337_FR	CAMK1D	115	24	0.002791	0.092599	20.87	0.288358

Table 20a. Type 2 diabetes mellitus probes – EpiSwitch™ markers to stratify type 2 diabetes mellitus vs. healthy controls

Probe	GeneLocus	Probe_Count_Total	Probe_Count_Sig	HyperG_Stats	FDR_HyperG	Percent_Sig	logFC
VEGFA_6_43701600_43705478_43718880_43723783_RF	VEGFA	16	6	0.006786	0.176922	37.5	0.285845
ADCY5_3_123037100_123044621_123133741_123143812_RF	ADCY5	90	18	0.013754	0.230556	20	0.283847
CAMK1D_10_12558950_12568337_12770482_12771684_RR	CAMK1D	115	24	0.002791	0.092599	20.87	0.282717
LTA_6_31498892_31502771_31552034_31554202_FF	LTA	17	6	0.009477	0.192177	35.29	0.282028
CYP2C9_10_96661464_96668745_96741594_96747469_FR	CYP2C9	8	5	0.000851	0.038824	62.5	0.281118
CACNA1C_12_2099248_2111840_2383231_2391100_RR	CACNA1C	197	35	0.006212	0.174409	17.77	0.280559
SREBF1_17_17722022_17726360_17743896_17753157_FR	SREBF1	19	9	0.000113	0.013705	47.37	0.279061
CACNA1C_12_2099248_2111840_2255353_2257963_FF	CACNA1C	197	35	0.006212	0.174409	17.77	0.276063
CYB5A_18_71929777_71931243_71965803_71970158_FF	CYB5A	19	6	0.016982	0.247935	31.58	0.275053
IDE_10_94207972_94216393_94232614_94236267_RF	IDE	7	6	1.49E-05	0.004309	85.71	0.270976
TASP1_20_13265932_13269301_13507251_13521471_RR	TASP1	172	30	0.013787	0.230556	17.44	0.26783
SDHB_1_17371319_17376758_17395655_17400949_FR	SDHB	13	8	2.36E-05	0.004309	61.54	0.267658
CYB5R4_6_84541872_84548862_84611173_84616879_FF	CYB5R4	39	10	0.011329	0.217632	25.64	0.265948
CAMK1D_10_12584612_12587236_12806730_12814088_FF	CAMK1D	115	24	0.002791	0.092599	20.87	0.262783
CYB5R4_6_84533887_84541872_84611173_84616879_FF	CYB5R4	39	10	0.011329	0.217632	25.64	0.262369
SREBF1_17_17722022_17726360_17754197_17760488_RR	SREBF1	19	9	0.000113	0.013705	47.37	0.258464
SREBF1_17_17743896_17753157_17764809_17767745_FR	SREBF1	19	9	0.000113	0.013705	47.37	0.258278
SDHB_1_17371319_17376758_17395655_17400949_RR	SDHB	13	8	2.36E-05	0.004309	61.54	0.256686

Table 20a. Type 2 diabetes mellitus probes – EpiSwitch™ markers to stratify type 2 diabetes mellitus vs. healthy controls

Probe	GeneLocus	Probe_Count_Total	Probe_Count_Sig	HyperG_Stats	FDR_HyperG	Percent_Sig	logFC
ADCY5_3_123098260_123106114_123133741_123143812_RF	ADCY5	90	18	0.013754	0.230556	20	0.256602
CACNA1C_12_2099248_2111840_2371355_2375397_FF	CACNA1C	197	35	0.006212	0.174409	17.77	0.251757
CACNA1C_12_2099248_2111840_2249555_2251873_RF	CACNA1C	197	35	0.006212	0.174409	17.77	0.250871
CYP2C9_10_96690028_96694118_96755577_96760846_FF	CYP2C9	8	5	0.000851	0.038824	62.5	0.248438
TASP1_20_13507251_13521471_13641645_13647312_FR	TASP1	172	30	0.013787	0.230556	17.44	0.246916
CAMK1D_10_12392639_12394405_12558950_12568337_FR	CAMK1D	115	24	0.002791	0.092599	20.87	0.246871
AVP_20_3082527_3084991_3109305_3112452_RR	AVP	8	4	0.00849	0.18229	50	0.245622
CYP2C9_10_96661464_96668745_96755577_96760846_FF	CYP2C9	8	5	0.000851	0.038824	62.5	0.245603
ICAM1_19_10341612_10343024_10368390_10370561_RR	ICAM1	9	5	0.001732	0.070257	55.56	0.245234
LTA_6_31498892_31502771_31523234_31525915_RF	LTA	17	6	0.009477	0.192177	35.29	0.242562
VEGFA_6_43711156_43718584_43754116_43756590_RR	VEGFA	16	6	0.006786	0.176922	37.5	0.241134
CAMK1D_10_12558950_12568337_12770482_12771684_FF	CAMK1D	115	24	0.002791	0.092599	20.87	0.240511
TASP1_20_13279725_13285391_13489615_13507251_RF	TASP1	172	30	0.013787	0.230556	17.44	0.239337
SDHB_1_17348194_17353079_17405102_17406505_FF	SDHB	13	8	2.36E-05	0.004309	61.54	0.238395

Table 20b. Type 2 diabetes mellitus probes – EpiSwitch™ markers to stratify type 2 diabetes mellitus vs. healthy controls

Probe	AveExpr	t	P.Value	adj.P.Val	B	FC	FC_1	LS	Loop detected
ICAM1_19_10368390_10370561_10406169_10407761_RF	0.454102	6.42338	0.000148	0.085141	1.368276	1.36993	1.36993	1	T2DM
SREBF1_17_17743896_17753157_17777190_17783023_RF	0.405312	4.847825	0.001034	0.085141	-0.376824	1.324375	1.324375	1	T2DM
CAMK1D_10_12558950_12568337_12770482_12771684_FR	0.389359	7.082112	7.22E-05	0.085141	1.981818	1.309812	1.309812	1	T2DM
SLC2A2_3_170700264_170710807_170738889_170750047_RF	0.37933	4.109419	0.0029	0.086908	-1.33958	1.300738	1.300738	1	T2DM
ICAM1_19_10341612_10343024_10406169_10407761_RF	0.374366	4.192347	0.002573	0.086505	-1.226909	1.29627	1.29627	1	T2DM
SREBF1_17_17722022_17726360_17743896_17753157_RR	0.370578	6.47337	0.00014	0.085141	1.417082	1.292871	1.292871	1	T2DM
IDE_10_94207972_94216393_94322805_94330672_RR	0.335806	4.411221	0.001884	0.085141	-0.934957	1.262082	1.262082	1	T2DM
CACNA1C_12_2099248_2111840_2394923_2398377_FR	0.335327	6.941313	8.38E-05	0.085141	1.85594	1.261663	1.261663	1	T2DM
KCNJ11_11_17401446_17405499_17419957_17422762_RF	0.334267	7.216543	6.27E-05	0.085141	2.099438	1.260737	1.260737	1	T2DM
SREBF1_17_17754197_17760488_17777190_17783023_RF	0.305866	4.192252	0.002573	0.086505	-1.227037	1.23616	1.23616	1	T2DM
CACNA1C_12_2099248_2111840_2221145_2224007_FR	0.304928	4.334594	0.0021	0.085141	-1.036262	1.235357	1.235357	1	T2DM
CYB5R4_6_84553857_84562119_84611173_84616879_FF	0.304406	3.987268	0.003466	0.086908	-1.507539	1.23491	1.23491	1	T2DM
SLC2A2_3_170700264_170710807_170767515_170774153_RF	0.304351	3.648477	0.005743	0.091143	-1.985152	1.234863	1.234863	1	T2DM
KCNJ11_11_17419957_17422762_17452295_17453614_FR	0.30432	5.539767	0.000423	0.085141	0.440492	1.234837	1.234837	1	T2DM
CAMK1D_10_12425560_12430245_12558950_12568337_RF	0.29721	5.92423	0.000265	0.085141	0.859646	1.228766	1.228766	1	T2DM

Table 20b. Type 2 diabetes mellitus probes – EpiSwitch™ markers to stratify type 2 diabetes mellitus vs. healthy controls

Probe	AveExpr	t	P.Value	adj.P.Val	B	FC	FC_1	LS	Loop detected
KCNJ11_11_17401446_17405499_17445199_17452295_RF	0.294294	6.734493	0.000105	0.085141	1.665928	1.226285	1.226285	1	T2DM
CAMK1D_10_12558950_12568337_12609856_12611356_FR	0.293636	6.449811	0.000144	0.085141	1.394129	1.225726	1.225726	1	T2DM
CAMK1D_10_12509013_12511923_12558950_12568337_FR	0.288358	3.608044	0.006106	0.091143	-2.043232	1.221249	1.221249	1	T2DM
VEGFA_6_43701600_43705478_43718880_43723783_RF	0.285845	3.220423	0.011102	0.098567	-2.609928	1.219124	1.219124	1	T2DM
ADCY5_3_123037100_123044621_123133741_123143812_RF	0.283847	5.443563	0.000477	0.085141	0.331754	1.217437	1.217437	1	T2DM
CAMK1D_10_12558950_12568337_12770482_12771684_RR	0.282717	5.210694	0.000641	0.085141	0.062038	1.216484	1.216484	1	T2DM
LTA_6_31498892_31502771_31552034_31554202_FF	0.282028	3.530375	0.006873	0.091324	-2.155392	1.215903	1.215903	1	T2DM
CYP2C9_10_96661464_96668745_96741594_96747469_FR	0.281118	3.845873	0.004271	0.086908	-1.704835	1.215136	1.215136	1	T2DM
CACNA1C_12_2099248_2111840_2383231_2391100_RR	0.280559	4.641664	0.001368	0.085141	-0.636294	1.214666	1.214666	1	T2DM
SREBF1_17_17722022_17726360_17743896_17753157_FR	0.279061	3.327419	0.009397	0.093872	-2.451875	1.213405	1.213405	1	T2DM
CACNA1C_12_2099248_2111840_2255353_2257963_FF	0.276063	3.581668	0.006356	0.091143	-2.081234	1.210886	1.210886	1	T2DM
CYB5A_18_71929777_71931243_71965803_71970158_FF	0.275053	5.581719	0.000401	0.085141	0.487422	1.210038	1.210038	1	T2DM
IDE_10_94207972_94216393_94232614_94236267_RF	0.270976	3.808438	0.004516	0.088035	-1.757569	1.206624	1.206624	1	T2DM
TASP1_20_13265932_13269301_13507251_13521471_RR	0.26783	4.183714	0.002605	0.086505	-1.238586	1.203995	1.203995	1	T2DM
SDHB_1_17371319_17376758_17395655_17400949_FR	0.267658	3.734784	0.005042	0.089145	-1.861916	1.203852	1.203852	1	T2DM
CYB5R4_6_84541872_84548862_84611173_84616879_FF	0.265948	3.914546	0.003857	0.086908	-1.608634	1.202426	1.202426	1	T2DM

Table 20b. Type 2 diabetes mellitus probes – EpiSwitch™ markers to stratify type 2 diabetes mellitus vs. healthy controls

Probe	AveExpr	t	P.Value	adj.P.Val	B	FC	FC_1	LS	Loop detected
CAMK1D_10_12584612_12587236_12806730_12814088_FF	0.262783	3.829993	0.004373	0.086908	-1.72718	1.199791	1.199791	1	T2DM
CYB5R4_6_84533887_84541872_84611173_84616879_FF	0.262369	3.516339	0.007022	0.091755	-2.175742	1.199447	1.199447	1	T2DM
SREBF1_17_17722022_17726360_17754197_17760488_RR	0.258464	4.593833	0.001461	0.085141	-0.697539	1.196205	1.196205	1	T2DM
SREBF1_17_17743896_17753157_17764809_17767745_FR	0.258278	4.299433	0.002207	0.085141	-1.083076	1.19605	1.19605	1	T2DM
SDHB_1_17371319_17376758_17395655_17400949_RR	0.256686	3.882266	0.004046	0.086908	-1.653765	1.194731	1.194731	1	T2DM
ADCY5_3_123098260_123106114_123133741_123143812_RF	0.256602	3.953353	0.003643	0.086908	-1.554585	1.194662	1.194662	1	T2DM
CACNA1C_12_2099248_2111840_2371355_2375397_FF	0.251757	5.392827	0.000508	0.085141	0.273777	1.190656	1.190656	1	T2DM
CACNA1C_12_2099248_2111840_2249555_2251873_RF	0.250871	3.572509	0.006445	0.091143	-2.094452	1.189926	1.189926	1	T2DM
CYP2C9_10_96690028_96694118_96755577_96760846_FF	0.248438	5.685135	0.000353	0.085141	0.601853	1.187921	1.187921	1	T2DM
TASP1_20_13507251_13521471_13641645_13647312_FR	0.246916	3.67084	0.005552	0.091143	-1.953122	1.186668	1.186668	1	T2DM
CAMK1D_10_12392639_12394405_12558950_12568337_FR	0.246871	4.321578	0.002139	0.085141	-1.053568	1.186631	1.186631	1	T2DM
AVP_20_3082527_3084991_3109305_3112452_RR	0.245622	3.833295	0.004351	0.086908	-1.72253	1.185604	1.185604	1	T2DM
CYP2C9_10_96661464_96668745_96755577_96760846_FF	0.245603	3.254351	0.010529	0.097267	-2.559693	1.185588	1.185588	1	T2DM
ICAM1_19_10341612_10343024_10368390_10370561_RR	0.245234	3.621185	0.005985	0.091143	-2.024332	1.185285	1.185285	1	T2DM
LTA_6_31498892_31502771_31523234_31525915_RF	0.242562	4.646403	0.001359	0.085141	-0.630248	1.183092	1.183092	1	T2DM

Table 20b. Type 2 diabetes mellitus probes – EpiSwitch™ markers to stratify type 2 diabetes mellitus vs. healthy controls

Probe	AveExpr	t	P.Value	adj.P.Val	B	FC	FC_1	LS	Loop detected
VEGFA_6_43711156_43718584_43754116_43756590_R R	0.241134	4.631302	0.001388	0.085141	-0.649529	1.181921	1.181921	1	T2DM
CAMK1D_10_12558950_12568337_12770482_12771684 _FF	0.240511	5.225549	0.000629	0.085141	0.07952	1.181411	1.181411	1	T2DM
TASP1_20_13279725_13285391_13489615_13507251_R F	0.239337	3.408863	0.008284	0.092903	-2.332342	1.18045	1.18045	1	T2DM
SDHB_1_17348194_17353079_17405102_17406505_FF	0.238395	4.19351	0.002568	0.086505	-1.225337	1.179679	1.179679	1	T2DM

Table 20c. Type 2 DM Probes - EpiSwitch™ markers to stratify Type 2 DM vs. healthy controls	Probe sequence
Probe	**60 mer**
ICAM1_19_10368390_10370561_10406169_10407761_RF	GGAAGGCCGAGGCGGCCAGATCACGAGGTCGAACCTCCTGATAACTTCAGCATTAACAGC
SREBF1_17_17743896_17753157_17777190_17783023_RF	ACATCTCAGACATGACTTTTGTGTTTCCTCGAGCCTTTTCGGGCAGGCGTCCAGCACGGG
CAMK1D_10_12558950_12568337_12770482_12771684_FR	CGTGGTTCTTCAAGTTGTAGTTTAATTCTCGAGAGCAGTGTTTTAAGTGGTCTGACGGGA
SLC2A2_3_170700264_170710807_170738889_170750047_RF	TTGGCTGTTTTCACTCAGTGAAATTCCTTCGAGCCCAGGAGGCAAAGGTTGCAGTGAGCT
ICAM1_19_10341612_10343024_10406169_10407761_RF	GGAAGGCCGAGGCGGCCAGATCACGAGGTCGAAAGCGCTCGGATTCAGCCTTCTCCCCGG
SREBF1_17_17722022_17726360_17743896_17753157_RR	ATGGACAGTAGGCAGGATGAATAAGTGCTCGAGCCTTTTCGGGCAGGCGTCCAGCACGGG
IDE_10_94207972_94216393_94322805_94330672_RR	GGGTTTCACCATGTTGGCCTGGCTGGGCTCGAGACCAGCCTGGCCAACATGGTGAAACCA
CACNA1C_12_2099248_2111840_2394923_2398377_FR	ACTGACAGTTTCTTGGGATTCTCCAGACTCGAGAGAGGCTGGTGCGCACCTACCCAGCGG
KCNJ11_11_17401446_17405499_17419957_17422762_RF	CTTAGAGCAAAGGCTAGGCTCAGTAATGTCGAGAGAGAGCCTGTGTGAGGAGTGCAGTCA
SREBF1_17_17754197_17760488_17777190_17783023_RF	ACATCTCAGACATGACTTTTGTGTTTCCTCGAGTCTCACCAGGTCGGTCCTGAGCCACAC
CACNA1C_12_2099248_2111840_2221145_2224007_FR	ACTGACAGTTTCTTGGGATTCTCCAGACTCGAGGCCTGGAGAAGCCCAGGAGGAGGCGTG
CYB5R4_6_84553857_84562119_84611173_84616879_FF	ATTATAACATTTATATATCATCTTTTCCTCGAGGTTGCAGTAAGCTGATCATGCCACTAC
SLC2A2_3_170700264_170710807_170767515_170774153_RF	GGAAAACAGGATTAAAAAAGAAATGGATTCGAGCCCAGGAGGCAAAGGTTGCAGTGAGCT
KCNJ11_11_17419957_17422762_17452295_17453614_FR	CTTAGAGCAAAGGCTAGGCTCAGTAATGTCGAGCAAGCCTTGAGGCTGACACAGGACCTG
CAMK1D_10_12425560_12430245_12558950_12568337_RF	CGTGGTTCTTCAAGTTGTAGTTTAATTCTCGAGCTTGTTATTTTCTCTTTCTTACCTAGT
KCNJ11_11_17401446_17405499_17445199_17452295_RF	GACCAAACAGCTGTGGTTTGGCCATCACTCGAGAGAGAGCCTGTGTGAGGAGTGCAGTCA
CAMK1D_10_12558950_12568337_12609856_12611356_FR	CGTGGTTCTTCAAGTTGTAGTTTAATTCTCGAGCTTGAATCAGAATGGTCAAGATACCTG
CAMK1D_10_12509013_12511923_12558950_12568337_FR	TGTGTTAGGGTACCATTCTTCTTAAGTATCGAATCTGTACATCAACTTTGGAAAAACTAA

Table 20c. Type 2 DM Probes - EpiSwitch™ markers to stratify Type 2 DM vs. healthy controls

Probe	Probe sequence
	60 mer
VEGFA_6_43701600_43705478_43718880_43723783_RF	TCCTACAGAAGTTAAAATAGAGCTAGGGTCGAATTGGCCCGGGTCCCTGCTGGGCTGGAG
ADCY5_3_123037100_123044621_123133741_123143812_RF	TTTAGCCAAAAAGAAAAAAAAGGTTCATTTCGAGAACCAGAGTCAAACTTAGACCCCAGGA
CAMK1D_10_12558950_12568337_12770482_12771684_RR	TTAGTTTTTCCAAAGTTGATGTACAGAATTCGAGAGCAGTGTTTTAAGTGGTCTGACGGGA
LTA_6_31498892_31502771_31552034_31554202_FF	TGGTGAGCAGAAGGCTCCAGCTGTACGCTCGACGGCCCAGGGAAACTCAAACCCATACTC
CYP2C9_10_96661464_96668745_96741594_96747469_FR	GAGTAGGTAAACAAAGCAGTCAGGAAGCTCGAGTCTTTGGTTTTCCCTAGATAATTAATA
CACNA1C_12_2099248_2111840_2383231_2391100_RR	ACACCACTTGAACCAAGAAACCTTAACTTCGAAGGAGTGGCATAAGGTCCCACTTGGGTG
SREBF1_17_17722022_17726360_17743896_17753157_FR	CCCTTTACCCCAGTCCGTGTGAGCCTCTTCGAGCCTTTTCGGGCAGGCGTCCAGCACGGG
CACNA1C_12_2099248_2111840_2255353_2257963_FF	ACTGACAGTTTCTTGGGATTCTCCAGACTCGAGGCAGGAGACAGCTTGAGCCCGGGAGT
CYB5A_18_71929777_71931243_71965803_71970158_FF	CCTAGGCAGATCACTTGAGTTCAGGAGTTCGAAACACTTGATCAAAACAGAATAACAGGT
IDE_10_94207972_94216393_94232614_94236267_RF	ATCTTTTTTAAAAAATATATTTATTTATTCGAGCCCAGCCAGGCCAACATGGTGAAACCC
TASP1_20_13265932_13269301_13507251_13521471_RR	TCCTTTCTTTTTTATTTTTTTAAGCTGTTTCGATTCAACATTAATTCATTTTTAGACTTCTC
SDHB_1_17371319_17376758_17395655_17400949_FR	CCAGGATGTACTACACTGAATATCTAAGTCGAGGCCCAGGGGCTCCAGGAGGCCACGCAC
CYB5R4_6_84541872_84548862_84611173_84616879_FF	TCCCGATCACAGCTGAAGATTGGAAAGGTCGAGGTTGCAGTAAGCTGATCATGCCACTAC
CAMK1D_10_12584612_12587236_12806730_12814088_FF	AGAAGCAATTGAGAAAAAACCTCAGGTGTTCGACTACTATGTTGTTGATTTCTATCAAAGC
CYB5R4_6_84533887_84541872_84611173_84616879_FF	TGTTCAATCAAAGGAAGGGATAACACTATCGAGGTTGCAGTAAGCTGATCATGCCACTAC
SREBF1_17_17722022_17726360_17754197_17760488_RR	ATGGACAGTAGGCAGGATGAATAAGTGCTCGAGTCTCACCAGGTCGGTCCTGAGCCACAC
SREBF1_17_17743896_17753157_17764809_17767745_FR	TTGCTTCTGTGAGAGAAGCAATTTCTTTTCGATTGTCTAGTGCAGAAGCAAGTCCTCCGA
SDHB_1_17371319_17376758_17395655_17400949_RR	CTCCCCGTATCAAGAAATTTGCCATCTATCGAGGCCCAGGGGCTCCAGGAGGCCACGCAC

Table 20c. Type 2 DM Probes - EpiSwitch™ markers to stratify Type 2 DM vs. healthy controls	Probe sequence
Probe	60 mer
ADCY5_3_123098260_123106114_123133741_123143812_RF	TTTAGCCAAAAAGAAAAAAAAGGTTCATTTCGAGGAATGTTTCCAAGCAATTCTCTCTGCT
CACNA1C_12_2099248_2111840_2371355_2375397_FF	ACTGACAGTTTCTTGGGATTCTCCAGACTCGAAGGCATTGTTCTGGAGGTGGAGGAAGGG
CACNA1C_12_2099248_2111840_2249555_2251873_RF	TCCTGACCAAGGATCCTGATCCTTGATATCGAAGTTAAGGTTTCTTGGTTCAAGTGGTGT
CYP2C9_10_96690028_96694118_96755577_96760846_FF	TGAGGTAGGCAGATCACAGGTCAGGAGATCGATCCAGTGTGCTTTTCACTTCAGACCTTG
TASP1_20_13507251_13521471_13641645_13647312_FR	CATGGTTATATACACATGTTAAAATTCATCGATTGAACCCTGGAGGAGGAGGTTGCAGTG
CAMK1D_10_12392639_12394405_12558950_12568337_FR	AGGCGAGCTGATCACTTAAGTCAGGAGTTCGAATCTGTACATCAACTTTGGAAAAACTAA
AVP_20_3082527_3084991_3109305_3112452_RR	CCCTTGTTTTCTGGAGATTCACTCTTCATCGAGATCAGCCCGGGCAACACAGCAAGACCC
CYP2C9_10_96661464_96668745_96755577_96760846_FF	GAGTAGGTAAACAAAGCAGTCAGGAAGCTCGATCCAGTGTGCTTTTCACTTCAGACCTTG
ICAM1_19_10341612_10343024_10368390_10370561_RR	CCGGGGAGAAGGCTGAATCCGAGCGCTTTCGAACCTCCTGATAACTTCAGCATTAACAGC
LTA_6_31498892_31502771_31523234_31525915_RF	AGCAGCAGCGAGAAGCAGAGGGATCCCGTCGATGTCCATGCCTCGGCCAAATAGGTTGGT
VEGFA_6_43711156_43718584_43754116_43756590_RR	AGCAGGATCGTTTCACAACCATGTGTGCTCGAGATATTCCGTAGTACATATTTATTTTTA
CAMK1D_10_12558950_12568337_12770482_12771684_FF	CGTGGTTCTTCAAGTTGTAGTTTAATTCTCGAATATTTAATCTCTCTACACCACTTAATC
TASP1_20_13279725_13285391_13489615_13507251_RF	ATTTTTTGACAATTATAGTAGTATGGATTCGACCGCATCAAGCGCAAGGACTTCCGCTGG
SDHB_1_17348194_17353079_17405102_17406505_FF	GGGTTTTATCACGTTGGCCAGGCTGGTCTCGAGACCAGCCTGGGCAACCCAGTGAAACCC

Table 20d. Type 2 diabetes mellitus probes - EpiSwitch™ markers to stratify type 2 diabetes vs. healthy controls	Probe Location					4 kb Sequence Location				
Probe	Chr	Start1	End1	Start2	End2	Chr	Start1	End1	Start2	End2
ICAM1_19_10368390_10370561_10406169_10407761_RF	19	10368391	10368420	10407732	10407761	19	10368391	10372390	10403762	10407761
SREBF1_17_17743896_17753157_17777190_17783023_RF	17	17743897	17743926	17782994	17783023	17	17743897	17747896	17779024	17783023
CAMK1D_10_12558950_12568337_12770482_12771684_FR	10	12568308	12568337	12770483	12770512	10	12564338	12568337	12770483	12774482
SLC2A2_3_170700264_170710807_170738889_170750047_RF	3	170700265	170700294	170750018	170750047	3	170700265	170704264	170746048	170750047
ICAM1_19_10341612_10343024_10406169_10407761_RF	19	10341613	10341642	10407732	10407761	19	10341613	10345612	10403762	10407761
SREBF1_17_17722022_17726360_17743896_17753157_RR	17	17722023	17722052	17743897	17743926	17	17722023	17726022	17743897	17747896
IDE_10_94207972_94216393_94322805_94330672_RR	10	94207973	94208002	94322806	94322835	10	94207973	94211972	94322806	94326805
CACNA1C_12_2099248_2111840_2394923_2398377_FR	12	2111811	2111840	2394924	2394953	12	2107841	2111840	2394924	2398923
KCNJ11_11_17401446_17405499_17419957_17422762_RF	11	17401447	17401476	17422733	17422762	11	17401447	17405446	17418763	17422762
SREBF1_17_17754197_17760488_17777190_17783023_RF	17	17754198	17754227	17782994	17783023	17	17754198	17758197	17779024	17783023
CACNA1C_12_2099248_2111840_2221145_2224007_FR	12	2111811	2111840	2221146	2221175	12	2107841	2111840	2221146	2225145
CYB5R4_6_84553857_84562119_84611173_84616879_FF	6	84562090	84562119	84616850	84616879	6	84558120	84562119	84612880	84616879
SLC2A2_3_170700264_170710807_170767515_170774153_RF	3	170700265	170700294	170774124	170774153	3	170700265	170704264	170770154	170774153
KCNJ11_11_17419957_17422762_17452295_17453614_FR	11	17422733	17422762	17452296	17452325	11	17418763	17422762	17452296	17456295

Table 20d. Type 2 diabetes mellitus probes - EpiSwitch™ markers to stratify type 2 diabetes vs. healthy controls	Probe Location					4 kb Sequence Location				
Probe	Chr	Start1	End1	Start2	End2	Chr	Start1	End1	Start2	End2
CAMK1D_10_12425560_12430245_12558950_12568337_RF	10	12425561	12425590	12568308	12568337	10	12425561	12429560	12564338	12568337
KCNJ11_11_17401446_17405499_17445199_17452295_RF	11	17401447	17401476	17452266	17452295	11	17401447	17405446	17448296	17452295
CAMK1D_10_12558950_12568337_12609856_12611356_FR	10	12568308	12568337	12609857	12609886	10	12564338	12568337	12609857	12613856
CAMK1D_10_12509013_12511923_12558950_12568337_FR	10	12511894	12511923	12558951	12558980	10	12507924	12511923	12558951	12562950
VEGFA_6_43701600_43705478_43718880_43723783_RF	6	43701601	43701630	43723754	43723783	6	43701601	43705600	43719784	43723783
ADCY5_3_123037100_123044621_123133741_123143812_RF	3	123037101	123037130	123143783	123143812	3	123037101	123041100	123139813	123143812
CAMK1D_10_12558950_12568337_12770482_12771684_RR	10	12558951	12558980	12770483	12770512	10	12558951	12562950	12770483	12774482
LTA_6_31498892_31502771_31552034_31554202_FF	6	31502742	31502771	31554173	31554202	6	31498772	31502771	31550203	31554202
CYP2C9_10_96661464_96668745_96741594_96747469_FR	10	96668716	96668745	96741595	96741624	10	96664746	96668745	96741595	96745594
CACNA1C_12_2099248_2111840_2383231_2391100_RR	12	2099249	2099278	2383232	2383261	12	2099249	2103248	2383232	2387231
SREBF1_17_17722022_17726360_17743896_17753157_FR	17	17726331	17726360	17743897	17743926	17	17722361	17726360	17743897	17747896
CACNA1C_12_2099248_2111840_2255353_2257963_FF	12	2111811	2111840	2257934	2257963	12	2107841	2111840	2253964	2257963
CYB5A_18_71929777_71931243_71965803_71970158_FF	18	71931214	71931243	71970129	71970158	18	71927244	71931243	71966159	71970158
IDE_10_94207972_94216393_94232614_94236267_RF	10	94207973	94208002	94236238	94236267	10	94207973	94211972	94232268	94236267

Table 20d. Type 2 diabetes mellitus probes - EpiSwitch™ markers to stratify type 2 diabetes vs. healthy controls	Probe Location					4 kb Sequence Location				
Probe	Chr	Start1	End1	Start2	End2	Chr	Start1	End1	Start2	End2
TASP1_20_13265932_13269301_13507251_13521471_RR	20	13265933	13265962	13507252	13507281	20	13265933	13269932	13507252	13511251
SDHB_1_17371319_17376758_17395655_17400949_FR	1	17376729	17376758	17395656	17395685	1	17372759	17376758	17395656	17399655
CYB5R4_6_84541872_84548862_84611173_84616879_FF	6	84548833	84548862	84616850	84616879	6	84544863	84548862	84612880	84616879
CAMK1D_10_12584612_12587236_12806730_12814088_FF	10	12587207	12587236	12814059	12814088	10	12583237	12587236	12810089	12814088
CYB5R4_6_84533887_84541872_84611173_84616879_FF	6	84541843	84541872	84616850	84616879	6	84537873	84541872	84612880	84616879
SREBF1_17_17722022_17726360_17754197_17760488_RR	17	17722023	17722052	17754198	17754227	17	17722023	17726022	17754198	17758197
SREBF1_17_17743896_17753157_17764809_17767745_FR	17	17753128	17753157	17764810	17764839	17	17749158	17753157	17764810	17768809
SDHB_1_17371319_17376758_17395655_17400949_RR	1	17371320	17371349	17395656	17395685	1	17371320	17375319	17395656	17399655
ADCY5_3_123098260_123106114_123133741_123143812_RF	3	123098261	123098290	123143783	123143812	3	123098261	123102260	123139813	123143812
CACNA1C_12_2099248_2111840_2371355_2375397_FF	12	2111811	2111840	2375368	2375397	12	2107841	2111840	2371398	2375397
CACNA1C_12_2099248_2111840_2249555_2251873_RF	12	2099249	2099278	2251844	2251873	12	2099249	2103248	2247874	2251873
CYP2C9_10_96690028_96694118_96755577_96760846_FF	10	96694089	96694118	96760817	96760846	10	96690119	96694118	96756847	96760846
TASP1_20_13507251_13521471_13641645_13647312_FR	20	13521442	13521471	13641646	13641675	20	13517472	13521471	13641646	13645645
CAMK1D_10_12392639_12394405_12558950_12568337_FR	10	12394376	12394405	12558951	12558980	10	12390406	12394405	12558951	12562950

Table 20d. Type 2 diabetes mellitus probes - EpiSwitch™ markers to stratify type 2 diabetes vs. healthy controls	Probe Location					4 kb Sequence Location				
Probe	Chr	Start1	End1	Start2	End2	Chr	Start1	End1	Start2	End2
AVP_20_3082527_3084991_3109305_3112452_RR	20	3082528	3082557	3109306	3109335	20	3082528	3086527	3109306	3113305
CYP2C9_10_96661464_96668745_96755577_96760846_FF	10	96668716	96668745	96760817	96760846	10	96664746	96668745	96756847	96760846
ICAM1_19_10341612_10343024_10368390_10370561_RR	19	10341613	10341642	10368391	10368420	19	10341613	10345612	10368391	10372390
LTA_6_31498892_31502771_31523234_31525915_RF	6	31498893	31498922	31525886	31525915	6	31498893	31502892	31521916	31525915
VEGFA_6_43711156_43718584_43754116_43756590_RR	6	43711157	43711186	43754117	43754146	6	43711157	43715156	43754117	43758116
CAMK1D_10_12558950_12568337_12770482_12771684_FF	10	12568308	12568337	12771655	12771684	10	12564338	12568337	12767685	12771684
TASP1_20_13279725_13285391_13489615_13507251_RF	20	13279726	13279755	13507222	13507251	20	13279726	13283725	13503252	13507251
SDHB_1_17348194_17353079_17405102_17406505_FF	1	17353050	17353079	17406476	17406505	1	17349080	17353079	17402506	17406505

Table 21a. Type 1 diabetes mellitus (T1DM) probes - EpiSwitch™ markers to stratify T1DM vs. healthy controls									
Probe	GeneLocus	Probe_Count_Total	Probe_Count_Sig	HyperG_Stats	FDR_HyperG	Percent_Sig	reps.	Avg_CV	logFC
11_923549_925733_976127_979142_FR	AP2A2	16	5	0.059154368	0.647796332	31.25	4	3.706	-0.529758172
3_3117964_3119702_3187910_3199411_RF	IL5RA	7	3	0.060129293	0.647796332	42.86	4	3.403	-0.472211842
16_4065887_4067896_4109379_4115518_FR	ADCY9	66	17	0.007121374	0.182781932	25.76	4	4.12	-0.443525263
1_172083100_172087823_172151185_172154127_FF	DNM3	902	153	0.002933237	0.114615211	16.96	4	2.695	-0.436858249
16_31228760_31230406_31342509_31344379_FR	ITGAM	28	11	0.000764097	0.108117529	39.29	4	3.617	-0.43527354
1_171936106_171939290_172083100_172087823_RF	DNM3	902	153	0.002933237	0.114615211	16.96	4	4.24	-0.423950437
1_172061602_172067357_172083100_172087823_RF	DNM3	902	153	0.002933237	0.114615211	16.96	4	4.369	-0.422397473
1_171811918_171813464_172083100_172087823_RF	DNM3	902	153	0.002933237	0.114615211	16.96	4	3.75	-0.412452012
11_36531355_36534043_36605543_36609927_RR	RAG1	44	14	0.001755155	0.108117529	31.82	4	3.185	-0.409161997
1_171887726_171889817_172083100_172087823_RF	DNM3	902	153	0.002933237	0.114615211	16.96	4	2.093	-0.4080218
11_1010876_1013083_964245_969445_FF	AP2A2	16	5	0.059154368	0.647796332	31.25	4	4.114	-0.403895599
1_172083100_172087823_172212232_172223166_FF	DNM3	902	153	0.002933237	0.114615211	16.96	4	3.339	-0.394277802
6_32135728_32138270_32149729_32154447_FF	AGER	3	3	0.002646464	0.114615211	100	4	4.106	-0.386842707
16_4065887_4067896_4204978_4209511_FF	ADCY9	66	17	0.007121374	0.182781932	25.76	4	3.536	-0.385489846
16_31342509_31344379_31355595_31363682_RF	ITGAM	28	11	0.000764097	0.108117529	39.29	4	3.29	-0.381926095
1_161590754_161594100_161627152_161631654_RR	FCGR2B;FCGR3A	96	20	0.037659864	0.56343312	20.83	4	3.793	-0.380537697

Table 21a. Type 1 diabetes mellitus (T1DM) probes - EpiSwitch™ markers to stratify T1DM vs. healthy controls									
Probe	GeneLocus	Probe_Count_Total	Probe_Count_Sig	HyperG_Stats	FDR_HyperG	Percent_Sig	reps.	Avg_CV	logFC
16_4004273_4006715_4065887_4067896_RF	ADCY9	66	17	0.007121374	0.182781932	25.76	4	3.34	-0.37973185
16_4065887_4067896_4209511_4211354_FF	ADCY9	66	17	0.007121374	0.182781932	25.76	4	3.447	-0.377158647
13_111748012_111752622_111942125_111944243_RR	ARHGEF7	61	17	0.002977018	0.114615211	27.87	4	3.57	-0.373760579
19_10341612_10343024_10406169_10407761_FF	ICAM1	6	4	0.004341765	0.134116446	66.67	4	4.066	-0.365760195
16_4044767_4047085_4065887_4067896_RF	ADCY9	66	17	0.007121374	0.182781932	25.76	4	4.183	-0.362629207
16_4065887_4067896_4145870_4149370_FF	ADCY9	66	17	0.007121374	0.182781932	25.76	4	3.24	-0.358825866
16_4065887_4067896_4169801_4171577_FF	ADCY9	66	17	0.007121374	0.182781932	25.76	4	3.257	-0.356727176
16_4065887_4067896_4209511_4211354_FR	ADCY9	66	17	0.007121374	0.182781932	25.76	4	2.966	-0.355168037
11_36524913_36530925_36605543_36609927_FR	RAG1	44	14	0.001755155	0.108117529	31.82	4	4.444	-0.350562005
1_172053648_172060321_172083100_172087823_RR	DNM3	902	153	0.002933237	0.114615211	16.96	4	4.067	-0.346486038
22_23509706_23512087_23566317_23569153_RR	BCR	51	11	0.086137864	0.787292123	21.57	4	3.926	-0.333558559
6_6621204_6623713_6637118_6642924_RR	LY86	53	14	0.01108912	0.231735442	26.42	4	4.149	-0.333492256
1_198564901_198567426_198666515_198673906_FF	PTPRC	138	28	0.022371015	0.430642048	20.29	4	3.936	-0.324552901
11_36531355_36534043_36605543_36609927_FR	RAG1	44	14	0.001755155	0.108117529	31.82	4	4.776	-0.314053685
8_131812677_131818201_131980638_131987302_FF	ADCY8	83	18	0.032875301	0.56343312	21.69	4	3.965	-0.307426412
8_131812677_131818201_131974285_131980638_FR	ADCY8	83	18	0.032875301	0.56343312	21.69	4	3.754	-0.306962662

Table 21a. Type 1 diabetes mellitus (T1DM) probes - EpiSwitch™ markers to stratify T1DM vs. healthy controls									
Probe	GeneLocus	Probe_Count_Total	Probe_Count_Sig	HyperG_Stats	FDR_HyperG	Percent_Sig	reps.	Avg_CV	logFC
8_131796786_131800910_131812677_131818201_RF	ADCY8	83	18	0.032875301	0.56343312	21.69	4	5.046	-0.305084735
X_19555372_19559004_19587789_19592813_FR	SH3KBP1	168	36	0.00435443	0.134116446	21.43	4	8.54	-0.303254166
8_131812677_131818201_131926196_131933918_FR	ADCY8	83	18	0.032875301	0.56343312	21.69	4	2.272	-0.300945102
8_131812677_131818201_132011208_132012836_FR	ADCY8	83	18	0.032875301	0.56343312	21.69	4	3.877	-0.299926052
1_171805618_171810940_171986876_171988822_FF	DNM3	902	153	0.002933237	0.114615211	16.96	4	5.663	-0.297441732
1_161576950_161581654_161627152_161631654_FR	FCGR2B;FCGR3A	96	20	0.037659864	0.56343312	20.83	4	5.054	-0.293499837
X_19644496_19650796_19796774_19799668_RR	SH3KBP1	168	36	0.00435443	0.134116446	21.43	4	3.798	-0.29153113
8_42099384_42103137_42121759_42128721_FF	IKBKB	11	5	0.011285817	0.231735442	45.45	4	5.228	-0.291180044
5_42419594_42423647_42597654_42605427_FR	GHR	84	18	0.03663135	0.56343312	21.43	4	4.497	-0.290654281
6_6569800_6579319_6621204_6623713_RR	LY86	53	14	0.01108912	0.231735442	26.42	4	4.024	-0.287951764
8_131812677_131818201_132023344_132028736_FR	ADCY8	83	18	0.032875301	0.56343312	21.69	4	3.631	-0.285057864
5_42419594_42423647_42515628_42519035_FF	GHR	84	18	0.03663135	0.56343312	21.43	4	4.019	-0.283604972
5_67483678_67490216_67602566_67610345_RF	PIK3R1	14	7	0.001348057	0.108117529	50	4	3.969	-0.282353934
5_42419594_42423647_42519035_42531458_FR	GHR	84	18	0.03663135	0.56343312	21.43	4	3.372	-0.282109082
8_131812677_131818201_132011208_132012836_FF	ADCY8	83	18	0.032875301	0.56343312	21.69	4	3.625	-0.281315812
5_42419594_42423647_42546292_42555639_FR	GHR	84	18	0.03663135	0.56343312	21.43	4	3.675	-0.280553106

Table 21a. Type 1 diabetes mellitus (T1DM) probes - EpiSwitch™ markers to stratify T1DM vs. healthy controls

Probe	GeneLocus	Probe_Count_Total	Probe_Count_Sig	HyperG_Stats	FDR_HyperG	Percent_Sig	reps.	Avg_CV	logFC
16_4071891_4073711_4204978_4209511_RF	ADCY9	66	17	0.007121374	0.182781932	25.76	4	2.982	-0.279952461
22_23509706_23512087_23570512_23575772_RR	BCR	51	11	0.086137864	0.787292123	21.57	4	3.893	-0.278366248

Table 21b. Type 1 diabetes mellitus (T1DM) probes - EpiSwitch™ markers to stratify T1DM vs. healthy controls

Probe	AveExpr	t	P.Value	adj.P.Val	B	FC	FC_1	LS	Loop detected
11_923549_925733_976127_979142_FR	-0.529758172	-8.092940735	2.70E-06	0.002478464	5.056585897	0.692670831	-1.443687181	-1	T1DM
3_3117964_3119702_3187910_3199411_RF	-0.472211842	-7.326745164	7.60E-06	0.002478464	4.088814905	0.720858579	-1.387234652	-1	T1DM
16_4065887_4067896_4109379_4115518_FR	-0.443525263	-4.897708137	0.000334556	0.018676874	0.441359698	0.7353356	-1.359923279	-1	T1DM
1_172083100_172087823_172151185_172154127_FF	-0.436858249	-8.008643893	3.02E-06	0.002478464	4.954100461	0.738741613	-1.35365327	-1	T1DM
16_31228760_31230406_31342509_31344379_FR	-0.43527354	-7.895023881	3.51E-06	0.002478464	4.814434563	0.739553519	-1.352167184	-1	T1DM
1_171936106_171939290_172083100_172087823_RF	-0.423950437	-7.864029648	3.66E-06	0.002478464	4.776027833	0.7453808	-1.341596135	-1	T1DM
1_172061602_172067357_172083100_172087823_RF	-0.422397473	-7.776469372	4.11E-06	0.002478464	4.666809028	0.746183584	-1.340152774	-1	T1DM
1_171811918_171813464_172083100_172087823_RF	-0.412452012	-7.671544816	4.73E-06	0.002478464	4.534523533	0.751345297	-1.330945976	-1	T1DM
11_36531355_36534043_36605543_36609927_RR	-0.409161997	-6.819776394	1.57E-05	0.003231046	3.401963442	0.753060669	-1.327914258	-1	T1DM
1_171887726_171889817_172083100_172087823_RF	-0.4080218	-7.529429148	5.74E-06	0.002478464	4.352875105	0.753656067	-1.32686519	-1	T1DM

Table 21b. Type 1 diabetes mellitus (T1DM) probes - EpiSwitch™ markers to stratify T1DM vs. healthy controls

Probe	AveExpr	t	P.Value	adj.P.Val	B	FC	FC_1	LS	Loop detected
11_1010876_1013083_964245_969445_FF	-0.403895599	-6.684109098	1.91E-05	0.003629502	3.211628494	0.755814657	-1.323075692	-1	T1DM
1_172083100_172087823_172212232_172223166_FF	-0.394277802	-7.26361383	8.31E-06	0.002478464	4.005351851	0.760870165	-1.314284678	-1	T1DM
6_32135728_32138270_32149729_32154447_FF	-0.386842707	-5.731657165	8.33E-05	0.009736268	1.795575772	0.764801518	-1.307528785	-1	T1DM
16_4065887_4067896_4204978_4209511_FF	-0.385489846	-4.888681066	0.000339809	0.018728454	0.426143725	0.765519033	-1.306303248	-1	T1DM
16_31342509_31344379_31355595_31363682_RF	-0.381926095	-6.703010937	1.86E-05	0.003629502	3.238314557	0.767412359	-1.303080395	-1	T1DM
1_161590754_161594100_161627152_161631654_RR	-0.380537697	-6.631403849	2.07E-05	0.003810738	3.136930233	0.768151245	-1.30182696	-1	T1DM
16_4004273_4006715_4065887_4067896_RF	-0.37973185	-4.884889904	0.000342041	0.018732137	0.419749987	0.768580431	-1.301100001	-1	T1DM
16_4065887_4067896_4209511_4211354_FF	-0.377158647	-5.013405675	0.00027427	0.017323041	0.635364748	0.769952501	-1.298781416	-1	T1DM
13_111748012_111752622_111942125_111944243_RR	-0.373760579	-6.566614764	2.28E-05	0.003979612	3.044523931	0.771768155	-1.295725917	-1	T1DM
19_10341612_10343024_10406169_10407761_FF	-0.365760195	-6.847126759	1.51E-05	0.003231046	3.439997052	0.77605984	-1.288560428	-1	T1DM

Table 21b. Type 1 diabetes mellitus (T1DM) probes - EpiSwitch™ markers to stratify T1DM vs. healthy controls

Probe	AveExpr	t	P.Value	adj.P.Val	B	FC	FC_1	LS	Loop detected
16_4044767_4047085_4065887_4067896_RF	-0.362629207	-4.41276426	0.000784271	0.025038962	-0.391357411	0.777745902	-1.28576698	-1	T1DM
16_4065887_4067896_4145870_4149370_FF	-0.358825866	-4.464550904	0.000715054	0.024359678	-0.301020595	0.779798959	-1.282381809	-1	T1DM
16_4065887_4067896_4169801_4171577_FF	-0.356727176	-4.448531827	0.00073576	0.024772487	-0.32893059	0.780934159	-1.280517683	-1	T1DM
16_4065887_4067896_4209511_4211354_FR	-0.355168037	-4.543545518	0.000621447	0.0233799	-0.163840278	0.781778581	-1.279134559	-1	T1DM
11_36524913_36530925_36605543_36609927_FR	-0.350562005	-5.497779151	0.000121787	0.012585299	1.426356702	0.784278521	-1.275057232	-1	T1DM
1_172053648_172060321_172083100_172087823_RR	-0.346486038	-6.509010811	2.49E-05	0.004135312	2.961825036	0.786497433	-1.271459967	-1	T1DM
22_23509706_23512087_23566317_23569153_RR	-0.333558559	-6.257680647	3.64E-05	0.005431251	2.59501906	0.793576627	-1.260117757	-1	T1DM
6_6621204_6623713_6637118_6642924_RR	-0.333492256	-5.635209705	9.73E-05	0.010795146	1.644336465	0.793613099	-1.260059846	-1	T1DM
1_198564901_198567426_198666515_198673906_FF	-0.324552901	-5.625071996	9.89E-05	0.010835398	1.628356124	0.798545821	-1.252276292	-1	T1DM
11_36531355_36534043_36605543_36609927_FR	-0.314053685	-5.234700644	0.000188513	0.015535298	1.001070959	0.804378438	-1.243195929	-1	T1DM

Table 21b. Type 1 diabetes mellitus (T1DM) probes - EpiSwitch™ markers to stratify T1DM vs. healthy controls

Probe	AveExpr	t	P.Value	adj.P.Val	B	FC	FC_1	LS	Loop detected
8_131812677_131818201_131980638_131987302_FF	-0.307426412	-3.665767474	0.003071423	0.045822458	-1.723581252	0.808081992	-1.237498187	-1	T1DM
8_131812677_131818201_131974285_131980638_FR	-0.306962662	-3.331746233	0.005739788	0.063202307	-2.329928992	0.808341789	-1.237100461	-1	T1DM
8_131796786_131800910_131812677_131818201_RF	-0.305084735	-3.709790489	0.00282993	0.04428099	-1.643918716	0.809394676	-1.2354912	-1	T1DM
X_19555372_19559004_19587789_19592813_FR	-0.303254166	-4.451820709	0.000731458	0.024723863	-0.323197898	0.810422331	-1.233924537	-1	T1DM
8_131812677_131818201_131926196_131933918_FR	-0.300945102	-3.610939996	0.003401862	0.048335494	-1.822913931	0.811720468	-1.231951194	-1	T1DM
8_131812677_131818201_132011208_132012836_FR	-0.299926052	-3.822687959	0.002295478	0.039410264	-1.440092801	0.812294031	-1.231081311	-1	T1DM
1_171805618_171810940_171986876_171988822_FF	-0.297441732	-4.378415333	0.000833987	0.025559591	-0.45144788	0.813694006	-1.228963213	-1	T1DM
1_161576950_161581654_161627152_161631654_FR	-0.293499837	-4.993456509	0.000283792	0.017602604	0.602048693	0.815920313	-1.225609884	-1	T1DM
X_19644496_19650796_19796774_19799668_RR	-0.29153113	-5.444999193	0.000132841	0.013212313	1.341873638	0.817034481	-1.223938553	-1	T1DM
8_42099384_42103137_42121759_42128721_FF	-0.291180044	-4.84874089	0.000364105	0.019220333	0.358685225	0.817233334	-1.223640738	-1	T1DM

Table 21b. Type 1 diabetes mellitus (T1DM) probes - EpiSwitch™ markers to stratify T1DM vs. healthy controls

Probe	AveExpr	t	P.Value	adj.P.Val	B	FC	FC_1	LS	Loop detected
5_42419594_42423647_42597654_42605427_FR	-0.290654281	-5.236418944	0.00018797	0.015535298	1.003882431	0.817531214	-1.223194886	-1	T1DM
6_6569800_6579319_6621204_6623713_RR	-0.287951764	-4.560501785	0.00060307	0.023192749	-0.134494067	0.819064083	-1.220905691	-1	T1DM
8_131812677_131818201_132023344_132028736_FR	-0.285057864	-3.395159822	0.00509506	0.059532252	-2.214691188	0.820708691	-1.218459133	-1	T1DM
5_42419594_42423647_42515628_42519035_FF	-0.283604972	-5.163591759	0.000212494	0.016129041	0.884339625	0.821535617	-1.217232679	-1	T1DM
5_67483678_67490216_67602566_67610345_RF	-0.282353934	-4.358632105	0.000864094	0.025847275	-0.486117992	0.822248323	-1.216177609	-1	T1DM
5_42419594_42423647_42519035_42531458_FR	-0.282109082	-5.019367142	0.00027149	0.017273522	0.645309644	0.822387886	-1.215971219	-1	T1DM
8_131812677_131818201_132011208_132012836_FF	-0.281315812	-3.314316703	0.005931032	0.064089653	-2.361599138	0.822840202	-1.215302798	-1	T1DM
5_42419594_42423647_42546292_42555639_FR	-0.280553106	-4.951991516	0.000304709	0.018144005	0.53261908	0.823275326	-1.214660477	-1	T1DM
16_4071891_4073711_4204978_4209511_RF	-0.279952461	-4.81303872	0.000387359	0.019869659	0.298198819	0.823618157	-1.214154875	-1	T1DM
22_23509706_23512087_23570512_23575772_RR	-0.278366248	-5.235317419	0.000188318	0.015535298	1.002080172	0.824524205	-1.212820671	-1	T1DM

Table 21c. Type 1 diabetes mellitus (T1DM) probes - EpiSwitch™ markers to stratify T1DM vs. healthy controls	Probes sequence
Probe	60 mer
11_923549_925733_976127_979142_FR	GCCTGCAGGGGGGCGCCCCCGCGCCTGCCTCGACCACACATCCACATGGACGCATGGCAGG
3_3117964_3119702_3187910_3199411_RF	TGTACAATGTGCTACACCACTCACACCCTCGACAACTTCAGGTAGGAGTGAGTGATAGCT
16_4065887_4067896_4109379_4115518_FR	CGCCGGGCCGACACCCACATTGTCTTCTTCGAAAAAAAAAAAAAAAAAAAGAAAAAAAAAGAAA
1_172083100_172087823_172151185_172154127_FF	TCACCTCTGTCACCCACCCGTTCCACTCTCGATGCTCTCTTAGTGTTCCAATTCTCAGCT
16_31228760_31230406_31342509_31344379_FR	GGTGGCATCCCCATCACTTCTCCATGCCTCGAGGTCCCCAACCCCCTGCCGCTCATCGTG
1_171936106_171939290_172083100_172087823_RF	TCACCTCTGTCACCCACCCGTTCCACTCTCGAATAGCTCCTATTGTTATGGAGTGTAGCA
1_172061602_172067357_172083100_172087823_RF	TCACCTCTGTCACCCACCCGTTCCACTCTCGATAAAGCACTTAGAACATGGCATATACTC
1_171811918_171813464_172083100_172087823_RF	TCACCTCTGTCACCCACCCGTTCCACTCTCGAATTAGGAATCAGCATTTCTTCCACTGAG
11_36531355_36534043_36605543_36609927_RR	CCGCCCCTGTCCTCTCGCTTCCCGCTGGTCGATCCACACCACCAGCAGTGGGGCACAA
1_171887726_171889817_172083100_172087823_RF	TCACCTCTGTCACCCACCCGTTCCACTCTCGAAATAGTAAAATTTGATTATCAAAATTTT
11_1010876_1013083_964245_969445_FF	GTGCCCTCCTCGCCCCTGATGGGTCTGGTCGAGACCAGCCTCAACATGGAGAAACACCAT
1_172083100_172087823_172211232_172223166_FF	TCACCTCTGTCACCCACCCGTTCCACTCTCGAGGCTGCAGTGAATCATAATCATAGCACT
6_32135728_32138270_32149729_32154447_FF	ACTGATGGCATCCCCCGTGCGCTTCCGGTCGATGGGGCCAGGGGGCTATGGGGATAACCT
16_4065887_4067896_4204978_4209511_FF	CGCCGGGCCGACACCCACATTGTCTTCTTCGATCCCTGGGCTACAAGGTGGGCGATTCTG
16_31342509_31344379_31355595_31363682_RF	AGTGGTCTCACCATGGCTTTCTTCCAATTCGAGGTCCCCAACCCCCTGCCGCTCATCGTG
1_161590754_161594100_161627152_161631654_RR	AGGACAGAGACCCCTAATTCCACCACCATCGACCCTTCTGCTTTCTCTCCAGGGGATGGC
16_4004273_4006715_4065887_4067896_RF	CGCCGGGCCGACACCCACATTGTCTTCTTCGACATCCACTCTTCTGGGCATTCCCAGCCT

Table 21c. Type 1 diabetes mellitus (T1DM) probes - EpiSwitch™ markers to stratify T1DM vs. healthy controls	Probes sequence
Probe	60 mer
16_4065887_4067896_4209511_4211354_FF	CGCCGGGCCGACACCCACATTGTCTTCTTCGATTTGCATTTCCCTAATGATCGGTGATGT
13_111748012_111752622_111942125_111944243_RR	TCCGTGACCCCCACAGCCGGTCGCCACATCGATTATCCAGAAGCTTCTTTTTTTTTAACC
19_10341612_10343024_10406169_10407761_FF	TGCGGAAATGATGGACACTACACCTTCATCGACCTCGTGATCTGGCCGCCTCGGCCTTCC
16_4044767_4047085_4065887_4067896_RF	CGCCGGGCCGACACCCACATTGTCTTCTTCGATTTTTATAGTATGTGAATTATATCTCAAC
16_4065887_4067896_4145870_4149370_FF	CGCCGGGCCGACACCCACATTGTCTTCTTCGAGTTCCTTGGAAGCTTTAATTTGCATTCC
16_4065887_4067896_4169801_4171577_FF	CGCCGGGCCGACACCCACATTGTCTTCTTCGAATCTCCCATCTGCTCTTTCAACCAAGCT
16_4065887_4067896_4209511_4211354_FR	CGCCGGGCCGACACCCACATTGTCTTCTTCGAACCCCTTTAAACCACTGACCTTGTCCCT
11_36524913_36530925_36605543_36609927_FR	TTATCAACCCGGCGTCTGGAACAATCGCTCGATCCACACCACCAGCAGTGGGGCACAA
1_172053648_172060321_172083100_172087823_RR	CTCCACGTCACCCCATGTCAATTCCAAGTCGATGCCAGACACTCTTCTGGGGGTGGGGTG
22_23509706_23512087_23566317_23569153_RR	CATCCCATCCCCCAGGCTGAAATGTGAGTCGACTGTGGCCGCCACACAGTGGTCACTGCT
6_6621204_6623713_6637118_6642924_RR	CTCCCCTCTCCCCCGGGCATGTGGGCCCTCGAACTGCAAAAAAAAAAAAAAAAAACAGAACTAA
1_198564901_198567426_198666515_198673906_FF	TTGAACCCAAGAGGTCACACCACTGCACTCGACGCCCAGCAAGTAGGCACAGTTCCCAAT
11_36531355_36534043_36605543_36609927_FR	AGTTCTTTCTTGAATTCTTTCCTGATACTCGATCCACACCACACCAGCAGTGGGGCACAA
8_131812677_131818201_131980638_131987302_FF	TCTTTAGCACCCGGGCCCCACAATTGTCTCGAAGCTTCTCTTCTGAACCTGGTGAAGCAG
8_131812677_131818201_131974285_131980638_FR	TCTTTAGCACCCGGGCCCCACAATTGTCTCGATGCTTTCATGGGACACTTTGAAAATAAA
8_131796786_131800910_131812677_131818201_RF	TCTTTAGCACCCGGGCCCCACAATTGTCTCGACCATATGGTCTTTGTTGTGACACTCAAC
X_19555372_19559004_19587789_19592813_FR	AGAAACAGCTAACTGATCCCTAAACTCCTCGAGTTGAGATCTGGCGGCCTGAATGCTGGT

Table 21c. Type 1 diabetes mellitus (T1DM) probes - EpiSwitch™ markers to stratify T1DM vs. healthy controls	Probes sequence
Probe	60 mer
8_131812677_131818201_131926196_131933918_FR	TCTTTAGCACCCGGGCCCCACAATTGTCTCGATAAAATGTTAATAACGTTGTCAAGATTA
8_131812677_131818201_132011208_132012836_FR	TCTTTAGCACCCGGGCCCCACAATTGTCTCGATCTGCTGCGGTGGGTCCATAGACTGGCA
1_171805618_171810940_171986876_171988822_FF	GGCCAGAGCGCCGGCAAGAGCTCGGTGCTCGAAAGAAAAAAAAAAATACTAGGGGGTAGG
1_161576950_161581654_161627152_161631654_FR	ACCCAGGATAAAACGCAGTGTTGACCGATCGACCCTTCTGCTTTCTCTCCAGGGGATGGC
X_19644496_19650796_19796774_19799668_RR	TTCATTCATTCATTCATTCATACATCGAAAGGCCAGTAGGTGTGATCTGAGGAAGG
8_42099384_42103137_42121759_42128721_FF	CAAGATAAAGGAAGAGTGAAATCCTGTCTCGACCGGGCGACTCCCCCGGGGCGGGGGTGG
5_42419594_42423647_42597654_42605427_FR	GCGGCACTCGGCCTCTCCGCAGCAGTTCTCGAGGAAAGACTTACTAGGTCCTGCAGTATT
6_6569800_6579319_6621204_6623713_RR	TCCCCAGCCTGCTCTCTGGTAGACCTCTTCGAGGGCCCACATGCCCGGGGGAGAGGGGAG
8_131812677_131818201_132023344_132028736_FR	TCTTTAGCACCCGGGCCCCACAATTGTCTCGAATCTAGGATAGACGCATGCAGCCCCCTGG
5_42419594_42423647_42515628_42519035_FF	GCGGCACTCGGCCTCTCCGCAGCAGTTCTCGAATACCAAGAAAAAAGTCACATGACTAACA
5_67483678_67490216_67602566_67610345_RF	CACTGCACCACCCTGTACATAAGTCCCCTCGACTTCAGCTCCAGTGAAGAAGACACTACT
5_42419594_42423647_42519035_42531458_FR	GCGGCACTCGGCCTCTCCGCAGCAGTTCTCGAGAGCCAGGAGGCTCTTGTGGTCTAATCT
8_131812677_131818201_132011208_132012836_FF	TCTTTAGCACCCGGGCCCCACAATTGTCTCGAGCTTCAGTTCCGGCATCTACAGAATGCT
5_42419594_42423647_42546292_42555639_FR	GCGGCACTCGGCCTCTCCGCAGCAGTTCTCGATTGAGCCTGAAAAATGAGGTGAAAAAAT
16_4071891_4073711_4204978_4209511_RF	CAGAATCGCCCCACCTTGTAGCCCAGGGATCGACGGCAAGCCACTCACCCTCAGCCCTATC
22_23509706_23512087_23570512_23575772_RR	CATCCCATCCCCCAGGCTGAAATGTGAGTCGAGACTTCCTTTTTCATCTGTGGATCATTT

Table 21d. Type 1 diabetes mellitus (T1DM) probes - EpiSwitch™ markers to stratify T1DM vs. healthy controls	Probe Location					4 kb Sequence Location				
Probe	Chr	Start1	End1	Start2	End2	Chr	Start1	End1	Start2	End2
11_923549_925733_976127_979142_FR	11	925704	925733	976128	976157	11	921734	925733	976128	980127
3_3117964_3119702_3187910_3199411_RF	3	3117965	3117994	3199382	3199411	3	3117965	3121964	3195412	3199411
16_4065887_4067896_4109379_4115518_FR	16	4067867	4067896	4109380	4109409	16	4063897	4067896	4109380	4113379
1_172083100_172087823_172151185_172154127_FF	1	17208779 4	17208782 3	17215409 8	17215412 7	1	17208382 4	17208782 3	17215012 8	17215412 7
16_31228760_31230406_31342509_31344379_FR	16	31230377	31230406	31342510	31342539	16	31226407	31230406	31342510	31346509
1_171936106_171939290_172083100_172087823_RF	1	17193610 7	17193613 6	17208779 4	17208782 3	1	17193610 7	17194010 6	17208382 4	17208782 3
1_172061602_172067357_172083100_172087823_RF	1	17206160 3	17206163 2	17208779 4	17208782 3	1	17206160 3	17206560 2	17208382 4	17208782 3
1_171811918_171813464_172083100_172087823_RF	1	17181191 9	17181194 8	17208779 4	17208782 3	1	17181191 9	17181591 8	17208382 4	17208782 3
11_36531355_36534043_36605543_36609927_RR	11	36531356	36531385	36605544	36605573	11	36531356	36535355	36605544	36609543
1_171887726_171889817_172083100_172087823_RF	1	17188772 7	17188775 6	17208779 4	17208782 3	1	17188772 7	17189172 6	17208382 4	17208782 3
11_1010876_1013083_964245_969445_FF	11	1013054	1013083	969416	969445	11	1009084	1013083	965446	969445
1_172083100_172087823_172212232_172223166_FF	1	17208779 4	17208782 3	17222313 7	17222316 6	1	17208382 4	17208782 3	17221916 7	17222316 6
6_32135728_32138270_32149729_32154447_FF	6	32138241	32138270	32154418	32154447	6	32134271	32138270	32150448	32154447

Table 21d. Type 1 diabetes mellitus (T1DM) probes - EpiSwitch™ markers to stratify T1DM vs. healthy controls

Probe	Probe Location					4 kb Sequence Location				
	Chr	Start1	End1	Start2	End2	Chr	Start1	End1	Start2	End2
16_4065887_4067896_4204978_4209511_FF	***16***	4067867	4067896	4209482	4209511	16	4063897	4067896	4205512	4209511
16_31342509_31344379_31355595_31363682_RF	16	31342510	31342539	31363653	31363682	16	31342510	31346509	31359683	31363682
1_161590754_161594100_161627152_161631654_RR	1	161590755	161590784	161627153	161627182	1	161590755	161594754	161627153	161631152
16_4004273_4006715_4065887_4067896_RF	16	4004274	4004303	4067867	4067896	16	4004274	4008273	4063897	4067896
16_4065887_4067896_4209511_4211354_FF	16	4067867	4067896	4211325	4211354	16	4063897	4067896	4207355	4211354
13_111748012_111752622_111942125_111942423_RR	13	111748013	111748042	111942126	111942155	13	111748013	111752013	111942126	111946126
19_10341612_10343024_10406169_10407761_FF	19	10342995	10343024	10407732	10407761	19	10339025	10343024	10403762	10407761
16_4044767_4047085_4065887_4067896_RF	16	4044768	4044797	4067867	4067896	16	4044768	4048767	4063897	4067896
16_4065887_4067896_4145870_4149370_FF	16	4067867	4067896	4149341	4149370	16	4063897	4067896	4145371	4149370
16_4065887_4067896_4169801_4171577_FF	16	4067867	4067896	4171548	4171577	16	4063897	4067896	4167578	4171577
16_4065887_4067896_4209511_4211354_FR	16	4067867	4067896	4209512	4209541	16	4063897	4067896	4209512	4213511
11_36524913_36530925_36605543_36609927_FR	11	36530896	36530925	36605544	36605573	11	36526926	36530925	36605544	36609543
1_172053648_172060321_172083100_172087823_RR	1	172053649	172053678	172060322	172060351	1	172053649	172057649	172060322	172083100
22_23509706_23512087_23566317_23569153_RR	22	23509707	23509736	23566318	23566347	22	23509707	23513706	23566318	23570317
6_6621204_6623713_6637118_6642924_RR	6	6621205	6621234	6637119	6637148	6	6621205	6625204	6637119	6641118

Table 21d. Type 1 diabetes mellitus (T1DM) probes - EpiSwitch™ markers to stratify T1DM vs. healthy controls	Probe Location					4 kb Sequence Location				
Probe	Chr	Start1	End1	Start2	End2	Chr	Start1	End1	Start2	End2
1_198564901_198567426_198666515_198673906_FF	1	198567397	198567426	198667377	198673906	1	198563427	198567426	198669907	198673906
11_36531355_36534043_36605543_36609927_FR	11	36534014	36534043	36605544	36605573	11	36530044	36534043	36605544	36609543
8_131812677_131818201_131980638_131987302_FF	8	131818172	131818201	131987273	131987302	8	131814202	131818201	131983303	131987302
8_131812677_131818201_131974285_131980638_FR	8	131818172	131818201	131974276	131974315	8	131814202	131818201	131974276	131978285
8_131796786_131800910_131812677_131818201_RF	8	131796787	131796816	131818172	131818201	8	131796787	131800786	131814202	131818201
X_19555372_19559004_19587789_19592813_FR	X	19558975	19559004	19587790	19587819	X	19555005	19559004	19587790	19591789
8_131812677_131818201_131926196_131933918_FR	8	131818172	131818201	131926197	131926226	8	131814202	131818201	131926197	131930196
8_131812677_131818201_132011208_132012836_FR	8	131818172	131818201	132011209	132011238	8	131814202	131818201	132011209	132015208
1_171805618_171810940_171986876_171988822_FF	1	171810911	171810940	171988793	171988822	1	171806941	171810940	171984823	171988822
1_161576950_161581654_161627152_161631654_FR	1	161581625	161581654	161627153	161627182	1	161577655	161581654	161627153	161631152
X_19644496_19650796_19796774_19799668_RR	X	19644497	19644526	19796775	19796804	X	19644497	19648496	19796775	19800774
8_42099384_42103137_42121759_42128721_FF	8	42103108	42103137	42128692	42128721	8	42099138	42103137	42124722	42128721

Table 21d. Type 1 diabetes mellitus (T1DM) probes - EpiSwitch™ markers to stratify T1DM vs. healthy controls	Probe Location					4 kb Sequence Location				
Probe	Chr	Start1	End1	Start2	End2	Chr	Start1	End1	Start2	End2
5_42419594_42423647_42597654_42605427_FR	5	42423618	42423647	42597655	42597684	5	42419648	42423647	42597655	42601654
6_6569800_6579319_6621204_6623713_RR	6	6569801	6569830	6621205	6621234	6	6569801	6573800	6621205	6625204
8_131812677_131818201_132023344_132028736_FR	8	131818172	131818201	132023345	132023374	8	131814202	131818201	132023345	132027344
5_42419594_42423647_42515628_42519035_FF	5	42423618	42423647	42519006	42519035	5	42419648	42423647	42515036	42519035
5_67483678_67490216_67602566_67610345_RF	5	67483679	67483708	67610316	67610345	5	67483679	67487678	67606346	67610345
5_42419594_42423647_42519035_42531458_FR	5	42423618	42423647	42519036	42519065	5	42419648	42423647	42519036	42523035
8_131812677_131818201_132011208_132012836_FF	8	131818172	131818201	132012807	132012836	8	131814202	131818201	132008837	132012836
5_42419594_42423647_42546292_42555639_FR	5	42423618	42423647	42546293	42546322	5	42419648	42423647	42546293	42550292
16_407y1891_4073711_4204978_4209511_RF	16	4071892	4071921	4209482	4209511	16	4071892	4075891	4205512	4209511
22_23509706_23512087_23570512_23575772_RR	22	23509707	23509736	23570513	23570542	22	23509707	23513706	23570513	23574512

Table 22a. Ulcerative colitis (UC) probes – EpiSwitch™ markers to stratify UC vs. healthy controls									
Probe	GeneLocus	Probe_Count_Total	Probe_Count_Sig	HyperG_Stats	FDR_HyperG	Percent_Sig	reps.	Avg_CV	logFC
7_45584884_45588878_45736475_45743273_RF	ADCY1	30	12	0.004580887	0.235152183	40	4	7.078	-0.446398112
1_161576950_161581654_161625371_161626958_FR	FCGR2B;FCGR3A	96	33	0.000124986	0.02420002	34.38	4	6.877	-0.423285329
7_55087969_55089963_55247129_55257611_RR	EGFR	196	53	0.001552393	0.119534297	27.04	4	7.023	-0.419269005
7_55087969_55089963_55276177_55281528_RF	EGFR	196	53	0.001552393	0.119534297	27.04	4	6.334	-0.405109539
7_55087969_55089963_55146890_55151406_RF	EGFR	196	53	0.001552393	0.119534297	27.04	4	7.084	-0.399784507
7_55087969_55089963_55113347_55115444_RR	EGFR	196	53	0.001552393	0.119534297	27.04	4	6.958	-0.352217394
1_161495318_161496726_161576950_161581654_RF	FCGR3A	37	12	0.028212278	0.511140091	32.43	4	5.212	-0.349947619
7_55087969_55089963_55159296_55163839_RF	EGFR	196	53	0.001552393	0.119534297	27.04	4	8.654	-0.34865568
19_6736190_6739207_6832841_6834474_FR	VAV1	16	7	0.016844872	0.370587187	43.75	4	6.787	-0.338622756
22_22718523_22726462_22744564_22754970_FR	IGLV7-43	6	3	0.079534188	0.846404874	50	4	2.861	-0.334996016
16_31228760_31230406_31342509_31344379_FR	ITGAM	28	9	0.056781917	0.675037525	32.14	4	3.617	-0.330551344
7_55087969_55089963_55294211_55302386_RR	EGFR	196	53	0.001552393	0.119534297	27.04	4	7.634	-0.328896083
19_10341612_10343024_10406169_10407761_FF	ICAM1	6	4	0.012352453	0.300931881	66.67	4	4.066	-0.325517106
1_161543531_161545118_161576950_161581654_RF	FCGR2B;FCGR3A	96	33	0.000124986	0.02420002	34.38	4	6.008	-0.320338689

Table 22a. Ulcerative colitis (UC) probes – EpiSwitch™ markers to stratify UC vs. healthy controls

Probe	GeneLocus	Probe_Count_Total	Probe_Count_Sig	HyperG_Stats	FDR_HyperG	Percent_Sig	reps.	Avg_CV	logFC
1_161576950_161581654_161627152_161631654_FR	FCGR2B;FCGR3A	96	33	0.000124986	0.02420002	34.38	4	5.054	-0.318424708
7_55087969_55089963_55224588_55235839_RR	EGFR	196	53	0.001552393	0.119534297	27.04	4	5.298	-0.314588705
6_32135728_32138270_32149729_32154447_FF	AGER	3	2	0.088576681	0.846404874	66.67	4	4.106	-0.313025185
8_42121759_42128721_42138740_42142593_FR	IKBKB	11	5	0.035894511	0.552775462	45.45	4	4.556	-0.308386023
11_118135384_118142619_118155813_118161617_RR	CD3E	9	4	0.065256334	0.744405584	44.44	3	2.805	-0.298082914
X_19555372_19559004_19587789_19592813_FR	SH3KBP1	168	49	0.000373076	0.038302514	29.17	4	8.54	-0.293447331
1_161519223_161525894_161625371_161626958_RR	FCGR2B;FCGR3A	96	33	0.000124986	0.02420002	34.38	4	4.896	-0.287540254
7_55087969_55089963_55116799_55120169_RR	EGFR	196	53	0.001552393	0.119534297	27.04	4	7.021	-0.286823372
8_42099384_42103137_42121759_42128721_FF	IKBKB	11	5	0.035894511	0.552775462	45.45	4	5.228	-0.284393396
1_161576950_161581654_161625371_161626958_RR	FCGR2B;FCGR3A	96	33	0.000124986	0.02420002	34.38	4	4.334	-0.282643839
1_161519223_161525894_161543531_161545118_RR	FCGR2B;FCGR3A	96	33	0.000124986	0.02420002	34.38	4	5.216	-0.277758539
10_98420739_98422156_98475835_98481698_FF	PIK3AP1	117	38	0.000157143	0.02420002	32.48	4	3.216	-0.27713633
11_923549_925733_976127_979142_FR	AP2A2	16	6	0.056983687	0.675037525	37.5	4	3.706	-0.276532824

Table 22a. Ulcerative colitis (UC) probes – EpiSwitch™ markers to stratify UC vs. healthy controls									
Probe	GeneLocus	Probe_Count_Total	Probe_Count_Sig	HyperG_Stats	FDR_HyperG	Percent_Sig	reps.	Avg_CV	logFC
X_19747473_19749276_19778202_19779729_RF	SH3KBP1	168	49	0.000373076	0.038302514	29.17	4	15.829	-0.272986417
X_19555372_19559004_19801817_19808062_FF	SH3KBP1	168	49	0.000373076	0.038302514	29.17	4	6.811	-0.269931263
7_55116799_55120169_55294211_55302386_RF	EGFR	196	53	0.001552393	0.119534297	27.04	4	4.233	-0.268950471
13_111740592_111744283_111955243_111957450_RR	ARHGEF7	61	18	0.022511064	0.462227188	29.51	4	5.616	-0.267816486
13_111740592_111744283_111951910_111954429_RF	ARHGEF7	61	18	0.022511064	0.462227188	29.51	4	7.583	-0.267054433
7_45584884_45588878_45641165_45652147_RR	ADCY1	30	12	0.004580887	0.235152183	40	4	12.069	-0.265005547
7_55087969_55089963_55247129_55257611_RF	EGFR	196	53	0.001552393	0.119534297	27.04	4	5.297	-0.262657522
19_6698247_6701314_6736190_6739207_RF	C3	10	4	0.093434304	0.846404874	40	4	3.227	-0.260946755
11_118135384_118142619_118155813_118161617_FR	CD3E	9	4	0.065256334	0.744405584	44.44	4	4.111	-0.260502589
11_65282265_65284907_65314616_65318092_RF	SCYL1	5	3	0.04594332	0.59107768	60	4	5.079	-0.260154428
10_98397707_98399014_98464393_98468588_FF	PIK3AP1	117	38	0.000157143	0.02420002	32.48	4	6.946	-0.259297107
X_19555372_19559004_19778202_19779729_FF	SH3KBP1	168	49	0.000373076	0.038302514	29.17	4	10.156	-0.258850322
X_19747473_19749276_19801817_19808062_RR	SH3KBP1	168	49	0.000373076	0.038302514	29.17	4	19.347	-0.258747317
7_55146890_55151406_55294211_55302386_RF	EGFR	196	53	0.001552393	0.119534297	27.04	4	4.893	-0.258444556

Table 22a. Ulcerative colitis (UC) probes – EpiSwitch™ markers to stratify UC vs. healthy controls

Probe	GeneLocus	Probe_Count_Total	Probe_Count_Sig	HyperG_Stats	FDR_HyperG	Percent_Sig	reps.	Avg_CV	logFC
7_55146890_55151406_55276177_55281528_FF	EGFR	196	53	0.001552393	0.119534297	27.04	4	18.078	-0.257369248
7_55159296_55163839_55294211_55302386_FF	EGFR	196	53	0.001552393	0.119534297	27.04	4	7.722	-0.2568125
8_42121759_42128721_42152856_42153945_FF	IKBKB	11	5	0.035894511	0.552775462	45.45	3	5.25	-0.255746698
10_98426247_98429729_98475835_98481698_FF	PIK3AP1	117	38	0.000157143	0.02420002	32.48	4	4.164	-0.255158509
7_55061795_55064635_55087969_55089963_FR	EGFR	196	53	0.001552393	0.119534297	27.04	4	4.1	-0.254266064
7_55061795_55064635_55159296_55163839_RF	EGFR	196	53	0.001552393	0.119534297	27.04	4	3.739	-0.254243219
22_22707693_22711085_22732515_22734197_FF	IGLV7-43	6	3	0.079534188	0.846404874	50	4	11.929	-0.2530292
X_19652532_19655511_19778202_19779729_RF	SH3KBP1	168	49	0.000373076	0.038302514	29.17	4	14.941	-0.251445257
13_111730571_111732652_111951910_111954429_FF	ARHGEF7	61	18	0.022511064	0.462227188	29.51	4	15.948	-0.25127638

Table 22b. Ulcerative colitis (UC) probes – EpiSwitch™ markers to stratify UC vs. healthy controls									
Probe	AveExpr	t	P.Value	adj.P.Val	B	FC	FC_1	LS	Loop detected
7_45584884_45588878_45736475_45743273_RF	-0.446398112	-9.435638924	8.85E-06	0.004888244	4.153848344	0.733872778	-1.362634002	-1	UC
1_161576950_161581654_161625371_161626958_FR	-0.423285329	-9.204965599	1.07E-05	0.004888244	3.975717007	0.745724513	-1.340977777	-1	UC
7_55087969_55089963_55247129_55257611_RR	-0.419269005	-6.369833493	0.00016899	0.009683903	1.315750587	0.747803431	-1.337249815	-1	UC
7_55087969_55089963_55276177_55281528_RF	-0.405109539	-7.588326295	4.69E-05	0.006547249	2.575442784	0.755178953	-1.324189448	-1	UC
7_55087969_55089963_55146890_55151406_RF	-0.399784507	-5.530622454	0.000452878	0.012730546	0.327975654	0.757971492	-1.319310833	-1	UC
7_55087969_55089963_55113347_55115444_RR	-0.352217394	-5.963318431	0.000269342	0.011344149	0.850286475	0.783379134	-1.276521108	-1	UC
1_161495318_161496726_161576950_161581654_RF	-0.349947619	-8.588507383	1.83E-05	0.005775865	3.474436751	0.784612585	-1.274514352	-1	UC
7_55087969_55089963_55159296_55163839_RF	-0.34865568	-6.004819682	0.000256579	0.011156666	0.89890943	0.785315523	-1.27337353	-1	UC
19_6736190_6739207_6832841_6834474_FR	-0.338622756	-5.016498633	0.000868153	0.014251641	-0.329969771	0.790795872	-1.264548837	-1	UC
22_22718523_22726462_22744564_22754970_FR	-0.334996016	-7.89866635	3.47E-05	0.006456046	2.866475514	0.792786326	-1.261373926	-1	UC
16_31228760_31230406_31342509_31344379_FR	-0.330551344	-8.609951248	1.80E-05	0.005775865	3.49251633	0.795232518	-1.25749385	-1	UC
7_55087969_55089963_55294211_55302386_RR	-0.328896083	-7.358953281	5.90E-05	0.007290908	2.352921549	0.796145443	-1.256051904	-1	UC

Table 22b. Ulcerative colitis (UC) probes – EpiSwitch™ markers to stratify UC vs. healthy controls									
Probe	AveExpr	t	P.Value	adj.P.Val	B	FC	FC_1	LS	Loop detected
19_10341612_10343024_10406169_10407761_FF	-0.325517106	-8.528225011	1.94E-05	0.005775865	3.423355584	0.798012303	-1.253113512	-1	UC
1_161543531_161545118_161576950_161581654_RF	-0.320338689	-8.393511114	2.19E-05	0.0059132	3.307822028	0.800881839	-1.248623643	-1	UC
1_161576950_161581654_161627152_161631654_FR	-0.318424708	-8.12686228	2.80E-05	0.006456046	3.073378688	0.801945051	-1.246968229	-1	UC
7_55087969_55089963_55224588_55235839_RR	-0.314588705	-5.391216831	0.000538302	0.012974733	0.153625606	0.804080192	-1.243657051	-1	UC
6_32135728_32138270_32149729_32154447_FF	-0.313025185	-5.602106309	0.000414904	0.012478833	0.41622014	0.804952085	-1.242309969	-1	UC
8_42121759_42128721_42138740_42142593_FR	-0.308386023	-7.622976448	4.53E-05	0.00653853	2.608502416	0.807544673	-1.238321585	-1	UC
11_118135384_118142619_118155813_118161617_RR	-0.298082914	-8.094870263	2.88E-05	0.006456046	3.044725378	0.813332453	-1.229509527	-1	UC
X_19555372_19559004_19587789_19592813_FR	-0.293447331	-7.444102967	5.41E-05	0.006996488	2.436279661	0.815950009	-1.225565279	-1	UC
1_161519223_161525894_161625371_161626958_RR	-0.287540254	-7.03430515	8.23E-05	0.008172517	2.026741952	0.819297743	-1.220557493	-1	UC
7_55087969_55089963_55116799_55120169_RR	-0.286823372	-6.401828897	0.000163044	0.009583602	1.351378276	0.819704957	-1.219951144	-1	UC
8_42099384_42103137_42121759_42128721_FF	-0.284393396	-6.612254602	0.00012922	0.00920378	1.582121005	0.821086775	-1.217898071	-1	UC
1_161576950_161581654_161625371_161626958_RR	-0.282643839	-7.052682312	8.08E-05	0.008172517	2.045566049	0.822083112	-1.216422021	-1	UC
1_161519223_161525894_161543531_161545118_RR	-0.277758539	-7.444555354	5.41E-05	0.006996488	2.436720143	0.824871594	-1.2123099	-1	UC

Table 22b. Ulcerative colitis (UC) probes – EpiSwitch™ markers to stratify UC vs. healthy controls

Probe	AveExpr	t	P.Value	adj.P.Val	B	FC	FC_1	LS	Loop detected
10_98420739_98422156_98475835_984816 98_FF	-0.27713633	-6.046853388	0.000244 323	0.011126993	0.947897504	0.825227424	-1.211787165	-1	UC
11_923549_925733_976127_979142_FR	-0.276532824	-5.676486002	0.000379 047	0.012018309	0.50721141	0.825572704	-1.211280358	-1	UC
X_19747473_19749276_19778202_1977972 9_RF	-0.272986417	-5.696390475	0.000370 035	0.012015418	0.531418605	0.827604608	-1.208306467	-1	UC
X_19555372_19559004_19801817_1980806 2_FF	-0.269931263	-6.52881124	0.000141 611	0.009455532	1.491358118	0.829359059	-1.205750379	-1	UC
7_55116799_55120169_55294211_5530238 6_RF	-0.268950471	-5.739838279	0.000351 166	0.011815747	0.584050005	0.829923077	-1.204930948	-1	UC
13_111740592_111744283_111955243_111 957450_RR	-0.267816486	-4.205996047	0.002616 378	0.022984284	-1.450517746	0.830575668	-1.203984222	-1	UC
13_111740592_111744283_111951910_111 954429_RF	-0.267054433	-6.52226367	0.000142 637	0.009455532	1.484195419	0.831014507	-1.203348428	-1	UC
7_45584884_45588878_45641165_4565214 7_RR	-0.265005547	-4.183322812	0.002702 107	0.023242532	-1.483290206	0.832195535	-1.20164067	-1	UC
7_55087969_55089963_55247129_5525761 1_RF	-0.262657522	-6.47694387	0.000149 967	0.009455532	1.4344543	0.833551058	-1.199686558	-1	UC
19_6698247_6701314_6736190_6739207_R F	-0.260946755	-6.928808517	9.20E-05	0.008557251	1.91782663	0.83454008	-1.198264797	-1	UC

Table 22b. Ulcerative colitis (UC) probes – EpiSwitch™ markers to stratify UC vs. healthy controls									
Probe	AveExpr	t	P.Value	adj.P.Val	B	FC	FC_1	LS	Loop detected
11_118135384_118142619_118155813_118161617_FR	-0.260502589	-6.591823929	0.00013214	0.00920378	1.559987043	0.834797052	-1.197895941	-1	UC
11_65282265_65284907_65314616_65318092_RF	-0.260154428	-6.459744124	0.000152857	0.009455532	1.415501514	0.834998535	-1.197606891	-1	UC
10_98397707_98399014_98464393_98468588_FF	-0.259297107	-6.141944944	0.000218896	0.010581613	1.057766824	0.83549488	-1.196895425	-1	UC
X_19555372_19559004_19778202_19779729_FF	-0.258850322	-5.163588632	0.000717941	0.013426134	-0.137531553	0.835753663	-1.196524819	-1	UC
X_19747473_19749276_19801817_19808062_RR	-0.258747317	-5.628459403	0.000401793	0.012388987	0.448555164	0.835813336	-1.196439392	-1	UC
7_55146890_55151406_55294211_55302386_RF	-0.258444556	-5.48941519	0.000476478	0.012730546	0.27675066	0.835988756	-1.196188337	-1	UC
7_55146890_55151406_55276177_55281528_FF	-0.257369248	-6.856937539	9.93E-05	0.008748963	1.842787206	0.83661209	-1.195297094	-1	UC
7_55159296_55163839_55294211_55302386_FF	-0.2568125	-5.445425032	0.00050316	0.012730546	0.22177796	0.836935008	-1.194835908	-1	UC
8_42121759_42128721_42152856_42153945_FF	-0.255746698	-6.333295655	0.000176072	0.009766371	1.274887498	0.837553529	-1.193953539	-1	UC
10_98426247_98429729_98475835_98481698_FF	-0.255158509	-5.308765695	0.000596982	0.01321755	0.049093344	0.83789507	-1.193466862	-1	UC

Table 22b. Ulcerative colitis (UC) probes – EpiSwitch™ markers to stratify UC vs. healthy controls

Probe	AveExpr	t	P.Value	adj.P.Val	B	FC	FC_1	LS	Loop detected
7_55061795_55064635_55087969_55089963_FR	-0.254266064	-6.603821021	0.000130416	0.00920378	1.572991286	0.838413548	-1.192728817	-1	UC
7_55061795_55064635_55159296_55163839_RF	-0.254243219	-5.394082975	0.000536379	0.012974733	0.157240388	0.838426825	-1.19270993	-1	UC
22_22707693_22711085_22732515_22734197_FF	-0.2530292	-4.020252229	0.003414746	0.026069411	-1.721154237	0.839132653	-1.191706694	-1	UC
X_19652532_19655511_19778202_19779729_RF	-0.251445257	-5.59071546	0.000420715	0.012478833	0.402210859	0.840054447	-1.190399031	-1	UC
13_111730571_111732652_111951910_111954429_FF	-0.25127638	-4.396690328	0.002000888	0.020387988	-1.17786842	0.840152787	-1.190259695	-1	UC

Table 22c. Ulcerative colitis (UC) probes – EpiSwitch™ markers to stratify UC vs. healthy controls	Probe Sequence
Probe	60 mer
7_45584884_45588878_45736475_45743273_RF	TCCATCCCCAACTTCAATGACTTCTACATCGACATAGTACTGAAAGTCTTTGCTAGAGTA
1_161576950_161581654_161625371_161626958_FR	ACCCAGGATAAAACGCAGTGTTGACCGATCGATTCTTGGGCCTTCCACCTTCACATTCTA
7_55087969_55089963_55247129_55257611_RR	AGACCCGGACGTCTCCGCGAGGCGGCCATCGAGGAAGGCTCCTCTGAGAAAGAGTCTGCT
7_55087969_55089963_55276177_55281528_RF	CTCCAGAAAGGACCTTTAAACACTCAGGTCGATGGCCGCCTCGCGGAGACGTCCGGGTCT
7_55087969_55089963_55146890_55151406_RF	TTCCTGAAAAAAAATGGCTACTTATTAGTCGATGGCCGCCTCGCGGAGACGTCCGGGTCT
7_55087969_55089963_55113347_55115444_RR	AGACCCGGACGTCTCCGCGAGGCGGCCATCGAGTGTCAACATGATGGCACCTAAAGCTGT
1_161495318_161496726_161576950_161581654_RF	ACCCAGGATAAAACGCAGTGTTGACCGATCGAGGGCGTGGACTTCTACACGTCCATCACT
7_55087969_55089963_55159296_55163839_RF	CACTTTTTATAGAAGAGAAAGTGAAGATTCGATGGCCGCCTCGCGGAGACGTCCGGGTCT
19_6736190_6739207_6832841_6834474_FR	CCTTGGCGAAGGCGCGTCCTGGGTTGGATCGAAGTGTATGATCGCATGGCATTTTGTACA
22_22718523_22726462_22744564_22754970_FR	CCTTCCCTCGTATTCAGTGAGATTCATTTCGAACTCCTGACCTCAGGTGAGGTGATCCAC
16_31228760_31230406_31342509_31344379_FR	GGTGGCATCCCCATCACTTCTCCATGCCTCGAGGTCCCCAACCCCCTGCCGCTCATCGTG
7_55087969_55089963_55294211_55302386_RR	AGACCCGGACGTCTCCGCGAGGCGGCCATCGAATGATCAGTGATGTTGATTTTTTTTTCT
19_10341612_10343024_10406169_10407761_FF	TGCGGAAATGATGGACACTACACCTTCATCGACCTCGTGATCTGGCCGCCTCGGCCTTCC
1_161543531_161545118_161576950_161581654_RF	ACCCAGGATAAAACGCAGTGTTGACCGATCGATTCTTGGGCCTTCCACCTTCACATTCTA
1_161576950_161581654_161627152_161631654_FR	ACCCAGGATAAAACGCAGTGTTGACCGATCGACCCTTCTGCTTTCTCTCCAGGGGATGGC
7_55087969_55089963_55224588_55235839_RR	AGACCCGGACGTCTCCGCGAGGCGGCCATCGACATATTTCCTGTTCCCTTGGAATAAAAA
6_32135728_32138270_32149729_32154447_FF	ACTGATGGCATCCCCCGTGCGCTTCCGGTCGATGGGGCCAGGGGGGCTATGGGGATAACCT
8_42121759_42128721_42138740_42142593_FR	CCACCCCCGCCCCGGGGGGAGTCGCCCGGTCGAGGGCCTGGCAAGAAGACAGAAGCCGACT

Table 22c. Ulcerative colitis (UC) probes – EpiSwitch™ markers to stratify UC vs. healthy controls	Probe Sequence
Probe	60 mer
11_118135384_118142619_118155813_118161617_RR	GAATTCCGACTCCCGTTTTGAAATTGTATCGAACTCCTGACCTCGGGTGACCCGTATGCC
X_19555372_19559004_19587789_19592813_FR	AGAAACAGCTAACTGATCCCTAAACTCCTCGAGTTGAGATCTGGCGGCCTGAATGCTGGT
1_161519223_161525894_161625371_161626958_RR	CAGAATCACTCTGTGGAACCAAAGAGCTTCGATTCTTGGGCCTTCCACCTTCACATTCTA
7_55087969_55089963_55116799_55120169_RR	AGACCCGGACGTCTCCGCGAGGCGGCCATCGATTTTGCTGATGCAATACAGTTTTACAGG
8_42099384_42103137_42121759_42128721_FF	CAAGATAAAGGAAGAGTGAAATCCTGTCTCGACCGGGCGACTCCCCCGGGGCGGGGGTGG
1_161576950_161581654_161625371_161626958_RR	AGTGATGGACTTGTAGAAGTCCACGCCCTCGATTCTTGGGCCTTCCACCTTCACATTCTA
1_161519223_161525894_161543531_161545118_RR	CAGAATCACTCTGTGGAACCAAAGAGCTTCGATTCTTGGGCCTTCCACCTTCACATTCTA
10_98420739_98422156_98475835_98481698_FF	GGCGGGTGGATCACCTGAGGTCAGGAGCTCGATCTCCTGACCTCGTGATCCGCCCGCCTC
11_923549_925733_976127_979142_FR	GCCTGCAGGGGGCGCCCCCGCGCCTGCCTCGACCACACATCCACATGGACGCATGGCAGG
X_19747473_19749276_19778202_19779729_RF	CATGATAGTTAAGAGATCATATCTAGAATCGATACAGTTCATAATTTATGAACATGTGGA
X_19555372_19559004_19801817_19808062_FF	AGAAACAGCTAACTGATCCCTAAACTCCTCGAGAGAGTCTTAAAAAGGGAACAAACCAAA
7_55116799_55120169_55294211_55302386_RF	ACCAAACCCAAGGTCCGCTGCTCGCTGCTCGATTTTGCTGATGCAATACAGTTTTACAGG
13_111740592_111744283_111955243_111957450_RR	AGTGACCTAATCACAGCTCACCGGAGCCTCGAGGCCTTAGCTCCTCAAGGATACACATTT
13_111740592_111744283_111951910_111954429_RF	AATTCTGTTGGAAGAATAATTTAAAATATCGAGGCTCCGGTGAGCTGTGATTAGGTCACT
7_45584884_45588878_45641165_45652147_RR	TACTCTAGCAAAGACTTTCAGTACTATGTCGATGGTGATTTTACCTTGTGGAGCAATGGC
7_55087969_55089963_55247129_55257611_RF	AGCAAGAGGCTGAGCCTAACTCTCCCTTTCGATGGCCGCCTCGCGGAGACGTCCGGGTCT
19_6698247_6701314_6736190_6739207_RF	CCTTGGCGAAGGCGCGTCCTGGGTTGGATCGATCTCTTGACCTCACGATCCACCCGCCTC
11_118135384_118142619_118155813_118161617_FR	GCAGAGGGAATTGAGAGAAGTTAAGAGTTCGAACTCCTGACCTCGGGTGACCCGTATGCC

Table 22c. Ulcerative colitis (UC) probes – EpiSwitch™ markers to stratify UC vs. healthy controls	Probe Sequence
Probe	60 mer
11_65282265_65284907_65314616_65318092_RF	GACACGGGCGCATCACGAGGTCAAGAGATCGATCTCTTGACCTGGTGATCTACCCGCCTC
10_98397707_98399014_98464393_98468588_FF	ATACTGACACACTATTCCACCCACAAAGTCGATAACATGTTTATAGAGAAATAGCCCTCT
X_19555372_19559004_19778202_19779729_FF	AGAAACAGCTAACTGATCCCTAAACTCCTCGATTCTAGATATGATCTCTTAACTATCATG
X_19747473_19749276_19801817_19808062_RR	TCCACATGTTCATAAATTATGAACTGTATCGAAATGTCTATTCATATTCATTAACTCAAG
7_55146890_55151406_55294211_55302386_RF	ACCAAACCCAAGGTCCGCTGCTCGCTGCTCGAGATGGGGAAGGAAAGGTCAGAAGAGGAG
7_55146890_55151406_55276177_55281528_FF	TTCCTGAAAAAAAAATGGCTACTTATTAGTCGACCTGAGTGTTTAAAGGTCCTTTCTGGAG
7_55159296_55163839_55294211_55302386_FF	CACTTTTTATAGAAGAGAAAGTGAAGATTCGAGCAGCGAGCAGCGGACCTTGGGTTTGGT
8_42121759_42128721_42152856_42153945_FF	CCACCCCCGCCCCGGGGGAGTCGCCCGGTCGAACTCCGGACCTCGTGATCTGCCCACCTC
10_98426247_98429729_98475835_98481698_FF	GAGGTGGGCGGATCCTAAGGTCAGGAGTTCGATCTCCTGACCTCGTGATCCGCCCGCCTC
7_55061795_55064635_55087969_55089963_FR	TTAACATGGTCTATGTGTCCCTGCATGATCGATGGCCGCCTCGCGGAGACGTCCGGGTCT
7_55061795_55064635_55159296_55163839_RF	CACTTTTTATAGAAGAGAAAGTGAAGATTCGACCTCCTGACCTCGGAACCACAATCACTC
22_22707693_22711085_22732515_22734197_FF	TTTTCCCTGGAAATCCTAGTTGGGGTGCTCGAGCCGCCAACGAGGATTTCTAGGAGAAGA
X_19652532_19655511_19778202_19779729_RF	CATGATAGTTAAGAGATCATATCTAGAATCGACTGTGCAGCTATGCTGTTTTATGTGTAA
13_111730571_111732652_111951910_111954429_FF	TCTTTGTTACTGGAATATACGAATAAAATCGATATTTTAAATTATTCTTCCAACAGAATT

Table 22d. Ulcerative colitis (UC) probes – EpiSwitch™ markers to stratify UC vs. healthy controls	Probe Location					4 kb Sequence Location				
Probe	Chr	Start1	End1	Start2	End2	Chr	Start1	End1	Start2	End2
7_45584884_45588878_45736475_45743273_RF	7	45584885	45584914	45743244	45743273	7	45584885	45588884	45739274	45743273
1_161576950_161581654_161625371_161626958_FR	1	161581625	161581654	161625372	161625401	1	161577655	161581654	161625372	161629371
7_55087969_55089963_55247129_55257611_RR	7	55087970	55087999	55247130	55247159	7	55087970	55091969	55247130	55251129
7_55087969_55089963_55276177_55281528_RF	7	55087970	55087999	55281499	55281528	7	55087970	55091969	55277529	55281528
7_55087969_55089963_55146890_55151406_RF	7	55087970	55087999	55151377	55151406	7	55087970	55091969	55147407	55151406
7_55087969_55089963_55113347_55115444_RR	7	55087970	55087999	55113348	55113377	7	55087970	55091969	55113348	55117347
1_161495318_161496726_161576950_161581654_RF	1	161495319	161495348	161581625	161581654	1	161495319	161499318	161577655	161581654
7_55087969_55089963_55159296_55163839_RF	7	55087970	55087999	55163810	55163839	7	55087970	55091969	55159840	55163839
19_6736190_6739207_6832841_6834474_FR	19	6739178	6739207	6832842	6832871	19	6735208	6739207	6832842	6836841
22_22718523_22726462_22744564_22754970_FR	22	22726433	22726462	22744565	22744594	22	22722463	22726462	22744565	22748564
16_31228760_31230406_31342509_31344379_FR	16	31230377	31230406	31342510	31342539	16	31226407	31230406	31342510	31346509
7_55087969_55089963_55294211_55302386_RR	7	55087970	55087999	55294212	55294241	7	55087970	55091969	55294212	55298211
19_10341612_10343024_10406169_10407761_FF	19	10342995	10343024	10407732	10407761	19	10339025	10343024	10403762	10407761
1_161543531_161545118_161576950_161581654_RF	1	161543532	161543561	161581625	161581654	1	161543532	161547531	161577655	161581654

Table 22d. Ulcerative colitis (UC) probes – EpiSwitch™ markers to stratify UC vs. healthy controls	Probe Location					4 kb Sequence Location				
Probe	Chr	Start1	End1	Start2	End2	Chr	Start1	End1	Start2	End2
1_161576950_161581654_161627152_161631654_FR	1	161581625	161581654	161627153	161627182	1	161577655	161581654	161627153	161631152
7_55087969_55089963_55224588_55235839_RR	7	55087970	55087999	55224589	55224618	7	55087970	55091969	55224589	55228588
6_32135728_32138270_32149729_32154447_FF	6	32138241	32138270	32154418	32154447	6	32134271	32138270	32150448	32154447
8_42121759_42128721_42138740_42142593_FR	8	42128692	42128721	42138741	42138770	8	42124722	42128721	42138741	42142740
11_118135384_118142619_118155813_118161617_RR	11	118135385	118135414	118155814	118155843	11	118135385	118139384	118155814	118159813
X_19555372_19559004_19587789_19592813_FR	X	19558975	19559004	19587790	19587819	X	19555005	19559004	19587790	19591789
1_161519223_161525894_161625371_161626958_RR	1	161519224	161519253	161625372	161625401	1	161519224	161523223	161625372	161629371
7_55087969_55089963_55116799_55120169_RR	7	55087970	55087999	55116800	55116829	7	55087970	55091969	55116800	55120799
8_42099384_42103137_42121759_42128721_FF	8	42103108	42103137	42128692	42128721	8	42099138	42103137	42124722	42128721
1_161576950_161581654_161625371_161626958_RR	1	161576951	161576980	161625372	161625401	1	161576951	161580950	161625372	161629371
1_161519223_161525894_161543531_161545118_RR	1	161519224	161519253	161543532	161543561	1	161519224	161523223	161543532	161547531
10_98420739_98422156_98475835_98481698_FF	10	98422127	98422156	98481669	98481698	10	98418157	98422156	98477699	98481698
11_923549_925733_976127_979142_FR	11	925704	925733	976128	976157	11	921734	925733	976128	980127
X_19747473_19749276_19778202_19779729_RF	X	19747474	19747503	19779700	19779729	X	19747474	19751473	19775730	19779729

Table 22d. Ulcerative colitis (UC) probes – EpiSwitch™ markers to stratify UC vs. healthy controls	Probe Location					4 kb Sequence Location				
Probe	Chr	Start1	End1	Start2	End2	Chr	Start1	End1	Start2	End2
X_19555372_19559004_19801817_19808062_FF	X	19558975	19559004	19808033	19808062	X	19555005	19559004	19804063	19808062
7_55116799_55120169_55294211_55302386_RF	7	55116800	55116829	55302357	55302386	7	55116800	55120799	55298387	55302386
13_111740592_111744283_111955243_111957450_RR	13	111740593	111740622	111955244	111955273	13	111740593	111744592	111955244	111959243
13_111740592_111744283_111951910_111954429_RF	13	111740593	111740622	111954400	111954429	13	111740593	111744592	111950430	111954429
7_45584884_45588878_45641165_45652147_RR	7	45584885	45584914	45641166	45641195	7	45584885	45588884	45641166	45645165
7_55087969_55089963_55247129_55257611_RF	7	55087970	55087999	55257582	55257611	7	55087970	55091969	55253612	55257611
19_6698247_6701314_6736190_6739207_RF	19	6698248	6698277	6739178	6739207	19	6698248	6702247	6735208	6739207
11_118135384_118142619_118155813_118161617_FR	11	118142590	118142619	118155814	118155843	11	118138620	118142619	118155814	118159813
11_65282265_65284907_65314616_65318092_RF	11	65282266	65282295	65318063	65318092	11	65282266	65286265	65314093	65318092
10_98397707_98399014_98464393_98468588_FF	10	98398985	98399014	98468559	98468588	10	98395015	98399014	98464589	98468588
X_19555372_19559004_19778202_19779729_FF	X	19558975	19559004	19779700	19779729	X	19555005	19559004	19775730	19779729
X_19747473_19749276_19801817_19808062_RR	X	19747474	19747503	19801818	19801847	X	19747474	19751473	19801818	19805817
7_55146890_55151406_55294211_55302386_RF	7	55146891	55146920	55302357	55302386	7	55146891	55150890	55298387	55302386
7_55146890_55151406_55276177_55281528_FF	7	55151377	55151406	55281499	55281528	7	55147407	55151406	55277529	55281528
7_55159296_55163839_55294211_55302386_FF	7	55163810	55163839	55302357	55302386	7	55159840	55163839	55298387	55302386

Table 22d. Ulcerative colitis (UC) probes – EpiSwitch™ markers to stratify UC vs. healthy controls

Probe	Probe Location					4 kb Sequence Location				
	Chr	Start1	End1	Start2	End2	Chr	Start1	End1	Start2	End2
8_421217 59_42128721_42152856_42153945_FF	8	42128692	42128721	42153916	42153945	8	42124722	42128721	42149946	42153945
10_98426247_98429729_98475835_98481698_F F	10	98429700	98429729	98481669	98481698	10	98425730	98429729	98477699	98481698
7_55061795_55064635_55087969_55089963_FR	7	55064606	55064635	55087970	55087999	7	55060636	55064635	55087970	55091969
7_55061795_55064635_55159296_55163839_RF	7	55061796	55061825	55163810	55163839	7	55061796	55065795	55159840	55163839
22_22707693_22711085_22732515_22734197_F F	22	22711056	22711085	22734168	22734197	22	22707086	22711085	22730198	22734197
X_19652532_19655511_19778202_19779729_RF	X	19652533	19652562	19779700	19779729	X	19652533	19656532	19775730	19779729
13_111730571_111732652_111951910_1119544 29_FF	13	111732623	111732652	111954400	111954429	13	111728653	111732652	111950430	111954429

Table 23a. SLE probes - EpiSwitch™ markers to stratify SLE vs. healthy controls									
Probe	GeneLocus	Probe_Count_Total	Probe_Count_Sig	HyperG_Stats	FDR_HyperG	Percent_Sig	reps.	Avg_CV	logFC
1_243635945_243637780_243655019_243656128_RR	AKT3	329	64	0.046948	0.964009	19.45	4	10.288	-1.11091
1_243655019_243656128_243727939_243733240_RF	AKT3	329	64	0.046948	0.964009	19.45	4	12.13	-1.046316
1_243655019_243656128_243954381_243957141_RF	AKT3	329	64	0.046948	0.964009	19.45	4	8.518	-1.021078
1_243655019_243656128_243680126_243690814_RF	AKT3	329	64	0.046948	0.964009	19.45	4	9.474	-1.004448
1_243655019_243656128_243867949_243871515_RF	AKT3	329	64	0.046948	0.964009	19.45	4	7.102	-0.959208
1_243655019_243656128_243860421_243862288_RF	AKT3	329	64	0.046948	0.964009	19.45	4	4.984	-0.955948
14_24795078_24798615_24843066_24844509_RR	ADCY4	10	4	0.060426	0.976846	40	4	3.707	-0.92139
1_243655019_243656128_243816190_243822519_RF	AKT3	329	64	0.046948	0.964009	19.45	4	7.955	-0.899817
14_24795078_24798615_24825321_24828950_RR	ADCY4	10	4	0.060426	0.976846	40	4	2.67	-0.883452
1_243655019_243656128_243938249_243942270_RF	AKT3	329	64	0.046948	0.964009	19.45	4	8.951	-0.797775
11_923549_925733_976127_979142_FR	AP2A2	16	5	0.097194	1	31.25	4	3.706	-0.750885
1_243655019_243656128_243864025_243867879_RF	AKT3	329	64	0.046948	0.964009	19.45	4	7.444	-0.7203
1_161590754_161594100_161627152_161631654_RR	FCGR2B;FCGR3A	96	21	0.076199	0.976846	21.88	4	3.793	-0.718037
1_243637780_243640834_243655019_243656128_RR	AKT3	329	64	0.046948	0.964009	19.45	4	3.009	-0.708974
7_45584884_45588878_45736475_45743273_RF	ADCY1	30	11	0.004679	0.356305	36.67	4	7.078	-0.694141
16_31228760_31230406_31342509_31344379_FR	ITGAM	28	10	0.008518	0.356305	35.71	4	3.617	-0.685914

Table 23a. SLE probes - EpiSwitch™ markers to stratify SLE vs. healthy controls

Probe	GeneLocus	Probe_Count_Total	Probe_Count_Sig	HyperG_Stats	FDR_HyperG	Percent_Sig	reps.	Avg_CV	logFC
5_7602410_7603529_7797003_7800572_FR	ADCY2	306	64	0.011305	0.356305	20.92	4	3.224	-0.683956
1_243635945_243637780_243655019_243656128_FR	AKT3	329	64	0.046948	0.964009	19.45	4	6.732	-0.673434
11_36583119_36588432_36605543_36609927_RR	RAG2;RAG1	10	5	0.012725	0.356305	50	4	3.345	-0.662419
1_243655019_243656128_243784071_243785870_RF	AKT3	329	64	0.046948	0.964009	19.45	4	4.885	-0.655741
1_243655019_243656128_243707136_243710471_RR	AKT3	329	64	0.046948	0.964009	19.45	4	4.221	-0.634957
16_31342509_31344379_31355595_31363682_RF	ITGAM	28	10	0.008518	0.356305	35.71	4	3.29	-0.634798
13_111748012_111752622_111942125_111944243_RR	ARHGEF7	61	15	0.052278	0.976846	24.59	4	3.57	-0.629905
11_36588999_36590845_36605543_36609927_FR	RAG2;RAG1	10	5	0.012725	0.356305	50	4	3.56	-0.616867
1_243637780_243640834_243655019_243656128_FR	AKT3	329	64	0.046948	0.964009	19.45	4	5.632	-0.609976
1_243655019_243656128_243784071_243785870_RR	AKT3	329	64	0.046948	0.964009	19.45	4	3.8	-0.605805
1_243655019_243656128_243790811_243793831_RR	AKT3	329	64	0.046948	0.964009	19.45	4	4.891	-0.603487
1_243655019_243656128_243669663_243671724_RF	AKT3	329	64	0.046948	0.964009	19.45	4	5.918	-0.603109
1_243655019_243656128_243946602_243948601_RR	AKT3	329	64	0.046948	0.964009	19.45	4	4.691	-0.598414
1_243655019_243656128_243674676_243679954_RR	AKT3	329	64	0.046948	0.964009	19.45	4	4.312	-0.594725
5_140009798_140011363_140052701_140055063_FR	CD14	23	7	0.060939	0.976846	30.43	4	3.095	-0.56733
1_243655019_243656128_243915703_243918596_RR	AKT3	329	64	0.046948	0.964009	19.45	4	4.647	-0.565895
3_111125030_111133059_111238151_111244343_FF	CD96	121	31	0.003927	0.356305	25.62	4	2.675	-0.56071

Table 23a. SLE probes - EpiSwitch™ markers to stratify SLE vs. healthy controls

Probe	GeneLocus	Probe_Count_Total	Probe_Count_Sig	HyperG_Stats	FDR_HyperG	Percent_Sig	reps.	Avg_CV	logFC
11_119059609_119061980_119165298_119170353_RF	CBL	19	6	0.068591	0.976846	31.58	4	4.022	-0.559209
1_243655019_243656128_243669663_243671724_RR	AKT3	329	64	0.046948	0.964009	19.45	4	3.629	-0.558549
1_243655019_243656128_243816190_243822519_RR	AKT3	329	64	0.046948	0.964009	19.45	4	4.429	-0.557515
1_243655019_243656128_243774056_243776138_RR	AKT3	329	64	0.046948	0.964009	19.45	4	3.649	-0.552494
21_46345789_46346831_46359648_46362975_FF	ITGB2	7	3	0.085633	0.976846	42.86	4	3.661	-0.546289
3_111080379_111085861_111238151_111244343_FF	CD96	121	31	0.003927	0.356305	25.62	4	3.59	-0.541985
3_111054275_111073125_111238151_111244343_FF	CD96	121	31	0.003927	0.356305	25.62	4	3.619	-0.538482
5_7602410_7603529_7787275_7792598_FF	ADCY2	306	64	0.011305	0.356305	20.92	4	3.602	-0.532192
13_111748012_111752622_111822569_111834523_RR	ARHGEF7	61	15	0.052278	0.976846	24.59	4	3.876	-0.530585
3_123010454_123013518_123033778_123037100_RF	ADCY5	123	29	0.016881	0.43328	23.58	4	3.106	-0.52203
5_7520707_7525339_7602410_7603529_RF	ADCY2	306	64	0.011305	0.356305	20.92	4	4.127	-0.520443
1_243655019_243656128_243954381_243957141_RR	AKT3	329	64	0.046948	0.964009	19.45	4	3.861	-0.517294
21_46345789_46346831_46359648_46362975_FR	ITGB2	7	3	0.085633	0.976846	42.86	4	5.114	-0.516056
6_111988059_111992304_112042041_112045568_FR	FYN	278	67	0.000218	0.067196	24.1	4	3.654	-0.486999
5_7425481_7432673_7602410_7603529_RF	ADCY2	306	64	0.011305	0.356305	20.92	4	3.405	-0.485758
1_243655019_243656128_243760927_243763803_RF	AKT3	329	64	0.046948	0.964009	19.45	4	6.485	-0.4791
11_923549_925733_976127_979142_RR	AP2A2	16	5	0.097194	1	31.25	4	3.228	-0.477125

Table 23b. SLE probes - EpiSwitch™ markers to stratify SLE vs. healthy controls

Probe	AveExpr	t	P.Value	adj.P.Val	B	FC	FC_1	LS	Loop detected
1_243635945_243637780_243655019_243656128_RR	-1.11091	-5.599889	0.001314	0.036644	-0.448311	0.463002	-2.159818	-1	SLE
1_243655019_243656128_243727939_243733240_RF	-1.046316	-6.292863	0.000708	0.036258	0.165125	0.484203	-2.065249	-1	SLE
1_243655019_243656128_243954381_243957141_RF	-1.021078	-5.726179	0.001169	0.036644	-0.331516	0.492748	-2.029435	-1	SLE
1_243655019_243656128_243680126_243690814_RF	-1.004448	-5.274858	0.00179	0.036644	-0.759704	0.498461	-2.006175	-1	SLE
1_243655019_243656128_243867949_243871515_RF	-0.959208	-6.127974	0.000816	0.036258	0.025116	0.514339	-1.944242	-1	SLE
1_243655019_243656128_243860421_243862288_RF	-0.955948	-5.470775	0.001483	0.036644	-0.570123	0.515503	-1.939854	-1	SLE
14_24795078_24798615_24843066_24844509_RR	-0.92139	-5.247772	0.001838	0.036644	-0.786372	0.528	-1.893939	-1	SLE
1_243655019_243656128_243816190_243822519_RF	-0.899817	-5.808019	0.001085	0.03651	-0.25705	0.535955	-1.86583	-1	SLE
14_24795078_24798615_24825321_24828950_RR	-0.883452	-5.055018	0.002223	0.036852	-0.979419	0.542069	-1.844784	-1	SLE
1_243655019_243656128_243938249_243942270_RF	-0.797775	-5.316164	0.00172	0.036644	-0.719252	0.575236	-1.738418	-1	SLE
11_923549_925733_976127_979142_FR	-0.750885	-6.20439	0.000764	0.036258	0.090449	0.594239	-1.682825	-1	SLE
1_243655019_243656128_243864025_243867879_RF	-0.7203	-5.090557	0.002146	0.036644	-0.943392	0.606971	-1.647525	-1	SLE
1_161590754_161594100_161627152_161631654_RR	-0.718037	-5.082248	0.002164	0.036652	-0.951797	0.607924	-1.644943	-1	SLE
1_243637780_243640834_243655019_243656128_RR	-0.708974	-5.13893	0.002045	0.036644	-0.894671	0.611755	-1.634641	-1	SLE
7_45584884_45588878_45736475_45743273_RF	-0.694141	-9.769901	6.04E-05	0.036258	2.430319	0.618077	-1.617921	-1	SLE
16_31228760_31230406_31342509_31344379_FR	-0.685914	-5.332127	0.001693	0.036644	-0.703688	0.621612	-1.608721	-1	SLE
5_7602410_7603529_7797003_7800572_FR	-0.683956	-6.410403	0.000641	0.036258	0.26276	0.622456	-1.606539	-1	SLE

Table 23b. SLE probes - EpiSwitch™ markers to stratify SLE vs. healthy controls

Probe	AveExpr	t	P.Value	adj.P.Val	B	FC	FC_1	LS	Loop detected
1_243635945_243637780_243655019_243656128_FR	-0.673434	-4.942038	0.002491	0.036991	-1.095274	0.627012	-1.594865	-1	SLE
11_36583119_36588432_36605543_36609927_RR	-0.662419	-6.265955	0.000724	0.036258	0.142522	0.631818	-1.582734	-1	SLE
1_243655019_243656128_243784071_243785870_RF	-0.655741	-4.92646	0.002531	0.037249	-1.111407	0.634749	-1.575425	-1	SLE
1_243655019_243656128_243707136_243710471_RR	-0.634957	-4.591917	0.003585	0.038783	-1.467292	0.64396	-1.552892	-1	SLE
16_31342509_31344379_31355595_31363682_RF	-0.634798	-4.822787	0.002815	0.037729	-1.219761	0.644031	-1.552721	-1	SLE
13_111748012_111752622_111942125_111944243_RR	-0.629905	-4.021529	0.006736	0.04662	-2.11649	0.646219	-1.547463	-1	SLE
11_36588999_36590845_36605543_36609927_FR	-0.616867	-6.119132	0.000823	0.036258	0.017506	0.652085	-1.533542	-1	SLE
1_243637780_243640834_243655019_243656128_FR	-0.609976	-4.687394	0.003241	0.038485	-1.363874	0.655207	-1.526234	-1	SLE
1_243655019_243656128_243784071_243785870_RR	-0.605805	-4.459183	0.004134	0.039948	-1.613554	0.657105	-1.521828	-1	SLE
1_243655019_243656128_243790811_243793831_RR	-0.603487	-4.631626	0.003437	0.038567	-1.424099	0.658161	-1.519385	-1	SLE
1_243655019_243656128_243669663_243671724_RF	-0.603109	-5.448	0.001516	0.036644	-0.591866	0.658334	-1.518987	-1	SLE
1_243655019_243656128_243946602_243948601_RR	-0.598414	-4.44854	0.004182	0.04016	-1.625407	0.66048	-1.514051	-1	SLE
1_243655019_243656128_243674676_243679954_RR	-0.594725	-5.239517	0.001853	0.036644	-0.794521	0.662171	-1.510185	-1	SLE
5_140009798_140011363_140052701_140055063_FR	-0.56733	-4.725427	0.003114	0.038193	-1.32309	0.674865	-1.481778	-1	SLE
1_243655019_243656128_243915703_243918596_RR	-0.565895	-4.478155	0.00405	0.039553	-1.59247	0.675536	-1.480306	-1	SLE
3_111125030_111133059_111238151_111244343_FF	-0.56071	-5.792929	0.0011	0.036553	-0.270709	0.677968	-1.474995	-1	SLE
11_119059609_119061980_119165298_119170353_RF	-0.559209	-6.367158	0.000665	0.036258	0.227046	0.678674	-1.473461	-1	SLE
1_243655019_243656128_243669663_243671724_RR	-0.558549	-4.215551	0.005406	0.043054	-1.889601	0.678985	-1.472787	-1	SLE

Table 23b. SLE probes - EpiSwitch™ markers to stratify SLE vs. healthy controls

Probe	AveExpr	t	P.Value	adj.P.Val	B	FC	FC_1	LS	Loop detected
1_243655019_243656128_243816190_243822519_RR	-0.557515	-4.417923	0.004324	0.040194	-1.659611	0.679472	-1.471732	-1	SLE
1_243655019_243656128_243774056_243776138_RR	-0.552494	-4.570167	0.003669	0.038783	-1.49106	0.68184	-1.466619	-1	SLE
21_46345789_46346831_46359648_46362975_FF	-0.546289	-5.929646	0.000972	0.036258	-0.148125	0.684779	-1.460324	-1	SLE
3_111080379_111085861_111238151_111244343_FF	-0.541985	-5.838613	0.001055	0.036258	-0.229456	0.686825	-1.455975	-1	SLE
3_111054275_111073125_111238151_111244343_FF	-0.538482	-5.700713	0.001197	0.036644	-0.354883	0.688495	-1.452443	-1	SLE
5_7602410_7603529_7787275_7792598_FF	-0.532192	-9.313451	7.95E-05	0.036258	2.194884	0.691503	-1.446125	-1	SLE
13_111748012_111752622_111822569_111834523_RR	-0.530585	-3.908474	0.007678	0.048749	-2.251568	0.692274	-1.444515	-1	SLE
3_123010454_123013518_123033778_123037100_RF	-0.52203	-7.099017	0.000367	0.036258	0.800425	0.696391	-1.435975	-1	SLE
5_7520707_7525339_7602410_7603529_RF	-0.520443	-8.338933	0.000149	0.036258	1.637153	0.697158	-1.434396	-1	SLE
1_243655019_243656128_243954381_243957141_RR	-0.517294	-4.34537	0.004681	0.041129	-1.741283	0.698681	-1.431268	-1	SLE
21_46345789_46346831_46359648_46362975_FR	-0.516056	-4.976539	0.002406	0.036852	-1.059681	0.699281	-1.430041	-1	SLE
6_111988059_111992304_112042041_112045568_FR	-0.486999	-7.427349	0.000286	0.036258	1.037454	0.713508	-1.401526	-1	SLE
5_7425481_7432673_7602410_7603529_RF	-0.485758	-9.720907	6.22E-05	0.036258	2.405775	0.714122	-1.400322	-1	SLE
1_243655019_243656128_243760927_243763803_RF	-0.4791	-4.579671	0.003632	0.038783	-1.480665	0.717425	-1.393874	-1	SLE
11_923549_925733_976127_979142_RR	-0.477125	-3.945042	0.007358	0.048126	-2.207646	0.718408	-1.391967	-1	SLE

Table 23c. SLE probes - EpiSwitch™ markers to stratify SLE vs. healthy controls	Probe sequence
Probe	60 mer
1_243635945_243637780_243655019_243656128_RR	CAAATAAATTAGAATGTATTTTCATTGCTCGAGCAGGTATTTTGGATGCGGTGCCGCCTG
1_243655019_243656128_243727939_243733240_RF	TACTGAAGAAGTCTTTGAAGAGATTTCTTCGAGCAGGTATTTTGGATGCGGTGCCGCCTG
1_243655019_243656128_243954381_243957141_RF	ATTTATTGACTCCCTAGGGTCTAGGAGCTCGAGCAGGTATTTTGGATGCGGTGCCGCCTG
1_243655019_243656128_243680126_243690814_RF	TGTTTTATAATCATTATAATTTTTTCTTTCGAGCAGGTATTTTGGATGCGGTGCCGCCTG
1_243655019_243656128_243867949_243871515_RF	TAGAACTGAACATGTTTAAATGATATCGTCGAGCAGGTATTTTGGATGCGGTGCCGCCTG
1_243655019_243656128_243860421_243862288_RF	TTATACCAGATTTCAGGTGCCTAGCTGTTCGAGCAGGTATTTTGGATGCGGTGCCGCCTG
14_24795078_24798615_24843066_24844509_RR	CCCACCTCCCACCAGACAGTGGAAGCAGTCGAGTGCTGTGAGCAAAGAGGCCCTGGGCCA
1_243655019_243656128_243816190_243822519_RF	TTCCACTTATGTGATGTGTCTAAAGTAGTCGAGCAGGTATTTTGGATGCGGTGCCGCCTG
14_24795078_24798615_24825321_24828950_RR	CCCACCTCCCACCAGACAGTGGAAGCAGTCGAAGCAAAACTGTGGAGATTGGGTCGGTGA
1_243655019_243656128_243938249_243942270_RF	TGAATGGACCTCATCCTACCATTCTTTTTCGAGCAGGTATTTTGGATGCGGTGCCGCCTG
11_923549_925733_976127_979142_FR	GCCTGCAGGGGGGCGCCCCCGCGCCTGCCTCGACCACACATCCACATGGACGCATGGCAGG
1_243655019_243656128_243864025_243867879_RF	CATCTCATGTGGATTCAGAAAAAAGGTAGTCGAGCAGGTATTTTGGATGCGGTGCCGCCTG
1_161590754_161594100_161627152_161631654_RR	AGGACAGAGACCCCTAATTCCACCCACCATCGACCCTTCTGCTTTCTCTCCAGGGGATGGC
1_243637780_243640834_243655019_243656128_RR	TGCCCACCCAGACCTCCCGGCGGCTGCTTCGAGCAGGTATTTTGGATGCGGTGCCGCCTG
7_45584884_45588878_45736475_45743273_RF	TCCATCCCCAACTTCAATGACTTCTACATCGACATAGTACTGAAAGTCTTTGCTAGAGTA
16_31228760_31230406_31342509_31344379_FR	GGTGGCATCCCCATCACTTCTCCATGCCTCGAGGTCCCCAACCCCCCTGCCGCTCATCGTG
5_7602410_7603529_7797003_7800572_FR	CACTGCCCCACCTCTTACTGGCATCTCCTCGACCCCGTGCCAAGTCCCCGGGTGGTAGAG
1_243635945_243637780_243655019_243656128_FR	CGGCCGAGCCCGGGCCTAGTATCCAGAGTCGAGCAGGTATTTTGGATGCGGTGCCGCCTG

Table 23c. SLE probes - EpiSwitch™ markers to stratify SLE vs. healthy controls	Probe sequence
Probe	60 mer
11_36583119_36588432_36605543_36609927_RR	CCACCTCATAGGGGAGGGCTTTACTCAGTCGATCCACACCACCAGCAGTGGGGCACAA
1_243655019_243656128_243784071_243785870_RF	GAGCAGTACCTAGCAAATAATTAGGTGTTCGAGCAGGTATTTTGGATGCGGTGCCGCCTG
1_243655019_243656128_243707136_243710471_RR	CAGGCGGCACCGCATCCAAAATACCTGCTCGAGTAGAGGTGTCTAATATGATGCACCTAT
16_31342509_31344379_31355595_31363682_RF	AGTGGTCTCACCATGGCTTTCTTCCAATTCGAGGTCCCCAACCCCCTGCCGCTCATCGTG
13_111748012_111752622_111942125_111944243_RR	TCCGTGACCCCCACAGCCGGTCGCCACATCGATTATCCAGAAGCTTCTTTTTTTTTAACC
11_36588999_36590845_36605543_36609927_FR	CCTGTAGCTCTGATGTCAGATGGCAATGTCGATCCACACCACCAGCAGTGGGGCACAA
1_243637780_243640834_243655019_243656128_FR	CCAAAGGTATTACAAACTCAGCCTTGGTTCGAGCAGGTATTTTGGATGCGGTGCCGCCTG
1_243655019_243656128_243784071_243785870_RR	CAGGCGGCACCGCATCCAAAATACCTGCTCGAGTATTGTGTTTGATACTTTGTTCTTGAT
1_243655019_243656128_243790811_243793831_RR	CAGGCGGCACCGCATCCAAAATACCTGCTCGAAGGGATTCTGACTTGATACAGGTCCAGA
1_243655019_243656128_243669663_243671724_RF	CTGCTGAACAGAGGTGCCTGCAGATGCGTCGAGCAGGTATTTTGGATGCGGTGCCGCCTG
1_243655019_243656128_243946602_243948601_RR	CAGGCGGCACCGCATCCAAAATACCTGCTCGATGGCCAATGATTTGATTAATTATGTCTA
1_243655019_243656128_243674676_243679954_RR	CAGGCGGCACCGCATCCAAAATACCTGCTCGACAGTAGAATCTGCTGCCTGTGACCATCT
5_140009798_140011363_140052701_140055063_FR	ATAAAGGTGGGGCAAAGGGTTGAATTGGTCGACGGGGCGGGTGGGACGTGGAGCCACAGTT
1_243655019_243656128_243915703_243918596_RR	CAGGCGGCACCGCATCCAAAATACCTGCTCGATGCTATAAAATGTTACGGAAATTATGTAC
3_111125030_111133059_111238151_111244343_FF	GGTCTCTGGTAATGGCCAAATAATCTAATCGACCGCCCTGCCCCCTACTGTGGAGTTCTA
11_119059609_119061980_119165298_119170353_RF	ACCGCCTCACCTCAGCTCTCCAGTGAGATCGATCCTTTGCTGCCTGATCGGTCTTCCTCT
1_243655019_243656128_243669663_243671724_RR	CAGGCGGCACCGCATCCAAAATACCTGCTCGATGTCCTCAAACCCATATAGGAAGTACAT
1_243655019_243656128_243816190_243822519_RR	CAGGCGGCACCGCATCCAAAATACCTGCTCGATGCAACAAAAAAGAGCTAACTATCCTAAA

Table 23c. SLE probes - EpiSwitch™ markers to stratify SLE vs. healthy controls	Probe sequence
Probe	60 mer
1_243655019_243656128_243774056_243776138_RR	CAGGCGGCACCGCATCCAAAATACCTGCTCGATCAATAGACAAACATATATACACATGTT
21_46345789_46346831_46359648_46362975_FF	GCCCGACCCTGAGCTCCAGAACAGACCATCGACCTCAACAGAGGTTTCTGAAGGGGGTCA
3_111080379_111085861_111238151_111244343_FF	ATACCAAGCCAGAGGTTTCTTGACTTAATCGACCGCCCTGCCCCCTACTGTGGAGTTCTA
3_111054275_111073125_111238151_111244343_FF	TACACAATGACTTCATTTTGTCCTCATATCGACCGCCCTGCCCCCTACTGTGGAGTTCTA
5_7602410_7603529_7787275_7792598_FF	CACTGCCCCACCTCTTACTGGCATCTCCTCGAGCTCCAGAGCTTTCCTCTGAGCCCATGT
13_111748012_111752622_111822569_111834523_RR	TCCGTGACCCCCCACAGCCGGTCGCCACATCGAGTAGCTGAGATTACAGGCATGTACCACC
3_123010454_123013518_123033778_123037100_RF	TGCAGCCCACTCCCACAACAGGGAAGACTCGAACTCTCTCTGCCAGCCTCTCTGGGGGTG
5_7520707_7525339_7602410_7603529_RF	CACTGCCCCACCTCTTACTGGCATCTCCTCGACTGCCCTATTTTGTCTATAGATTATTTC
1_243655019_243656128_243954381_243957141_RR	CAGGCGGCACCGCATCCAAAATACCTGCTCGACTCAAGGTTGCCACAAATCTTCAATTTG
21_46345789_46346831_46359648_46362975_FR	GCCCGACCCTGAGCTCCAGAACAGACCATCGACTGCCGCGGGGGTCGCGTCCTCTCCATC
6_111988059_111992304_112042041_112045568_FR	GGAACTGCATCCATACTTGTTACACATCTCGAGTTGTTGCCACCCCACCCTCCTCAAACC
5_7425481_7432673_7602410_7603529_RF	CACTGCCCCACCTCTTACTGGCATCTCCTCGAGCATTAAGTCTTGGATGCTGTTGTTCTA
1_243655019_243656128_243760927_243763803_RF	CAATACAACAGAATGCAGAGTCCAGAAATCGAGCAGGTATTTTGGATGCGGTGCCGCCTG
11_923549_925733_976127_979142_RR	AGTGGTACAATCATGAATCACTACAGCCTCGACCACACATCCACATGGACGCATGGCAGG

Table 23d. SLE probes - EpiSwitch™ markers to stratify SLE vs. healthy controls	Probe location					4 kb sequence location				
Probe	Chr	Start1	End1	Start2	End2	Chr	Start1	End1	Start2	End2
1_243635945_243637780_243655019_243656128_RR	1	2436359 46	2436359 75	2436550 20	2436550 49	1	2436359 46	2436399 45	2436550 20	2436590 19
1_243655019_243656128_243727939_243733240_RF	1	2436550 20	2436550 49	2437332 11	2437332 40	1	2436550 20	2436590 19	2437292 41	2437332 40
1_243655019_243656128_243954381_243957141_RF	1	2436550 20	2436550 49	2439571 12	2439571 41	1	2436550 20	2436590 19	2439531 42	2439571 41
1_243655019_243656128_243680126_243690814_RF	1	2436550 20	2436550 49	2436907 85	2436908 14	1	2436550 20	2436590 19	2436868 15	2436908 14
1_243655019_243656128_243867949_243871515_RF	1	2436550 20	2436550 49	2438714 86	2438715 15	1	2436550 20	2436590 19	2438675 16	2438715 15
1_243655019_243656128_243860421_243862288_RF	1	2436550 20	2436550 49	2438622 59	2438622 88	1	2436550 20	2436590 19	2438582 89	2438622 88
14_24795078_24798615_24843066_24844509_RR	14	2479507 9	2479510 8	2484306 7	2484309 6	14	2479507 9	2479907 8	2484306 7	2484706 6
1_243655019_243656128_243816190_243822519_RF	1	2436550 20	2436550 49	2438224 90	2438225 19	1	2436550 20	2436590 19	2438185 20	2438225 19
14_24795078_24798615_24825321_24828950_RR	14	2479507 9	2479510 8	2482532 2	2482535 1	14	2479507 9	2479907 8	2482532 2	2482932 1
1_243655019_243656128_243938249_243942270_RF	1	2436550 20	2436550 49	2439422 41	2439422 70	1	2436550 20	2436590 19	2439382 71	2439422 70
11_923549_925733_976127_979142_FR	11	925704	925733	976128	976157	11	921734	925733	976128	980127

Table 23d. SLE probes - EpiSwitch™ markers to stratify SLE vs. healthy controls	Probe location					4 kb sequence location				
Probe	Chr	Start1	End1	Start2	End2	Chr	Start1	End1	Start2	End2
1_243655019_243656128_243864025_243867879_RF	1	243655020	243655049	243867850	243867879	1	243655020	243659019	243863880	243867879
1_161590754_161594100_161627152_161631654_RR	1	161590755	161590784	161627153	161627182	1	161590755	161594754	161627153	161631152
1_243637780_243640834_243655019_243656128_RR	1	243637781	243637810	243655020	243655049	1	243637781	243641780	243655020	243659019
7_45584884_45588878_45736475_45743273_RF	7	45584885	45584914	45743244	45743273	7	45584885	45588884	45739274	45743273
16_31228760_31230406_31342509_31344379_FR	16	31230377	31230406	31342510	31342539	16	31226407	31230406	31342510	31346509
5_7602410_7603529_7797003_7800572_FR	5	7603500	7603529	7797004	7797033	5	7599530	7603529	7797004	7801003
1_243635945_243637780_243655019_243656128_FR	1	243637751	243637780	243655020	243655049	1	243633781	243637780	243655020	243659019
11_36583119_36588432_36605543_36609927_RR	11	36583120	36583149	36605544	36605573	11	36583120	36587119	36605544	36609543
1_243655019_243656128_243784071_243785870_RF	1	243655020	243655049	243785841	243785870	1	243655020	243659019	243781871	243785870
1_243655019_243656128_243707136_243710471_RR	1	243655020	243655049	243707137	243707166	1	243655020	243659019	243707137	243711136
16_31342509_31344379_31355595_31363682_RF	16	31342510	31342539	31363653	31363682	16	31342510	31346509	31359683	31363682

Table 23d. SLE probes - EpiSwitch™ markers to stratify SLE vs. healthy controls	Probe location					4 kb sequence location				
Probe	Chr	Start1	End1	Start2	End2	Chr	Start1	End1	Start2	End2
13_111748012_111752622_111942125_111944243_RR	13	111748013	111748042	111942126	111942155	13	111748013	111752012	111942126	111946125
11_36588999_36590845_36605543_36609927_FR	11	36590816	36590845	36605544	36605573	11	36586846	36590845	36605544	36609543
1_243637780_243640834_243655019_243656128_FR	1	243640805	243640834	243655020	243655049	1	243636835	243640834	243655020	243659019
1_243655019_243656128_243784071_243785870_RR	1	243655020	243655049	243784072	243784101	1	243655020	243659019	243784072	243788071
1_243655019_243656128_243790811_243793831_RR	1	243655020	243655049	243790812	243790841	1	243655020	243659019	243790812	243794811
1_243655019_243656128_243669663_243671724_RF	1	243655020	243655049	243671695	243671724	1	243655020	243659019	243667725	243671724
1_243655019_243656128_243946602_243948601_RR	1	243655020	243655049	243946603	243946632	1	243655020	243659019	243946603	243950602
1_243655019_243656128_243674676_243679954_RR	1	243655020	243655049	243674677	243674706	1	243655020	243659019	243674677	243678676
5_140009798_140011363_140052701_140055063_FR	5	140011334	140011363	140052702	140052731	5	140007364	140011363	140052702	140056701
1_243655019_243656128_243915703_243918596_RR	1	243655020	243655049	243915704	243915733	1	243655020	243659019	243915704	243919703

Table 23d. SLE probes - EpiSwitch™ markers to stratify SLE vs. healthy controls	Probe location					4 kb sequence location				
Probe	Chr	Start1	End1	Start2	End2	Chr	Start1	End1	Start2	End2
3_111125030_111133059_111238151_111244343_FF	3	111133030	111133059	111238151	111244343	3	111129060	111133059	111238144	111244343
11_119059609_119061980_119165298_119170353_RF	11	119059610	119061980	119165298	119170353	11	119059609	119063609	119165424	119170353
1_243655019_243656128_243669663_243671724_RR	1	243655020	243656049	243669664	243671724	1	243655020	243656019	243669664	243671763
1_243655019_243656128_243816190_243822519_RR	1	243655020	243656049	243816191	243822519	1	243655020	243656019	243816191	243822590
1_243655019_243656128_243774056_243776138_RR	1	243655020	243656049	243774057	243776138	1	243655020	243656019	243774057	243776186
21_46345789_46346831_46359648_46362975_FF	21	46346802	46346831	46359648	46362975	21	46342832	46346831	46359648	46362975
3_111080379_111085861_111238151_111244343_FF	3	111085832	111085861	111238151	111244343	3	111106862	111108561	111238144	111244343
3_111054275_111073125_111238151_111244343_FF	3	111073096	111073125	111238151	111244343	3	111069126	111073125	111238144	111244343
5_7602410_7603529_7787275_7792598_FF	5	7603500	7603529	7792569	7792598	5	7599530	7603529	7788599	7792598
13_111748012_111752622_111822569_111834523_RR	13	111748013	111752622	111822570	111834523	13	111748013	111752620	111822570	111834569
3_123010454_123013518_123033778_123037100_RF	3	123013055	123013084	123033771	123037100	3	123010455	123013054	123033701	123037100

Table 23d. SLE probes - EpiSwitch™ markers to stratify SLE vs. healthy controls	Probe location					4 kb sequence location				
Probe	Chr	Start1	End1	Start2	End2	Chr	Start1	End1	Start2	End2
5_7520707_7525339_7602410_7603529_RF	5	7520708	7520737	7603500	7603529	5	7520708	7524707	7599530	7603529
1_243655019_243656128_243954381_243957141_RR	1	2436550 20	2436550 49	2439543 82	2439544 11	1	2436550 20	2436590 19	2439543 82	2439583 81
21_46345789_46346831_46359648_46362975_FR	21	4634680 2	4634683 1	4635964 9	4635967 8	21	4634283 2	4634683 1	4635964 9	4636364 8
6_111988059_111992304_112042041_112045568_FR	6	1119922 75	1119923 04	1120420 42	1120420 71	6	1119883 05	1119923 04	1120420 42	1120460 41
5_7425481_7432673_7602410_7603529_RF	5	7425482	7425511	7603500	7603529	5	7425482	7429481	7599530	7603529
1_243655019_243656128_243760927_243763803_RF	1	2436550 20	2436550 49	2437637 74	2437638 03	1	2436550 20	2436590 19	2437598 04	2437638 03
11_923549_925733_976127_979142_RR	11	923550	923579	976128	976157	11	923550	927549	976128	980127

Table 24a. Relapsing-Remitting Multiple Sclerosis (MSRR) probes – EpiSwitch™ markers to stratify MSRR vs. healthy controls

Probe	GeneLocus	Probe_Count_Total	Probe_Count_Sig	HyperG_Stats	FDR_HyperG	Percent_Sig	reps.	Avg_CV	logFC
1_171811918_171813464_172083100_172087823_RF	DNM3	902	68	0.08859	1	7.54	4	3.75	-0.549300177
1_171887726_171889817_172083100_172087823_RF	DNM3	902	68	0.08859	1	7.54	4	2.093	-0.537146861
11_36588999_36590845_36605543_36609927_FR	RAG2;RAG1	10	3	0.022581	0.695488	30	4	3.56	-0.537123703
11_36583119_36588432_36605543_36609927_RR	RAG2;RAG1	10	3	0.022581	0.695488	30	4	3.345	-0.536970673
1_172083100_172087823_172151185_172154127_FF	DNM3	902	68	0.08859	1	7.54	4	2.695	-0.52875345
1_172061602_172067357_172083100_172087823_RF	DNM3	902	68	0.08859	1	7.54	4	4.369	-0.516042591
11_36531355_36534043_36605543_36609927_FR	RAG1	44	6	0.060775	1	13.64	4	4.776	-0.514259356
11_36524913_36530925_36605543_36609927_FR	RAG1	44	6	0.060775	1	13.64	4	4.444	-0.512456898
X_19644496_19650796_19753406_19760963_RR	SH3KBP1	168	22	0.001083	0.136367	13.1	4	4.453	-0.497267732
X_19644496_19650796_19801817_19808062_RR	SH3KBP1	168	22	0.001083	0.136367	13.1	4	3.856	-0.490178577
1_171936106_171939290_172083100_172087823_RF	DNM3	902	68	0.08859	1	7.54	4	4.24	-0.489770025
1_172083100_172087823_172212232_172223166_FF	DNM3	902	68	0.08859	1	7.54	4	3.339	-0.479550197
11_923549_925733_976127_979142_FR	AP2A2	16	3	0.079231	1	18.75	4	3.706	-0.466762178
6_150252084_150255951_150278503_150282998_FF	ULBP1	13	4	0.007581	0.295659	30.77	4	3.854	-0.465746785
X_19644496_19650796_19796774_19799668_RR	SH3KBP1	168	22	0.001083	0.136367	13.1	4	3.798	-0.457016079
11_36489037_36490716_36605543_36609927_FR	RAG1	44	6	0.060775	1	13.64	4	4.796	-0.440356879

Table 24a. Relapsing-Remitting Multiple Sclerosis (MSRR) probes – EpiSwitch™ markers to stratify MSRR vs. healthy controls

Probe	GeneLocus	Probe_Count_Total	Probe_Count_Sig	HyperG_Stats	FDR_HyperG	Percent_Sig	reps.	Avg_CV	logFC
12_53578817_53581303_53603928_53605952_RF	ITGB7	1	1	0.064304	1	100	4	3.431	-0.435531598
11_36531355_36534043_36605543_36609927_RR	RAG1	44	6	0.060775	1	13.64	4	3.185	-0.42982656
10_6530169_6531558_6639985_6645189_FR	PRKCQ	125	22	1.30E-05	0.003989	17.6	4	3.137	-0.426811638
10_6530169_6531558_6632086_6637212_FR	PRKCQ	125	22	1.30E-05	0.003989	17.6	4	2.911	-0.424093073
11_923549_925733_976127_979142_RR	AP2A2	16	3	0.079231	1	18.75	4	3.228	-0.41421442
20_43244575_43248985_43318009_43319077_FR	ADA	7	2	0.069859	1	28.57	3	3.441	-0.413256671
10_6510600_6515355_6530169_6531558_RF	PRKCQ	125	22	1.30E-05	0.003989	17.6	4	4.194	-0.400405262
6_112042041_112045568_112135380_112149905_RF	FYN	278	29	0.006553	0.295659	10.43	4	3.36	-0.399738531
6_112042041_112045568_112071383_112076102_RF	FYN	278	29	0.006553	0.295659	10.43	4	2.355	-0.394579607
19_40813634_40815315_40897327_40898354_RF	PLD3	5	2	0.036239	0.93013	40	4	6.096	-0.389654595
6_111988059_111992304_112042041_112045568_FR	FYN	278	29	0.006553	0.295659	10.43	4	3.654	-0.389003289
11_36583119_36588432_36600417_36605543_RR	RAG2;RAG1	10	3	0.022581	0.695488	30	4	3.602	-0.385757062
10_6474855_6481197_6632086_6637212_RR	PRKCQ	125	22	1.30E-05	0.003989	17.6	4	3.662	-0.385687884
1_171773003_171774629_171883013_171884075_FF	DNM3	902	68	0.08859	1	7.54	4	3.231	-0.378954576
6_150252084_150255951_150307780_150309507_FF	ULBP1	13	4	0.007581	0.295659	30.77	4	4.266	-0.376981869
10_6530169_6531558_6601540_6605133_FF	PRKCQ	125	22	1.30E-05	0.003989	17.6	4	4.493	-0.37476066
5_67483678_67490216_67602566_67610345_RF	PIK3R1	14	5	0.001328	0.136367	35.71	4	3.969	-0.374337026

Table 24a. Relapsing-Remitting Multiple Sclerosis (MSRR) probes – EpiSwitch™ markers to stratify MSRR vs. healthy controls

Probe	GeneLocus	Probe_Count_Total	Probe_Count_Sig	HyperG_Stats	FDR_HyperG	Percent_Sig	reps.	Avg_CV	logFC
1_171813464_171818896_171883013_171884075_FF	DNM3	902	68	0.08859	1	7.54	4	3.041	-0.373722216
1_172053648_172060321_172083100_172087823_RR	DNM3	902	68	0.08859	1	7.54	4	4.067	-0.372802641
11_36507808_36510397_36605543_36609927_RR	RAG1	44	6	0.060775	1	13.64	4	4.148	-0.370291136
6_112042041_112045568_112058283_112061400_RF	FYN	278	29	0.006553	0.295659	10.43	4	3.078	-0.368727065
6_112042041_112045568_112109707_112111662_RF	FYN	278	29	0.006553	0.295659	10.43	4	4.037	-0.367010214
19_10341612_10343024_10406169_10407761_FF	ICAM1	6	2	0.052074	1	33.33	4	4.066	-0.364917001
6_112008166_112013438_112042041_112045568_RR	FYN	278	29	0.006553	0.295659	10.43	4	4.186	-0.361100403
10_6530169_6531558_6567582_6570484_FR	PRKCQ	125	22	1.30E-05	0.003989	17.6	4	3.089	-0.360875261
X_19737340_19741050_19801817_19808062_RF	SH3KBP1	168	22	0.001083	0.136367	13.1	4	4.018	-0.35429493
10_6474855_6481197_6663527_6669234_RR	PRKCQ	125	22	1.30E-05	0.003989	17.6	4	3.669	-0.346972125
10_6474855_6481197_6639985_6645189_RR	PRKCQ	125	22	1.30E-05	0.003989	17.6	4	3.325	-0.346904516
6_112042041_112045568_112210969_112216626_RF	FYN	278	29	0.006553	0.295659	10.43	4	4.094	-0.346182416
X_19737340_19741050_19778202_19779729_RF	SH3KBP1	168	22	0.001083	0.136367	13.1	4	4.731	-0.346178617
1_171770367_171771990_171883013_171884075_FF	DNM3	902	68	0.08859	1	7.54	4	3.37	-0.345712766
5_7402050_7407728_7602410_7603529_RF	ADCY2	306	33	0.002281	0.175665	10.78	4	3.192	-0.345212375
6_111982743_111987540_112042041_112045568_RR	FYN	278	29	0.006553	0.295659	10.43	4	3.27	-0.343509788
10_6530169_6531558_6639985_6645189_FF	PRKCQ	125	22	1.30E-05	0.003989	17.6	4	4.012	-0.341094327

Table 24b. Relapsing-Remitting Multiple Sclerosis (MSRR) probes – EpiSwitch™ markers to stratify MSRR vs. healthy controls

Probe	AveExpr	t	P.Value	adj.P.Val	B	FC	FC_1	LS	Loop detected
1_171811918_171813464_172083100_172087823_RF	-0.5493	-4.878904	2.52E-05	0.016541	2.522812	0.683352	-1.463376	-1	MSRR
1_171887726_171889817_172083100_172087823_RF	-0.537147	-4.776621	3.41E-05	0.016541	2.254684	0.689132	-1.4511	-1	MSRR
11_36588999_36590845_36605543_36609927_FR	-0.537124	-4.759332	3.58E-05	0.016541	2.209419	0.689143	-1.451077	-1	MSRR
11_36583119_36588432_36605543_36609927_RR	-0.536971	-4.754908	3.63E-05	0.016541	2.197839	0.689217	-1.450923	-1	MSRR
1_172083100_172087823_172151185_172154127_FF	-0.528753	-4.671798	4.64E-05	0.020085	1.980532	0.693153	-1.442682	-1	MSRR
1_172061602_172067357_172083100_172087823_RF	-0.516043	-4.577701	6.12E-05	0.023334	1.735112	0.699287	-1.430027	-1	MSRR
11_36531355_36534043_36605543_36609927_FR	-0.514259	-4.546753	6.71E-05	0.023334	1.654558	0.700152	-1.428261	-1	MSRR
11_36524913_36530925_36605543_36609927_FR	-0.512457	-4.551028	6.62E-05	0.023334	1.66568	0.701028	-1.426477	-1	MSRR
X_19644496_19650796_19753406_19760963_RR	-0.497268	-3.909962	0.000424	0.089384	0.02369	0.708447	-1.411538	-1	MSRR
X_19644496_19650796_19801817_19808062_RR	-0.490179	-3.837951	0.000519	0.098494	-0.156436	0.711937	-1.404619	-1	MSRR
1_171936106_171939290_172083100_172087823_RF	-0.48977	-4.328915	0.000127	0.040649	1.090307	0.712139	-1.404221	-1	MSRR
1_172083100_172087823_172212232_172223166_FF	-0.47955	-4.25668	0.000156	0.048352	0.904453	0.717201	-1.394309	-1	MSRR
11_923549_925733_976127_979142_FR	-0.466762	-4.078247	0.000262	0.068397	0.448614	0.723587	-1.382004	-1	MSRR
6_150252084_150255951_150278503_150282998_FF	-0.465747	-4.05913	0.000277	0.068397	0.400082	0.724096	-1.381032	-1	MSRR
X_19644496_19650796_19796774_19799668_RR	-0.457016	-3.577031	0.001077	0.150238	-0.799075	0.728491	-1.3727	-1	MSRR
11_36489037_36490716_36605543_36609927_FR	-0.440357	-3.841588	0.000514	0.098494	-0.147364	0.736952	-1.35694	-1	MSRR

Table 24b. Relapsing-Remitting Multiple Sclerosis (MSRR) probes – EpiSwitch™ markers to stratify MSRR vs. healthy controls

Probe	AveExpr	t	P.Value	adj.P.Val	B	FC	FC_1	LS	Loop detected
12_53578817_53581303_53603928_53605952_RF	-0.435532	-3.842051	0.000513	0.098494	-0.146209	0.739421	-1.352409	-1	MSRR
11_36531355_36534043_36605543_36609927_RR	-0.429827	-3.806914	0.000567	0.100546	-0.233725	0.742351	-1.347072	-1	MSRR
10_6530169_6531558_6639985_6645189_FR	-0.426812	-3.569871	0.001099	0.150238	-0.816466	0.743904	-1.344259	-1	MSRR
10_6530169_6531558_6632086_6637212_FR	-0.424093	-3.56223	0.001122	0.150238	-0.83501	0.745307	-1.341729	-1	MSRR
11_923549_925733_976127_979142_RR	-0.414214	-3.673148	0.000825	0.12543	-0.564294	0.750428	-1.332573	-1	MSRR
20_43244575_43248985_43318009_43319077_FR	-0.413257	-3.675048	0.00082	0.12543	-0.559628	0.750926	-1.331689	-1	MSRR
10_6510600_6515355_6530169_6531558_RF	-0.400405	-3.346683	0.002021	0.205187	-1.351146	0.757645	-1.319879	-1	MSRR
6_112042041_112045568_112135380_112149905_RF	-0.399739	-3.554581	0.001146	0.150238	-0.853557	0.757996	-1.319269	-1	MSRR
6_112042041_112045568_112071383_112076102_RF	-0.39458	-3.353416	0.001984	0.205187	-1.33524	0.760711	-1.31456	-1	MSRR
19_40813634_40815315_40897327_40898354_RF	-0.389655	-3.381122	0.001841	0.205187	-1.269629	0.763312	-1.31008	-1	MSRR
6_111988059_111992304_112042041_112045568_FR	-0.389003	-3.314793	0.002202	0.205187	-1.42629	0.763657	-1.309488	-1	MSRR
11_36583119_36588432_36600417_36605543_RR	-0.385757	-3.148846	0.003425	0.236519	-1.81172	0.765377	-1.306545	-1	MSRR
10_6474855_6481197_6632086_6637212_RR	-0.385688	-3.191411	0.003061	0.228339	-1.713785	0.765414	-1.306483	-1	MSRR
1_171773003_171774629_171883013_171884075_FF	-0.378955	-3.245663	0.00265	0.212785	-1.588019	0.768995	-1.300399	-1	MSRR
6_150252084_150255951_150307780_150309507_FF	-0.376982	-3.212931	0.002891	0.221395	-1.66402	0.770047	-1.298622	-1	MSRR
10_6530169_6531558_6601540_6605133_FF	-0.374761	-3.177187	0.003178	0.229196	-1.746585	0.771233	-1.296624	-1	MSRR
5_67483678_67490216_67602566_67610345_RF	-0.374337	-3.314195	0.002206	0.205187	-1.427696	0.77146	-1.296244	-1	MSRR

Table 24b. Relapsing-Remitting Multiple Sclerosis (MSRR) probes – EpiSwitch™ markers to stratify MSRR vs. healthy controls

Probe	AveExpr	t	P.Value	adj.P.Val	B	FC	FC_1	LS	Loop detected
1_171813464_171818896_171883013_171884075_FF	-0.373722	-3.180371	0.003152	0.229184	-1.739249	0.771789	-1.295691	-1	MSRR
1_172053648_172060321_172083100_172087823_RR	-0.372803	-3.314532	0.002204	0.205187	-1.426903	0.772281	-1.294866	-1	MSRR
11_36507808_36510397_36605543_36609927_RR	-0.370291	-3.240667	0.002686	0.212785	-1.599644	0.773626	-1.292614	-1	MSRR
6_112042041_112045568_112058283_112061400_RF	-0.368727	-3.124672	0.00365	0.240436	-1.867045	0.774466	-1.291213	-1	MSRR
6_112042041_112045568_112109707_112111662_RF	-0.36701	-3.143782	0.003471	0.236519	-1.823328	0.775388	-1.289677	-1	MSRR
19_10341612_10343024_10406169_10407761_FF	-0.364917	-3.24435	0.002659	0.212785	-1.591073	0.776514	-1.287808	-1	MSRR
6_112008166_112013438_112042041_112045568_RR	-0.3611	-3.089639	0.004001	0.240436	-1.946832	0.778571	-1.284405	-1	MSRR
10_6530169_6531558_6567582_6570484_FR	-0.360875	-2.991279	0.005165	0.241157	-2.168299	0.778692	-1.284205	-1	MSRR
X_19737340_19741050_19801817_19808062_RF	-0.354295	-3.129581	0.003604	0.240436	-1.855828	0.782252	-1.278361	-1	MSRR
10_6474855_6481197_6663527_6669234_RR	-0.346972	-2.851366	0.007382	0.259517	-2.476483	0.786232	-1.271888	-1	MSRR
10_6474855_6481197_6639985_6645189_RR	-0.346905	-2.865775	0.007118	0.258492	-2.445132	0.786269	-1.271829	-1	MSRR
6_112042041_112045568_112210969_112216626_RF	-0.346182	-2.979451	0.005325	0.241616	-2.19467	0.786663	-1.271192	-1	MSRR
X_19737340_19741050_19778202_19779729_RF	-0.346179	-3.021513	0.004777	0.240831	-2.100633	0.786665	-1.271189	-1	MSRR
1_171770367_171771990_171883013_171884075_FF	-0.345713	-2.99466	0.005121	0.240831	-2.160749	0.786919	-1.270779	-1	MSRR
5_7402050_7407728_7602410_7603529_RF	-0.345212	-3.028269	0.004694	0.240831	-2.085461	0.787192	-1.270338	-1	MSRR
6_111982743_111987540_112042041_112045568_RR	-0.34351	-3.036106	0.0046	0.240831	-2.06784	0.788122	-1.26884	-1	MSRR
10_6530169_6531558_6639985_6645189_FF	-0.341094	-2.843592	0.007528	0.259517	-2.49336	0.789442	-1.266717	-1	MSRR

Table 24c. Relapsing-Remitting Multiple Sclerosis (MSRR) probes – EpiSwitch™ markers to stratify MSRR vs. healthy controls

Probe	Probe sequence
	60 mer
1_171811918_171813464_172083100_172087823_RF	TCACCTCTGTCACCCACCCGTTCCACTCTCGAATTAGGAATCAGCATTTCTTCCACTGAG
1_171887726_171889817_172083100_172087823_RF	TCACCTCTGTCACCCACCCGTTCCACTCTCGAAATAGTAAAATTTGATTATCAAAATTTT
11_36588999_36590845_36605543_36609927_FR	CCTGTAGCTCTGATGTCAGATGGCAATGTCGATCCACACCACCAGCAGTGGGGCACAA
11_36583119_36588432_36605543_36609927_RR	CCACCTCATAGGGGAGGGCTTTACTCAGTCGATCCACACCACCAGCAGTGGGGCACAA
1_172083100_172087823_172151185_172154127_FF	TCACCTCTGTCACCCACCCGTTCCACTCTCGATGCTCTCTTAGTGTTCCAATTCTCAGCT
1_172061602_172067357_172083100_172087823_RF	TCACCTCTGTCACCCACCCGTTCCACTCTCGATAAAGCACTTAGAACATGGCATATACTC
11_36531355_36534043_36605543_36609927_FR	AGTTCTTTCTTGAATTCTTTCCTGATACTCGATCCACACCACCAGCAGTGGGGCACAA
11_36524913_36530925_36605543_36609927_FR	TTATCAACCCGGCGTCTGGAACAATCGCTCGATCCACACCACCAGCAGTGGGGCACAA
X_19644496_19650796_19753406_19760963_RR	TTCATTCATTCATTCATTCATTCATACATCGATTCTCTATTTCATTTATTTCCACTGTAA
X_19644496_19650796_19801817_19808062_RR	TTCATTCATTCATTCATTCATTCATACATCGAAATGTCTATTCATATTCATTAACTCAAG
1_171936106_171939290_172083100_172087823_RF	TCACCTCTGTCACCCACCCGTTCCACTCTCGAATAGCTCCTATTGTTATGGAGTGTAGCA
1_172083100_172087823_172212232_172223166_FF	TCACCTCTGTCACCCACCCGTTCCACTCTCGAGGCTGCAGTGAATCATAATCATAGCACT
11_923549_925733_976127_979142_FR	GCCTGCAGGGGGGCGCCCCCGCGCCTGCCTCGACCACACATCCACATGGACGCATGGCAGG
6_150252084_150255951_150278503_150282998_FF	GGGTGGGATGGGGACAGACACAAGAACTCTCGAGGTTGTAGACCTCATGGCTGGCACAAGT
X_19644496_19650796_19796774_19799668_RR	TTCATTCATTCATTCATTCATTCATACATCGAAAGGCCAGTAGGTGTGATCTGAGGAAGG
11_36489037_36490716_36605543_36609927_FR	AGTGTTGGTGAGATATTGTCTCTCAGTTTCGATCCACACCACACCAGCAGTGGGGCACAA
12_53578817_53581303_53603928_53605952_RF	CCAACCCCACTCCCCAAGTACCCCACTCTCGAGTCAGGTACAGCGCTTGAGTCCATTGTG

Table 24c. Relapsing-Remitting Multiple Sclerosis (MSRR) probes -- Epi5witch™ markers to stratify MSRR vs. healthy controls

Probe	Probe sequence
	60 mer
11_36531355_36534043_36605543_36609927_RR	CCGCCCCTGTCCTCTCGCTTCCCGCTGGTCGATCCACACCACACCAGCAGTGGGGCACAA
10_6530169_6531558_6639985_6645189_FR	AGAGAGCTGGAGAAGAGGGCGAGAAGAGTCGAAAGAATTGTGAGTAGCAGTTGTGTGGTT
10_6530169_6531558_6632086_6637212_FR	AGAGAGCTGGAGAAGAGGGCGAGAAGAGTCGATAAAGGAAAAAGTTCAGTAAAGTGTGAA
11_923549_925733_976127_979142_RR	AGTGGTACAATCATGAATCACTACAGCCTCGACCACACATCCACATGGACGCATGGCAGG
20_43244575_43248985_43318009_43319077_FR	TGGCATCCCATAGGCTTTATAGAGCAGGTCGACCTCCTGACCTCGTGATCCACCTGCCTC
10_6510600_6515355_6530169_6531558_RF	AGAGAGCTGGAGAAGAGGGCGAGAAGAGTCGAGGTATCTTTTTTCTCCGAAGGCTAGTAA
6_112042041_112045568_112135380_112149905_RF	ATCCACTTACATGAGGTACCTAGAGGAGTCGAGTTGTTGCCACCCCACCCTCCTCAAACC
6_112042041_112045568_112071383_112076102_RF	GTTAACAGTAATACGATGTTAAAAGGACTCGAGTTGTTGCCACCCCACCCTCCTCAAACC
19_40813634_40815315_40897327_40898354_RF	TGGGGAAGAGGAGCAAGTGTCAGGAAGATCGACTCATTTAATCCCCAAAACCATTCCATG
6_111988059_111992304_112042041_112045568_FR	GGAACTGCATCCATACTTGTTACACATCTCGAGTTGTTGCCACCCCACCCTCCTCAAACC
11_36583119_36588432_36600417_36605543_RR	CCACCTCATAGGGGAGGGGCTTTACTCAGTCGAGCATTTGTGTGTATGTGTGAAGTATA
10_6474855_6481197_6632086_6637212_RR	TTTAAAGATGAGGGGAGGGAAGCAGGAGTCGATAAAGGAAAAAGTTCAGTAAAGTGTGAA
1_171773003_171774629_171883013_171884075_FF	TGTAATCTGTTTTGCTATCCAATCAAGATCGAGGTCCCCCCACCCCCACATGTCTCTACC
6_150252084_150255951_150307780_150309507_FF	GGGTGGGATGGGACAGACACAAGAACTCTCGAACACTCAGCTATCAGTTTTGTTGAGTTC
10_6530169_6531558_6601540_6605133_FF	AGAGAGCTGGAGAAGAGGGCGAGAAGAGTCGACTGAATATCTTCACTCTTGAGCCAAAGT
5_67483678_67490216_67602566_67610345_RF	CACTGCACCACCCTGTACATAAGTCCCCTCGACTTCAGCTCCAGTGAAGAAGACACTACT
1_171813464_171818896_171883013_171884075_FF	AAGCAGTTTTTATCATTTCATTAATCCTTCGAGGTCCCCCCACCCCCACATGTCTCTACC

Table 24c. Relapsing-Remitting Multiple Sclerosis (MSRR) probes -- Epi5witch™ markers to stratify MSRR vs. healthy controls	Probe sequence
Probe	60 mer
1_172053648_172060321_172083100_172087823_RR	CTCCACGTCACCCCATGTCAATTCCAAGTCGATGCCAGACACTCTTCTGGGGGTGGGGTG
11_36507808_36510397_36605543_36609927_RR	GGCTGGCGGATTACTTGAAGCCAGGAGTTCGATCCACACCACACCAGCAGTGGGGCACAA
6_112042041_112045568_112058283_112061400_RF	TAAATACAGATGAAACCAACTAATAGACTCGAGTTGTTGCCACCCCACCCTCCTCAAACC
6_112042041_112045568_112109707_112111662_RF	AAGTCCTAAGAACACTGAAAATCTCAGATCGAGTTGTTGCCACCCCACCCTCCTCAAACC
19_10341612_10343024_10406169_10407761_FF	TGCGGAAATGATGGACACTACACCTTCATCGACCTCGTGATCTGGCCGCCTCGGCCTTCC
6_112008166_112013438_112042041_112045568_RR	CTCAGGAAGAAGTGGATCCCTGTTTCTTTCGAGTTGTTGCCACCCCACCCTCCTCAAACC
10_6530169_6531558_6567582_6570484_FR	AGAGAGCTGGAGAAGAGGGCGAGAAGAGTCGAAGATGTCAAAAGGAAAAATGGAAATAGT
X_19737340_19741050_19801817_19808062_RF	TTTGGTTTGTTCCCTTTTTAAGACTCTCTCGACTCACTCACATCTGCCTCATGATGGTTA
10_6474855_6481197_6663527_6669234_RR	TTTAAAGATGAGGGGAGGGAAGCAGGAGTCGAAACCAGAAGACCCAATATAATATCTAGT
10_6474855_6481197_6639985_6645189_RR	TTTAAAGATGAGGGGAGGGAAGCAGGAGTCGAAAGAATTGTGAGTAGCAGTTGTGTGGTT
6_112042041_112045568_112210969_112216626_RF	ATCTAAACACAGTCCATGCTAAAAAGCTTCGAGTTGTTGCCACCCCACCCTCCTCAAACC
X_19737340_19741050_19778202_19779729_RF	CATGATAGTTAAGAGATCATATCTAGAATCGACTCACTCACATCTGCCTCATGATGGTTA
1_171770367_171771990_171883013_171884075_FF	CTTCACCAGACATTTTAAATAAAATCTATCGAGGTCCCCCCACCCCCACATGTCTCTACC
5_7402050_7407728_7602410_7603529_RF	CACTGCCCCACCTCTTACTGGCATCTCCTCGAGACAATTCATTGAACCTGACTCATTTCT
6_111982743_111987540_112042041_112045568_RR	CCAAATCCGAACCTCCTCTGTGAAGCATTCGAGTTGTTGCCACCCCACCCTCCTCAAACC
10_6530169_6531558_6639985_6645189_FF	AGAGAGCTGGAGAAGAGGGCGAGAAGAGTCGAATTGTGCTCCATTGTTACCTTTTTGTGT

Table 24d. Relapsing-Remitting Multiple Sclerosis (MSRR) probes – EpiSwitch™ markers to stratify MSRR vs. healthy controls	Probe Location					4 kb Sequence Location				
Probe	Chr	Start1	End1	Start2	End2	Chr	Start1	End1	Start2	End2
1_171811918_171813464_172083100_172087823_RF	1	171811919	171811948	172087794	172087823	1	171811919	171815918	172083824	172087823
1_171887726_171889817_172083100_172087823_RF	1	171887727	171887756	172087794	172087823	1	171887727	171891726	172083824	172087823
11_36588999_36590845_36605543_36609927_FR	11	36590816	36590845	36605544	36605573	11	36586846	36590845	36605544	36609543
11_36583119_36588432_36605543_36609927_RR	11	36583120	36583149	36605544	36605573	11	36583120	36587119	36605544	36609543
1_172083100_172087823_172151185_172154127_FF	1	172087794	172087823	172154098	172154127	1	172083824	172087823	172150128	172154127
1_172061602_172067357_172083100_172087823_RF	1	172061603	172061632	172087794	172087823	1	172061603	172065602	172083824	172087823
11_36531355_36534043_36605543_36609927_FR	11	36534014	36534043	36605544	36605573	11	36530044	36534043	36605544	36609543
11_36524913_36530925_36605543_36609927_FR	11	36530896	36530925	36605544	36605573	11	36526926	36530925	36605544	36609543
X_19644496_19650796_19753406_19760963_RR	X	19644497	19644526	19753407	19753436	X	19644497	19648496	19753407	19757406
X_19644496_19650796_19801817_19808062_RR	X	19644497	19644526	19801818	19801847	X	19644497	19648496	19801818	19805817
1_171936106_171939290_172083100_172087823_RF	1	171936107	171936136	172087794	172087823	1	171936107	171940106	172083824	172087823
1_172083100_172087823_172212232_172223166_FF	1	172087794	172087823	172223137	172223166	1	172083824	172087823	172219167	172223166
11_923549_925733_976127_979142_FR	11	925704	925733	976128	976157	11	921734	925733	976128	980127
6_150252084_150255951_150278503_150282998_FF	6	150255922	150255951	150282969	150282998	6	150251952	150255951	150278999	150282998
X_19644496_19650796_19796774_19799668_RR	X	19644497	19644526	19796775	19796804	X	19644497	19648496	19796775	19800774

Table 24d. Relapsing-Remitting Multiple Sclerosis (MSRR) probes – EpiSwitch™ markers to stratify MSRR vs. healthy controls	Probe Location					4 kb Sequence Location				
Probe	Chr	Start1	End1	Start2	End2	Chr	Start1	End1	Start2	End2
11_36489037_36490716_36605543_36609927_FR	11	36490687	36490716	36605544	36605573	11	36486717	36490716	36605544	36609543
12_53578817_53581303_53603928_53605952_RF	12	53578818	53578847	53605923	53605952	12	53578818	53582817	53601953	53605952
11_36531355_36534043_36605543_36609927_RR	11	36531356	36531385	36605544	36605573	11	36531356	36535355	36605544	36609543
10_6530169_6531558_6639985_6645189_FR	10	6531529	6531558	6639986	6640015	10	6527559	6531558	6639986	6643985
10_6530169_6531558_6632086_6637212_FR	10	6531529	6531558	6632087	6632116	10	6527559	6531558	6632087	6636086
11_923549_925733_976127_979142_RR	11	923550	923579	976128	976157	11	923550	927549	976128	980127
20_43244575_43248985_43318009_43319077_FR	20	43248956	43248985	43318010	43318039	20	43244986	43248985	43318010	43322009
10_6510600_6515355_6530169_6531558_RF	10	6510601	6510630	6531529	6531558	10	6510601	6514600	6527559	6531558
6_112042041_112045568_112135380_112149905_RF	6	112042042	112042071	112149876	112149905	6	112042042	112046041	112145906	112149905
6_112042041_112045568_112071383_112076102_RF	6	112042042	112042071	112076073	112076102	6	112042042	112046041	112072103	112076102
19_40813634_40815315_40897327_40898354_RF	19	40813635	40813664	40898325	40898354	19	40813635	40817634	40894355	40898354
6_111988059_111992304_112042041_112045568_FR	6	111992275	111992304	112042042	112042071	6	111988305	111992304	112042042	112046041
11_36583119_36588432_36600417_36605543_RR	11	36583120	36583149	36600418	36600447	11	36583120	36587119	36600418	36604417
10_6474855_6481197_6632086_6637212_RR	10	6474856	6474885	6632087	6632116	10	6474856	6478855	6632087	6636086
1_171773003_171774629_171883013_171884075_FF	1	171774600	171774629	171884046	171884075	1	171770630	171774629	171880076	171884075

Table 24d. Relapsing-Remitting Multiple Sclerosis (MSRR) probes – EpiSwitch™ markers to stratify MSRR vs. healthy controls	Probe Location					4 kb Sequence Location				
Probe	Chr	Start1	End1	Start2	End2	Chr	Start1	End1	Start2	End2
6_150252084_150255951_150307780_150309507_FF	6	150255922	150255951	150309478	150309507	6	150251952	150255951	150305508	150309507
10_6530169_6531558_6601540_6605133_FF	10	6531529	6531558	6605104	6605133	10	6527559	6531558	6601134	6605133
5_67483678_67490216_67602566_67610345_RF	5	67483679	67483708	67610316	67610345	5	67483679	67487678	67606346	67610345
1_171813464_171818896_171883013_171884075_FF	1	171818867	171818896	171884046	171884075	1	171814897	171818896	171880076	171884075
1_172053648_172060321_172083100_172087823_RR	1	172053649	172053678	172083101	172083130	1	172053649	172057648	172083101	172087100
11_36507808_36510397_36605543_36609927_RR	11	36507809	36507838	36605544	36605573	11	36507809	36511808	36605544	36609543
6_112042041_112045568_112058283_112061400_RF	6	112042042	112042071	112061371	112061400	6	112042042	112046041	112057401	112061400
6_112042041_112045568_112109707_112111662_RF	6	112042042	112042071	112111633	112111662	6	112042042	112046041	112107663	112111662
19_10341612_10343024_10406169_10407761_FF	19	10342995	10343024	10407732	10407761	19	10339025	10343024	10403762	10407761
6_112008166_112013438_112042041_112045568_RR	6	112008167	112008196	112042042	112042071	6	112008167	112012166	112042042	112046041
10_6530169_6531558_6567582_6570484_FR	10	6531529	6531558	6567583	6567612	10	6527559	6531558	6567583	6571582
X_19737340_19741050_19801817_19808062_RF	X	19737341	19737370	19808033	19808062	X	19737341	19741340	19804063	19808062
10_6474855_6481197_6663527_6669234_RR	10	6474856	6474885	6663528	6663557	10	6474856	6478855	6663528	6667527
10_6474855_6481197_6639985_6645189_RR	10	6474856	6474885	6639986	6640015	10	6474856	6478855	6639986	6643985
6_112042041_112045568_112210969_112216626_RF	6	112042042	112042071	112216597	112216626	6	112042042	112046041	112212627	112216626

Table 24d. Relapsing-Remitting Multiple Sclerosis (MSRR) probes – EpiSwitch™ markers to stratify MSRR vs. healthy controls

	Probe Location					4 kb Sequence Location				
Probe	**Chr**	**Start1**	**End1**	**Start2**	**End2**	**Chr**	**Start1**	**End1**	**Start2**	**End2**
X_19737340_19741050_19778202_19779729_RF	X	19737341	19737370	19779700	19779729	X	19737341	19741340	19775730	19779729
1_171770367_171771990_171883013_171884075_FF	1	171771961	171771990	171884046	171884075	1	171767991	171771990	171880076	171884075
5_7402050_7407728_7602410_7603529_RF	5	7402051	7402080	7603500	7603529	5	7402051	7406050	7599530	7603529
6_111982743_111987540_112042041_112045568_RR	6	111982744	111982773	112042042	112042071	6	111982744	111986743	112042042	112046041
10_6530169_6531558_6639985_6645189_FF	10	6531529	6531558	6645160	6645189	10	6527559	6531558	6641190	6645189

Table 25a. Multiple Sclerosis (MS) probes - EpiSwitch™ monitoring markers to stratify MS patients who are responders (B) to IFN-B treatment vs. non-responders (A)

Probes	GeneLocus	Probe_Count_ Total	Probe_Count_ Sig	HyperG_Stats	FDR_HyperG	Percent _Sig	logFC
A							
14_24795078_24798615_24843066_24844509_RR	ADCY4	8	5	0.039348	0.471151	62.5	-1.02593
14_24795078_24798615_24825321_24828950_RR	ADCY4	8	5	0.039348	0.471151	62.5	-0.999378
11_923549_925733_976127_979142_FR	AP2A2	10	6	0.030192	0.428435	60	-0.813494
16_4065887_4067896_4209511_4211354_FR	ADCY9	60	30	0.000146	0.011194	50	-0.771915
16_4065887_4067896_4145870_4149370_FF	ADCY9	60	30	0.000146	0.011194	50	-0.76637
7_55087969_55089963_55116799_55120169_RR	EGFR	196	77	0.00015	0.011194	39.29	-0.756155
16_4065887_4067896_4169801_4171577_FF	ADCY9	60	30	0.000146	0.011194	50	-0.752947
16_4004273_4006715_4065887_4067896_RF	ADCY9	60	30	0.000146	0.011194	50	-0.73992
6_32135728_32138270_32149729_32154447_FF	AGER	2	2	0.07449	0.599944	100	-0.729578
16_4044767_4047085_4065887_4067896_RF	ADCY9	60	30	0.000146	0.011194	50	-0.715327
6_167527869_167530791_167549754_167555064_FR	CCR6	11	6	0.051332	0.52748	54.55	-0.711289
16_4071891_4073711_4204978_4209511_RF	ADCY9	60	30	0.000146	0.011194	50	-0.704294
16_31255309_31261374_31329916_31335980_RF	ITGAM	24	11	0.039526	0.471151	45.83	-0.703943
7_45584884_45588878_45736475_45743273_RF	ADCY1	30	16	0.002216	0.073388	53.33	-0.698983
7_55087969_55089963_55224588_55235839_RR	EGFR	196	77	0.00015	0.011194	39.29	-0.697432
16_4065887_4067896_4209511_4211354_FF	ADCY9	60	30	0.000146	0.011194	50	-0.692904
1_161590754_161594100_161627152_161631654_RR	FCGR2B;FCGR3A	95	41	0.000591	0.029335	43.16	-0.688738

Table 25a. Multiple Sclerosis (MS) probes - EpiSwitch™ monitoring markers to stratify MS patients who are responders (B) to IFN-B treatment vs. non-responders (A)

Probes	GeneLocus	Probe_Count_ Total	Probe_Count_ Sig	HyperG_Stats	FDR_HyperG	Percent _Sig	logFC
16_4065887_4067896_4204978_4209511_FF	ADCY9	60	30	0.000146	0.011194	50	-0.673206
7_55087969_55089963_55146890_55151406_RF	EGFR	196	77	0.00015	0.011194	39.29	-0.670616
19_50479474_50480574_50495462_50498507_FF	SIGLEC16	5	4	0.021663	0.358647	80	-0.661358
7_55087969_55089963_55159296_55163839_RF	EGFR	196	77	0.00015	0.011194	39.29	-0.66015
11_923549_925733_976127_979142_RF	AP2A2	10	6	0.030192	0.428435	60	-0.648337
16_4065887_4067896_4109379_4115518_FR	ADCY9	60	30	0.000146	0.011194	50	-0.642688
1_25048331_25049906_25138048_25141786_RR	CLIC4	171	60	0.014508	0.33256	35.09	-0.628657
11_1010876_1013083_964245_969445_FF	AP2A2	10	6	0.030192	0.428435	60	-0.626498
B							
19_55265127_55271536_55301130_55304400_FR	KIR2DL1;KIR2DL4;KIR 3DL1;KIR2DL3	5	4	0.021663	0.358647	80	0.882342
15_45005395_45007515_45023742_45026509_FR	B2M	18	8	0.089181	0.680673	44.44	0.79992
19_55265127_55271536_55301130_55304400_FF	KIR2DL1;KIR2DL4;KIR 3DL1;KIR2DL3	5	4	0.021663	0.358647	80	0.784363
15_44986846_44994405_45005395_45007515_RF	B2M	18	8	0.089181	0.680673	44.44	0.724237
15_44962061_44965177_45005395_45007515_RF	B2M	18	8	0.089181	0.680673	44.44	0.703463
17_4709602_4710899_4724773_4727780_RR	PLD2	5	4	0.021663	0.358647	80	0.583764
15_44994405_44997599_45023742_45026509_RR	B2M	18	8	0.089181	0.680673	44.44	0.560989

Table 25a. Multiple Sclerosis (MS) probes - EpiSwitch™ monitoring markers to stratify MS patients who are responders (R) to IFN-B treatment vs. non-responders (A)

Probes	GeneLocus	Probe_Count_Total	Probe_Count_Sig	HyperG_Stats	FDR_HyperG	Percent_Sig	logFC
19_55275870_55279952_55301130_55304400_FF	KIR2DL1;KIR2DL4;KIR3DL1;KIR2DL3	5	4	0.021663	0.358647	80	0.549219
15_44986846_44994405_45005395_45007515_FF	B2M	18	8	0.089181	0.680673	44.44	0.521549
1_207739376_207741296_207803544_207805928_RF	CR1	108	37	0.065707	0.593356	34.26	0.51017
2_65447148_65449472_65486660_65489594_FF	ACTR2	24	10	0.091366	0.680673	41.67	0.501463
1_9722966_9724614_9740102_9742515_RR	PIK3CD	71	32	0.000945	0.040077	45.07	0.499905
20_1570332_1585721_1606778_1615074_RR	SIRPB1	2	2	0.07449	0.599944	100	0.497866
2_65429854_65434619_65447148_65449472_FR	ACTR2	24	10	0.091366	0.680673	41.67	0.48838
1_161588628_161590754_161603284_161607252_RR	FCGR2B;FCGR3A	95	41	0.000591	0.029335	43.16	0.473798
1_25039149_25042248_25060201_25061315_RR	CLIC4	171	60	0.014508	0.33256	35.09	0.469989
19_6765111_6771260_6808215_6810512_FF	VAV1	16	9	0.013621	0.33256	56.25	0.461142
15_44986846_44994405_45005395_45007515_FR	B2M	18	8	0.089181	0.680673	44.44	0.460579
1_25106841_25109990_25121474_25132059_RR	CLIC4	171	60	0.014508	0.33256	35.09	0.456162
1_207803544_207805928_207823127_207825662_FR	CR1	108	37	0.065707	0.593356	34.26	0.452664
1_161532168_161534007_161588628_161590754_RR	FCGR2B;FCGR3A	95	41	0.000591	0.029335	43.16	0.451751
1_207803544_207805928_207823127_207825662_FF	CR1	108	37	0.065707	0.593356	34.26	0.449375
21_34811256_34815025_34867137_34868523_RR	IFNGR2	28	18	4.59E-05	0.006832	64.29	0.446599
2_65407538_65411209_65486660_65489594_FF	ACTR2	24	10	0.091366	0.680673	41.67	0.430665

Table 25a. Multiple Sclerosis (MS) probes - EpiSwitch™ monitoring markers to stratify MS patients who are responders (B) to IFN-B treatment vs. non-responders (A)							
Probes	GeneLocus	Probe_Count_ Total	Probe_Count_ Sig	HyperG_Stats	FDR_HyperG	Percent _Sig	logFC
2_65429854_65434619_65461265_65464595_FF	ACTR2	24	10	0.091366	0.680673	41.67	0.427971

Table 25b. Multiple Sclerosis (MS) probes - EpiSwitch™ monitoring markers to stratify MS patients who are responders (B) to IFN-B treatment vs. non-responders (A)									
Probes	AveExpr	t	P.Value	adj.P.Val	B	FC	FC_1	LS	Loop detected
A									
14_24795078_24798615_24843066_24844509_RR	-1.02593	-8.353134	1.94E-07	0.001326	7.269095	0.491094	-2.036271	-1	IFN-B NR
14_24795078_24798615_24825321_24828950_RR	-0.999378	-8.011946	3.44E-07	0.001326	6.753681	0.500216	-1.999138	-1	IFN-B NR
11_923549_925733_976127_979142_FR	-0.813494	-6.68296	3.74E-06	0.002986	4.573795	0.569002	-1.757463	-1	IFN-B NR
16_4065887_4067896_4209511_4211354_FR	-0.771915	-5.520398	3.67E-05	0.005146	2.441367	0.585639	-1.707535	-1	IFN-B NR
16_4065887_4067896_4145870_4149370_FF	-0.76637	-5.439371	4.33E-05	0.005435	2.285404	0.587895	-1.700985	-1	IFN-B NR
7_55087969_55089963_55116799_55120169_RR	-0.756155	-4.377827	0.000405	0.016027	0.172054	0.592072	-1.688983	-1	IFN-B NR
16_4065887_4067896_4169801_4171577_FF	-0.752947	-5.697975	2.56E-05	0.004189	2.780024	0.59339	-1.685232	-1	IFN-B NR
16_4004273_4006715_4065887_4067896_RF	-0.73992	-5.840209	1.92E-05	0.004189	3.048058	0.598773	-1.670083	-1	IFN-B NR
6_32135728_32138270_32149729_32154447_FF	-0.729578	-5.804952	2.07E-05	0.004189	2.98189	0.60308	-1.658154	-1	IFN-B NR
16_4044767_4047085_4065887_4067896_RF	-0.715327	-5.175447	7.47E-05	0.007103	1.771458	0.609067	-1.641855	-1	IFN-B NR
6_167527869_167530791_167549754_167555064_FR	-0.711289	-5.75873	2.27E-05	0.004189	2.894871	0.610774	-1.637267	-1	IFN-B NR

Table 25b. Multiple Sclerosis (MS) probes - EpiSwitch™ monitoring markers to stratify MS patients who are responders (B) to IFN-B treatment vs. non-responders (A)

Probes	AveExpr	t	P.Value	adj.P.Val	B	FC	FC_1	LS	Loop detected
16_4071891_4073711_4204978_4209511_RF	-0.704294	-6.032689	1.31E-05	0.004179	3.406069	0.613743	-1.629347	-1	IFN-B NR
16_31255309_31261374_31329916_31335980_RF	-0.703943	-5.996948	1.41E-05	0.004179	3.340008	0.613892	-1.628951	-1	IFN-B NR
7_45584884_45588878_45736475_45743273_RF	-0.698983	-5.89072	1.74E-05	0.004189	3.142539	0.616006	-1.62336	-1	IFN-B NR
7_55087969_55089963_55224588_55235839_RR	-0.697432	-4.563863	0.000272	0.013616	0.550153	0.616669	-1.621616	-1	IFN-B NR
16_4065887_4067896_4209511_4211354_FF	-0.692904	-5.338064	5.34E-05	0.00614	2.089177	0.618607	-1.616534	-1	IFN-B NR
1_161590754_161594100_161627152_161631654_RR	-0.688738	-5.719547	2.45E-05	0.004189	2.820863	0.620396	-1.611872	-1	IFN-B NR
16_4065887_4067896_4204978_4209511_FF	-0.673206	-5.142187	8.01E-05	0.007264	1.706076	0.627112	-1.594612	-1	IFN-B NR
7_55087969_55089963_55146890_55151406_RF	-0.670616	-3.987991	0.000943	0.023813	-0.626034	0.628238	-1.591753	-1	IFN-B NR
19_50479474_50480574_50495462_50498507_FF	-0.661358	-5.741299	2.35E-05	0.004189	2.861975	0.632283	-1.581571	-1	IFN-B NR
7_55087969_55089963_55159296_55163839_RF	-0.66015	-4.047471	0.000828	0.022441	-0.503956	0.632812	-1.580247	-1	IFN-B NR
11_923549_925733_976127_979142_RF	-0.648337	-4.908682	0.000131	0.00981	1.243458	0.638015	-1.56736	-1	IFN-B NR
16_4065887_4067896_4109379_4115518_FR	-0.642688	-4.6626	0.00022	0.011998	0.749772	0.640518	-1.561236	-1	IFN-B NR
1_25048331_25049906_25138048_25141786_RR	-0.628657	-5.393526	4.76E-05	0.005734	2.19677	0.646778	-1.546126	-1	IFN-B NR
11_1010876_1013083_964245_969445_FF	-0.626498	-4.803983	0.000163	0.010835	1.034127	0.647747	-1.543813	-1	IFN-B NR
B									
19_55265127_55271536_55301130_55304400_FR	0.882342	7.654384	6.39E-07	0.001642	6.194412	1.843366	1.843366	1	IFN-B R
15_45005395_45007515_45023742_45026509_FR	0.79992	6.845926	2.76E-06	0.002986	4.856081	1.741005	1.741005	1	IFN-B R

Table 25b. Multiple Sclerosis (MS) probes - EpiSwitch™ monitoring markers to stratify MS patients who are responders (B) to IFN-B treatment vs. non-responders (A)

Probes	AveExpr	t	P.Value	adj.P.Val	B	FC	FC_1	LS	Loop detected
19_55265127_55271536_55301130_55304400_FF	0.784363	6.631301	4.13E-06	0.002986	4.483437	1.722331	1.722331	1	IFN-B R
15_44986846_44994405_45005395_45007515_RF	0.724237	6.236561	8.81E-06	0.003975	3.779199	1.652026	1.652026	1	IFN-B R
15_44962061_44965177_45005395_45007515_RF	0.703463	5.83783	1.93E-05	0.004189	3.0436	1.628409	1.628409	1	IFN-B R
17_4709602_4710899_4724773_4727780_RR	0.583764	4.979741	0.000113	0.009131	1.384883	1.498755	1.498755	1	IFN-B R
15_44994405_44997599_45023742_45026509_RR	0.560989	4.537838	0.000287	0.013851	0.497407	1.47528	1.47528	1	IFN-B R
19_55275870_55279952_55301130_55304400_FF	0.549219	4.770727	0.000175	0.011147	0.967408	1.463293	1.463293	1	IFN-B R
15_44986846_44994405_45005395_45007515_FF	0.521549	4.339727	0.00044	0.016549	0.094345	1.435495	1.435495	1	IFN-B R
1_207739376_207741296_207803544_207805928_RF	0.51017	3.705654	0.001742	0.033948	-1.20555	1.424218	1.424218	1	IFN-B R
2_65447148_65449472_65486660_65489594_FF	0.501463	4.32279	0.000456	0.016999	0.059773	1.415648	1.415648	1	IFN-B R
1_9722966_9724614_9740102_9742515_RR	0.499905	3.916502	0.001101	0.025709	-0.772813	1.41412	1.41412	1	IFN-B R
20_1570332_1585721_1606778_1615074_RR	0.497866	4.140936	0.000676	0.019902	-0.312278	1.412123	1.412123	1	IFN-B R
2_65429854_65434619_65447148_65449472_FR	0.48838	4.240472	0.000545	0.018315	-0.108462	1.402869	1.402869	1	IFN-B R
1_161588628_161590754_161603284_161607252_RR	0.473798	4.078336	0.000775	0.021483	-0.440632	1.38876	1.38876	1	IFN-B R
1_25039149_25042248_25060201_25061315_RR	0.469989	3.946322	0.001032	0.024818	-0.711583	1.385099	1.385099	1	IFN-B R
19_6765111_6771260_6808215_6810512_FF	0.461142	3.8272	0.001337	0.028716	-0.95617	1.376632	1.376632	1	IFN-B R
15_44986846_44994405_45005395_45007515_FR	0.460579	3.904482	0.00113	0.026088	-0.797495	1.376094	1.376094	1	IFN-B R
1_25106841_25109990_25121474_25132059_RR	0.456162	3.950375	0.001023	0.024818	-0.703261	1.371888	1.371888	1	IFN-B R

Table 25b. Multiple Sclerosis (MS) probes - EpiSwitch™ monitoring markers to stratify MS patients who are responders (B) to IFN-B treatment vs. non-responders (A)									
Probes	**AveExpr**	**t**	**P.Value**	**adj.P.Val**	**B**	**FC**	**FC_1**	**LS**	**Loop detected**
1_207803544_207805928_207823127_207825662_FR	0.452664	3.129845	0.00607	0.059844	-2.37481	1.368565	1.368565	1	IFN-B R
1_161532168_161534007_161588628_161590754_RR	0.451751	3.815746	0.001371	0.029036	-0.979682	1.367699	1.367699	1	IFN-B R
1_207803544_207805928_207823127_207825662_FF	0.449375	3.254497	0.00464	0.053711	-2.124448	1.365449	1.365449	1	IFN-B R
21_34811256_34815025_34867137_34868523_RR	0.446599	3.662075	0.001915	0.03533	-1.294865	1.362824	1.362824	1	IFN-B R
2_65407538_65411209_65486660_65489594_FF	0.430665	3.625717	0.002073	0.036207	-1.369322	1.347855	1.347855	1	IFN-B R
2_65429854_65434619_65461265_65464595_FF	0.427971	3.645565	0.001985	0.036019	-1.328682	1.34534	1.34534	1	IFN-B R

Table 25c. Multiple Sclerosis (MS) probes - EpiSwitch™ monitoring markers to stratify MS patients who are responders to IFN-B treatment (B) vs. non-responders (A)	
Probes	**60 mer Probe sequence**
A	
14_24795078_24798615_24843066_24844509_RR	CCCACCTCCCACCAGACAGTGGAAGCAGTCGAGTGCTGTGAGCAAAGAGGCCCTGGGCCA
14_24795078_24798615_24825321_24828950_RR	CCCACCTCCCACCAGACAGTGGAAGCAGTCGAAGCAAAACTGTGGAGATTGGGTCGGTGA
11_923549_925733_976127_979142_FR	GCCTGCAGGGGGCGCCCCCGCGCCTGCCTCGACCACACATCCACATGGACGCATGGCAGG
16_4065887_4067896_4209511_4211354_FR	CGCCGGGCCGACACCCACATTGTCTTCTTCGAACCCCTTTAAACCACTGACCTTGTCCCT
16_4065887_4067896_4145870_4149370_FF	CGCCGGGCCGACACCCACATTGTCTTCTTCGAGTTCCTTGGAAGCTTTAATTTGCATTCC
7_55087969_55089963_55116799_55120169_RR	AGACCCGGACGTCTCCGCGAGGCGGCCATCGATTTTGCTGATGCAATACAGTTTTACAGG
16_4065887_4067896_4169801_4171577_FF	CGCCGGGCCGACACCCACATTGTCTTCTTCGAATCTCCCATCTGCTCTTTCAACCAAGCT

Table 25c. Multiple Sclerosis (MS) probes - EpiSwitch™ monitoring markers to stratify MS patients who are responders to IFN-B treatment (B) vs. non-responders (A)

Probes	60 mer Probe sequence
16_4004273_4006715_4065887_4067896_RF	CGCCGGGCCGACACCCACATTGTCTTCTTCGACATCCACTCTTCTGGGCATTCCCAGCCT
6_32135728_32138270_32149729_32154447_FF	ACTGATGGCATCCCCCGTGCGCTTCCGGTCGATGGGGCCAGGGGGCTATGGGGATAACCT
16_4044767_4047085_4065887_4067896_RF	CGCCGGGCCGACACCCACATTGTCTTCTTCGATTTTATAGTATGTGAATTATATCTCAAC
6_167527869_167530791_167549754_167555064_FR	ACAGCTGCATCTTATGTCAGAAGAGTGTTCGACTCCAGTGAAGATTATTTTGTGTCAGTC
16_4071891_4073711_4204978_4209511_RF	CAGAATCGCCCACCTTGTAGCCCAGGGATCGACGGCAAGCCACTCACCCTCAGCCCTATC
16_31255309_31261374_31329916_31335980_RF	CAAATCCCGGCTATCTCTTAGAATTGCATCGAGTTTATCTTGAGTTTATATATTTTAATG
7_45584884_45588878_45736475_45743273_RF	TCCATCCCCAACTTCAATGACTTCTACATCGACATAGTACTGAAAGTCTTTGCTAGAGTA
7_55087969_55089963_55224588_55235839_RR	AGACCCGGACGTCTCCGCGAGGCGGCCATCGACATATTTCCTGTTCCCTTGGAATAAAAA
16_4065887_4067896_4209511_4211354_FF	CGCCGGGCCGACACCCACATTGTCTTCTTCGATTTGCATTTCCCTAATGATCGGTGATGT
1_161590754_161594100_161627152_161631654_RR	AGGACAGAGACCCCTAATTCCACCACCATCGACCCTTCTGCTTTCTCTCCAGGGGATGGC
16_4065887_4067896_4204978_4209511_FF	CGCCGGGCCGACACCCACATTGTCTTCTTCGATCCCTGGGCTACAAGGTGGGCGATTCTG
7_55087969_55089963_55146890_55151406_RF	TTCCTGAAAAAAAATGGCTACTTATTAGTCGATGGCCGCCTCGCGGAGACGTCCGGGTCT
19_50479474_50480574_50495462_50498507_FF	AGCACAGGCAAGATGACCTTCAAGGTGCTCGACCCCACTGCTGGCCATCCCTACCTGCAT
7_55087969_55089963_55159296_55163839_RF	CACTTTTTATAGAAGAGAAAGTGAAGATTCGATGGCCGCCTCGCGGAGACGTCCGGGTCT
11_923549_925733_976127_979142_RF	CCACGTGTCGCGGGCCTGAGTGTGCCCCTCGAGGCTGTAGTGATTCATGATTGTACCACT
16_4065887_4067896_4109379_4115518_FR	CGCCGGGCCGACACCCACATTGTCTTCTTCGAAAAAAAAAAAAAAAAAAAAAAAAAAGAAA
1_25048331_25049906_25138048_25141786_RR	GTGCCCACACTCCTCAGCCCTCCGGTGGTCGACCGCCTGGGCTCAACCAATCCTCCCATC

Table 25c. Multiple Sclerosis (MS) probes - EpiSwitch™ monitoring markers to stratify MS patients who are responders to IFN-B treatment (B) vs. non-responders (A)	
Probes	**60 mer Probe sequence**
11_1010876_1013083_964245_969445_FF	GTGCCCTCCTCGCCCCTGATGGGTCTGGTCGAGACCAGCCTCAACATGGAGAAACACCAT
B	
19_55265127_55271536_55301130_55304400_FR	ATAGGCACCGAATAGATAAATAGATAGATCGATAGATAATAGATAGAAATATGCAGAAAG
15_45005395_45007515_45023742_45026509_FR	GCCAGAGTGGAAATGGAATTGGGAGAAATCGAAGAGTTTTAATATCTGCTGTAAACCTTG
19_55265127_55271536_55301130_55304400_FF	ATAGGCACCGAATAGATAAATAGATAGATCGAAGATTCTGACAATAACTAAGAGCAGAGG
15_44986846_44994405_45005395_45007515_RF	GCCAGAGTGGAAATGGAATTGGGAGAAATCGAAATGAGTCAAGGAAACTTACAAGCTTTT
15_44962061_44965177_45005395_45007515_RF	GCCAGAGTGGAAATGGAATTGGGAGAAATCGATTCGGACCACTGCATGAGAAGAGAGGCA
17_4709602_4710899_4724773_4727780_RR	ATCTTGGGTAACTAGGGAGTGGAGTTGTTCGACTTCGCCAGCTGAAGTGATCCTCCCACT
15_44994405_44997599_45023742_45026509_RR	ATTCCTAGACACATACAACCTGCCAAGATCGAAGAGTTTTAATATCTGCTGTAAACCTTG
19_55275870_55279952_55301130_55304400_FF	TACAGATTTTGGTATCTGAGTGGAGATCTCGAAGATTCTGACAATAACTAAGAGCAGAGG
15_44986846_44994405_45005395_45007515_FF	CTGTTCTGGTTTTGGATTTCTTCAAGGTTCGATTTCTCCCAATTCCATTTCCACTCTGGC
1_207739376_207741296_207803544_207805928_RF	CGAGGCGAGTGGATCATGAGTCAGGAGATCGATTTAAAAATAGTTTATTTTAATAATGTT
2_65447148_65449472_65486660_65489594_FF	ATAAAGAAAATGCAGTACACATACACAATCGAGACCAGCCTGGTCAATACGGCAAAACCC
1_9722966_9724614_9740102_9742515_RR	GGCAGGTGGATCACCTGAGGTCAGGAGTTCGAACTCTTAACCTCAGGTGATCCACCCGCA
20_1570332_1585721_1606778_1615074_RR	GTAGTAGGGATTCATTCAAAAGCACCACTCGAGGATTTACGATGCAGTGCGACAACCCTG
2_65429854_65434619_65447148_65449472_FR	TATATTTATATCCCAGATTCAATCATCATCGAGACCAGCCTAGCTAACATGGTGAAACCC
1_161588628_161590754_161603284_161607252_RR	TGATAAACATCTTAACAGGAAACAGGGTTCGATTGTCATCCTCTAGGACTTACAGTTTCT

Table 25c. Multiple Sclerosis (MS) probes - EpiSwitch™ monitoring markers to stratify MS patients who are responders to IFN-B treatment (B) vs. non-responders (A)	
Probes	**60 mer Probe sequence**
1_25039149_25042248_25060201_25061315_RR	GGCAGGCAGATCACTTGAGGTCAGGAGTTCGAACACCTGACCTCAGGTGATCTGCCCACC
19_6765111_6771260_6808215_6810512_FF	GGCAGGTGGATCACCTGAGGTCAGGAGTTCGAACTCCTGACCTCAGGGGATCCACCCACC
15_44986846_44994405_45005395_45007515_FR	CTGTTCTGGTTTTGGATTTCTTCAAGGTTCGAAAGCAGAATGTTTTGATCATGAGAAAAT
1_25106841_25109990_25121474_25132059_RR	AACAAATGTTTACCAAGTACCTACTATGTCGAAAATCAGATGGTTATAGGTGTGTGGCCT
1_207803544_207805928_207823127_207825662_FR	CGAGGCGAGTGGATCATGAGTCAGGAGATCGAAAGGTATCTGTCTTGGAAAAACCTTGAT
1_161532168_161534007_161588628_161590754_RR	AAAGATGTTGAGTGGAGTTTGCAGTTGTTCGAACCCTGTTTCCTGTTAAGATGTTTATCA
1_207803544_207805928_207823127_207825662_FF	CGAGGCGAGTGGATCATGAGTCAGGAGATCGACAATAAACTGAAGAGACAGCATTAATGT
21_34811256_34815025_34867137_34868523_RR	AAGGTGGGTGGATCATGAGGTCAGGAGTTCGAACCCCTGACCTCAAATGATCCACCTAGG
2_65407538_65411209_65486660_65489594_FF	AAGGAAGGAATCAAACACTTCTGAAAAGTCGAGACCAGCCTGGTCAATACGGCAAAACCC
2_65429854_65434619_65461265_65464595_FF	TATATTTATATCCCAGATTCAATCATCATCGAGACCAGTATGGGCAACACGGCAAGATTC

Table 25d. Multiple Sclerosis (MS) probes - EpiSwitch™ monitoring markers to stratify MS patients who are responders (B) to IFN-B treatment vs. non-responders (A)

Table 25 d	Probe Location					4 kb Sequence Location				
Probes	**Chr**	**Start1**	**End1**	**Start2**	**End2**	**Chr**	**Start1**	**End1**	**Start2**	**End2**
A										
14_24795078_24798615_24843066_24844509_RR	14	24795079	24795108	24843067	24843096	14	24795079	24799078	24843067	24847066
14_24795078_24798615_24825321_24828950_RR	14	24795079	24795108	24825322	24825351	14	24795079	24799078	24825322	24829321
11_923549_925733_976127_979142_FR	11	925704	925733	976128	976157	11	921734	925733	976128	980127

Table 25 d

Probes	Probe Location					4 kb Sequence Location				
	Chr	Start1	End1	Start2	End2	Chr	Start1	End1	Start2	End2
16_4065887_4067896_4209511_4211354_FR	16	4067867	4067896	4209512	4209541	16	4063897	4067896	4209512	4213511
16_4065887_4067896_4145870_4149370_FF	16	4067867	4067896	4149341	4149370	16	4063897	4067896	4145371	4149370
7_55087969_55089963_55116799_55120169_RR	7	55087970	55087999	55116800	55116829	7	55087970	55091969	55116800	55120799
16_4065887_4067896_4169801_4171577_FF	16	4067867	4067896	4171548	4171577	16	4063897	4067896	4167578	4171577
16_4004273_4006715_4065887_4067896_RF	16	4004274	4004303	4067867	4067896	16	4004274	4008273	4063897	4067896
6_32135728_32138270_32149729_32154447_FF	6	32138241	32138270	32154418	32154447	6	32134271	32138270	32150448	32154447
16_4044767_4047085_4065887_4067896_RF	16	4044768	4044797	4067867	4067896	16	4044768	4048767	4063897	4067896
6_167527869_167530791_167549754_167555064_FR	6	167530762	167530791	167549755	167549784	6	167526792	167530791	167549755	167553754
16_4071891_4073711_4204978_4209511_RF	16	4071892	4071921	4209482	4209511	16	4071892	4075891	4205512	4209511
16_31255309_31261374_31329916_31335980_RF	16	31255310	31255339	31335951	31335980	16	31255310	31259309	31331981	31335980
7_45584884_45588878_45736475_45743273_RF	7	45584885	45584914	45743244	45743273	7	45584885	45588884	45739274	45743273
7_55087969_55089963_55224588_55235839_RR	7	55087970	55087999	55224589	55224618	7	55087970	55091969	55224589	55228588
16_4065887_4067896_4209511_4211354_FF	16	4067867	4067896	4211325	4211354	16	4063897	4067896	4207355	4211354
1_161590754_161594100_161627152_161631654_RR	1	161590755	161590784	161627153	161627182	1	161590755	161594754	161627153	161631152
16_4065887_4067896_4204978_4209511_FF	16	4067867	4067896	4209482	4209511	16	4063897	4067896	4205512	4209511
7_55087969_55089963_55146890_55151406_RF	7	55087970	55087999	55151377	55151406	7	55087970	55091969	55147407	55151406
19_50479474_50480574_50495462_50498507_FF	19	50480545	50480574	50498478	50498507	19	50476575	50480574	50494508	50498507
7_55087969_55089963_55159296_55163839_RF	7	55087970	55087999	55163810	55163839	7	55087970	55091969	55159840	55163839

Table 25 d	Probe Location					4 kb Sequence Location				
Probes	Chr	Start1	End1	Start2	End2	Chr	Start1	End1	Start2	End2
11_923549_925733_976127_979142_RF	11	923550	923579	979113	979142	11	923550	927549	975143	979142
16_4065887_4067896_4109379_4115518_FR	16	4067867	4067896	4109380	4109409	16	4063897	4067896	4109380	4113379
1_25048331_25049906_25138048_25141786_RR	1	25048332	25048361	25138049	25138078	1	25048332	25052331	25138049	25142048
11_1010876_1013083_964245_969445_FF	11	1013054	1013083	969416	969445	11	1009084	1013083	965446	969445
B										
19_55265127_55271536_55301130_55304400_FR	19	55271507	55271536	55301131	55301160	19	55267537	55271536	55301131	55305130
15_45005395_45007515_45023742_45026509_FR	15	45007486	45007515	45023743	45023772	15	45003516	45007515	45023743	45027742
19_55265127_55271536_55301130_55304400_FF	19	55271507	55271536	55304371	55304400	19	55267537	55271536	55300401	55304400
15_44986846_44994405_45005395_45007515_RF	15	44986847	44986876	45007486	45007515	15	44986847	44990846	45003516	45007515
15_44962061_44965177_45005395_45007515_RF	15	44962062	44962091	45007486	45007515	15	44962062	44966061	45003516	45007515
17_4709602_4710899_4724773_4727780_RR	17	4709603	4709632	4724774	4724803	17	4709603	4713602	4724774	4728773
15_44994405_44997599_45023742_45026509_RR	15	44994406	44994435	45023743	45023772	15	44994406	44998405	45023743	45027742
19_55275870_55279952_55301130_55304400_FF	19	55279923	55279952	55304371	55304400	19	55275953	55279952	55300401	55304400
15_44986846_44994405_45005395_45007515_FF	15	44994376	44994405	45007486	45007515	15	44990406	44994405	45003516	45007515
1_207739376_207741296_207803544_207805928_RF	1	207739377	207739406	207805899	207805928	1	207739377	207743376	207801929	207805928
2_65447148_65449472_65486660_65489594_FF	2	65449443	65449472	65489565	65489594	2	65445473	65449472	65485595	65489594
1_9722966_9724614_9740102_9742515_RR	1	9722967	9722996	9740103	9740132	1	9722967	9726966	9740103	9744102

Table 25 d	Probe Location					4 kb Sequence Location				
Probes	Chr	Start1	End1	Start2	End2	Chr	Start1	End1	Start2	End2
20_1570332_1585721_1606778_1615074_RR	20	1570333	1570362	1606779	1606808	20	1570333	1574332	1606779	1610778
2_65429854_65434619_65447148_65449472_FR	2	65434590	65434619	65447149	65447178	2	65430620	65434619	65447149	65451148
1_161588628_161590754_161603284_161607252_RR	1	161588629	161588658	161603285	161603314	1	161588629	161592628	161603285	161607284
1_25039149_25042248_25060201_25061315_RR	1	25039150	25039179	25060202	25060231	1	25039150	25043149	25060202	25064201
19_6765111_6771260_6808215_6810512_FF	19	6771231	6771260	6810483	6810512	19	6767261	6771260	6806513	6810512
15_44986846_44994405_45005395_45007515_FR	15	44994376	44994405	45005396	45005425	15	44990406	44994405	45005396	45009395
1_25106841_25109990_25121474_25132059_RR	1	25106842	25106871	25121475	25121504	1	25106842	25110841	25121475	25125474
1_207803544_207805928_207823127_207825662_FR	1	207805899	207805928	207823128	207823157	1	207801929	207805928	207823128	207827127
1_161532168_161534007_161588628_161590754_RR	1	161532169	161532198	161588629	161588658	1	161532169	161536168	161588629	161592628
1_207803544_207805928_207823127_207825662_FF	1	207805899	207805928	207825633	207825662	1	207801929	207805928	207821663	207825662
21_34811256_34815025_34867137_34868523_RR	21	34811257	34811286	34867138	34867167	21	34811257	34815256	34867138	34871137
2_65407538_65411209_65486660_65489594_FF	2	65411180	65411209	65489565	65489594	2	65407210	65411209	65485595	65489594
2_65429854_65434619_65461265_65464595_FF	2	65434590	65434619	65464566	65464595	2	65430620	65434619	65460596	65464595

Table 26a. Neurofibromatosis (NF) probes - EpiSwitch™ markers to stratify (A) Benign plexiform vs. (B) Malignant Peripheral Nerve Sheath Tumours (MPNSTs)

Probe	LS	Loop detected	60 mer Probe sequence
A			
10_114686118_114690592_114727613_114729725_FF	1	Benign plexiform	AAGCTCAATAAATCCCAAGCACACACTCGACCTTCATCACAACAGTGCTCATAGGTTT
10_114686118_114690592_114743749_114745454_FF	1	Benign plexiform	AAGCTCAATAAATCCCAAGCACACACTCGAGGACCCTTCCACCCAAAAAAAAGCAAGG
10_114686118_114690592_114773872_114776404_FF	1	Benign plexiform	AAGCTCAATAAATCCCAAGCACACACTCGAAGTCAGCTGGGATGAAGGAAGGGAAAGA
10_114686118_114690592_114794603_114795614_FF	1	Benign plexiform	AAGCTCAATAAATCCCAAGCACACACTCGAAAGCAGCCACAGGCAGTCAGTATATGTC
10_114686118_114690592_114804200_114807457_FF	1	Benign plexiform	AAGCTCAATAAATCCCAAGCACACACTCGAATAAATAGTATCTTTGCCCAATAATATG
10_114686118_114690592_114821603_114822761_FF	1	Benign plexiform	AAGCTCAATAAATCCCAAGCACACACTCGAATGTAAAATGAGAGACCTGATGCACAGT
10_114686118_114690592_114845287_114849773_FF	1	Benign plexiform	AAGCTCAATAAATCCCAAGCACACACTCGAGGCAAAGTGGGCATTTTCCAGCACCCTG
10_114686118_114690592_114885061_114889442_FF	1	Benign plexiform	AAGCTCAATAAATCCCAAGCACACACTCGAAATGGCTCCAGATTCCTGGCCGAGTAGG
11_128342943_128345136_128481262_128489818_FF	1	Benign plexiform	ACCTGAATACATTGAGATTATTTTGCAATCGAGATCTGAGTGTGAGGGTGGGGGGCTGAG
11_128410884_128413638_128489818_128498866_FF	1	Benign plexiform	AAGGTTGTGAAAATTTTATCTTACGTGATCGATGACACACAAAGTGTGTTTAAATACAGGGT
5_131857043_131861763_131874140_131875551_RF	1	Benign plexiform	GTATGTCAGGGGTCAGAGGGGGCAGAGGTCGAGGAGACTACTTAGGAATAATACACAACAAA
5_131874140_131875551_131894531_131901964_FF	1	Benign plexiform	GTATGTCAGGGGTCAGAGGGGGCAGAGGTCGAGACCTAGCTACCCGGCAAACATCAAAT
5_131874140_131875551_131920774_131922322_FF	1	Benign plexiform	GTATGTCAGGGGTCAGAGGGGGCAGAGGTCGACTTTAACATAATTTATTAAAATTATACT
5_131874140_131875551_131942647_131945574_FF	1	Benign plexiform	GTATGTCAGGGGTCAGAGGGGGCAGAGGTCGAACTTTTACCATGAGTCTTTTACTGAAAA
5_131874140_131875551_131985852_131989475_FF	1	Benign plexiform	GTATGTCAGGGGTCAGAGGGGGCAGAGGTCGACTTTGATGAACAAAAATGGATATCTAAC
5_131882513_131883559_131942647_131945574_FF	1	Benign plexiform	GGTGGGTGGATTGGTTGAAGTCAGCAGTTCGAACTTTTACCATGAGTCTTTTACTGAAAA
5_131882513_131883559_131966700_131972322_FF	1	Benign plexiform	GGTGGGTGGATTGGTTGAAGTCAGCAGTTCGAACTGCCACCTTGTCCCTCTTCTATCACT
6_41890642_41893643_42057606_42059682_RR	1	Benign plexiform	AGGGAGAGAGAGGAGTCTAAAGTTTATCTCGAGGGGGTGGGAGGGCATGTCTATTTGCTC
7_137557828_137562242_137656982_137661712_FF	1	Benign plexiform	TTTACAATATCCCTTTTTAAGTGCAAAGTCGATGGTTGATGTTGTGTGTGGGTGTGTACG
7_50818806_50825328_50840056_50842638_RR	1	Benign plexiform	TGGTGAGGAGGGCAGTGTCCAAGGCAAGTCGATGCAAGAGTCCCAGGACAGTCAAAGAAT
7_519231_522690_557100_558462_FF	1	Benign plexiform	ATGGGTAAGTGATGAATGGGTGGATAGTTCGATGTTTAGATTTTCCCAACTGGGTTCTAT
7_519231_522690_594007_596370_FF	1	Benign plexiform	ATGGGTAAGTGATGAATGGGTGGATAGTTCGACGTGCCGGAGGTGCGTGGGGGAACTGTTC
9_36907980_36909849_36932342_36938946_FF	1	Benign plexiform	TTTTTTTTTTTTTTTAGATATAGGGTTTCGAGGCTAATCTGGCTGAGAGAGGAGGGTCT
9_36951690_36954534_36987524_36991745_RF	1	Benign plexiform	CCCTGGACAGCAACTAAGCTGTCCTGGGTCGAGACTACTCAAATATTTTTATTTATTTCT
9_36961116_36962831_37038244_37041179_FF	1	Benign plexiform	AGACACACACTGAGACAGCTCAATCTGCTCGAGGATCAAAGGATGTTGTGTGTGAGGCTTGC

Table 26a. Neurofibromatosis (NF) probes - EpiSwitch™ markers to stratify (A) Benign plexiform vs. (B) Malignant Peripheral Nerve Sheath Tumours (MPNSTs)			
Probe	**LS**	**Loop detected**	**60 mer Probe sequence**
B			
1_26993831_26995281_27050122_27052726_FF	-1	MPNSTs	GACCAGGCTGGAGTGCAGTGGCACAATCTCGAGCCACTGCACTCCATCCTGGGCAGCAGA
17_67495529_67497867_67514127_67521454_RF	-1	MPNSTs	GATTCCTTATAGTTTAAAATTAAATTATTCGAGTCTCTTAATGACCTGCGGAGATTGTAC
19_11040234_11041901_11194011_11195243_FF	-1	MPNSTs	CAGTCAGGTGGATCACGAGGTCAGGAGATCGATCTCCTGACCTCGTGATCCGCCCGCCTC
19_11062377_11065717_11194011_11195243_RF	-1	MPNSTs	GAGGCGGGCGGATCACGAGGTCAGGAGATCGATCTCCTGACCTCGTGATCCGCCCGCCTC
19_52666823_52670053_52700693_52702643_FF	-1	MPNSTs	GGGTTTCACCTTGTTAGCCAGGATGGTCTCGAGACCATCCTGGCTAACACGGTGAAACCC
21_39757299_39761915_39949058_39951313_FF	-1	MPNSTs	ACACTGATTAAATCTTAATTATTCCATTTCGATCCCTCAAGGATCAGGACTGTGTTGCAT
21_39757299_39761915_40055526_40064997_FF	-1	MPNSTs	ACACTGATTAAATCTTAATTATTCCATTTCGAGGGAATAATCTCCTAAACATTTCTGGTG
21_39762207_39763468_40021022_40024449_FF	-1	MPNSTs	CTTGGGCCCTATCTTATGTATGGAGCTGTCGAGTTTATGTTCTTACCCTTGTTTCTCTTT
5_42377143_42386021_42652698_42659568_FF	-1	MPNSTs	ATGCTAAATTATGTAAAATGGAATATGTTCGAGTTCATAGATACTCAAGGGCCCCTCAGT
5_42543850_42546292_42676184_42678827_RF	-1	MPNSTs	CAACAATTTTATTAATTTTCAACTTTCATCGATTTTATAAAATTATCAGTAATAACCTTT
6_41953588_41955459_42036433_42038022_RF	-1	MPNSTs	GAGGTGGGCAGATCACGAGGTCAGGAGATCGATCTCCTGACCTCGTGATCCGCCCGCCTC
6_41953588_41955459_42040682_42041908_RR	-1	MPNSTs	GAGGCGGGCGGATCACGAGGTCAGGAGATCGATCTCCCGACCTCGTGATCCGCCCGCCTC
7_116279520_116285670_116319380_116323843_RF	-1	MPNSTs	TGACACCATACATTTTATTTCTCCCTTCTCGAGATTTTGTTATTAAGCTTCCGTCTCGTT
7_116279520_116285670_116419719_116422284_RF	-1	MPNSTs	AGTCCTTTATTTCTGTTACAATCTTAAATCGAGATTTTGTTATTAAGCTTCCGTCTCGTT
7_116308668_116319380_116371770_116373950_RR	-1	MPNSTs	TACCTTTTTAGAGCTATGTCATGTATGTTCGAACAGAGTTTACCACAGCTTTGCAGCGCG
7_137545600_137549019_137668037_137669463_RR	-1	MPNSTs	TGTATTCTGTATCACTTAGACTCTTCTTTCGAAGAAGGAATCTTAAACAAGAGAAGCAAG
7_50657698_50658729_50784135_50786449_FF	-1	MPNSTs	AGTTGTTTTTCCTTGAAAAGGGTTTACCTCGACGGTTACAATTTCAGTATGCACGGGACT
8_108267104_108269307_108407566_108418839_RR	-1	MPNSTs	TTAACCTAGCAGATCTGGTTCTTCTGGTTCGAGGTATTTATATCACCTTGAGTATTATTT
8_108277745_108282069_108528062_108532217_FF	-1	MPNSTs	CCTAATAAAGAAAAAAAAAATGAGTCCCTTCGAAGCACAAAGTTACAGGACATGGCATCCA
8_108444846_108453607_108528062_108532217_FF	-1	MPNSTs	TCCTTTGGCCTGGTAATCTTTTCAATATTCGAAGCACAAAGTTACAGGACATGGCATCCA
8_99432076_99435027_99521801_99527715_RF	-1	MPNSTs	CTGCTCCATGTCTGTATTCCTACTTTATTCGAAAGCATCTTTGTGTCATTGTCCATGCTC
8_99486386_99490632_99554813_99560156_FF	-1	MPNSTs	CCTAAACTAAGCTTGGGCTTAAGATCCATCGAAAGGATACTTTTATAGGAACCAGGCTAG
8_99521801_99527715_99826498_99828247_RF	-1	MPNSTs	ATATATATATATCACAATGCCTAAGGGATCGAATAGCTTTTTAAGAACAGTGTATAAAAT
8_99541449_99550447_99646209_99658080_RR	-1	MPNSTs	CTCTCTGATTTGCCACATAAAGTAGGCATCGATTCCAAATAAATTAGTTGGTGATGTGGA
8_99792735_99799194_99962638_99967147_RF	-1	MPNSTs	ACTTCATGCACAAGTTAGGTATTTACTCTCGAGATTATAAACATTTTCATTTGGATTTTG

Table 26b. Neurofibromatosis (NF) probes - EpiSwitch™ markers to stratify (A) Benign plexiform vs. (B) Malignant Peripheral Nerve Sheath Tumours (MPNSTs)

Table 26b	Probe Location					4 kb Sequence Location				
Probe	Chr	Start1	End1	Start2	End2	Chr	Start1	End1	Start2	End2
A										
10_114686118_114690592_114727613_114729725_FF	10	114690563	114690592	114729696	114729725	10	114686593	114690592	114725726	114729725
10_114686118_114690592_114743749_114745454_FF	10	114690563	114690592	114745425	114745454	10	114686593	114690592	114741455	114745454
10_114686118_114690592_114773872_114776404_FF	10	114690563	114690592	114776375	114776404	10	114686593	114690592	114772405	114776404
10_114686118_114690592_114794603_114795614_FF	10	114690563	114690592	114795585	114795614	10	114686593	114690592	114791615	114795614
10_114686118_114690592_114804200_114807457_FF	10	114690563	114690592	114807428	114807457	10	114686593	114690592	114803458	114807457
10_114686118_114690592_114821603_114822761_FF	10	114690563	114690592	114822732	114822761	10	114686593	114690592	114818762	114822761
10_114686118_114690592_114845287_114849773_FF	10	114690563	114690592	114849744	114849773	10	114686593	114690592	114845774	114849773
10_114686118_114690592_114885061_114889442_FF	10	114690563	114690592	114889413	114889442	10	114686593	114690592	114885443	114889442
11_128342943_128345136_128481262_128489818_FF	11	128345107	128345136	128489789	128489818	11	128341137	128345136	128485819	128489818
11_128410884_128413638_128489818_128498866_FF	11	128413609	128413638	128498837	128498866	11	128409639	128413638	128494867	128498866
5_131857043_131861763_131874140_131875551_RF	5	131857044	131857073	131875522	131875551	5	131857044	131861043	131871552	131875551
5_131874140_131875551_131894531_131901964_FF	5	131875522	131875551	131901935	131901964	5	131871552	131875551	131897965	131901964
5_131874140_131875551_131920774_131922322_FF	5	131875522	131875551	131922293	131922322	5	131871552	131875551	131918323	131922322
5_131874140_131875551_131942647_131945574_FF	5	131875522	131875551	131945545	131945574	5	131871552	131875551	131941575	131945574
5_131874140_131875551_131985852_131989475_FF	5	131875522	131875551	131989446	131989475	5	131871552	131875551	131985476	131989475
5_131882513_131883559_131942647_131945574_FF	5	131883530	131883559	131945545	131945574	5	131879560	131883559	131941575	131945574

Table 26b	Probe Location					4 kb Sequence Location				
Probe	Chr	Start1	End1	Start2	End2	Chr	Start1	End1	Start2	End2
5_131882513_131883559_131966700_131972322_FF	5	131883530	131883559	131972293	131972322	5	131879560	131883559	131968323	131972322
6_41890642_41893643_42057606_42059682_RR	6	41890643	41890672	42057607	42057636	6	41890643	41894642	42057607	42061606
7_137557828_137562242_137656982_137661712_FF	7	137562213	137562242	137661683	137661712	7	137558243	137562242	137657713	137661712
7_50818806_50825328_50840056_50842638_RR	7	50818807	50818836	50840057	50840086	7	50818807	50822806	50840057	50844056
7_519231_522690_557100_558462_FF	7	522661	522690	558433	558462	7	518691	522690	554463	558462
7_519231_522690_594007_596370_FF	7	522661	522690	596341	596370	7	518691	522690	592371	596370
9_36907980_36909849_36932342_36938946_FF	9	36909820	36909849	36938917	36938946	9	36905850	36909849	36934947	36938946
9_36951690_36954534_36987524_36991745_RF	9	36951691	36951720	36991716	36991745	9	36951691	36955690	36987746	36991745
9_36961116_36962831_37038244_37041179_FF	9	36962802	36962831	37041150	37041179	9	36958832	36962831	37037180	37041179
B										
1_26993831_26995281_27050122_27052726_FF	1	26995252	26995281	27052697	27052726	1	26991282	26995281	27048727	27052726
17_67495529_67497867_67514127_67521454_RF	17	67495530	67495559	67521425	67521454	17	67495530	67499529	67517455	67521454
19_11040234_11041901_11194011_11195243_FF	19	11041872	11041901	11195214	11195243	19	11037902	11041901	11191244	11195243
19_11062377_11065717_11194011_11195243_RF	19	11062378	11062407	11195214	11195243	19	11062378	11066377	11191244	11195243
19_52666823_52670053_52700693_52702643_FF	19	52670024	52670053	52702614	52702643	19	52666054	52670053	52698644	52702643
21_39757299_39761915_39949058_39951313_FF	21	39761886	39761915	39951284	39951313	21	39757916	39761915	39947314	39951313
21_39757299_39761915_40055526_40064997_FF	21	39761886	39761915	40064968	40064997	21	39757916	39761915	40060998	40064997
21_39762207_39763468_40021022_40024449_FF	21	39763439	39763468	40024420	40024449	21	39759469	39763468	40020450	40024449

Table 26b	Probe Location					4 kb Sequence Location				
Probe	Chr	Start1	End1	Start2	End2	Chr	Start1	End1	Start2	End2
5_42377143_42386021_42652698_42659568_FF	5	42385992	42386021	42659539	42659568	5	42382022	42386021	42655569	42659568
5_42543850_42546292_42676184_42678827_RF	5	42543851	42543880	42678798	42678827	5	42543851	42547850	42674828	42678827
6_41953588_41955459_42036433_42038022_RF	6	41953589	41953618	42037993	42038022	6	41953589	41957588	42034023	42038022
6_41953588_41955459_42040682_42041908_RR	6	41953589	41953618	42040683	42040712	6	41953589	41957588	42040683	42044682
7_116279520_116285670_116319380_116323843_RF	7	116279521	116279550	116323814	116323843	7	116279521	116283520	116319844	116323843
7_116279520_116285670_116419719_116422284_RF	7	116279521	116279550	116422255	116422284	7	116279521	116283520	116418285	116422284
7_116308668_116319380_116371770_116373950_RR	7	116308669	116308698	116371771	116371800	7	116308669	116312668	116371771	116375770
7_137545600_137549019_137668037_137669463_RR	7	137545601	137545630	137668038	137668067	7	137545601	137549600	137668038	137672037
7_50657698_50658729_50784135_50786449_FF	7	50658700	50658729	50786420	50786449	7	50654730	50658729	50782450	50786449
8_108267104_108269307_108407566_108418839_RR	8	108267105	108267134	108407567	108407596	8	108267105	108271104	108407567	108411566
8_108277745_108282069_108528062_108532217_FF	8	108282040	108282069	108532188	108532217	8	108278070	108282069	108528218	108532217
8_108444846_108453607_108528062_108532217_FF	8	108453578	108453607	108532188	108532217	8	108449608	108453607	108528218	108532217
8_99432076_99435027_99521801_99527715_RF	8	99432077	99432106	99527686	99527715	8	99432077	99436076	99523716	99527715
8_99486386_99490632_99554813_99560156_FF	8	99490603	99490632	99560127	99560156	8	99486633	99490632	99556157	99560156
8_99521801_99527715_99826498_99828247_RF	8	99521802	99521831	99828218	99828247	8	99521802	99525801	99824248	99828247
8_99541449_99550447_99646209_99658080_RR	8	99541450	99541479	99646210	99646239	8	99541450	99545449	99646210	99650209
8_99792735_99799194_99962638_99967147_RF	8	99792736	99792765	99967118	99967147	8	99792736	99796735	99963148	99967147

Table 27. ALS Gene Data

GENE	Description	Comments	p-value
FCGR2B;FCGR3A	Fc Fragment Of IgG, Low Affinity Iib and IIa, Receptor	IgG binding	9.75E-05
CR1	Complement Component (3b/4b) Receptor 1 (Knops Blood Group)	complement component C3b binding and complement component C4b receptor activity	0.00010036
DNM3	Dynamin 3	GTP binding and GTPase activity	0.00067328
RAG1	Recombination Activating Gene 1	ubiquitin-protein ligase activity and protein homodimerization activity	0.00165575
PIK3R1	Phosphoinositide-3-Kinase, Regulatory Subunit 1 (Alpha)	protein phosphatase binding and1-phosphatidylinositol binding	0.00350494
TRAF6	TNF Receptor-Associated Factor 6, E3 Ubiquitin Protein Ligase	protein kinase binding and signal transducer activity	0.00408044
AP2A2	Adaptor-Related Protein Complex 2, Alpha 2 Subunit	protein transporter activity and lipid binding	0.00666831
ARHGEF7	Rho Guanine Nucleotide Exchange Factor (GEF) 7	phospholipid binding and guanyl-nucleotide exchange factor activity	0.00771418
CLEC5A	C-Type Lectin Domain Family 5, Member A	carbohydrate binding and virus receptor activity	0.00788381
TREM1	Triggering Receptor Expressed On Myeloid Cells 1	receptor activity	0.00795844
FYN	FYN Oncogene Related To SRC, FGR, YES	ion channel binding and identical protein binding	0.01316089
KIR2DL4;KIR3DL1; KIR2DL3	Killer Cell Immunoglobulin-Like Receptor, Two Domains, Long Cytoplasmic Tail, 4/Killer Cell Immunoglobulin-Like Receptor, Three Domains, Long Cytoplasmic Tail, 1/Killer Cell Immunoglobulin-Like Receptor, Two Domains, Long Cytoplasmic Tail, 3	transmembrane signaling receptor activity/HLA-B specific inhibitory MHC class I receptor activity/antigen binding and receptor activity	0.01380768
PTPRC	Protein Tyrosine Phosphatase, Receptor Type, C	protein kinase binding and transmembrane receptor protein tyrosine phosphatase activity	0.01507433
ICAM1	Intercellular Adhesion Molecule 1	integrin binding and receptor activity	0.01604022
ULBP1	UL16 Binding Protein 1	antigen binding and natural killer cell lectin-like receptor binding	0.01680033
MYD88	Myeloid Differentiation Primary Response 88	identical protein binding and TIR domain binding	0.028
ITGAM	Integrin, Alpha M (Complement Component 3 Receptor 3 Subunit)	heparin binding and heparan sulfate proteoglycan binding	0.03116451
LILRB4	Leukocyte Immunoglobulin-Like Receptor, Subfamily B (With TM And ITIM Domains), Member 4	antigen binding and receptor activity	0.04403324
IKBKB	Inhibitor Of Kappa Light Polypeptide Gene Enhancer In B-Cells, Kinase Beta	protein heterodimerization activity and protein homodimerization activity	0.04625161

GENE	Description	Comments	p-value
FCGR3A	Fc Fragment Of IgG, Low Affinity IIIa, Receptor (CD16a)	IgG binding	0.0579917
GLYCAM1	Glycosylation Dependent Cell Adhesion Molecule 1 (Pseudogene)	regulation of immune response	0.05817306
DDOST	Dolichyl-Diphosphooligosaccharide--Protein Glycosyltransferase Subunit (Non-Catalytic)	oligosaccharyl transferase activity and dolichyl-diphosphooligosaccharide-protein glycotransferase activity	0.06418361
RAG2;RAG1	Recombination Activating Gene 2 and 1	chromatin binding and methylated histone residue binding/ubiquitin-protein ligase activity and protein homodimerization activity	0.06418361
VCAM1	Vascular Cell Adhesion Molecule 1	integrin binding and primary amine oxidase activity	0.06418361
IGKV3-11	Immunoglobulin Kappa Variable 3-11	antigen/protein binding	0.07051211
IGKV3-20	Immunoglobulin Kappa Variable 3-20	antigen binding	0.07051211
IRAK1	Interleukin-1 Receptor-Associated Kinase 1	protein serine/threonine kinase activity andprotein homodimerization activity	0.07051211
SYK	Spleen Tyrosine Kinase	protein tyrosine kinase activity and protein kinase binding	0.0812399
FGFR1	Fibroblast Growth Factor Receptor 1	heparin binding and protein homodimerization activity	0.08977269
IGKV3-7	Immunoglobulin Kappa Variable 3-7 (Non-Functional)	protein binding	0.08977269
PRKCQ	Protein Kinase C, Theta	ubiquitin-protein ligase activity and identical protein binding	0.0976878
GHR	Growth Hormone Receptor	protein phosphatase binding and protein homodimerization activity	0.10265608
SH3KBP1	SH3-Domain Kinase Binding Protein 1	SH3 domain binding	0.11086917
MS4A2	Membrane-Spanning 4-Domains, Subfamily A, Member 2	SH2 domain binding and protein kinase binding	0.11608661
EGFR	Epidermal Growth Factor Receptor	chromatin binding and identical protein binding	0.11651883
BLNK	B-Cell Linker	SH3/SH2 adaptor activity and transmembrane receptor protein tyrosine kinase adaptor activity	0.1175276
CD96	CD96 Molecule	protein binding	0.12443215
DAPP1	Dual Adaptor Of Phosphotyrosine And 3-Phosphoinositides	phospholipid binding and phosphatidylinositol-3,4,5-trisphosphate binding	0.1574769
ART1	ADP-Ribosyltransferase 1	NAD(P)+-protein-arginine ADP-ribosyltransferase activity and NAD+ ADP-ribosyltransferase activity	0.16237882
C4B	Complement Component 4B	endopeptidase inhibitor activity	0.16237882

GENE	Description	Comments	p-value
CCR2	Chemokine (C-C Motif) Receptor 2	C-C chemokine receptor activity and protein homodimerization activity	0.16237882
CD180	CD180 Molecule	protein binding	0.16237882
CD274	CD274 Molecule	protein binding	0.16237882
CD28	CD28 Molecule	SH3/SH2 adaptor activity and identical protein binding	0.16237882
CD3D	CD3d Molecule, Delta (CD3-TCR Complex)	transmembrane signaling receptor activity and protein heterodimerization activity	0.16237882
CD3G;CD3D	CD3g Molecule, Gamma (CD3-TCR Complex)/CD3d Molecule, Delta (CD3-TCR Complex)	receptor signaling complex scaffold activity and protein heterodimerization activity/transmembrane signaling receptor activity and protein heterodimerization activity	0.16237882
CD40LG	CD40 Ligand	CD40 receptor binding and cytokine activity	0.16237882
ICAM1;ICAM4	Intercellular Adhesion Molecule 1 and 4	integrin binding and receptor activity	0.16237882
IFITM1;IFITM2	Interferon Induced Transmembrane Protein 1 and 2	receptor signaling protein activity	0.16237882
IFITM3	Interferon Induced Transmembrane Protein 3	receptor signaling and protein binding activity	0.16237882
IGLC3;IGLC7;IGLC2; IGLC1;IGLC6	Immunoglobulin Lambda Constant 3/7/2/1/6	antigen binding	0.16237882
IKBKG	Inhibitor Of Kappa Light Polypeptide Gene Enhancer In B-Cells, Kinase Gamma	protein homodimerization activity and signal transducer activity	0.16237882
IRS2	Insulin Receptor Substrate 2	phospholipid binding and signal transducer activity	0.16237882
ITGA4	Integrin, Alpha 4 (Antigen CD49D, Alpha 4 Subunit Of VLA-4 Receptor)	fibronectin binding	0.16237882
ITGAV	Integrin, Alpha V	protein kinase C binding and virus receptor activity	0.16237882
KIR2DS4;KIR3DL1	Killer Cell Immunoglobulin-Like Receptor, Two Domains, Short Cytoplasmic Tail, 4/Killer Cell Immunoglobulin-Like Receptor, Three Domains, Long Cytoplasmic Tail, 1	receptor activity/HLA-B specific inhibitory MHC class I receptor activity	0.16237882
LILRB2	Leukocyte Immunoglobulin-Like Receptor, Subfamily B (With TM And ITIM Domains), Member 2	MHC class I protein binding and receptor activity	0.16237882
PDCD1LG2	Programmed Cell Death 1 Ligand 2	protein binding	0.16237882
SIGIRR	Single Immunoglobulin And Toll-Interleukin 1 Receptor (TIR) Domain	protein binding	0.16237882

GENE	Description	Comments	p-value
TLR1;TLR6	Toll-Like Receptor 1 and 6	transmembrane signaling receptor activity and protein heterodimerization activity	0.16237882
VPREB1	Pre-B Lymphocyte 1	antigen binding	0.16237882
DNM2	Dynamin 2	protein kinase binding and GTP binding	0.16968984
AGER	Advanced Glycosylation End Product-Specific Receptor	S100 protein binding and receptor activity	0.1879858
CCNO	Cyclin O	protein kinase binding and uracil DNA N-glycosylase activity	0.1879858
KRAS	Kirsten Rat Sarcoma Viral Oncogene Homolog	GDP binding and GTP binding	0.1879858
LILRB1	Leukocyte Immunoglobulin-Like Receptor, Subfamily B (With TM And ITIM Domains), Member 1	MHC class I protein binding andprotein homodimerization activity	0.1879858
TLR2	Toll-Like Receptor 2	transmembrane signaling receptor activity and protein heterodimerization activity	0.1879858
B2M	beta-2-microglobulin	identical protein binding	0.20978301
ADCY4	Adenylate Cyclase 4	adenylate cyclase activity	0.21283252
IL7R	Interleukin 7 Receptor	antigen binding and interleukin-7 receptor activity	0.21283252
CR1;CR2	Complement Component (3b/4b) Receptor 1/ Complement component C3b binding and complement component C4b receptor activity	complement component C3b binding and complement component C4b receptor activity/ protein homodimerization activity and complement receptor activity	0.25289217
FCGR1A	Fc Fragment Of IgG, High Affinity Ia, Receptor (CD64)	IgG binding and receptor signaling protein activity	0.2547195
CCR6	Chemokine (C-C Motif) Receptor 6	C-C chemokine receptor activity and receptor activity	0.25953148
ITGB2	Integrin, Beta 2 (Complement Component 3 Receptor 3 And 4 Subunit)	protein kinase binding andglycoprotein binding	0.25953148
RFXAP	Regulatory Factor X-Associated Protein	transcription coactivator activity andsequence-specific DNA binding transcription factor activity	0.25953148
ITGB5	Integrin, Beta 5	integrin binding and receptor activity	0.27876985
ADCY8	Adenylate Cyclase 8 (Brain)	calcium- and calmodulin-responsive adenylate cyclase activity and adenylate cyclase activity	0.29005636
AICDA	Activation-Induced Cytidine Deaminase	cytidine deaminase activity	0.29840344
ATPIF1;PTAFR	ATPase Inhibitory Factor 1/Platelet-Activating Factor Receptor	enzyme inhibitor activity and protein homodimerization activity/G-protein coupled receptor activity and lipopolysaccharide binding	0.29840344

GENE	Description	Comments	p-value
CD3G	CD3g Molecule, Gamma (CD3-TCR Complex)	receptor signaling complex scaffold activity and protein heterodimerization activity	0.29840344
CD81	CD81 Molecule	MHC class II protein complex binding	0.29840344
CFB	Complement Factor B	complement binding and serine-type endopeptidase activity	0.29840344
CXADR	Coxsackie Virus And Adenovirus Receptor	PDZ domain binding and identical protein binding	0.29840344
ERBB2	V-Erb-B2 Avian Erythroblastic Leukemia Viral Oncogene Homolog 2	protein C-terminus bindingand identical protein binding	0.29840344
ERBB3	V-Erb-B2 Avian Erythroblastic Leukemia Viral Oncogene Homolog 3	protein heterodimerization activity and protein homodimerization activity	0.29840344
FCER1A	Fc Fragment Of IgE, High Affinity I, Receptor For; Alpha Polypeptide	IgE receptor activity and IgE binding	0.29840344
HCST	Hematopoietic Cell Signal Transducer	phosphatidylinositol 3-kinase binding	0.29840344
IGHV1-46	Immunoglobulin Heavy Variable 1-46	protein binding	0.29840344
IL3RA;CSF2RA	Interleukin 3 Receptor, Alpha (Low Affinity)/Colony Stimulating Factor 2 Receptor, Alpha, Low-Affinity	interleukin-3 receptor activity/cytokine receptor activity and receptor activity	0.29840344
ITGB7	Integrin, Beta 7	virus receptor activity	0.29840344
KIR2DS4;KIR3DL1;KIR3DL2	Killer Cell Immunoglobulin-Like Receptor, Two Domains, Short Cytoplasmic Tail, 4/Killer Cell Immunoglobulin-Like Receptor, Three Domains, Long Cytoplasmic Tail, 1/Killer Cell Immunoglobulin-Like Receptor, Three Domains, Long Cytoplasmic Tail, 2	signalling activity/HLA-B specific inhibitory MHC class I receptor activity/Receptor on natural killer (NK) cells for HLA-A alleles	0.29840344
KIR3DL1	Killer Cell Immunoglobulin-Like Receptor, Three Domains, Long Cytoplasmic Tail, 1	HLA-B specific inhibitory MHC class I receptor activity	0.29840344
MADCAM1	Mucosal Vascular Addressin Cell Adhesion Molecule 1	protrin binding	0.29840344
MAP3K7	Mitogen-Activated Protein Kinase Kinase Kinase 7	protein serine/threonine kinase activity and protein kinase activity	0.29840344
NFKB2	Nuclear Factor Of Kappa Light Polypeptide Gene Enhancer In B-Cells 2 (P49/P100)	transcription coactivator activity and sequence-specific DNA binding transcription factor activity	0.29840344
PDCD1	Programmed Cell Death 1	signal transducer activity	0.29840344
SIGLEC14	Sialic Acid Binding Ig-Like Lectin 14	protein binding	0.29840344
SIGLEC15	Sialic Acid Binding Ig-Like Lectin 15	protein binding	0.29840344
SIRPB1	Signal-Regulatory Protein Beta 1	protein binding	0.29840344

GENE	Description	Comments	p-value
TIRAP	Toll-Interleukin 1 Receptor (TIR) Domain Containing Adaptor Protein	protein binding, bridging and protein homodimerization activity	0.29840344
TLR10	Toll-Like Receptor 10	transmembrane signaling receptor activity	0.29840344
TYROBP;HCST	TYRO Protein Tyrosine Kinase Binding Protein/Hematopoietic Cell Signal Transducer	receptor signaling protein activity and identical protein binding/Hematopoietic Cell Signal Transducer	0.29840344
VAV1;C3	Vav 1 Guanine Nucleotide Exchange Factor/Complement Component 3	sequence-specific DNA binding transcription factor activity and guanyl-nucleotide exchange factor activity/C5L2 anaphylatoxin chemotactic receptor binding and receptor binding	0.29840344

Table 28. Pre –Type 2 Diabetes Gene Data

GENE	Description	Table 28 Comments	p-value
ABCC8	ATP-Binding Cassette, Sub-Family C (CFTR/MRP), Member 8	ion channel binding andpotassium ion transmembrane transporter activity	0.005571163
ADCY5	Adenylate Cyclase 5	adenylate cyclase binding and protein heterodimerization activity	0.000309237
CACNA1C	Calcium Channel, Voltage-Dependent, L Type, Alpha 1C Subunit	alpha-actinin binding and calmodulin binding	0.004207097
CDKN2A	Cyclin-Dependent Kinase Inhibitor 2A	protein kinase binding and p53 binding	0.001156338
CYB5R4	Cytochrome B5 Reductase 4	NAD(P)H oxidase activity and heme binding	0.001648199
CYP2C9	Cytochrome P450, Family 2, Subfamily C, Polypeptide 9	electron carrier activity and heme binding	3.00E-05
DGKB	Diacylglycerol Kinase, Beta 90kDa	diacylglycerol kinase activity andcalcium ion binding	0.000440459
ICAM1	Intercellular Adhesion Molecule 1	integrin binding and receptor activity	0.009727539
IGF2	Insulin-Like Growth Factor 2 (Somatomedin A)	growth factor activity and insulin receptor binding	0.013781657
INS	Insulin	protease binding and identical protein binding	0.005779532
KCNJ11	Potassium Inwardly-Rectifying Channel, Subfamily J, Member 11	protein C-terminus binding andvoltage-gated potassium channel activity	0.000203298
LEP	Leptin	growth factor activity and peptide hormone receptor binding	0.010562363
MAPK10	Mitogen-Activated Protein Kinase 10	JUN kinase activity and MAP kinase kinase activity	0.010774536
PAX4	Paired Box 4	double-stranded DNA binding and sequence-specific DNA binding transcription factor activity	0.009727539

GENE	Description	Table 28 Comments	p-value
PIK3R3	Phosphoinositide-3-Kinase, Regulatory Subunit 3 (Gamma)	1-phosphatidylinositol-3-kinase activity and phosphatidylinositol 3-kinase regulator activity	0.005779532
PTPRD	Protein Tyrosine Phosphatase, Receptor Type, D	transmembrane receptor protein tyrosine phosphatase activity and receptor binding	0.010774536
SREBF1	Sterol Regulatory Element Binding Transcription Factor 1	chromatin binding and sequence-specific DNA binding transcription factor activity	0.00036609
TASP1	Taspase, Threonine Aspartase, 1	threonine-type endopeptidase activity	0.003377072
TNFRSF1B	Tumor Necrosis Factor Receptor Superfamily, Member 1B	tumor necrosis factor-activated receptor activity and ubiquitin protein ligase binding	0.005226941
TSPAN8	Tetraspanin 8	signal transducer activity	0.016203495
ASIP	Agouti Signaling Protein	type 4 melanocortin receptor binding and receptor binding	0.021488806
INSR	Insulin Receptor	SH2 domain binding and GTP binding	0.021488806
CAMK1D	Calcium/Calmodulin-Dependent Protein Kinase ID	calmodulin binding and calmodulin-dependent protein kinase activity	0.029182439
UBA52P6	Ubiquitin A-52 Residue Ribosomal Protein Fusion Product 1 Pseudogene 6	pseudogene	0.030482606
SLC30A8	Solute Carrier Family 30 (Zinc Transporter), Member 8	zinc ion transmembrane transporter activityand protein homodimerization activity	0.033480808
CYB5A	Cytochrome B5 Type A (Microsomal)	cytochrome-c oxidase activity and enzyme binding	0.041435693
CDKN2B	Cyclin-Dependent Kinase Inhibitor 2B (P15, Inhibits CDK4)	cyclin-dependent protein serine/threonine kinase inhibitor activityand protein kinase binding	0.059165859
ZFAND6	Zinc Finger, AN1-Type Domain 6	polyubiquitin binding	0.059165859
NOTCH2	Neurogenic Locus Notch Homolog Protein 2	receptor activity and calcium ion binding	0.064334474
TIMP1	Tissue Inhibitor Of Metalloproteinases 1	metalloendopeptidase inhibitor activity	0.063526643
AGT	Angiotensinogen (Serpin Peptidase Inhibitor, Clade A, Member 8)	growth factor activity and hormone activity	0.072394301
HSD17B3	Hydroxysteroid (17-Beta) Dehydrogenase 3	testosterone 17-beta-dehydrogenase (NADP+) activity	0.072394301
RBP4	Retinol Binding Protein 4, Plasma	retinal binding and protein heterodimerization activity	0.072394301
ADIPOR1	Adiponectin Receptor 1	protein kinase binding and identical protein binding	0.077957576
AKT1	V-Akt Murine Thymoma Viral Oncogene Homolog 1	enzyme binding and identical protein binding	0.077957576
VEGFA	Vascular Endothelial Growth Factor A	protein heterodimerization activity and protein homodimerization activity	0.077957576

GENE	Description	Table 28 Comments	p-value
ARAP1	ArfGAP With RhoGAP Domain, Ankyrin Repeat And PH Domain 1	ARF GTPase activator activity and phosphatidylinositol-3,4,5-trisphosphate binding	0.091540286
SUCLG2	Succinate-CoA Ligase, GDP-Forming, Beta Subunit	succinate-CoA ligase (GDP-forming) activity and GTP binding	0.204362567

Table 29. Type 2 Diabetes Gene Data

GENE	Description	Table 29 Comments	p-value
IDE	Insulin-Degrading Enzyme	ATPase activity and protein homodimerization activity	1.49E-05
SDHB	Succinate Dehydrogenase Complex, Subunit B, Iron Sulfur (Ip)	electron carrier activity and 2 iron, 2 sulfur cluster binding	2.36E-05
SREBF1	Sterol Regulatory Element Binding Transcription Factor 1	chromatin binding and sequence-specific DNA binding transcription factor activity	0.00011264
AGT	Angiotensinogen (Serpin Peptidase Inhibitor, Clade A, Member 8)	growth factor activity and hormone activity	0.00043908
CDKN2B-AS1	CDKN2B Antisense RNA 1	interacts with both polycomb repressive complex-1 (PRC1) and -2 (PRC2), and may function as a regulator for epigenetic transcriptional repression	0.00054565
ANKRD55	Ankyrin Repeat Domain 55	protein binding	0.00065244
SLC2A2	Solute Carrier Family 2 (Facilitated Glucose Transporter), Member 2	hexose transmembrane transporter activity and dehydroascorbic acid transporter activity	0.00080874
CYP2C9	Cytochrome P450, Family 2, Subfamily C, Polypeptide 9	electron carrier activity and heme binding	0.00085093
ICAM1	Intercellular Adhesion Molecule 1	integrin binding and receptor activity	0.00173236
KCNJ11	Potassium Inwardly-Rectifying Channel, Subfamily J, Member 11	protein C-terminus binding andvoltage-gated potassium channel activity	0.00225223
CAMK1D	Calcium/Calmodulin-Dependent Protein Kinase ID	calmodulin binding and calmodulin-dependent protein kinase activity	0.00279065
GIPR	Gastric Inhibitory Polypeptide Receptor	transmembrane signaling receptor activity and gastric inhibitory peptide receptor activity	0.003136
CACNA1C	Calcium Channel, Voltage-Dependent, L Type, Alpha 1C Subunit	alpha-actinin binding and calmodulin binding	0.00621182
VEGFA	Vascular Endothelial Growth Factor A	protein heterodimerization activity and protein homodimerization activity	0.00678606

GENE	Description	Table 29 Comments	p-value
GHRL	Ghrelin/Obestatin Prepropeptide	growth hormone-releasing hormone activity and G-protein coupled receptor binding	0.00808286
TLE1	Transducin-Like Enhancer Of Split 1 (E(Sp1) Homolog, Drosophila)	chromatin binding and RNA polymerase II transcription corepressor activity	0.00808286
AVP	Arginine Vasopressin	protein kinase activity and receptor binding	0.00849023
LTA	Lymphotoxin Alpha	tumor necrosis factor receptor binding and receptor binding	0.00947722
CYB5R4	Cytochrome B5 Reductase 4	NAD(P)H oxidase activity and heme binding	0.01132881
ADCY5	Adenylate Cyclase 5	adenylate cyclase binding and protein heterodimerization activity	0.0137542
TASP1	Taspase, Threonine Aspartase, 1	hreonine-type endopeptidase activity	0.01378654
PAX4	Paired Box 4	double-stranded DNA binding and sequence-specific DNA binding transcription factor activity	0.01389652
DGKB	Diacylglycerol Kinase, Beta 90kDa	diacylglycerol kinase activity andcalcium ion binding	0.01468697
SOCS2	Suppressor Of Cytokine Signaling 2	SH3/SH2 adaptor activity and growth hormone receptor binding	0.01677982
CYB5A	Cytochrome B5 Type A (Microsomal)	cytochrome-c oxidase activity and enzyme binding	0.01698184
SOCS3	Suppressor Of Cytokine Signaling 3	protein kinase inhibitor activity	0.02282234
TNF	Tumor Necrosis Factor	cytokine activity and identical protein binding	0.02282234
H19	H19, Imprinted Maternally Expressed Transcript (Non-Protein Coding)	expresses a non-coding RNA, and functions as a tumor suppressor	0.02357461
EDN1	Endothelin 1	endothelin A receptor binding and cytokine activity	0.02779399
HSD3B2	Hydroxy-Delta-5-Steroid Dehydrogenase, 3 Beta- And Steroid Delta-Isomerase 2	3-beta-hydroxy-delta5-steroid dehydrogenase activity and steroid delta-isomerase activity	0.02779399
SELE	Selectin E	transmembrane signaling receptor activity and sialic acid binding	0.03638118
ADIPOQ	Adiponectin, C1Q And Collagen Domain Containing	protein homodimerization activity and receptor binding	0.03775263
GIP	Gastric Inhibitory Polypeptide	hormone activity	0.03775263
TCF7L2	Transcription Factor 7-Like 2 (T-Cell Specific, HMG-Box)	chromatin binding and sequence-specific DNA binding transcription factor activity	0.04116208
NFKB1	Nuclear Factor Of Kappa Light Polypeptide Gene Enhancer In B-Cells 1	transcription factor binding andsequence-specific DNA binding transcription factor activity	0.04503238

GENE	Description	Table 29 Comments	p-value
MTOR	Mechanistic Target Of Rapamycin (Serine/Threonine Kinase)	drug binding and protein serine/threonine kinase activity	0.05115907
TSPAN8	Tetraspanin 8	signal transducer activity	0.05432511
GSTT1	Glutathione S-Transferase Theta 1	glutathione transferase activity and glutathione peroxidase activity	0.05531008
PRC1	Protein Regulator Of Cytokinesis 1	microtubule binding and identical protein binding	0.05531008
VPS26A	Vacuolar Protein Sorting 26 Homolog A (S. Pombe)	protein transporter activity	0.05531008
KCNQ1	Potassium Voltage-Gated Channel, KQT-Like Subfamily, Member 1	calmodulin binding and voltage-gated potassium channel activity	0.05682953
ATP5A1	ATP Synthase, H+ Transporting, Mitochondrial F1 Complex, Alpha Subunit 1, Cardiac Muscle	ATPase activity and proton-transporting ATPase activity, rotational mechanism	0.06838534
WFS1	Wolfram Syndrome 1 (Wolframin)	ATPase binding and transporter activity	0.0718483
CCL2	Chemokine (C-C Motif) Ligand 2	heparin binding and receptor binding	0.0726416
ELOVL6	ELOVL Fatty Acid Elongase 6	transferase activity, transferring acyl groups other than amino-acyl groups	0.0726416
IL6	Interleukin 6 (Interferon, Beta 2)	interleukin-6 receptor binding and cytokine activity	0.0726416
UCP2	Uncoupling Protein 2 (Mitochondrial, Proton Carrier)	mitochondrial transporter proteins	0.0726416
ESR1	Estrogen Receptor 1	chromatin binding and sequence-specific DNA binding transcription factor activity	0.07850912
NR3C1	Nuclear Receptor Subfamily 3, Group C, Member 1 (Glucocorticoid Receptor	protein dimerization activity and sequence-specific DNA binding transcription factor activity	0.08595811
ACADM	Acyl-CoA Dehydrogenase, C-4 To C-12 Straight Chain	acyl-CoA dehydrogenase activity and identical protein binding	0.08665649
PNISR	PNN-Interacting Serine/Arginine-Rich Protein	poly(A) RNA binding	0.08665649
PTPRD	Protein Tyrosine Phosphatase, Receptor Type, D	transmembrane receptor protein tyrosine phosphatase activity and receptor binding	0.08744676
PSMG1	Proteasome (Prosome, Macropain) Assembly Chaperone 1	protein binding	0.09956542
LDLR	Low Density Lipoprotein Receptor	low-density lipoprotein particle binding and calcium ion binding	0.10538293
PDHB	Pyruvate Dehydrogenase (Lipoamide) Beta	pyruvate dehydrogenase activity andpyruvate dehydrogenase (acetyl-transferring) activity	0.10538293

GENE	Description	Table 29 Comments	p-value
CCKAR	Cholecystokinin A Receptor	cholecystokinin receptor activity	0.12483961
INS	insulin	protease binding and identical protein binding	0.12483961
MT1X	Metallothionein 1X	metal ion binding	0.12483961
PIK3R3	Phosphoinositide-3-Kinase, Regulatory Subunit 3 (Gamma)	1-phosphatidylinositol-3-kinase activity and phosphatidylinositol 3-kinase regulator activity	0.12483961
SHBG	Sex Hormone-Binding Globulin	androgen binding and protein homodimerization activity	0.12483961
ZBED3	Zinc Finger, BED-Type Containing 3	DNA/protein/metal ion binding	0.12483961
MAPK8IP1	Mitogen-Activated Protein Kinase 8 Interacting Protein 1	protein kinase binding and kinesin binding	0.12560157
CRHR1	Corticotropin Releasing Hormone Receptor 1	corticotrophin-releasing factor receptor activity and protein complex binding	0.14071272
CDK10	Cyclin-Dependent Kinase 10	cyclin-dependent protein serine/threonine kinase activity	0.1462871
CYBA	Cytochrome B-245, Alpha Polypeptide	protein heterodimerization activity and heme binding	0.1462871
GCDH	Glutaryl-CoA Dehydrogenase	fatty-acyl-CoA binding and flavin adenine dinucleotide binding	0.1462871
GPX1	Glutathione Peroxidase 1	SH3 domain binding and glutathione peroxidase activity	0.1462871
SLC9A1	Solute Carrier Family 9, Subfamily A (NHE1, Cation Proton Antiporter 1), Member 1	sodium:hydrogen antiporter activityand calmodulin binding	0.1462871
ATF3	Activating Transcription Factor 3	identical protein binding and sequence-specific DNA binding transcription factor activity	0.14660664
CCR5	Chemokine (C-C Motif) Receptor 5 (Gene/Pseudogene)	actin binding and coreceptor activity	0.14660664
FADS1	Fatty Acid Desaturase 1	oxidoreductase activity and iron ion binding	0.14660664
AP3S2	Adaptor-Related Protein Complex 3, Sigma 2 Subunit	protein transporter activity	0.15374807
CTRB1	Chymotrypsinogen B1	serine-type endopeptidase activity	0.15374807
CDKN2A	Cyclin-Dependent Kinase Inhibitor 2A	protein kinase binding and p53 binding	0.18362238
HLA-DQA1	Major Histocompatibility Complex, Class II, DQ Alpha 1	MHC class II receptor activity	0.18970088
SOD1	Superoxide Dismutase 1, Soluble	copper ion binding and protein homodimerization activity	0.18970088
RND3	Rho Family GTPase 3	GTP binding and GTPase activity	0.19352045

GENE	Description	Table 29 Comments	p-value
MAPK9	Mitogen-Activated Protein Kinase 9	transcription factor binding andmitogen-activated protein kinase kinase kinase binding	0.19397784
SDHA	Succinate Dehydrogenase Complex, Subunit A, Flavoprotein (Fp)	succinate dehydrogenase (ubiquinone) activity and flavin adenine dinucleotide binding	0.19397784
SOD2	Superoxide Dismutase 2, Mitochondrial	oxygen binding and identical protein binding	0.21484978
CARTPT	Cocaine And Amphetamine Regulated Transcript	protein binding	0.21922992
CCL13	Chemokine (C-C Motif) Ligand 13	chemokine activity and receptor binding	0.23449781
HSD17B3	Hydroxysteroid (17-Beta) Dehydrogenase 3	testosterone 17-beta-dehydrogenase (NADP+) activity	0.24528753
PDX1	Pancreatic And Duodenal Homeobox 1	chromatin binding and sequence-specific DNA binding transcription factor activity	0.24528753
SRC	V-Src Avian Sarcoma (Schmidt-Ruppin A-2) Viral Oncogene Homolog	protein kinase activity and identical protein binding	0.2470727
GLIS3	GLIS Family Zinc Finger 3	sequence-specific DNA binding transcription factor activity	0.25858972
CDKN2B	Cyclin-Dependent Kinase Inhibitor 2B (P15, Inhibits CDK4)	cyclin-dependent protein serine/threonine kinase inhibitor activity and protein kinase binding	0.27977809
PIK3R2	Phosphoinositide-3-Kinase, Regulatory Subunit 2 (Beta)	receptor tyrosine kinase binding and phosphatidylinositol 3-kinase regulator activity	0.27977809
ZFAND6	Zinc Finger, AN1-Type Domain 6	polyubiquitin binding	0.27977809

Table 30. Type 1 Diabetes Gene Data

GENE	Description	Table 30 Comments	p-value
ITGAM	Integrin, Alpha M (Complement Component 3 Receptor 3 Subunit)	heparin binding and heparan sulfate proteoglycan binding	0.0007641
ULBP1	UL16 Binding Protein 1	antigen binding and natural killer cell lectin-like receptor binding	0.000765
PIK3R1	Phosphoinositide-3-Kinase, Regulatory Subunit 1 (Alpha)	protein phosphatase binding and1-phosphatidylinositol binding	0.00134806
CCNO	Cyclin O	protein kinase binding and uracil DNA N-glycosylase activity	0.00162587
RAG1	Recombination Activating Gene 1	ubiquitin-protein ligase activity and protein homodimerization activity	0.00175515
AGER	Advanced Glycosylation End Product-Specific Receptor	S100 protein binding and receptor activity	0.00264646
DNM3	Dynamin 3	GTP binding and GTPase activity	0.00293324
ARHGEF7	Rho Guanine Nucleotide Exchange Factor (GEF) 7	phospholipid binding and guanyl-nucleotide exchange factor activity	0.00297702
ICAM1	Intercellular Adhesion Molecule 1	integrin binding and receptor activity	0.00434176
SH3KBP1	SH3-Domain Kinase Binding Protein 1	SH3 domain binding	0.00435443
DAPP1	Dual Adaptor Of Phosphotyrosine And 3-Phosphoinositides	phospholipid binding and phosphatidylinositol-3,4,5-trisphosphate binding	0.00523553
ADCY9	Adenylate Cyclase 9	adenylate cyclase activity	0.00712137
PLD1	Phospholipase D1, Phosphatidylcholine-Specific	NAPE-specific phospholipase D activity and phosphatidylinositol binding	0.00999977
LY86	Lymphocyte Antigen 86	mediate innate immune response to bacterial lipopolysaccharide (LPS) and cytokine production	0.01108912
IKBKB	Inhibitor Of Kappa Light Polypeptide Gene Enhancer In B-Cells, Kinase Beta	protein heterodimerization activity and protein homodimerization activity	0.01128582
PTPRC	Protein Tyrosine Phosphatase, Receptor Type, C	protein kinase binding and transmembrane receptor protein tyrosine phosphatase activity	0.02237102
ADCY8	Adenylate Cyclase 8 (Brain)	calcium- and calmodulin-responsive adenylate cyclase activity and adenylate cyclase activity	0.0328753
PRKCQ	Protein Kinase C, Theta	ubiquitin-protein ligase activity and identical protein binding	0.03480357
GHR	Growth Hormone Receptor	protein phosphatase binding and protein homodimerization activity	0.03663135
FCGR2B;FCGR3A	Fc Fragment Of IgG, Low Affinity IIb and IIIa, Receptor	IgG binding	0.03765986
VCAM1	Vascular Cell Adhesion Molecule 1	integrin binding and primary amine oxidase activity	0.03841589
TAP2;TAP1	Transporter 2, ATP-Binding Cassette, Sub-Family B /Transporter 1, ATP-Binding Cassette, Sub-Family B	transporter activity and MHC class I protein binding/ADP binding and protein homodimerization activity	0.05214662

GENE	Description	Table 30 Comments	p-value
CCR6	Chemokine (C-C Motif) Receptor 6	C-C chemokine receptor activity and receptor activity	0.0539188
AP2A2	Adaptor-Related Protein Complex 2, Alpha 2 Subunit	protein transporter activity and lipid binding	0.05915437
PRKCSH	Protein Kinase C Substrate 80K-H	protein kinase C binding and calcium ion binding	0.05915437
DNM1	Dynamin 1	phospholipid binding and identical protein binding	0.06012929
IL5RA	Interleukin 5 Receptor, Alpha	interleukin-5 receptor activity	0.06012929
PLCG1	Phospholipase C, Gamma 1	receptor signaling protein activity and calcium ion binding	0.06012929
FCGR3A	Fc Fragment Of IgG, Low Affinity IIIa, Receptor (CD16a)	IgG binding	0.06099381
FCGR1A	Fc Fragment Of IgG, High Affinity Ia, Receptor (CD64)	IgG binding and receptor signaling protein activity	0.07229075
BCR	Breakpoint Cluster Region	protein serine/threonine kinase activity and enzyme binding	0.08613786
RAG1;TRAF6	Recombination Activating Gene 1/TNF Receptor-Associated Factor 6, E3 Ubiquitin Protein Ligase	ubiquitin-protein ligase activity and protein homodimerization activity/protein kinase binding and signal transducer activity	0.08655541
B2M	beta-2-microglobulin	identical protein binding	0.08762339
AP2B1	Adaptor-Related Protein Complex 2, Beta 1 Subunit	clathrin bindingand protein complex binding	0.08822935
CD38	CD38 Molecule	phosphorus-oxygen lyase activity and NAD+ nucleosidase activity	0.09202116
KIT	V-Kit Hardy-Zuckerman 4 Feline Sarcoma Viral Oncogene Homolog	protein homodimerization activity and protease binding	0.09202116
CBL	Cbl Proto-Oncogene, E3 Ubiquitin Protein Ligase	ubiquitin-protein ligase activity and sequence-specific DNA binding transcription factor activity	0.11131925
TREM1	Triggering Receptor Expressed On Myeloid Cells 1	receptor activity	0.11692072
CDH1	Cadherin 1, Type 1, E-Cadherin (Epithelial)	beta-catenin binding and calcium ion binding	0.1313431
AICDA	Activation-Induced Cytidine Deaminase	cytidine deaminase activity	0.13842069
CD180	CD180 Molecule	protein binding	0.13842069
CD274	CD274 Molecule	protein binding	0.13842069
CD3D	CD3d Molecule, Delta (CD3-TCR Complex)	transmembrane signaling receptor activity and protein heterodimerization activity	0.13842069
CD81	CD81 Molecule	MHC class II protein complex binding	0.13842069
HCST	Hematopoietic Cell Signal Transducer	phosphatidylinositol 3-kinase binding	0.13842069
ITGAV	Integrin, Alpha V	protein kinase C binding and virus receptor activity	0.13842069
ITGB7	Integrin, Beta 7	virus receptor activity	0.13842069
NFKB2	Nuclear Factor Of Kappa Light Polypeptide Gene Enhancer In B-Cells 2 (P49/P100)	include transcription coactivator activity and sequence-specific DNA binding transcription factor activity	0.13842069
IRS1	Insulin Receptor Substrate 1	protein kinase C binding and phospholipid binding	0.14381711

GENE	Description	Table 30 Comments	p-value
SCYL1	SCY1-Like 1 (S. Cerevisiae)	protein tyrosine kinase activity	0.14381711
SYK	Spleen Tyrosine Kinase	protein tyrosine kinase activity and protein kinase binding	0.1709489
FYN	FYN Oncogene Related To SRC, FGR, YES	ion channel binding and identical protein binding	0.18657498
HRAS	Harvey Rat Sarcoma Viral Oncogene Homolog	protein C-terminus binding and GTP binding	0.19661222
PVR	Poliovirus Receptor	receptor activity and cell adhesion molecule binding	0.19661222
LCK	Lymphocyte-Specific Protein Tyrosine Kinase	protein C-terminus binding and identical protein binding	0.20079822
PANX1	Pannexin 1	actin filament binding and protein heterodimerization activity	0.20454126
PPAPDC1A	Phosphatidic Acid Phosphatase Type 2 Domain Containing 1A	phosphatidate phosphatase activity	0.23161338
CR1	Complement Component (3b/4b) Receptor 1 (Knops Blood Group)	complement component C3b binding and complement component C4b receptor activity	0.23203701
ADA	Adenosine Deaminase	purine nucleoside binding and adenosine deaminase activity	0.25120539
CHUK	Conserved Helix-Loop-Helix Ubiquitous Kinase	protein heterodimerization activity and protein homodimerization activity	0.25120539
FGFR1	Fibroblast Growth Factor Receptor 1	heparin binding and protein homodimerization activity	0.25120539
ITGB2	Integrin, Beta 2 (Complement Component 3 Receptor 3 And 4 Subunit)	protein kinase binding andglycoprotein binding	0.25120539
RFXAP	Regulatory Factor X-Associated Protein	transcription coactivator activity andsequence-specific DNA binding transcription factor activity	0.25120539
TNFRSF13B	Tumor Necrosis Factor Receptor Superfamily, Member 13B	receptor activity	0.25120539
CD19	CD19 Molecule	receptor signaling protein activity	0.25769486
CD74	CD74 Molecule, Major Histocompatibility Complex, Class II Invariant Chain	cytokine receptor activity and identical protein binding	0.25769486
FCER1A	Fc Fragment Of IgE, High Affinity I, Receptor For; Alpha Polypeptide	IgE receptor activity and IgE binding	0.25769486
PDCD1	Programmed Cell Death 1	signal transducer activity	0.25769486
PIK3AP1	Phosphoinositide-3 Kinase Adaptor Protein 1	phosphatidylinositol 3-kinase regulatory subunit binding and identical protein binding	0.2609107
PDPK1	3-Phosphoinositide Dependent Protein Kinase 1	protein serine/threonine kinase activity and insulin receptor binding	0.26369181

Table 31. Ulcerative Colitis Gene Data

GENE	Description	Table 31 Comments	p-value
FCGR2B;FCGR3A	Fc Fragment Of IgG, Low Affinity IIb and IIIa, Receptor	IgG binding	0.00012499
PIK3AP1	Phosphoinositide-3-Kinase Adaptor Protein 1	phosphatidylinositol 3-kinase regulatory subunit binding and identical protein binding	0.00015714
SH3KBP1	SH3-Domain Kinase Binding Protein 1	SH3 domain binding	0.00037308
EGFR	Epidermal Growth Factor Receptor	chromatin binding and identical protein binding	0.00155239
DLEU2	Deleted In Lymphocytic Leukemia 2 (Non-Protein Coding)	RNA gene affiliated with the lncRNA class	0.00226369
ADCY1	Adenylate Cyclase 1 (Brain)	calcium- and calmodulin-responsive adenylate cyclase activity and calmodulin binding	0.00458089
ZAP70	Zeta-Chain (TCR) Associated Protein Kinase 70kDa	phosphotyrosine binding and protein tyrosine kinase activity	0.00706531
CBLB	Cbl Proto-Oncogene B, E3 Ubiquitin Protein Ligase	signal transducer activity and calcium ion binding	0.00835978
CD96	CD96 Molecule	protein binding	0.00964315
GLYCAM1	Glycosylation Dependent Cell Adhesion Molecule 1 (Pseudogene)	pseudogene affiliated with the lncRNA class	0.01235245
ICAM1	Intercellular Adhesion Molecule 1	integrin binding and receptor activity	0.01235245
TRAC	T Cell Receptor Alpha Constant	peptide antigen binding and MHC protein binding	0.01235245
FCGR1A	Fc Fragment Of IgG, High Affinity Ia, Receptor (CD64)	IgG binding and receptor signaling protein activity	0.01270167
VAV1	Vav 1 Guanine Nucleotide Exchange Factor	sequence-specific DNA binding transcription factor activity and guanyl-nucleotide exchange factor activity	0.01684487
ARHGEF7	Rho Guanine Nucleotide Exchange Factor (GEF) 7	phospholipid binding and guanyl-nucleotide exchange factor activity	0.02251106
C4BPB	Complement Component 4 Binding Protein, Beta	controls activation of the complement cascade through the classical pathway	0.02466186
FCGR3A	Fc Fragment Of IgG, Low Affinity IIIa, Receptor (CD16a)	IgG binding	0.02821228
PLD1	Phospholipase D1, Phosphatidylcholine-Specific	NAPE-specific phospholipase D activity and phosphatidylinositol binding	0.03197958
NFKB1	Nuclear Factor Of Kappa Light Polypeptide Gene Enhancer In B-Cells 1	transcription factor binding andsequence-specific DNA binding transcription factor activity	0.03543356
IKBKB	Inhibitor Of Kappa Light Polypeptide Gene Enhancer In B-Cells, Kinase Beta	protein heterodimerization activity and protein homodimerization activity	0.03589451
IRS1	Insulin Receptor Substrate 1	protein kinase C binding and phospholipid binding	0.04594332
SCYL1	SCY1-Like 1 (S. Cerevisiae)	protein tyrosine kinase activity	0.04594332

GENE	Description	Table 31 Comments	p-value
CD36	CD36 Molecule (Thrombospondin Receptor)	lipid binding and transforming growth factor beta binding	0.046058
ITGAM	Integrin, Alpha M (Complement Component 3 Receptor 3 Subunit)	heparin binding and heparan sulfate proteoglycan binding	0.05678192
AP2A2	Adaptor-Related Protein Complex 2, Alpha 2 Subunit	protein transporter activity and lipid binding	0.05698369
CD3E	CD3e Molecule, Epsilon (CD3-TCR Complex)	SH3 domain binding and protein heterodimerization activity	0.06525633
IGLV7-43	Immunoglobulin Lambda Variable 7-43	antigen binding	0.07953419
IFI6	Interferon, Alpha-Inducible Protein 6	protein binding	0.08776649
AGER	Advanced Glycosylation End Product-Specific Receptor	S100 protein binding and receptor activity	0.08857668
TLR1;TLR10	Toll-Like Receptor 1 and 10	transmembrane signaling receptor activity and protein heterodimerization activity/transmembrane signaling receptor activity	0.08857668
PTGIR	Prostaglandin I2 (Prostacyclin) Receptor (IP)	G-protein coupled receptor activity and guanyl-nucleotide exchange factor activity	0.09239109
C3	Complement Component 3	C5L2 anaphylatoxin chemotactic receptor binding and receptor binding	0.0934343
PVRL2	Poliovirus Receptor-Related 2 (Herpesvirus Entry Mediator B)	virus receptor activity and protein homodimerization activity	0.0934343
B2M	beta-2-microglobulin	identical protein binding	0.1127473
PDPK1	3-Phosphoinositide Dependent Protein Kinase 1	protein serine/threonine kinase activity and insulin receptor binding	0.11897734
ADA	Adenosine Deaminase	purine nucleoside binding and adenosine deaminase activity	0.12068843
IL5RA	Interleukin 5 Receptor, Alpha	interleukin-5 receptor activity	0.12068843
ITGB2	Integrin, Beta 2 (Complement Component 3 Receptor 3 And 4 Subunit)	protein kinase binding andglycoprotein binding	0.12068843
CCR6	Chemokine (C-C Motif) Receptor 6	C-C chemokine receptor activity and receptor activity	0.12631419
FAS	Fas Cell Surface Death Receptor	receptor activity and identical protein binding	0.12631419
PTPRC	Protein Tyrosine Phosphatase, Receptor Type, C	protein kinase binding and transmembrane receptor protein tyrosine phosphatase activity	0.12636817
PRKCQ	Protein Kinase C, Theta	ubiquitin-protein ligase activity and identical protein binding	0.14418364
RAP1B	RAP1B, Member Of RAS Oncogene Family	GDP binding and GTP binding	0.14746966
CXCR5	Chemokine (C-X-C Motif) Receptor 5	G-protein coupled receptor activity and C-X-C chemokine receptor activity	0.15588515
FCGR3A;FCGR2A	Fc Fragment Of IgG, Low Affinity IIIa and IIa, Receptor	IgG binding	0.15588515
TREM2	Triggering Receptor Expressed On Myeloid Cells 2	lipopolysaccharide binding and receptor activity	0.15588515
AP2B1	Adaptor-Related Protein Complex 2, Beta 1 Subunit	clathrin bindingand protein complex binding	0.15685807

GENE	Description	Table 31 Comments	p-value
ITGAL	Integrin, Alpha L (Antigen CD11A (P180), Lymphocyte Function-Associated Antigen 1; Alpha Polypeptide)	cell adhesion molecule binding	0.16324087
CSF2RA	Colony Stimulating Factor 2 Receptor, Alpha, Low-Affinity (Granulocyte-Macrophage)	cytokine receptor activity and receptor activity	0.16774645
KIR2DL4;KIR3DL1;KIR2DL3	Killer Cell Immunoglobulin-Like Receptor, Two Domains, Long Cytoplasmic Tail, 3 and 4/Killer Cell Immunoglobulin-Like Receptor, Three Domains, Long Cytoplasmic Tail, 1	receptor activity/HLA-B specific inhibitory MHC class I receptor activity	0.16774645
RASGRP1	RAS Guanyl Releasing Protein 1 (Calcium And DAG-Regulated)	guanyl-nucleotide exchange factor activity and calcium ion binding	0.16774645
RAG1	Recombination Activating Gene 1	ubiquitin-protein ligase activity and protein homodimerization activity	0.16996471
CD274	CD274 Molecule	protein binding	0.18344493
CD28	CD28 Molecule	SH3/SH2 adaptor activity and identical protein binding	0.18344493
CD3D	CD3d Molecule, Delta (CD3-TCR Complex)	transmembrane signaling receptor activity and protein heterodimerization activity	0.18344493
ITGAV	Integrin, Alpha V	protein kinase C binding and virus receptor activity	0.18344493
TIRAP	Toll-Interleukin 1 Receptor (TIR) Domain Containing Adaptor Protein	protein binding, bridging and protein homodimerization activity	0.18344493
TYROBP	TYRO Protein Tyrosine Kinase Binding Protein	receptor signaling protein activity and identical protein binding	0.18344493
PRKCB	Protein Kinase C, Beta	chromatin binding and histone binding	0.18954531
ULBP1	UL16 Binding Protein 1	antigen binding and natural killer cell lectin-like receptor binding	0.20345466
AMICA1	Adhesion Molecule, Interacts With CXADR Antigen 1	cell adhesion molecule binding	0.2189915
TREM1	Triggering Receptor Expressed On Myeloid Cells 1	receptor activity	0.2189915
TAB3	TGF-Beta Activated Kinase 1/MAP3K7 Binding Protein 3	protein binding/zinc ion binding	0.22139123
PPAPDC1A	Phosphatidic Acid Phosphatase Type 2 Domain Containing 1A	phosphatidate phosphatase activity	0.22331897
ACP5	Acid Phosphatase 5, Tartrate Resistant	ferrous iron binding and acid phosphatase activity	0.2291797
LAT	Linker For Activation Of T Cells	SH3/SH2 adaptor activity and protein kinase binding	0.2291797
SIGLEC16	Sialic Acid Binding Ig-Like Lectin 16 (Gene/Pseudogene)	pseudogene affiliated with the lncRNA class	0.2291797
GINS1	GINS Complex Subunit 1 (Psf1 Homolog)	plays a role in the initiation of DNA replication, and progression of DNA replication forks	0.24615224
CDH1	Cadherin 1, Type 1, E-Cadherin (Epithelial)	beta-catenin binding and calcium ion binding	0.25428788

GENE	Description	Table 31 Comments	p-value
CBL	Cbl Proto-Oncogene, E3 Ubiquitin Protein Ligase	ubiquitin-protein ligase activity and sequence-specific DNA binding transcription factor activity	0.26058383
GHR	Growth Hormone Receptor	protein phosphatase binding and protein homodimerization activity	0.27057824
ATPIF1	ATPase Inhibitory Factor 1	enzyme inhibitor activity and protein homodimerization activity	0.27280173
CD8A;CD8B	CD8a and 8b Molecules	protein homodimerization activity and coreceptor activity/MHC class I protein binding and coreceptor activity	0.27280173
IGKV3-15	Immunoglobulin Kappa Variable 3-15	protein binding	0.27280173

Table 32. SLE Gene Data

GENE	Description	Table 32. Comments	p-value
FYN	FYN Oncogene Related To SRC, FGR, YES	ion channel binding and identical protein binding	0.00021817
MKL1	Megakaryoblastic Leukemia (Translocation) 1	transcription regulatory region sequence-specific DNA binding and sequence-specific DNA binding transcription factor activity	0.00055943
CD96	CD96 Molecule	protein binding	0.00392655
ADCY1	Adenylate Cyclase 1 (Brain)	calcium- and calmodulin-responsive adenylate cyclase activity and calmodulin binding	0.00467913
PRKCQ	Protein Kinase C, Theta	ubiquitin-protein ligase activity and identical protein binding	0.00655819
TREM1	Triggering Receptor Expressed On Myeloid Cells 1	receptor activity	0.0073133
ITGAM	Integrin, Alpha M (Complement Component 3 Receptor 3 Subunit)	heparin binding and heparan sulfate proteoglycan binding	0.00851784
ULBP1	UL16 Binding Protein 1	antigen binding and natural killer cell lectin-like receptor binding	0.01009946
ADCY2	Adenylate Cyclase 2 (Brain)	adenylate cyclase activity and protein heterodimerization activity	0.01130519
PLD1	Phospholipase D1, Phosphatidylcholine-Specific	NAPE-specific phospholipase D activity and phosphatidylinositol binding	0.01230118
RAG2;RAG1	Recombination Activating Gene 2 and 1	chromatin binding and methylated histone residue binding/ubiquitin-protein ligase activity and protein homodimerization activity	0.01272518

GENE	Description	Table 32. Comments	p-value
ADCY5	Adenylate Cyclase 5	adenylate cyclase binding and protein heterodimerization activity	0.01688104
CCNO	Cyclin O	protein kinase binding and uracil DNA N-glycosylase activity	0.03134733
MALT1	Mucosa Associated Lymphoid Tissue Lymphoma Translocation Gene 1	ubiquitin-protein ligase activity and peptidase activity	0.04135861
AKT3	V-Akt Murine Thymoma Viral Oncogene Homolog 3	protein serine/threonine kinase activity and protein kinase activity	0.04694848
ARHGEF7	Rho Guanine Nucleotide Exchange Factor (GEF) 7	phospholipid binding and guanyl-nucleotide exchange factor activity	0.0522776
CR1;CR2	Complement Component (3b/4b) Receptor 1/Complement Component (3d/Epstein Barr Virus) Receptor 2	complement component C3b binding and complement component C4b receptor activity/protein homodimerization activity and complement receptor activity	0.05535272
ADCY4	Adenylate Cyclase 4	adenylate cyclase activity	0.06042648
CD14	CD14 Molecule	lipoteichoic acid binding and lipopolysaccharide binding	0.06093891
TNFRSF13C	Tumor Necrosis Factor Receptor Superfamily, Member 13C	enhances B-cell survival in vitro and is a regulator of the peripheral B-cell population	0.06802621
CBL	Cbl Proto-Oncogene, E3 Ubiquitin Protein Ligase	ubiquitin-protein ligase activity and sequence-specific DNA binding transcription factor activity	0.0685906
SELL	Selectin L	carbohydrate binding and protease binding	0.07467257
FCGR2B;FCGR3A	Fc Fragment Of IgG, Low Affinity IIb and IIIa, Receptor	IgG binding	0.07619895
SH3KBP1	SH3-Domain Kinase Binding Protein 1	SH3 domain binding	0.0788614
IKBKB	Inhibitor Of Kappa Light Polypeptide Gene Enhancer In B-Cells, Kinase Beta	protein heterodimerization activity and protein homodimerization activity	0.08334932
ADA	Adenosine Deaminase	purine nucleoside binding and adenosine deaminase activity	0.08563263
ITGB2	Integrin, Beta 2 (Complement Component 3 Receptor 3 And 4 Subunit)	protein kinase binding andglycoprotein binding	0.08563263
TLR5	Toll-Like Receptor 5	interleukin-1 receptor binding	0.09151248
AP2A2	Adaptor-Related Protein Complex 2, Alpha 2 Subunit	protein transporter activity and lipid binding	0.09719424

GENE	Description	Table 32. Comments	p-value
PTPRC	Protein Tyrosine Phosphatase, Receptor Type, C	protein kinase binding and transmembrane receptor protein tyrosine phosphatase activity	0.10051777
CD55	CD55 Molecule, Decay Accelerating Factor For Complement	enzyme inhibitor activity andvirus receptor activity	0.10406481
CR1	Complement Component (3b/4b) Receptor 1	complement component C3b binding and complement component C4b receptor activity	0.10918275
DAPP1	Dual Adaptor Of Phosphotyrosine And 3-Phosphoinositides	phospholipid binding and phosphatidylinositol-3,4,5-trisphosphate binding	0.12045909
FGFR4	Fibroblast Growth Factor Receptor 4	fibroblast growth factor binding and heparin binding	0.12128
IGKV1D-16	Immunoglobulin Kappa Variable 1D-16	protein binding	0.12128
IL7R	Interleukin 7 Receptor	antigen binding and interleukin-7 receptor activity	0.12128
KIR2DL4;KIR3DL1	Killer Cell Immunoglobulin-Like Receptor, Two Domains, Short Cytoplasmic Tail, 4/Killer Cell Immunoglobulin-Like Receptor, Three Domains, Long Cytoplasmic Tail, 1	receptor activity/HLA-B specific inhibitory MHC class I receptor activity	0.12128
NFKB1	Nuclear Factor Of Kappa Light Polypeptide Gene Enhancer In B-Cells 1	transcription factor binding andsequence-specific DNA binding transcription factor activity	0.12476294
CDH1	Cadherin 1, Type 1, E-Cadherin (Epithelial)	beta-catenin binding and calcium ion binding	0.13542507
RAG1	Recombination Activating Gene 1	ubiquitin-protein ligase activity and protein homodimerization activity	0.15168578
AICDA	Activation-Induced Cytidine Deaminase	cytidine deaminase activity	0.15931656
CD274	CD274 Molecule	protein binding	0.15931656
ERBB2	V-Erb-B2 Avian Erythroblastic Leukemia Viral Oncogene Homolog 2	protein C-terminus bindingand identical protein binding	0.15931656
HCST	Hematopoietic Cell Signal Transducer	phosphatidylinositol 3-kinase binding	0.15931656
IGLC3;IGLC7;IGLC2;IGLC1;IGLC6	Immunoglobulin Lambda Constant 3/7/2/1/6	antigen binding	0.15931656
IRS2	Insulin Receptor Substrate 2	phospholipid binding and signal transducer activity	0.15931656
ITGB7	Integrin, Beta 7	virus receptor activity	0.15931656

GENE	Description	Table 32. Comments	p-value
NFKB2	Nuclear Factor Of Kappa Light Polypeptide Gene Enhancer In B-Cells 2	transcription coactivator activity and sequence-specific DNA binding transcription factor activity	0.15931656
TLR1;TLR6	Toll-Like Receptor 1 and 6	transmembrane signaling receptor activity and protein heterodimerization activity	0.15931656
AP2B1	Adaptor-Related Protein Complex 2, Beta 1 Subunit	clathrin bindingand protein complex binding	0.16253886
EPHB4	EPH Receptor B4	ephrin receptor activity and transmembrane receptor protein tyrosine kinase activity	0.17370523
CD200R1	CD200 Receptor 1	protein binding	0.18215624
GUCY2D	Guanylate Cyclase 2D, Membrane (Retina-Specific)	receptor activity and identical protein binding	0.18215624
IRS1	Insulin Receptor Substrate 1	protein kinase C binding and phospholipid binding	0.18215624
SCYL1	SCY1-Like 1 (S. Cerevisiae)	protein tyrosine kinase activity	0.18215624
TLR2	Toll-Like Receptor 2	transmembrane signaling receptor activity and protein heterodimerization activity	0.18215624
CD8A;CD8B	CD8a and 8b Molecules	protein homodimerization activity and coreceptor activity/MHC class I protein binding and coreceptor activity	0.20445582
ICOS	Inducible T-Cell Co-Stimulator	protein binding	0.20445582
KLB	Klotho Beta	fibroblast growth factor binding and hydrolase activity, hydrolyzing O-glycosyl compounds	0.20445582
LYPLA2	Lysophospholipase II	hydrolase activity	0.20445582
PIK3CD	Phosphatidylinositol-4,5-Bisphosphate 3-Kinase, Catalytic Subunit Delta	phosphatidylinositol 3-kinase activity and 1-phosphatidylinositol-3-kinase activity	0.20457531
LY86	Lymphocyte Antigen 86	mediate innate immune response to bacterial lipopolysaccharide (LPS) and cytokine production	0.21428543
LYN	V-Yes-1 Yamaguchi Sarcoma Viral Related Oncogene Homolog	SH3 domain binding and enzyme binding	0.21831744
ACTR2	ARP2 Actin-Related Protein 2 Homolog (Yeast)	actin binding	0.23943002
GLYCAM1	Glycosylation Dependent Cell Adhesion Molecule 1 (Pseudogene)	pseudogene affiliated with the lncRNA class	0.245558
ICAM1	Intercellular Adhesion Molecule 1	integrin binding and receptor activity	0.245558
UNG	Uracil-DNA Glycosylase	uracil DNA N-glycosylase activity	0.245558
CCR6	Chemokine (C-C Motif) Receptor 6	C-C chemokine receptor activity and receptor activity	0.24987076

GENE	Description	Table 32. Comments	p-value
CD8B	CD8b Molecule	MHC class I protein binding and coreceptor activity	0.24987076
AKT2;PLD3	V-Akt Murine Thymoma Viral Oncogene Homolog 2/Phospholipase D Family, Member 3	protein serine/threonine kinase activity and kinase activity/phospholipase D activity and NAPE-specific phospholipase D activity	0.29326681
CD74	CD74 Molecule, Major Histocompatibility Complex, Class II Invariant Chain	cytokine receptor activity and identical protein binding	0.29326681
SIGLEC15	Sialic Acid Binding Ig-Like Lectin 15	protein binding	0.29326681
FCGR1A	Fc Fragment Of IgG, High Affinity Ia, Receptor (CD64)	IgG binding and receptor signaling protein activity	0.29654271

Table 33. Multiple Sclerosis Relapse Remitting Gene Data

GENE	Description	Table 33. Comments	p-value
PRKCQ	Protein Kinase C, Theta	ubiquitin-protein ligase activity and identical protein binding	1.30E-05
SH3KBP1	SH3-Domain Kinase Binding Protein 1	SH3 domain binding	0.00108322
PIK3R1	Phosphoinositide-3-Kinase, Regulatory Subunit 1 (Alpha)	protein phosphatase binding and1-phosphatidylinositol binding	0.00132825
ADCY2	Adenylate Cyclase 2 (Brain)	adenylate cyclase activity and protein heterodimerization activity	0.00228137
PPAPDC1A	Phosphatidic Acid Phosphatase Type 2 Domain Containing 1A	phosphatidate phosphatase activity	0.00458647
FYN	FYN Oncogene Related To SRC, FGR, YES	ion channel binding and identical protein binding	0.0065531
ULBP1	UL16 Binding Protein 1	antigen binding and natural killer cell lectin-like receptor binding	0.00758094
ITGAM	Integrin, Alpha M (Complement Component 3 Receptor 3 Subunit)	heparin binding and heparan sulfate proteoglycan binding	0.00767946
KRAS	Kirsten Rat Sarcoma Viral Oncogene Homolog	GDP binding and GTP binding	0.011855
RAG2;RAG1	Recombination Activating Gene 2 and 1	chromatin binding and methylated histone residue binding/ubiquitin-protein ligase activity and protein homodimerization activity	0.02258078
IRS1	Insulin Receptor Substrate 1	protein kinase C binding and phospholipid binding	0.03623882
PLD3	Phospholipase D Family, Member 3	phospholipase D activity and NAPE-specific phospholipase D activity	0.03623882

GENE	Description	Table 33. Comments	p-value
ICAM1	Intercellular Adhesion Molecule 1	integrin binding and receptor activity	0.05207439
PVR	Poliovirus Receptor	receptor activity and cell adhesion molecule binding	0.05207439
RAG1	Recombination Activating Gene 1	ubiquitin-protein ligase activity and protein homodimerization activity	0.06077487
IFNAR1	Interferon (Alpha, Beta And Omega) Receptor 1	type I interferon receptor activity	0.06430386
ITGB7	Integrin, Beta 7	virus receptor activity	0.06430386
NFKB2	Nuclear Factor Of Kappa Light Polypeptide Gene Enhancer In B-Cells 2 (P49/P100)	transcription coactivator activity and sequence-specific DNA binding transcription factor activity	0.06430386
ADA	Adenosine Deaminase	purine nucleoside binding and adenosine deaminase activity	0.06985867
TNFRSF13B	Tumor Necrosis Factor Receptor Superfamily, Member 13B	receptor activity	0.06985867
AP2A2	Adaptor-Related Protein Complex 2, Alpha 2 Subunit	protein transporter activity and lipid binding	0.07923074
SYK	Spleen Tyrosine Kinase	protein tyrosine kinase activity and protein kinase binding	0.07923074
DNM3	Dynamin 3	GTP binding and GTPase activity	0.08859048
ARHGEF7	Rho Guanine Nucleotide Exchange Factor (GEF) 7	phospholipid binding and guanyl-nucleotide exchange factor activity	0.09504564
PTPRC	Protein Tyrosine Phosphatase, Receptor Type, C	protein kinase binding and transmembrane receptor protein tyrosine phosphatase activity	0.10621879
BCR	Breakpoint Cluster Region	protein serine/threonine kinase activity and enzyme binding	0.10715318
TREM1	Triggering Receptor Expressed On Myeloid Cells 1	receptor activity	0.11004513
ADCY1	Adenylate Cyclase 1 (Brain)	calcium- and calmodulin-responsive adenylate cyclase activity and calmodulin binding	0.12363153
CD74	CD74 Molecule, Major Histocompatibility Complex, Class II Invariant Chain	cytokine receptor activity and identical protein binding	0.12447967
PDCD1	Programmed Cell Death 1	signal transducer activity	0.12447967
TLR10	Toll-Like Receptor 10	transmembrane signaling receptor activity	0.12447967
ADCY4	Adenylate Cyclase 4	adenylate cyclase activity	0.13191122
CD8A;CD8B	CD8a and 8b Molecules	protein homodimerization activity and coreceptor activity/MHC class I protein binding and coreceptor activity	0.13191122

GENE	Description	Table 33. Comments	p-value
GINS2	GINS Complex Subunit 2 (Psf2 Homolog)	ole in the initiation of DNA replication, and progression of DNA replication forks	0.13386225
LYN	V-Yes-1 Yamaguchi Sarcoma Viral Related Oncogene Homolog	SH3 domain binding and enzyme binding.	0.14259452
CLTA	Clathrin, Light Chain A	peptide binding and structural molecule activity	0.15014664
CCR6	Chemokine (C-C Motif) Receptor 6	C-C chemokine receptor activity and receptor activity	0.15464838
IKBKB	Inhibitor Of Kappa Light Polypeptide Gene Enhancer In B-Cells, Kinase Beta	protein heterodimerization activity and protein homodimerization activity	0.15464838
NFKB1	Nuclear Factor Of Kappa Light Polypeptide Gene Enhancer In B-Cells 1	transcription factor binding andsequence-specific DNA binding transcription factor activity	0.16493065
AGER	Advanced Glycosylation End Product-Specific Receptor	S100 protein binding and receptor activity	0.18079201
ICOSLG;AIRE	Inducible T-Cell Co-Stimulator Ligand/Autoimmune Regulator	receptor binding/transcription regulatory region DNA binding and identical protein binding	0.18079201
TAP2;TAP1	Transporter 2, ATP-Binding Cassette, Sub-Family B /Transporter 1, ATP-Binding Cassette, Sub-Family B	transporter activity and MHC class I protein binding/ADP binding and protein homodimerization activity	0.18079201
TLR1;TLR10	Toll-Like Receptor 1 and 10	transmembrane signaling receptor activity and protein heterodimerization activity/transmembrane signaling receptor activity	0.18079201
B2M	beta-2-microglobulin	identical protein binding	0.18119302
CD14	CD14 Molecule	lipoteichoic acid binding and lipopolysaccharide binding	0.18119302
CD226	CD226 Molecule	protein kinase binding and cell adhesion molecule binding	0.20195054
KLRG1	Killer Cell Lectin-Like Receptor Subfamily G, Member 1	carbohydrate binding and receptor activity	0.22617654
IL6R	Interleukin 6 Receptor	interleukin-6 receptor binding and protein homodimerization activity	0.22772527
IL1RAP	Interleukin 1 Receptor Accessory Protein	interleukin-1 receptor activity and signal transducer activity	0.23219152
AP2S1	Adaptor-Related Protein Complex 2, Sigma 1 Subunit	protein transporter activity and transporter activity	0.23348849
CD40	CD40 Molecule, TNF Receptor Superfamily Member 5	receptor activity and signal transducer activity	0.23348849
PRKCSH	Protein Kinase C Substrate 80K-H	protein kinase C binding and calcium ion binding	0.27507189
EGFR	Epidermal Growth Factor Receptor	chromatin binding and identical protein binding	0.27872539
CD59	CD59 Molecule, Complement Regulatory Protein	complement binding	0.28280091

GENE	Description	Table 33. Comments	p-value
IGKV2-30	Immunoglobulin Kappa Variable 2-30	protein binding	0.28280091
KIR2DL1;KIR2DL4;KIR3DL1;KIR2DL3	Killer Cell Immunoglobulin-Like Receptor, Two Domains, Long Cytoplasmic Tail, 1, 3 and 4/Killer Cell Immunoglobulin-Like Receptor, Three Domains, Long Cytoplasmic Tail, 1	receptor activity/HLA-B specific inhibitory MHC class I receptor activity	0.28280091
SIGLEC16	Sialic Acid Binding Ig-Like Lectin 16 (Gene/Pseudogene)	pseudogene affiliated with the lncRNA class	0.28280091
TLR2	Toll-Like Receptor 2	transmembrane signaling receptor activity and protein heterodimerization activity	0.28280091

Table 34. Multiple Sclerosis IFN- β Responder Gene Data

GENE	Description	Table 34. Comments	p-value
TLR5	Toll-Like Receptor 5	interleukin-1 receptor binding	4.96E-06
IFNGR2	Interferon Gamma Receptor 2 (Interferon Gamma Transducer 1)	interferon-gamma receptor activity	4.59E-05
ADCY9	Adenylate Cyclase 9	adenylate cyclase activity	0.00014626
EGFR	Epidermal Growth Factor Receptor	chromatin binding and identical protein binding	0.00015025
FCGR3A	Fc Fragment Of IgG, Low Affinity IIIa, Receptor (CD16a)	IgG binding	0.0004003
FCGR2B;FCGR3A	Fc Fragment Of IgG, Low Affinity IIb and IIIa, Receptor	IgG binding	0.00059065
PIK3CD	Phosphatidylinositol-4,5-Bisphosphate 3-Kinase, Catalytic Subunit Delta	phosphatidylinositol 3-kinase activity and 1-phosphatidylinositol-3-kinase activity	0.00094547
PDGFRA	Platelet-Derived Growth Factor Receptor, Alpha Polypeptide	platelet-derived growth factor receptor bindingand protein homodimerization activity	0.0010759
ADCY1	Adenylate Cyclase 1 (Brain)	calcium- and calmodulin-responsive adenylate cyclase activity and calmodulin binding	0.00221641
PTGIR	Prostaglandin I2 (Prostacyclin) Receptor (IP)	G-protein coupled receptor activity and guanyl-nucleotide exchange factor activity	0.01047073
ADCY8	Adenylate Cyclase 8 (Brain)	calcium- and calmodulin-responsive adenylate cyclase activity and adenylate cyclase activity	0.01116758
VAV1	Vav 1 Guanine Nucleotide Exchange Factor	sequence-specific DNA binding transcription factor activity and guanyl-nucleotide exchange factor activity	0.0136214

GENE	Description	Table 34. Comments	p-value
CLIC4	Chloride Intracellular Channel 4	chloride channel activity and voltage-gated chloride channel activity	0.01450765
IGKV3-20	Immunoglobulin Kappa Variable 3-20	antigen binding	0.02031975
ADA	Adenosine Deaminase	purine nucleoside binding and adenosine deaminase activity	0.02166327
KIR2DL1;KIR2DL4;KIR3DL1;KIR2DL3	Killer Cell Immunoglobulin-Like Receptor, Two Domains, Long Cytoplasmic Tail, 1, 3 and 4/Killer Cell Immunoglobulin-Like Receptor, Three Domains, Long Cytoplasmic Tail, 1	receptor activity/HLA-B specific inhibitory MHC class I receptor activity	0.02166327
PLD2	Phospholipase D2	NAPE-specific phospholipase D activity and phosphatidylinositol binding	0.02166327
SIGLEC16	Sialic Acid Binding Ig-Like Lectin 16 (Gene/Pseudogene)	signallibg activity	0.02166327
CD34	CD34 Molecule	sulfate binding and transcription factor binding	0.0264282
AP2A2	Adaptor-Related Protein Complex 2, Alpha 2 Subunit	protein transporter activity and lipid binding	0.0301917
GINS1	GINS Complex Subunit 1 (Psf1 Homolog)	protein binding	0.0301917
ULBP1	UL16 Binding Protein 1	antigen binding and natural killer cell lectin-like receptor binding	0.0385112
ADCY4	Adenylate Cyclase 4	adenylate cyclase activity	0.03934766
TREM1	Triggering Receptor Expressed On Myeloid Cells 1	receptor activity	0.03934766
ITGAM	Integrin, Alpha M (Complement Component 3 Receptor 3 Subunit)	heparin binding and heparan sulfate proteoglycan binding	0.03952611
CD55	CD55 Molecule, Decay Accelerating Factor For Complement (Cromer Blood Group)	enzyme inhibitor activity andvirus receptor activity	0.0487537
CR1;CR2	Complement Component (3b/4b) Receptor 1 (Knops Blood Group)/Complement Component (3d/Epstein Barr Virus) Receptor 2	complement component C3b binding and complement component C4b receptor activity/protein homodimerization activity and complement receptor activity	0.05098024
CCR6	Chemokine (C-C Motif) Receptor 6	C-C chemokine receptor activity and receptor activity	0.05133199
IL6ST	Interleukin 6 Signal Transducer (Gp130, Oncostatin M Receptor)	interleukin-6 receptor binding and protein homodimerization activity	0.05133199
CDH1	Cadherin 1, Type 1, E-Cadherin (Epithelial)	beta-catenin binding and calcium ion binding	0.05524598

GENE	Description	Table 34. Comments	p-value
FCER1G	Fc Fragment Of IgE, High Affinity I, Receptor For; Gamma Polypeptide	IgG binding and IgE receptor activity	0.06448065
ANGPTL2	Angiopoietin-Like 2	receptor binding	0.06465591
CR1	Complement Component (3b/4b) Receptor 1 (Knops Blood Group)	complement component C3b binding and complement component C4b receptor activity	0.06570725
IFI6	Interleukin 6 Signal Transducer (Gp130, Oncostatin M Receptor)	interleukin-6 receptor binding and protein homodimerization activity	0.06840941
AGER	Advanced Glycosylation End Product-Specific Receptor	S100 protein binding and receptor activity	0.07448963
IL2RB	Interleukin 2 Receptor, Beta	interleukin-2 receptor activity and interleukin-2 binding	0.07448963
SIRPB1	Signal-Regulatory Protein Beta 1	signallibg activity	0.07448963
C3	Complement Component 3	C5L2 anaphylatoxin chemotactic receptor binding and receptor binding	0.07952454
B2M	beta-2-microglobulin	identical protein binding	0.089181
ACTR2	ARP2 Actin-Related Protein 2 Homolog (Yeast)	actin binding	0.09136556
AKT2	V-Akt Murine Thymoma Viral Oncogene Homolog 2	protein serine/threonine kinase activity and kinase activity	0.10771954
PAG1	Phosphoprotein Associated With Glycosphingolipid Microdomains 1	SH3/SH2 adaptor activity and SH2 domain binding	0.10796035
DNM2	Dynamin 2	protein kinase binding and GTP binding	0.11207314
IRAK2	Interleukin-1 Receptor-Associated Kinase 2	protein kinase activityand protein homodimerization activity	0.11467884
DLEU2	Deleted In Lymphocytic Leukemia 2 (Non-Protein Coding)	affiliated with the lncRNA class	0.11776746
IL6R	Interleukin 6 Receptor	interleukin-6 receptor binding and protein homodimerization activity	0.12113785
GHR	Growth Hormone Receptor	protein phosphatase binding and protein homodimerization activity	0.1256734
KIR2DL4;KIR3DL1;KIR2DL3	Killer Cell Immunoglobulin-Like Receptor, Two Domains, Long Cytoplasmic Tail, 4 and 3/ Killer Cell Immunoglobulin-Like Receptor, Three Domains, Long Cytoplasmic Tail, 1	receptor activity/HLA-B specific inhibitory MHC class I receptor activity	0.14790547
MS4A2	Membrane-Spanning 4-Domains, Subfamily A, Member 2	SH2 domain binding and protein kinase binding	0.14790547

GENE	Description	Table 34. Comments	p-value
CD8B	CD8b Molecule	MHC class I protein binding and coreceptor activity	0.15470915
FCGR1A	Fc Fragment Of IgG, High Affinity Ia, Receptor (CD64)	IgG binding and receptor signaling protein activity	0.15470915
IKBKB	Inhibitor Of Kappa Light Polypeptide Gene Enhancer In B-Cells, Kinase Beta	protein heterodimerization activity and protein homodimerization activity	0.15470915
PRKCQ	Protein Kinase C, Theta	ubiquitin-protein ligase activity and identical protein binding	0.16963402
C4BPB;C4BPA	Complement Component 4 Binding Protein, Beta and Alpha	both control activation of the complement cascade through the classical pathway	0.18282939
GUCY2D	Guanylate Cyclase 2D, Membrane (Retina-Specific)	receptor activity and identical protein binding	0.18282939
IL3RA	Interleukin 3 Receptor, Alpha (Low Affinity)	interleukin-3 receptor activity	0.18282939
IRAK1	Interleukin-1 Receptor-Associated Kinase 1	protein serine/threonine kinase activity andprotein homodimerization activity	0.18282939
TNFRSF13C	Tumor Necrosis Factor Receptor Superfamily, Member 13C	signallibg activity	0.18282939
RAP1B	RAP1B, Member Of RAS Oncogene Family	GDP binding and GTP binding	0.18357409
CD36	CD36 Molecule (Thrombospondin Receptor)	lipid binding and transforming growth factor beta binding	0.18747042
IL21R	Interleukin 21 Receptor	interleukin-21 receptor activity	0.20323726
AP2S1	Adaptor-Related Protein Complex 2, Sigma 1 Subunit	protein transporter activity and transporter activity	0.20730949
CRTAM	Cytotoxic And Regulatory T Cell Molecule	receptor binding	0.20730949
FGFR1	Fibroblast Growth Factor Receptor 1	heparin binding and protein homodimerization activity	0.20730949
GLYCAM1	Glycosylation Dependent Cell Adhesion Molecule 1 (Pseudogene)	pseudogene affiliated with the lncRNA class	0.20730949
JAK3	Janus Kinase 3	non-membrane spanning protein tyrosine kinase activity and protein tyrosine kinase activity	0.20730949
TRAC	T Cell Receptor Alpha Constant	peptide antigen binding and MHC protein binding	0.20730949
MRC2	Mannose Receptor, C Type 2	carbohydrate binding	0.21155921
AP2B1	Adaptor-Related Protein Complex 2, Beta 1 Subunit	clathrin bindingand protein complex binding	0.22129944
CBLB	Cbl Proto-Oncogene B, E3 Ubiquitin Protein Ligase	signal transducer activity and calcium ion binding	0.24873708

GENE	Description	Table 34. Comments	p-value
FYN	FYN Oncogene Related To SRC, FGR, YES	ion channel binding and identical protein binding	0.24940226
PRKCB	Protein Kinase C, Beta	chromatin binding and histone binding	0.25190937
AICDA	Activation-Induced Cytidine Deaminase	cytidine deaminase activity	0.27297508
CD81	CD81 Molecule	MHC class II protein complex binding	0.27297508
CLEC5A	C-Type Lectin Domain Family 5, Member A	carbohydrate binding and virus receptor activity	0.27297508
CXCR5	Chemokine (C-X-C Motif) Receptor 5	G-protein coupled receptor activity and C-X-C chemokine receptor activity	0.27297508
DONSON	Downstream Neighbor Of SON	molecular function	0.27297508
ERBB2	V-Erb-B2 Avian Erythroblastic Leukemia Viral Oncogene Homolog 2	protein C-terminus bindingand identical protein binding	0.27297508
IGLC3;IGLC7;IGLC2;IGLC1;IGLC6	Immunoglobulin Lambda Constant 3/7/2/1/6	antigen binding	0.27297508
KIR2DS4;KIR3DL1	Killer Cell Immunoglobulin-Like Receptor, Two Domains, Short Cytoplasmic Tail, 4/Killer Cell Immunoglobulin-Like Receptor, Three Domains, Long Cytoplasmic Tail, 1	receptor activity/HLA-B specific inhibitory MHC class I receptor activity	0.27297508
NFKB2	Nuclear Factor Of Kappa Light Polypeptide Gene Enhancer In B-Cells 2 (P49/P100)	transcription coactivator activity and sequence-specific DNA binding transcription factor activity	0.27297508
TIRAP	Toll-Interleukin 1 Receptor (TIR) Domain Containing Adaptor Protein	protein binding, bridging and protein homodimerization activity	0.27297508
TLR1;TLR6	Toll-Like Receptor 1 and 6	transmembrane signaling receptor activity and protein heterodimerization activity	0.27297508
FAS	Fas Cell Surface Death Receptor	receptor activity and identical protein binding	0.27996257
CD96	CD96 Molecule	protein binding	0.28265813
ATPIF1	ATPase Inhibitory Factor 1	enzyme inhibitor activity and protein homodimerization activity	0.29257168
ITGAL	Integrin, Alpha L (Antigen CD11A (P180), Lymphocyte Function-Associated Antigen 1; Alpha Polypeptide)	cell adhesion molecule binding	0.29257168
LILRB4	Leukocyte Immunoglobulin-Like Receptor, Subfamily B (With TM And ITIM Domains), Member 4	antigen binding and receptor activity	0.29257168
ATK	Megakaryocyte-Associated Tyrosine Kinase	non-membrane spanning protein tyrosine kinase activity and protein tyrosine kinase activity	0.29257168

Table 35. Neurofibromatosis

GENE	Description	Table 35. Comments	p-value
PAX5	Paired Box 5	sequence-specific DNA binding transcription factor activity	7.34E-05
MAPK1	Mitogen-Activated Protein Kinase 1	phosphatase binding and protein serine/threonine kinase activity	0.000242763
TCF7L2	Transcription Factor 7-Like 2 (T-Cell Specific, HMG-Box)	chromatin binding and sequence-specific DNA binding transcription factor activity	0.001722166
RAD50	DNA Repair Protein RAD50	3'-5' exonuclease activity and protein binding, bridging	0.00248408
MET	Met Proto-Oncogene	hepatocyte growth factor-activated receptor activity and protein tyrosine kinase activity	0.003610583
HSPA1A	Heat Shock 70kDa Protein 1A	stabilizes existing proteins against aggregation and mediates the folding of newly translated proteins	0.003808074
ETS1	V-Ets Avian Erythroblastosis Virus E26 Oncogene Homolog 1	transcription factor binding and sequence-specific DNA binding transcription factor activity	0.005352442
CCND3	Cyclin D3	protein kinase binding and cyclin-dependent protein serine/threonine kinase activity	0.009209629
PDGFA	Platelet-Derived Growth Factor Alpha Polypeptide	growth factor activity and protein homodimerization activity	0.013450723
ANGPT1	Angiopoietin 1	receptor tyrosine kinase binding	0.018084653
YWHAE	Tyrosine 3-Monooxygenase/Tryptophan 5-Monooxygenase Activation Protein, Epsilon	protein heterodimerization activity and protein domain specific binding	0.0195928
IGF2	Insulin-Like Growth Factor 2 (Somatomedin A)	growth factor activity and insulin receptor binding	0.024402387
CRLF2	Cytokine Receptor-Like Factor 2	protein binding	0.024528379
GSK3B	Glycogen Synthase Kinase 3 Beta	protein kinase binding and identical protein binding	0.025098881
SMARCA4	SWI/SNF Related, Matrix Associated, Actin Dependent Regulator of Chromatin, Subfamily A, Member 4	chromatin binding and transcription corepressor activity	0.039826881
ARID1A	AT Rich Interactive Domain 1A (SWI-Like)	transcription coactivator activity and ligand-dependent nuclear receptor binding	0.039899362
PHLPP1	PH Domain And Leucine Rich Repeat Protein Phosphatase 1	phospholipid binding and phosphoprotein phosphatase activity	0.045755956

GENE	Description	Table 35. Comments	p-value
MAP2K6	Mitogen-Activated Protein Kinase Kinase 6	protein serine/threonine kinase activity and protein tyrosine kinase activity	0.049695395
CDKN1A	Cyclin-Dependent Kinase Inhibitor 1A (P21, Cip1)	cyclin-dependent protein serine/threonine kinase inhibitor activity and protein complex binding	0.056825878
CREB3L2	CAMP Responsive Element Binding Protein 3-Like 2	transcription regulatory region DNA binding and sequence-specific DNA binding transcription factor activity	0.061543489
MED12	Mediator Complex Subunit 12	chromatin binding and receptor activity	0.065591011
RPS6	Ribosomal Protein S6	structural constituent of ribosome and protein kinase binding	0.065591011
ERG	V-Ets Avian Erythroblastosis Virus E26 Oncogene Homolog	sequence-specific DNA binding transcription factor activity and signal transducer activity	0.066666216
STK3	Serine/Threonine Kinase 3	protein serine/threonine kinase activity andprotein kinase activity	0.071007547
PPP2R1A	Protein Phosphatase 2, Regulatory Subunit A, Alpha	protein serine/threonine phosphatase activity and protein heterodimerization activity	0.071334665
HSP90AA1	Heat Shock Protein 90kDa Alpha (Cytosolic), Class A Member 1	GTP binding andprotein homodimerization activity	0.07858404
CRKL	V-Crk Avian Sarcoma Virus CT10 Oncogene Homolog-Like	SH3/SH2 adaptor activity and signal transducer activity	0.081613204
MEN1	Multiple Endocrine Neoplasia I	sequence-specific DNA binding and transcription regulatory region DNA binding	0.081613204
TCF3	Transcription Factor 3	sequence-specific DNA binding and sequence-specific DNA binding transcription factor activity	0.081613204
GHR	Growth Hormone Receptor	protein phosphatase binding and protein homodimerization activity	0.081618354
GRB10	Growth Factor Receptor-Bound Protein 10	phospholipid binding and insulin receptor binding	0.092067488
CBLB	Methylmalonic Aciduria (Cobalamin Deficiency) CblB Type	cob(II)alamin reductase activity and cob(I)yrinic acid a,c-diamide adenosyltransferase activity	0.096651683
IDH1	Isocitrate Dehydrogenase 1 (NADP+), Soluble	magnesium ion binding and protein homodimerization activity	0.103835035
KDR	Kinase Insert Domain Receptor (A Type III Receptor Tyrosine Kinase)	transmembrane receptor protein tyrosine kinase activity and protein tyrosine kinase activity	0.1177313
LEPR	Leptin Receptor	cytokine receptor activity and identical protein binding	0.137331474

GENE	Description	Table 35. Comments	p-value
PAK1	P21 Protein (Cdc42/Rac)-Activated Kinase 1	protein kinase binding and identical protein binding	0.145173658
BRCA2	Breast Cancer 2, Early Onset	histone acetyltransferase activity and single-stranded DNA binding	0.154405702
STAT5B	Signal Transducer And Activator Of Transcription 5B	sequence-specific DNA binding transcription factor activity and signal transducer activity	0.155660564
BAD	BCL2-Associated Agonist Of Cell Death	protein kinase binding and protein heterodimerization activity	0.156265727
E2F1	Transcription Factor 1	transcription factor binding and sequence-specific DNA binding transcription factor activity	0.156265727
NGFR	Nerve Growth Factor Receptor	ubiquitin protein ligase binding and signal transducer activity	0.156265727
APC	Adenomatous Polyposis Coli	beta-catenin binding and protein kinase binding	0.161824001
SPRED3	Sprouty-Related, EVH1 Domain Containing 3	signalling activity	0.163428114
FGFR2	Fibroblast Growth Factor Receptor 2	heparin bindingand protein homodimerization activity	0.171306539
BDNF	Brain-Derived Neurotrophic Factor	growth factor activity and neurotrophin TRKB receptor binding	0.176400063
CASP2	Caspase 2, Apoptosis-Related Cysteine Peptidase	cysteine-type endopeptidase activity and enzyme binding	0.176400063
VEGFA	Vascular Endothelial Growth Factor A	protein heterodimerization activity and protein homodimerization activity	0.176400063
NF2	Neurofibromin 2	cytoskeletal protein binding	0.19198831
CREB3L1	CAMP Responsive Element Binding Protein 3-Like 1	sequence-specific DNA binding and RNA polymerase II core promoter proximal region sequence-specific DNA binding transcription factor activity involved in positive regulation of transcription	0.196225627
SUZ12	SUZ12 Polycomb Repressive Complex 2 Subunit	sequence-specific DNA binding and methylated histone residue binding	0.221781006
PAK2	P21 Protein (Cdc42/Rac)-Activated Kinase 2	protein kinase binding and identical protein binding	0.232346927
NGF	Nerve Growth Factor (Beta Polypeptide)	nerve growth factor receptor binding and growth factor activity	0.240341223
PML	Promyelocytic Leukemia	transcription coactivator activity and protein homodimerization activity	0.240341223
RELA	V-Rel Avian Reticuloendotheliosis Viral Oncogene Homolog A	identical protein binding and sequence-specific DNA binding transcription factor activity	0.240341223

GENE	Description	Table 35. Comments	p-value
EIF4B	Eukaryotic Translation Initiation Factor 4B	RNA binding andtranslation initiation factor activity	0.252840719
CDK6	Cyclin-Dependent Kinase 6	cyclin binding and cyclin-dependent protein serine/threonine kinase activity	0.280990258
CHUK	Conserved Helix-Loop-Helix Ubiquitous Kinase	protein heterodimerization activity and protein homodimerization activity	0.285843285
CASP7	Caspase 7, Apoptosis-Related Cysteine Peptidase	cysteine-type peptidase activity and aspartic-type endopeptidase activity	0.288129068
CCNA2	Cyclin A2	protein kinase binding	0.288129068
CDKN1B	Cyclin-Dependent Kinase Inhibitor 1B (P27, Kip1)	cyclin-dependent protein serine/threonine kinase inhibitor activity and protein phosphatase binding	0.288129068
CDKN2C	Cyclin-Dependent Kinase Inhibitor 2C (P18, Inhibits CDK4)	cyclin-dependent protein serine/threonine kinase inhibitor activity and protein kinase binding	0.288129068
HRAS	Harvey Rat Sarcoma Viral Oncogene Homolog	protein C-terminus binding and GTP binding	0.288129068
SPRED1	Sprouty-Related, EVH1 Domain Containing 1	protein kinase binding and stem cell factor receptor binding	0.288129068

Table 36a. Top Probes – Anti PD1 (Melanoma) - responders

Probes	Gene Locus	ProbeCount_Total	Probe Count_Sig	HyperG_ Stats	FDR_ HyperG	Percent _Sig	Avg_CV	logFC	Ave Expr	t	B
PVRL1_11_119575859_119577309_119599998_119609544_FR	PVRL1	95	44	3.65E-05	0.003027108	46	7.635	1.226061632	1.226061632	5.78144807	0.132665646
HLA-DQB1_6_32607972_32614493_32669132_32671838_RR	HLA-DQB1	12	8	0.004571	0.126456634	67	22.3213	1.087554243	1.087554243	4.681620255	-1.14002515
HLA-DQB1_6_32607972_32614493_32630138_32632737_RR	HLA-DQB1	12	8	0.004571	0.126456634	67	11.4997	1.063195633	1.063195633	3.723996585	-2.400733019
BOK_2_242498607_242505838_242528424_242532109_RF	BOK	9	6	0.014565	0.185978822	67	12.1167	1.052556037	1.052556037	5.736345926	0.084050827
CSK_15_75042637_75047345_75083504_75088622_FR	CSK	11	8	0.001994	0.066190912	73	4.2993	1.017645742	1.017645742	10.5480604	3.93908303
CSK_15_75042637_75047345_75075209_75080043_FF	CSK	11	8	0.001994	0.066190912	73	3.5337	0.976259273	0.976259273	10.17749745	3.718233225
CSK_15_75042637_75047345_75072257_75074709_FR	CSK	11	8	0.001994	0.066190912	73	7.7027	0.956377371	0.956377371	8.607527484	2.66302761
HLA-DQB1_6_32630138_32632737_32669132_32671838_RR	HLA-DQB1	12	8	0.004571	0.126456634	67	6.4587	0.947727381	0.947727381	6.812472203	1.167235963
STAT5B_17_40403935_40406459_40464294_40468456_FR	STAT5B	20	12	0.001867	0.066190912	60	3.7883	0.870424687	0.870424687	6.817040924	1.17150928
BOK_2_242498607_242505838_242517411_242520415_RR	BOK	9	6	0.014565	0.185978822	67	5.5887	0.80624455	0.80624455	6.460070524	0.829620615
PTPRA_20_2853761_2858838_2943750_2948659_RF	PTPRA	137	57	0.000127	0.00842741	42	6.3143	0.771442283	0.771442283	9.132304403	3.038874107
FCGR2B_1_161562782_161569954_161615627_161622991_FR	FCGR2B	72	28	0.017535	0.207920508	39	7.6063	0.764546463	0.764546463	12.05142341	4.74221712
BOK_2_242474875_242482300_242498607_242505838_RR	BOK	9	6	0.014565	0.185978822	67	5.514	0.7579354	0.7579354	6.572418004	0.938990195
FCGR2B_1_161519223_161525894_161562782_161569954_RF	FCGR2B	72	28	0.017535	0.207920508	39	11.9687	0.753793658	0.753793658	10.0691174	3.651754924
HLA-DQB1_6_32634654_32639610_32669132_32671838_RR	HLA-DQB1	12	8	0.004571	0.126456634	67	18.3157	0.744863383	0.744863383	12.87752031	5.127893879

Probes	Gene Locus	ProbeCount_Total	Probe Count_Sig	HyperG_Stats	FDR_HyperG	Percent_Sig	Avg_CV	logFC	Ave Expr	t	B
PTPRA_20_2853761_2858838_3001591_3004582_RF	PTPRA	137	57	0.000127	0.00842741	42	7.6363	0.730046719	0.730046719	7.043346164	1.379956688
AKT1_14_105266348_105267359_105309658_FF	AKT1	18	11	0.002366	0.071417842	61	11.7737	0.722145646	0.722145646	7.844164755	2.069431262
PTPRA_20_2797355_2801691_3001591_3004582_RF	PTPRA	137	57	0.000127	0.00842741	42	11.6457	0.708900064	0.708900064	8.071412072	2.252281349
FCGR2B_1_161534237_161535923_161562782_161569954_RF	FCGR2B	72	28	0.017535	0.207920508	39	9.799	0.705863487	0.705863487	11.77453541	4.604637192
BOK_2_242454060_242458194_242498607_242505838_RR	BOK	9	6	0.014565	0.185978822	67	7.4167	0.697538177	0.697538177	5.281758629	-0.422695361
CSK_15_75042637_75047345_75075209_75080043_FR	CSK	11	8	0.001994	0.066190912	73	3.5587	0.685347379	0.685347379	9.554135055	3.323606724
TNFRSF25_1_6521664_6526267_6554648_6558108_FR	TNFRSF25	23	16	2.37E-05	0.002619074	70	5.036	0.683997693	0.683997693	4.543960331	-1.31251778
SHH_7_155593268_155595881_155627543_155630456_FF	SHH	25	12	0.019288	0.22081874	48	2.0403	0.681239755	0.681239755	10.97966954	4.184300851
PTPRA_20_2797355_2801691_2943750_29048659_RF	PTPRA	137	57	0.000127	0.00842741	42	3.26	0.665384587	0.665384587	7.762694435	2.002552201
TNFRSF25_1_6521664_6526267_6554648_6558108_FF	TNFRSF25	23	16	2.37E-05	0.002619074	70	3.634	0.664203164	0.664203164	4.841523516	-0.943405234

Table 36b. Top Probes – Anti PD1 (Melanoma) – responders - probe sequences

Probes	FC	FC_1	LS	Loop present	60 mer
PVRL1_11_119575859_119577309_119599998_119609544_FR	2.33927526	2.33927526	1	BL R	AGAAAATATAGTATTGATTGCTTTCAAGTCGATGCGCGCCCGCCGGGGCCCGGTCGGAGC
HLA-DQB1_6_32607972_32614493_32669132_32671838_RR	2.125134633	2.125134633	1	BL R	TACTGTAGTAAGTTCTCTGAGGAGGATATCGATTTTTTATTGTATCCTATATTTTTTCTA
HLA-DQB1_6_32607972_32614493_32630138_32632737_RR	2.089554856	2.089554856	1	BL R	TACTGTAGTAAGTTCTCTGAGGAGGATATCGAAGTCTTGGATTAAGGTTCATTCAACAAA
BOK_2_242498607_242505838_242528424_242532109_RF	2.074201477	2.074201477	1	BL R	CACTTCCCCAACATAAGCCTCGGTCTCTTCGAGGGCGGGCCCGGCGGCCCCGGAGCAAAC
CSK_15_75042637_75047345_75083504_75088622_FR	2.024612404	2.024612404	1	BL R	GAGTTCAGCGTGCCGCCGGGCGTGAAAGTCGAGGCATATTTGAGTTTAGGGAGGTGTTGC
CSK_15_75042637_75047345_75075209_75080043_FF	1.967357679	1.967357679	1	BL R	GAGTTCAGCGTGCCGCCGGGCGTGAAAGTCGACTCTGGGCCCAGACCACAGAAGGAGGGG
CSK_15_75042637_75047345_75072257_75074709_FR	1.94043132	1.94043132	1	BL R	GAGTTCAGCGTGCCGCCGGGCGTGAAAGTCGATTTGTTTATGGTTTTATCCCCAGTGCCT
HLA-DQB1_6_32630138_32632737_32669132_32671838_RR	1.928831852	1.928831852	1	BL R	TTTGTTGAATGAACCTTAATCCAAGACTTCGATTTTTTATTGTATCCTATATTTTTTCTA
STAT5B_17_40403935_40406459_40464294_40468456_FR	1.82820099	1.82820099	1	BL R	TTCCATAGATTACTTTTCAAATCATCCTTCGAAGCTGGCGGCTGAGGGCCCCGGCGCCAAG
BOK_2_242498607_242505838_242517411_242520415_RR	1.748653628	1.748653628	1	BL R	GTTTGCTCCGGGGCCGCCGGGCCCGCCCTCGATTTTAACACCACCATGGTTTGAATGAAT
PTPRA_20_2853761_2858838_2943750_2948659_RF	1.706975419	1.706975419	1	BL R	TCCATTGTCTTATTCCAGTCTAGGCTTGTCGAGTTGCAGGCCGCCCTGGTGGCTAGACAT
FCGR2B_1_161562782_161569954_161615627_161622991_FR	1.698835854	1.698835854	1	BL R	AAAAAACAATTATGTAATTGAAAACCCATCGAGGGGCTTACTAATGCCTTTTAGCTCCCT
BOK_2_242474875_242482300_242498607_242505838_RR	1.691068852	1.691068852	1	BL R	GACCCCCGGGAATTGGCTCCAGCACATCTCGAGGGCGGGCCCGGCGGCCCCGGAGCAAAC
FCGR2B_1_161519223_161525894_161562782_161569954_RF	1.686221031	1.686221031	1	BL R	AAAAAACAATTATGTAATTGAAAACCCATCGAAGCTCTTTGGTTCCACAGAGTGATTCTG

Probes	FC	FC_1	LS	Loop present	60 mer
HLA-DQB1_6_32634654_32639610_32669132_32671838_RR	1.67581557	1.67581557	1	BL R	AGGCATTCGTTCTTCAGCTCTTCTATAATCGATTTT TTATTGTATCCTATATTTTTTCTA
PTPRA_20_2853761_2858838_3001591_3004582_RF	1.658692805	1.658692805	1	BL R	GCTCTTATAAATTATGTATTCAAAGAAATCGAGTTG CAGGCCGCCCTGGTGGCTAGACAT
AKT1_14_105266348_105267359_105305709_10530965 8_FF	1.649633626	1.649633626	1	BL R	CCCGCGGCGGAGCTGCTACTGTTTACTTTCGAAGCT TCTTCCTTTCGGCCCCCAGGCCTA
PTPRA_20_2797355_2801691_3001591_3004582_RF	1.634557427	1.634557427	1	BL R	GCTCTTATAAATTATGTATTCAAAGAAATCGAACTG GCGGCAACCGCTGCAGCGCCTGCT
FCGR2B_1_161534237_161535923_161562782_1615699 54_RF	1.631120636	1.631120636	1	BL R	AAAAAACAATTATGTAATTGAAAACCCATCGAGGGG CTTACTAATGCCTTTTAGCTCCCT
BOK_2_242454060_242458194_242498607_242505838_ RR	1.621735092	1.621735092	1	BL R	TCTCCTGCCTACCACACTGTGAGAAAGCTCGAGGGC GGGCCCGGCGGCCCCGGAGCAAAC
CSK_15_75042637_75047345_75075209_75080043_FR	1.608089138	1.608089138	1	BL R	GAGTTCAGCGTGCCGCCGGGCGTGAAAGTCGAATTC TCCCAGCAGCCCACTGTCAGAACCC
TNFRSF25_1_6521664_6526267_6554648_6558108_FR	1.606585424	1.606585424	1	BL R	CCGCGCCCCGCCAGGGCCCGCCCCGCGCCGTCGACAAT GTTATTCTTTGTTTCTCTTACCAA
SHH_7_155593268_155595881_155627543_155630456_ FF	1.603517118	1.603517118	1	BL R	GAAGGCCCGGTGCGCCCAGCTGTGCTCCTCGAGAAC AGCCAGGCTAACACGGAGAAACCC
PTPRA_20_2797355_2801691_2943750_2948659_RF	1.585991003	1.585991003	1	BL R	TCCATTGTCTTATTCCAGTCTAGGCTTGTCGAACTG GCGGCAACCGCTGCAGCGCCTGCT
TNFRSF25_1_6521664_6526267_6554648_6558108_FF	1.584692766	1.584692766	1	BL R	CCGCGCCCCGCAGGGCCCGCCCCGCGCCGTCGATGTG TTGGAAGTCAGGGCGGCGGTGCCC

Table 36c. Top Probes – Anti PD1 (Melanoma) – Responders - Loci

Probes	Chr	Start1	End1	Start2	End2	Chr	Start1	End1	Start2	End2
PVRL1_11_119575859_119577309_119599998_119609544_FR	11	119577280	119577309	119599999	119600028	11	11957 3310	119577309	119599999	119603998
HLA-DQB1_6_32607972_32614493_32669132_32671838_RR	6	32607973	32608002	32669133	32669162	6	32607 973	32611972	32669133	32673132
HLA-DQB1_6_32607972_32614493_32630138_32632737_RR	6	32607973	32608002	32630139	32630168	6	32607 973	32611972	32630139	32634138
BOK_2_242498607_242505838_242528424_242532109_RF	2	242498608	242498637	242532080	242532109	2	24249 8608	242502607	242528110	242532109
CSK_15_75042637_75047345_75083504_75088622_FR	15	75047316	75047345	75083505	75083534	15	75043 346	75047345	75083505	75087504
CSK_15_75042637_75047345_75075209_75080043_FF	15	75047316	75047345	75080014	75080043	15	75043 346	75047345	75076044	75080043
CSK_15_75042637_75047345_75072257_75074709_FR	15	75047316	75047345	75072258	75072287	15	75043 346	75047345	75072258	75076257
HLA-DQB1_6_32630138_32632737_32669132_32671838_RR	6	32630139	32630168	32669133	32669162	6	32630 139	32634138	32669133	32673132
STAT5B_17_40403935_40406459_40464294_40468456_FR	17	40406430	40406459	40464295	40464324	17	40402 460	40406459	40464295	40468294
BOK_2_242498607_242505838_242517411_242520415_RR	2	242498608	242498637	242517412	242517441	2	24249 8608	242502607	242517412	242521411
PTPRA_20_2853761_2858838_2943750_2948659_RF	20	2853762	2853791	2948630	2948659	20	28537 62	2857761	2944660	2948659
FCGR2B_1_161562782_161569954_161615627_161622991_FR	1	161569925	161569954	161615628	161615657	1	16156 5955	161569954	161615628	161619627
BOK_2_242474875_242482300_242498607_242505838_RR	2	242454061	242454090	242498608	242498637	2	24245 4061	242458060	242498608	242502607

Probes	Chr	Start1	End1	Start2	End2	Chr	Start1	End1	Start2	End2
FCGR2B_1_161519223_161525894_161562782_161569954_RF	15	75047316	75047345	75075210	75075239	15	75043346	75047345	75075210	75079209
HLA-DQB1_6_32634654_32639610_32669132_32671838_RR	1	6526238	6526267	6554649	6554678	1	6522268	6526267	6554649	6558648
PTPRA_20_2853761_2858838_3001591_3004582_RF	7	155595852	155595881	155630427	155630456	7	155591882	155595881	155626457	155630456
AKT1_14_105266348_105267359_105305709_105309658_FF	20	2797356	2797385	2948630	2948659	20	2797356	2801355	2944660	2948659
PTPRA_20_2797355_2801691_3001591_3004582_RF	1	6526238	6526267	6558079	6558108	1	6522268	6526267	6554109	6558108
FCGR2B_1_161534237_161535923_161562782_161569954_RF	2	242454061	242454090	242498608	242498637	2	242454061	242458060	242498608	242502607
BOK_2_242454060_242458194_242498607_242505838_RR	15	75047316	75047345	75075210	75075239	15	75043346	75047345	75075210	75079209
CSK_15_75042637_75047345_75075209_75080043_FR	1	6526238	6526267	6554649	6554678	1	6522268	6526267	6554649	6558648
TNFRSF25_1_6521664_6526267_6554648_6558108_FR	7	155595852	155595881	155630427	155630456	7	155591882	155595881	155626457	155630456
SHH_7_155593268_155595881_155627543_155630456_FF	20	2797356	2797385	2948630	2948659	20	2797356	2801355	2944660	2948659
PTPRA_20_2797355_2801691_2943750_2948659_RF	1	6526238	6526267	6558079	6558108	1	6522268	6526267	6554109	6558108
TNFRSF25_1_6521664_6526267_6554648_6558108_FF	2	242454061	242454090	242498608	242498637	2	242454061	242458060	242498608	242502607

Table 36d. Top Probes – Anti PD1 (Melanoma) Non—responders

Probes	Gene Locus	Probe_Count_Total	Probe_Count_Sig	HyperG_Stats	FDR_HyperG	Percent_Sig	Avg_CV	logFC
PVRL1_11_119523735_119528121_119599998_119609544_RF	PVRL1	95	44	3.65E-05	0.003027108	46	5.822	-0.534218713
IL12B_5_158737480_158738689_158805563_158807407_FF	IL12B	11	7	0.011584	0.182699883	64	4.1377	-0.531233304
MYD88_3_38139864_38141788_38192489_38194027_RR	MYD88	18	10	0.009424	0.173813506	56	11.04	-0.520757975
PVRL1_11_119599998_119609544_119620830_119624585_FR	PVRL1	95	44	3.65E-05	0.003027108	46	5.2193	-0.516406696
PIK3R3_1_46633134_46639474_46678880_46685388_FR	PIK3R3	55	24	0.005396	0.137801433	44	4.378	-0.488392104
CD6_11_60744556_60751199_60768894_60771404_RR	CD6	62	33	9.60E-06	0.001593482	53	3.2567	-0.488334118
TREM1_6_41229998_41238663_41295986_41297320_RR	TREM1	32	15	0.012077	0.182699883	47	5.1013	-0.486331515
PVRL1_11_119508824_119511197_119599998_119609544_RF	PVRL1	95	44	3.65E-05	0.003027108	46	5.0377	-0.480648315
IL12B_5_158737480_158738689_158781589_158783887_FF	IL12B	11	7	0.011584	0.182699883	64	4.282	-0.476087861
IL12A_3_159657523_159676447_159701524_159705330_FR	IL12A	19	10	0.015159	0.186399228	53	0.9037	-0.473957047
PVRL1_11_119599998_119609544_119640015_119642535_FR	PVRL1	95	44	3.65E-05	0.003027108	46	6.073	-0.470148979
CD6_11_60768894_60771404_60785339_60793057_RF	CD6	62	33	9.60E-06	0.001593482	53	3.216	-0.468856196
IL12B_5_158737480_158738689_158805563_158807407_FR	IL12B	11	7	0.011584	0.182699883	64	6.2313	-0.464794636
PVRL1_11_119539363_119541214_119599998_119609544_RF	PVRL1	95	44	3.65E-05	0.003027108	46	5.525	-0.460783807
IL12A_3_159657523_159676447_159701524_159705330_RR	IL12A	19	10	0.015159	0.186399228	53	3.6993	-0.457786304

Probes	Gene Locus	Probe_Count _ Total	Probe_Count _ Sig	HyperG_ Stats	FDR_ HyperG	Percent _ Sig	Avg_ CV	logFC
PVRL1_11_119479071_119480091_119599998_119609544_RF	PVRL1	95	44	3.65E-05	0.003027108	46	3.7273	0.455986104
PIK3CA_3_178832360_178841413_178871576_178873671_FF	PIK3CA	25	13	0.006619	0.146507027	52	2.733	0.445211521
PIK3R3_1_46609200_46612260_46633134_46639474_RF	PIK3R3	55	24	0.005396	0.137801433	44	10.7787	0.443513439
MYD88_3_38164895_38166955_38192489_38194027_RR	MYD88	18	10	0.009424	0.173813506	56	2.8267	0.439771491
PVRL1_11_119570787_119575859_119599998_119609544_RF	PVRL1	95	44	3.65E-05	0.003027108	46	4.0827	0.431853241
CD6_11_60744556_60751199_60768894_60771404_FR	CD6	62	33	9.60E-06	0.001593482	53	5.8293	-0.42873082
PIK3R3_1_46488955_46494355_46633134_46639474_RF	PIK3R3	55	24	0.005396	0.137801433	44	2.7617	0.427126062
PVRL1_11_119599998_119609544_119620830_119624585_FF	PVRL1	95	44	3.65E-05	0.003027108	46	8.9813	0.424995751
PIK3R3_1_46633134_46639474_46662272_46666981_FR	PIK3R3	55	24	0.005396	0.137801433	44	5.5577	0.4180861 22
PIK3R3_1_46605407_46608166_46633134_46639474_RF	PIK3R3	55	24	0.005396	0.137801433	44	5.008	0.411050272

Table 36e. Top Probes – Anti PD1 (Melanoma) Non—responders

Probes	Ave Expr	T	P.Value	adj.P.Val	B	FC	FC_1	LS	Loop present
PVRL1_11_119539363_119541214_119599998_119609544_RF	-0.534218713	-9.570025943	2.35E-05	0.008847609	3.334045114	0.690532531	-1.448157697	-1	BL NR
IL12A_3_159657523_159676447_159701524_159705330_RR	-0.531233304	-7.016342932	0.000181305	0.009942962	1.35541306	0.691962949	-1.445164083	-1	BL NR
PVRL1_11_119479071_119480091_119599998_119609544_RF	-0.520757975	-3.831304203	0.006089906	0.044194094	-2.252601523	0.697005539	-1.434708829	-1	BL NR
PIK3CA_3_178832360_178841413_178871576_178873671_FF	-0.516406696	-8.795272062	4.14E-05	0.008847609	2.800356612	0.699110934	-1.430388156	-1	BL NR
PIK3R3_1_46609200_46612260_46633134_46639474_RF	-0.488392104	-5.61212648	0.000725486	0.015727218	-0.051375364	0.712819098	-1.402880481	-1	BL NR
MYD88_3_38164895_38166955_38192489_38194027_RR	-0.488334118	-8.047360963	7.46E-05	0.009617494	2.23318282	0.712847749	-1.402824097	-1	BL NR
PVRL1_11_119570787_119575859_119599998_119609544_RF	-0.486331515	-8.738479042	4.32E-05	0.008847609	2.759158258	0.713837939	-1.40087819	-1	BL NR
CD6_11_60744556_60751199_60768894_60771404_FR	-0.480648315	-8.6418614	4.66E-05	0.008945528	2.688386536	0.716655502	-1.395370574	-1	BL NR
PIK3R3_1_46488955_46494355_46633134_46639474_RF	-0.476087861	-6.114799585	0.000430223	0.012658979	0.482977345	0.718924482	-1.39096668	-1	BL NR
PVRL1_11_119599998_119609544_119620830_119624585_FF	-0.473957047	-7.58766065	0.000109483	0.00978135	1.856437949	0.719987095	-1.388913783	-1	BL NR
PIK3R3_1_46633134_46639474_46662272_46666981_FR	-0.470148979	-8.578336694	4.89E-05	0.008945528	2.641380204	0.721890048	-1.385252508	-1	BL NR
PIK3R3_1_46605407_46608166_46633134_46639474_RF	-0.468856196	-8.542957327	5.03E-05	0.008945528	2.615035493	0.722537216	-1.384011755	-1	BL NR
	-0.464794636	-7.023464829	0.000180133	0.009942962	1.361894813	0.724574211	-1.380120883	-1	BL NR
PVRL1_11_119539363_119541214_119599998_119609544_RF	-0.460783807	-8.332777274	5.93E-05	0.009591857	2.456053048	0.726591399	-1.376289344	-1	BL NR

Probes	Ave Expr	t	P.Value	adj.P.Val	B	FC	FC_1	LS	Loop present
PVRL1_11_119479071_119480091_119599998_119609544_RF	-0.455986104	-7.517911586	0.000116245	0.00978135	1.797273524	0.729011711	-1.371720076	-1	BL NR
PIK3CA_3_178832360_178841413_178871576_178873671_FF	-0.445211521	-7.531076446	0.000114934	0.00978135	1.808482074	0.734476623	-1.36151372	-1	BL NR
PIK3R3_1_46609200_46612260_46633134_46639474_RF	-0.443513439	-5.674070937	0.000679088	0.015238097	0.016439762	0.735341627	-1.359912133	-1	BL NR
MYD88_3_38164895_38166955_38192489_38194027_RR	-0.439771491	-7.048947048	0.00017601	0.009942962	1.38503639	0.737251373	-1.356389472	-1	BL NR
PVRL1_11_119570787_119575859_119599998_119609544_RF	-0.431853241	-7.498223987	0.000118238	0.00978135	1.780475318	0.741308911	-1.348965303	-1	BL NR
CD6_11_60744556_60751199_60768894_61771404_FR	-0.42873082	-7.398571649	0.000128932	0.00978135	1.694777806	0.742915061	-1.346048899	-1	BL NR
PIK3R3_1_46488955_46494355_46633134_46639474_RF	-0.427126062	-4.901162068	0.001606582	0.0221991	-0.871100352	0.74374189	-1.344552476	-1	BL NR
PVRL1_11_119599998_119609544_119620830_119624585_FF	-0.424995751	-7.614744268	0.000106977	0.00978135	1.879266088	0.744840925	-1.342568549	-1	BL NR
PIK3R3_1_46633134_46639474_46662272_46666981_FR	-0.418086122	-4.651195344	0.002160496	0.025812366	-1.177891691	0.748416815	-1.336153838	-1	BL NR
PIK3R3_1_46605407_46608166_46633134_46639474_RF	-0.411050272	-4.731761481	0.001961829	0.024339948	-1.077937879	0.752075669	-1.32965344	-1	BL NR

Table 36f. Top Probes – Anti PD1 (Melanoma) Non–responders – probe sequences

Probes	60 mer
TNFRSF25_1_6521664_6526267_6541388_6544308_FF	CCGCGCCCCGCAGGGCCCGCCCCGCGCCGTCGAGGCTTTCAAGGGATCCAGGGTGGGGTGC
TNFRSF25_1_6521664_6526267_6554648_6558108_FR	CCGCGCCCCGCAGGGCCCGCCCCGCGCCGTCGACAAATGTIATTCTTTGTTTCTCTTACCAA
TNFRSF25_1_6521664_6526267_6554648_6558108_FF	CCGCGCCCCGCAGGGCCCGCCCCGCGCCGTCGATGTGTTGGAAGTCAGGGCGGCGGTGCCC
BOK_2_242498607_242505838_242528424_242532109_RF	CACTTCCCCAACATAAGCCTCGGTCTCTTCGAGGGCGGGCCCGGCGCCCCGGAGCAAACC
TNFRSF25_1_6521664_6526267_6574084_6575375_FR	CCGCGCCCCGCAGGGCCCGCCCCGCGCCGTCGAGAAGCATAAAGCAGGGACAGGGTATGGAG
BOK_2_242474875_242482300_242498607_242505838_RR	GACCCCCGGGGAATTGGCTCCAGCACATCTCGAGGGCGGGCCCGGCGCCCCGGAGCAAACC
BOK_2_242498607_242505838_242517411_242520415_RR	GTTTGCTCCGGGGCCGCCGGGCCCGCCCTCGATTTTAACACCACCATGGTTTGAATGAAT
IRF1_5_131808352_131813604_131831068_131832754_FF	GTGTCTCGGCCCCCTGGGGCCCCACCCTTCGATTTCCCTGTTGCCGCCGCGTTTGCAAGA
BOK_2_242454060_242458194_242498607_242505838_RR	TCTCCTGCCTACCACACACTGTGAGAAAGCTCGAGGGCGGGCCCGGCGCCCCGGAGCAAAC
CSK_15_75042637_75047345_75083504_75088622_FR	GAGTTCAGCGTGCCGCCGGGCGTGAAAGTCGAGGCATATTTGAGTTTAGGGAGGTGTTGC
TNFRSF25_1_6521664_6526267_6554648_6558108_RF	GGGCACCGCGCCGCCCTGACTTCCAACACATCGATCTCTGCCTCGCGCAGCCCCAGCGTGCG
IKBKB_8_42121759_42128721_42148497_42149642_FR	CCACCCCCGCCCCCGGGGGAGTCGCCCGGTCGATTTCCAAAAGCTCACACATGGGTGCACA
TNFRSF25_1_6510663_6512333_6554648_6558108_RF	GGGCACCGCGCCGCCCTGACTTCCAACACATCGAAGAATGGGTGGGGCCTTGCACCTCATAC
IKBKB_8_42121759_42128721_42188562_42190317_FR	CCACCCCCGCCCCCGGGGGAGTCGCCCGGTCGACCCCCCTGACATGGGGCTGCCTGGAGCAG
TNFRSF25_1_6554648_6558108_6574084_6575375_FR	GGGCACCGCGCCGCCCTGACTTCCAACACATCGAGAAGCATAAAGCAGGGACAGGGTATGGAG

Table 36f continued. Top Probes – Anti PD1 (Melanoma) Non—responders – probe sequences

Probes	60 mer
CSK_15_75042637_75047345_75075209_75080043_FF	GAGTTCAGCGTGCCGCCGGGCGTGAAAGTCGACTCTGGGCCCAGACCACACAGAAGGAGGGG
ARHGEF7_13_111748012_111752622_111951910_111954429_RF	AATTCTGTTGGAAGAATAATTTAAAATATCGATGTGGCGACCGGCTGTGGGGGTCACGGA
STAT5B_17_40403935_40406459_40464294_40468456_FR	TTCCATAGATTACTTTTCAAATCATCCTTCGAAGCTGGCGGCTGAGGGCCCGGCGCCAAG
CSK_15_75042637_75047345_75072257_75074709_FR	GAGTTCAGCGTGCCGCCGGGCGTGAAAGTCGATTTGTTTATGGTTTTATCCCCAGTGCCT
IRF3_19_50158039_50163617_50184391_50185455_RF	CACCCTCCCTTCTTCCTGGGCCCTCAGATCGACCCCCCCCCACCCCACCGGGCTGGCTGC
IKBKB_8_42121759_42128721_42138740_42142593_FR	CCACCCCCGCCCCGGGGGAGTCGCCCGGTCGAGGGCCTGGCAAGAAGACAGAAGCCGACT
TRAF1_9_123675824_123681988_123698802_123702746_RF	TATGAGTAATAATTACAATTTCCCCCTTTCGACCTCCAGGTCCCCCGCCACTTCCACGGC
BAD_11_64023977_64025423_64060063_64064396_RR	CAGAAACTGCTGGTTGGGCTCATACTTTTCGAGGGCCAGCTCCCCGCACCCCCACCAAGC
ICOSLG_21_45663614_45665471_45687442_45689916_FR	TTCCCCTGTAAGATTCATTTCCTGTGATTCGAGTCACAGCTGTAGTGGGGTGGGGGGTGA
ARHGEF7_13_111730571_111732652_111748012_111752622_FR	TCTTTGTTACTGGAATATACGAATAAATCGATGTGGCGACCGGCTGTGGGGGTCACGGA

Table 36g. Top Probes – Anti PD1 (Melanoma) Non—responders – probes sequences and loci

60 mer	Chr	Start1	End1	Start2	End2	Chr	Start1	End1	Start2	End2
CCGCGCCCGCAGGGCCCGCCCCGCGCCGTCGA GGCTTTCAAGGGATCCAGGGTGGGGTGC	1	6526238	6526267	6544279	6544308	1	6522268	6526267	6540309	6544308
CCGCGCCCGCAGGGCCCGCCCCGCGCCGTCG ACAATGTTATTCTTTGTTTCTCTTACCAA	1	6526238	6526267	6554649	6554678	1	6522268	6526267	6554649	6558648
CCGCGCCCGCAGGGCCCGCCCCGCGCCGTCGATG TGTTGGAAGTCAGGGCGGCGGTGCCC	1	6526238	6526267	6558079	6558108	1	6522268	6526267	6554109	6558108
CACTTCCCCAACATAAGCCTCGGTCTCTTCGAGGG CGGGCCCGGCGGCCCCGGAGCAAAC	2	242498608	242498637	242532080	242532109	2	242498608	242502607	242528110	242532109
CCGCGCCCGCAGGGCCCGCCCCGCGCCGTCGAGA AGCATAAAGCAGGGACAGGTATGGAG	1	6526238	6526267	6574085	6574114	1	6522268	6526267	6574085	6578084
GACCCCCGGGAATTGGCTCCAGCACATCTCGAGGGC GGGCCCGGCGGCCCCGGAGCAAAC	2	242474876	242474905	242498608	242498637	2	242474876	242478875	242498608	242502607
GTTTGCTCCGGGGCCGCCGGGCCCGCCCTCGATTT TAACACCACCATGGTTTGAATGAAT	2	242498608	242498637	242517412	242517441	2	242498608	242502607	242517412	242521411
GTGTCTCGGCCCCCTGGGGCCCCACCCTTCGATTTC CCTGTTGCCGCCGCGTTTGCAAGA	5	131813575	131813604	131832725	131832754	5	131809605	131813604	131828755	131832754
TCTCCTGCCTACCACACTGTGAGAAAGCTCGAGGG CGGGCCCGGCGGCCCCGGAGCAAAC	2	242454061	242454090	242498608	242498637	2	242454061	242458060	242498608	242502607
GAGTTCAGCGTGCCGCCGGGCGTGAAAGTCGAGGC ATATTTGAGTTTAGGGAGGTGTTGC	15	75047316	75047345	75083505	75083534	15	75043346	75047345	75083505	75087504
GGGCACCGCCGCCCTGACTTCCAACACATCGATCTC TGCCTCGCGCAGCCCCAGCGTGCG	1	6521665	6521694	6558079	6558108	1	6521665	6525664	6554109	6558108
CCACCCCCGCCCCGGGGGAGTCGCCCGGTCGATTTCC AAAAGCTCACACATGGGTGCACA	8	42128692	42128721	42148498	42148527	8	42124722	42128721	42148498	42152497
GGGCACCGCCGCCCTGACTTCCAACACATCGAAGAAT GGGTGGGGCCTTGCACCTCATAC	1	6510664	6510693	6558079	6558108	1	6510664	6514663	6554109	6558108
CCACCCCCGCCCCGGGGGAGTCGCCCGGTCGACCCC CTGACATGGGGCTGCCTGGAGCAG	8	42128692	42128721	42188563	42188592	8	42124722	42128721	42188563	42192562
GGGCACCGCCGCCCTGACTTCCAACACATCGAGAAG CATAAAGCAGGGACAGGTATGGAG	1	6558079	6558108	6574085	6574114	1	6554109	6558108	6574085	6578084
GAGTTCAGCGTGCCGCCGGGCGTGAAAGTCGACT CTGGGCCCAGACCACAGAAGGAGGGG	15	75047316	75047345	75080014	75080043	15	75043346	75047345	75076044	75080043
AATTCTGTTGGAAGAATAATTTAAAATATCGATGTG GCGACCGGCTGTGGGGGTCACGGA	13	111748013	111748042	111954400	111954429	13	111748013	111752012	111950430	111954429

Table 36g continued. Top Probes – Anti PD1 (Melanoma) Non—responders – probes sequences and loci

60 mer	Chr	Start1	End1	Start2	End2	Chr	Start1	End1	Start2	End2
TTCCATAGATTACTTTTCAAATCATCCTTCGAAGC TGGCGGCTGAGGGCCCGGCGCCAAG	17	40406430	40406459	40464295	40464324	17	40402460	40406459	40464295	40468294
GAGTTCAGCGTGCCGCCGGGCGTGAAAGTCGAT TTGTTTATGGTTTTATCCCCAGTGCCT	15	75047316	75047345	75072258	75072287	15	75043346	75047345	75072258	75076257
CACCCTCCCTTCTTCCTGGGCCCTCAGATCGACC CCCCCCACCCCCACCGGGCTGGCTGC	19	50158040	50158069	50185426	50185455	19	50158040	50162039	50181456	50185455
CCACCCCCGCCCCGGGGGAGTCGCCCGGTCGAG GGCCTGGCAAGAAGACAGAAGCCGACT	8	42128692	42128721	42138741	42138770	8	42124722	42128721	42138741	42142740
TATGAGTAATAATTACAATTTCCCCCTTTCGACC TCCAGGTCCCCCGCCACTTCCACGGC	9	123675825	123675854	123702717	123702746	9	123675825	123679824	123698747	123702746
CAGAAACTGCTGGTTGGGCTCATACTTTTCGAGG GCCAGCTCCCCGCACCCCCACCAAGC	11	64023978	64024007	64060064	64060093	11	64023978	64027977	64060064	64064063
TTCCCCTGTAAGATTCATTTCCTGTGATTCGAG TCACAGCTGTAGTGGGGTGGGGGGTGA	21	45665442	45665471	45687443	45687472	21	45661472	45665471	45687443	45691442
TCTTTGTTACTGGAATATACGAATAAAATCGATG TGGCGACCGGCTGTGGGGGTCACGGA	13	111732623	111732652	111748013	111748042	13	111728653	111732652	111748013	111752012

Table 37a. Anti-PD1: pharmacodynamic response markers

Probes	Gene Locus	X12w_ adj.P.Val	X12w_FC_1	X12w_ LS	Loop detected	60 mer
BAX_19_49417533_49419970_49471563_49474829_FF	BAX	0.014	1.2508	1	BL R	AAGGCAGGCAGATCAGGAGCTCAAGAGA TCGAAAGAAAAAAAAAAAAGCATAAAAATCCA
BAX_19_49417533_49419970_49435499_49438567_FF	BAX	0.014	1.2346	1	BL R	AAGGCAGGCAGATCAGGAGCTCAAGAGATCGAA CGCTAAGTGTAGTTTAACACCTACTAG
CASP1_11_104941451_104946789_104994205_105005564_RR	CASP1	0.015	1.2201	1	BL R	ATAGTAAAATGTGAAAATGTTACAGTTATCGAA GTTCAGCGAGTATATTTTTACTGATAC
NCK2_2_106375590_106379449_106457772_106460967_RR	NCK2	0.014	1.2178	1	BL R	AAGGCCCAAGAACCAGGAATCTAGGTATTCGAA AAGCCCTAAAGTTGGCTTAATAAACTT
JAM2_21_26994168_26998383_27012522_27024636_FR	JAM2	0.014	1.2083	1	BL R	GGTGGGCAGATCACTTAAGGCCAGGAATTCGAA TGCAAAACTCACTACCCACTGGTAAGA
JAM2_21_26994168_26998383_27070793_27073958_FF	JAM2	0.014	1.2076	1	BL R	GGTGGGCAGATCACTTAAGGCCAGGAATTCGAT TCTATCAACTCTAGAATTTTTTTAAAT
BAX_19_49417533_49419970_49471563_49474829_FR	BAX	0.014	1.2071	1	BL R	AAGGCAGGCAGATCAGGAGCTCAAGAGATCGAG GTAAATGTGGGGGTTCTAGAACCCAGT
JAM2_21_26994168_26998383_27075383_27076758_FF	JAM2	0.014	1.205	1	BL R	GGTGGGCAGATCACTTAAGGCCAGGAATTCGAA ATTCTTTCCTAATGCCAAGTGTGTTAT
CXCL2_4_74949499_74952659_74968426_74975311_RR	CXCL2	0.014	1.2039	1	BL R	GGTCCCCTGATTTCCATCCTAGTGCTTCTCGAA ACATGTGCTCTGGAGATAAAGCGCCAA
JAM2_21_26994168_26998383_27056447_27060410_FR	JAM2	0.014	1.2038	1	BL R	GGTGGGCAGATCACTTAAGGCCAGGAATTCGAT ATTCAATAAAAGACCGGATGTGCAAAG
JAM2_21_26994168_26998383_27056447_27060410_FF	JAM2	0.014	1.2033	1	BL R	GGTGGGCAGATCACTTAAGGCCAGGAATTCGAG AAATGGTTTATCCAATTCATCCAAAAT
JAM2_21_26994168_26998383_27047035_27050041_FR	JAM2	0.014	1.1995	1	BL R	GGTGGGCAGATCACTTAAGGCCAGGAATTCGAG AGACTGTAAAGACATGTGTCTGCCTCT
JAM2_21_26994168_26998383_27028107_27035825_FF	JAM2	0.015	1.1972	1	BL R	GGTGGGCAGATCACTTAAGGCCAGGAATTCGAT CACTTCTTAAAGGCCCTACCTCTTAAT
IL2_4_123399246_123404439_123417475_123422774_FF	IL2	0.014	1.1962	1	BL R	GTTGGGTTGAAGATGAAATCATAGGAAGTCGAG CTGTAACCTCTGCTTGGTATTCTCCCT

Probes	Gene Locus	X12w_ adj.P.Val	X12w_FC_1	X12w_ LS	Loop detected	60 mer
JAM2_21_26994168_26998383_27 028107_27035825_FR	JAM2	0.014	1.1953	1	BL R	GGTGGGCAGATCACTTAAGGCCAGGAATTCGAA ACACCAGCTCTCTTAAATCCTGTGCCT
JAM2_21_26994168_26998383_27 047035_27050041_FF	JAM2	0.014	1.1924	1	BL R	GGTGGCCAGATCACTTAAGGCCCAGGAATTCGAG GAAAACCTCGGGGCAAAATAGGGAAAG
BAX_19_49421751_49425642_494 75136_49476327_RR	BAX	0.015	1.1898	1	BL R	TGAGAATGGAATAGATCAAAGGGAGGGTTCGAG ACAAGGTCTCACTTTATCACCCAACCT
JAM2_21_26994168_26998383_27 070793_27073958_FR	JAM2	0.014	1.1879	1	BL R	GGTGGGCAGATCACTTAAGGCCAGGAATTCGA CTGTGTGCCCATGAAGAAAGAAGATGGG
IL4_5_131966700_131972322_131 985852_131989475_FR	IL4	0.024	1.1852	1	BL R	AGTGATAGAAGAGGGACAAGGTGGCAGTTCGA TTTTAAAACACGCTCTTCAATAAAAAGA
CBLB_3_105390159_105394525_1 05627700_105635575_FF	CBLB	0.015	1.1828	1	BL R	AGCAGGGGGATCACATAAGGCCAG GAGTTCGATAAAATAAATTAGAGAAGATATAAA TAA
JAM2_21_26994168_26998383_27 080812_27083366_FF	JAM2	0.016	1.1816	1	BL R	GGTGGGCAGATCACTTAAGGCCAGGAAT TCGATTTCTCTGCTTCTCTCACAGCCCACATC
NCK2_2_106344684_106358282_1 06457772_106460967_FR	NCK2	0.019	1.1805	1	BL R	TCTTTGCAGATGTTGTAAGATAAGGATGTCG AAAAGCCCTAAAGTTGGCTTAATAAACTT
CXCL2_4_74949499_74952659_74 983628_74990858_RR	CXCL2	0.015	1.1794	1	BL R	GGTCCCCTGATTTCCATCCTAGTGCTTCTCGAT GATATAATACTCTGCTGACTACATTTT
NCK2_2_106375590_106379449_1 06435340_106439151_RR	NCK2	0.015	1.1767	1	BL R	AAGGCCCAAGAACCAGGAATCTAGGTATTCGAC CACCTTAAAAGAAAAATCTCTTGCAAC
CBLB_3_105390159_105394525_1 05606664_105615153_FR	CBLB	0.015	1.176	1	BL R	AGCAGGGGGATCACATAAGGCCAGGAGTTCGAT GAACGTTTACCCAATTATTTCTAAACA

Table 37b. Anti-PD1: pharmacodynamic response markers

Probes	Chr	Start1	End1	Start2	End2	Chr	Start1	End1	Start2	End2
BAX_19_49417533_49419970_49471563_49474829_FF	19	49419941	49419970	49474800	49474829	19	49415971	49419970	49470830	5E+07
BAX_19_49417533_49419970_49435499_49438567_FF	19	49419941	49419970	49438538	49438567	19	49415971	49419970	49434568	5E+07
CASP1_11_104941451_104946789_104994205_105005564_RR	11	104941452	104941481	104994206	104994235	11	104941452	104945451	104994206	1E+08
NCK2_2_106375590_106379449_106457772_106460967_RR	2	106375591	106375620	106457773	106457802	2	106375591	106379590	106457773	1E+08
JAM2_21_26994168_26998383_27012522_27024636_FR	21	26998354	26998383	27012523	27012552	21	26994384	26998383	27012523	3E+07
JAM2_21_26994168_26998383_27070793_27073958_FF	21	26998354	26998383	27073929	27073958	21	26994384	26998383	27069959	3E+07
BAX_19_49417533_49419970_49471563_49474829_FR	19	49419941	49419970	49471564	49471593	19	49415971	49419970	49471564	5E+07
JAM2_21_26994168_26998383_27075383_27076758_FF	21	26998354	26998383	27076729	27076758	21	26994384	26998383	27072759	3E+07
CXCL2_4_74949499_74952659_74968426_74975311_RR	4	74949500	74949529	74968427	74968456	4	74949500	74953499	74968427	7E+07
JAM2_21_26994168_26998383_27056447_27060410_FR	21	26998354	26998383	27056448	27056477	21	26994384	26998383	27056448	3E+07
JAM2_21_26994168_26998383_27056447_27060410_FF	21	26998354	26998383	27060381	27060410	21	26994384	26998383	27056411	3E+07
JAM2_21_26994168_26998383_27047035_27050041_FR	21	26998354	26998383	27047036	27047065	21	26994384	26998383	27047036	3E+07
JAM2_21_26994168_26998383_27028107_27035825_FF	21	26998354	26998383	27035796	27035825	21	26994384	26998383	27031826	3E+07
IL2_4_123399246_123404439_123417475_123422774_FF	4	123404410	123404439	123422745	123422774	4	123404400	123404439	123418775	1E+08
JAM2_21_26994168_26998383_27028107_27035825_FR	21	26998354	26998383	27028108	27028137	21	26994384	26998383	27028108	3E+07

Probes	Chr	Start1	End1	Start2	End2	Chr	Start1	End1	Start2	End2
JAM2_21_26994168_26998383_27047035_27050041_FF	21	26998354	26998383	27050012	27050041	21	26994384	26998383	27046042	3E+07
BAX_19_49421751_49425642_49475136_49476327_RR	19	49421752	49421781	49475137	49475166	19	49421752	49425751	49475137	5E+07
JAM2_21_26994168_26998383_27070793_27073958_FR	21	26998354	26998383	27070794	27070823	21	26994384	26998383	27070794	3E+07
IL4_5_131966700_131972322_131985852_131989475_FR	5	131972293	13197232	13198585	13198588	5	13196832	13197232	13198585	1E+08
CBLB_3_105390159_105394525_105627700_105635575_FF	3	105394496	10539452	10563554	10563557	3	10539052	10539452	10563157	1E+08
JAM2_21_26994168_26998383_27080812_27083366_FF	21	26998354	26998383	27083337	27083366	21	26994384	26998383	27079367	3E+07
NCK2_2_106344684_106358282_106457772_106460967_FR	2	106358253	10635828	10645777	10645780	2	10635428	10635828	10645777	1E+08
CXCL2_4_74949499_74952659_74983628_74990858_RR	4	74949500	74949529	74983629	74983658	4	74949500	74953499	74983629	7E+07
NCK2_2_106375590_106379449_106435340_106439151_RR	2	106375591	10637562	10643534	10643537	2	10637559	10637959	10643534	1E+08
CBLB_3_105390159_105394525_105606664_105615153_FR	3	105394496	10539452	10560666	10560669	3	10539052	10539452	10560666	1E+08

Table 38a. Anti-PD1: pharmacodynamic response markers
No difference in baseline Responders and baseline Non-Responders but show a significant change in 12 week Responder

Probes	Gene Locus	X12w_ adj.P.Val	X12w_ FC_1	X12w_ LS	Loop detected	60 mer
MAP3K14_17_43375304_43380378_43409961_43415408_FF	MAP3K14	0.085	-1.382	-1	12 W R	GATGCGGACTGTTTCCTGCTTTGATTTATCGACT TCTTATTTCTATTTTGTGACTTAGGA
MAP3K14_17_43360790_43364282_43375304_43380378_RF	MAP3K14	0.065	-1.366	-1	12 W R	GATGCGGACTGTTTCCTGCTTTGATTTATCGACA CAGTGTGTCTGAAGTTTGGGGTGGTA
MAP3K14_17_43375304_43380378_43399352_43402185_FR	MAP3K14	0.062	-1.365	-1	12 W R	GATGCGGACTGTTTCCTGCTTTGATTTATCGATA TCTCCCTCCTTTCGCTTCTTCCTTTC
MAP3K14_17_43375304_43380378_43416164_43419166_FF	MAP3K14	0.077	-1.348	-1	12 W R	GATGCGGACTGTTTCCTGCTTTGATTTATCGAGT CATTAAGAGACTCTCCGCCTGGGTGG
PRKCQ_10_6474855_6481197_6530169_6531558_FF	PRKCQ	0.014	-1.332	-1	12 W R	TTCCACCTGTAATACTGTGCCTGTATTCTCGACT CTTCTCGCCCTCTTCTCCAGCTCTCT
SIRPA_20_1838201_1841874_1872135_1877996_FF	SIRPA	0.014	-1.296	-1	12 W R	TAAAGTACTGTGTCCCACATATAAGTACTCGACC AAGAAATTCATTCTTACCTCCTAAGA
MAPK1_22_22175466_22178188_22210841_22217782_RR	MAPK1	0.019	-1.232	-1	12 W R	ACCCCACCAATCTATAATAAGATTGATTTCGACA CAAGGGTTTGTAACAAAAAACAAAAA
SIRPA_20_1857090_1859261_1905279_1911608_FF	SIRPA	0.014	-1.219	-1	12 W R	AGCGCTTTATTTGTCAGGACGATAGACCTCGACA ATGTCCTATTCTTCCAGAAACTCATT
CBLB_3_105466912_105471108_105514190_105519713_FR	CBLB	0.039	-1.217	-1	12 W R	TTATTACTTTATTCTGACTGAATATCATTCGAAA GAAACCAAAAACACAAGTATACATCA
CBLB_3_105442255_105450516_105471108_105479961_RR	CBLB	0.018	-1.211	-1	12 W R	TATCCTTTGGTTTAGAAGTATTTCTTATTCGACA AAATTTTAACATGTTATGCAGTTACA
PRKCQ_10_6474855_6481197_6544129_6548414_RF	PRKCQ	0.014	-1.211	-1	12 W R	TTCAGCTATTCACTGGTTTTTCTTCAGATCGACT CCTGCTTCCCTCCCCTCATCTTTAAA
CBLB_3_105471108_105479961_105538128_105544723_RF	CBLB	0.023	-1.21	-1	12 W R	TCCAGTACAATAAACAATGTACCAAAGATCGACA AAATTTTAACATGTTATGCAGTTACA
IGKC_2_89162710_89164067_89175040_89179794_FF	IGKC	0.019	-1.204	-1	12 W R	TAAACTCTGACATTGCCTATTAGCATTCTCGAAT GCATGGCTCACTGTAACCTCCAACTC
CBLB_3_105442255_105450516_105466912_105471108_RR	CBLB	0.047	-1.202	-1	12 W R	TATCCTTTGGTTTAGAAGTATTTCTTATTCGACA ACTACTGGCTTAAAAAAGGCAAAACA

Probes	Gene Locus	X12w_ adj.P.Val	X12w_ FC_1	X12w_ LS	Loop detected	60 mer
PRKCQ_10_6474855_6481197_6593817_6595662_RF	PRKCQ	0.016	-1.202	-1	12 W R	TACCTCCTTGGGAACATATTTGAGAGTTTCGACT CCTGCTTCCCTCCCCCTCATCTCTTTAAA
SIRPA_20_1905279_1911608_1931241_1933334_RF	SIRPA	0.014	-1.201	-1	12 W R	ACACTTGATTTTTGCTTTCCAAGCTGACTCGAGA CATCTAAGAAGGTCCAGCCAGATGTT
SIRPA_20_1872135_1877996_1900304_1902024_RR	SIRPA	0.014	-1.199	-1	12 W R	GCGCCCTATTTCCACCTTGTGCCTTCTGTCGACA CACCAAGATGTCACGGAGGAGTCTGT
NCK2_2_106403393_106408079_106473847_106478190_RR	NCK2	0.016	-1.193	-1	12 W R	CCAGCTGAAGTTTCGCAGGTCCCCTGCTTCGAGT AGGCCAATCCCATTTTGGCCGAAAAC
PRKCQ_10_6474855_6481197_6593817_6595662_RF	PRKCQ	0.016	-1.202	-1	12 W R	TACCTCCTTGGGAACATATTTGAGAGTTTCGACT CCTGCTTCCCTCCCCCTCATCTCTTTAAA
SIRPA_20_1905279_1911608_1931241_1933334_RF	SIRPA	0.014	-1.201	-1	12 W R	ACACTTGATTTTTGCTTTCCAAGCTGACTCGAGA CATCTAAGAAGGTCCAGCCAGATGTT
SIRPA_20_1872135_1877996_1900304_1902024_RR	SIRPA	0.014	-1.199	-1	12 W R	GCGCCCTATTTCCACCTTGTGCCTTCTGTCGACA CACCAAGATGTCACGGAGGAGTCTGT
NCK2_2_106403393_106408079_106473847_106478190_RR	NCK2	0.016	-1.193	-1	12 W R	CCAGCTGAAGTTTCGCAGGTCCCCTGCTTCGAGT AGGCCAATCCCATTTTGGCCGAAAAC
PRKCQ_10_6474855_6481197_6601540_6605133_RF	PRKCQ	0.018	-1.191	-1	12 W R	ACTTTGGCTCAAGAGTGAACGATATTCAGTCGACT CCTGCTTCCCTCCCCCTCATCTCTTTAAA
MAPK1_22_22122470_22123582_22210841_22217782_FR	MAPK1	0.041	-1.19	-1	12 W R	TTCCTTAGGCAAGTCATCCCAATTCCATGTCGACA CAAGGGTTTGTAACAAAAAACAAAAA
SIRPA_20_1830612_1833775_1872135_1877996_RF	SIRPA	0.05	-1.189	-1	12 W R	TCTTAGGAGGTAAGAATGAATTTCTTGGTCGAAC TCCTGACCAGGAGGCTGGGAGGGGGT
CASP7_10_115416083_115421410_115478671_11548142_FF	CASP7	0.021	-1.188	-1	12 W R	CATCATTTTAATAGGTGCAAGAGTTCCGTCGAAC GCCCATACCTGTGTGGGAATCAAGCAAT
NCK2_2_106383183_106387147_106435340_106439151_RF	NCK2	0.015	-1.188	-1	12 W R	AAAAACAAAAAAGCCAATTCTGTACCCCTCGAAC CAGCCCTGGCTCTGTCCCCAGACCTT
SIRPA_20_1872135_1877996_1905279_1911608_RR	SIRPA	0.014	-1.188	-1	12 W R	GCGCCCTATTTCCACCTTGTGCCTTCTGTCGAGA CATCTAAGAAGGTCCAGCCAGATGTT
PRKCQ_10_6474855_6481197_6510600_6515355_RF	PRKCQ	0.016	-1.185	-1	12 W R	TTGATTATTTCAGGTTGACAGCTGTAAATCGACT CCTGCTTCCCTCCCCCTCATCTCTTTAAA

Table 38b. Probe location - Anti-PD1: pharmacodynamic response markers - No difference in baseline Responders and baseline Non-Responders but show a significant change in 12 week Responder

Probes	Chr	Start1	End1	Start2	End2	Chr	Start1	End1	Start2	End2
PRKCQ_10_6474855_6481197_6544129_6548414_RF	10	6474856	6474885	6548385	6548414	10	6474856	6478855	6544415	7E+06
CBLB_3_105471108_105479961_105538128_105544723_RF	3	105471109	105471138	105544694	105544723	3	105471109	105475108	105540724	1E+08
IGKC_2_89162710_89164067_89175040_89179794_FF	2	89164038	89164067	89179765	89179794	2	89160068	89164067	89175795	9E+07
CBLB_3_105442255_105450516_105466912_105471108_RR	3	105442256	105442285	105466913	105466942	3	105442256	105446255	105466913	1E+08
PRKCQ_10_6474855_6481197_6593817_6595662_RF	10	6474856	6474885	6595633	6595662	10	6474856	6478855	6591663	7E+06
SIRPA_20_1905279_1911608_1931241_1933334_RF	20	1905280	1905309	1933305	1933334	20	1905280	1909279	1929335	2E+06
SIRPA_20_1872135_1877996_1900304_1902024_RR	20	1872136	1872165	1900305	1900334	20	1872136	1876135	1900305	2E+06
NCK2_2_106403393_106408079_106473847_106478190_RR	2	106403394	106403423	106473848	106473877	2	106403394	106407393	106473848	1E+08
PRKCQ_10_6474855_6481197_6601540_6605133_RF	10	6474856	6474885	6605104	6605133	10	6474856	6478855	6601134	7E+06
MAPK1_22_22122470_22123582_22210841_22217782_FR	22	22123553	22123582	22210842	22210871	22	22119583	22123582	22210842	2E+07
SIRPA_20_1830612_1833775_1872135_1877996_RF	20	1830613	1830642	1877967	1877996	20	1830613	1834612	1873997	2E+06
CASP7_10_115416083_115421410_115478671_115481421_FF	10	115421381	115421410	115481392	115481421	10	115417411	115421410	115477422	1E+08
NCK2_2_106383183_106387147_106435340_106439151_RF	2	106383184	106383213	106439122	106439151	2	106383184	106387183	106435152	1E+08
SIRPA_20_1872135_1877996_1905279_1911608_RR	20	1872136	1872165	1905280	1905309	20	1872136	1876135	1905280	2E+06
PRKCQ_10_6474855_6481197_6510600_6515355_RF	10	6474856	6474885	6515326	6515355	10	6474856	6478855	6511356	7E+06

Table 39

Array Interaction	Outer Primers	Inner Primers	Chi.Square	p.value
IL15_4_142530356_142539177_142656375_142659066_RF	IL15-70/72	IL15-69/71	4.8	0.129
MYD88_3_38139864_38141788_38192489_38194027_RR	MYD88-10/12	MYD88-9/11	4.8	0.129
HLA-DQB1_6_32607972_32614493_32630138_32632737_RR	HLA-DQB1-86/88	HLA-DQB1-85/87	4.8	0.135
STAT5B_17_40403935_40406459_40464294_40468456_FR	STAT5B -74/76	STAT5B -73/75	4.8	0.142
IL12B_5_158737480_158738689_158781589_158783887_FF	IL12B -30/32	IL12B -29/31	4.8	0.143
PVRL1_11_119599998_119609544_119620830_119624585_FR	PVRL1-14/16	PVRL1-13/15	4.8	0.147
PIK3R3_1_46633134_46639474_46678880_46685388_FR	PIK3R3-18/20	PIK3R3-17/19	2.667	0.426
CD6_11_60744556_60751199_60768894_60771404_RR	CD6-22/24	CD6-21/23	2.667	0.443

Table 40

PCR Probe	GeneLocus	Responder				Non-Responder				Array Probe	Array
		1370 (BL)	1372 (BL)	1393 (BL)	1414 (BL)	1482 (BL)	1426 (BL)	1458 (BL)	1440 (BL)		
IL15-69/71	IL15	1	1	1	1	0	0	1	0	IL15_4_142530356_142539177_142656375_142659066_RF	R
STAT5B-73/75	STAT5B	1	1	1	1	0	0	0	1	STAT5B_17_40403935_40406459_40464294_40468456_FR	R
HLA-DQB1-85/87	HLA-DQB1	1	1	0	1	0	0	0	0	HLA-DQB1_6_32607972_32614493_32630138_32632737_RR	R
MYD88-9/11	MYD88	1	1	1	1	1	0	0	0	MYD88_3_38139864_38141788_38192489_38194027_RR	NR
IL12B-29/31	IL12B	1	0	0	0	1	1	1	1	IL12B_5_158737480_158738689_158781589_158783887_FF	NR
PVRL1-13/15	PVRL1	0	0	1	0	1	1	1	1	PVRL1_11_119599998_119609544_119620830_119624585_FR	NR

Table 41. Top ALS PCR Markers

No	PCR Marker	Corresponding Array Probe	Gene	GLMNET	GLMNET_1	FP	Coef	S.E.	Wald	Pr(>|Z|)
1	ALS.61.63_8	7_80060926_80068170_80299255_80301429_RF	CD36	0.257668	0.272798	0.003	-1.779	0.803	-2.2	0.027
2	NEALS.213.215_8	6_149533510_149536508_149623404_149626512_RF	TAB2	0.237181	0.271083	0.098	-0.857	0.935	-0.9	0.36
3	NEALS.101.103_32	12_54983093_54985391_55002281_55007763_RR	GLYCAM1	0.237255	0.261601	0.213	-0.958	0.943	-1	0.31
4	NEALS.249.251_4	17_73313347_73315473_73407153_73409693_FR	GRB2	0.162296	0.180288	0.055	-0.811	0.912	-0.9	0.374
5	NEALS.45.47_8	6_112058283_112061400_112189648_112191961_RR	FYN	0.148914	0.170383	0.276	-2.087	0.931	-2.2	0.025
6	ALS.49.51_4	1_198660142_198665086_198737979_198744955_RR	PTPRC	0.150202	0.16467	0.027	-1.706	1.423	-1.2	0.231
7	NEALS.65.67_8	1_172053648_172060321_172083100_172087823_RR	DNM3	0.114247	0.131721	0.142	-2.023	0.915	-2.2	0.027
8	NEALS.97.99_16	8_42121759_42128721_42138740_42142593_FR	IKBKB	0.082939	0.099489	0.117	-1.395	1.32	-1.1	0.291
9	DNM3.5.7_16	1_171936106_171939290_171988822_171992948_RF	DNM3	0.062886	0.07767	0.185	-0.609	1.09	-0.6	0.576
10	CLIC4 1.3_1	1_25106841_25109990_25142389_25144224_RF	CLIC4	0.272660	0.1432879	1	0.7161	1.243	0.58	0.565
11	NEALS.5.7_64	1_161590754_161594100_161627152_161631654_RR	FCGR2B;FCGR3A_1	0						
12	NEALS.57.59_1	10_6474855_6481197_6530169_6531558_FR	PRKCQ_10	0.043413						
13	ALS.21.23_32	7_55089963_55093430_55294211_55302386_RF	EGFR_7	0						

Table 42a Primer Sequences of top PCR markers

No	PCR Marker	PCR Primer 1 Sequence	PCR Primer 2 Sequence
1	ALS.61.63_8	GGAACCTCGCTGTCCATAAAC	TCTGTATGCAAGTCCTGATGTTTC
2	NEALS.213.215_8	GGTAGGAGTGTGCCTTATTAAC	GAGGCTGTTAGGCATTCTAAG
3	NEALS.101.103_32	GAAACCAACCCTATCTGTAAAC	AAAGAAAGGAGGCTGTGG
4	NEALS.249.251_4	GCTCTGGACTGCCTTTAAC	AAGTCAGACTCCTCTTCTCTAC
5	NEALS.45.47_8	GTGAAACTAAGCCCTCAACC	TACCCTCCTTCCATTCAGAC
6	ALS.49.51_4	GCTACAGAGGTGAAGGAGATC	AAGTCTGGAGCTGGGCAAAG
7	NEALS.65.67_8	GAAACAGCATTCTTGCCAAC	GCTTCATGAGAGAGTGAGAAC
8	NEALS.97.99_16	AAAGAGAACAGGGTGTAACG	GAGCCGGGAATAAACGAC
9	DNM3.5.7_16	AGGTCTAGGGTTCAGGGCTC	GGGTTCATTTGACTGGACTGG
10	CLIC4 1.3_1	GCCAGTGTGACAAGATTGCC	GACATCAGTGGAGGGAGGAAC
11	NEALS.5.7_64	ATGCCTGCAACTTAAGGAC	GAGGACAAAGAGATAGCTTACTG
12	NEALS.57.59_1	CTGTCTAGAGTCCAGATCTTTC	AAACTACAGGTGAGGGTTG
13	ALS.21.23_32	TGACTTGTCCACCTTCACCC	TACGGCAGTGTGGGTCTAAC

Table 42b ALS Probes - EpiSwitch™ markers to stratify ALS vs. healthy controls

Probe	Probe sequence 60 mer
7_80060926_80068170_80299255_80301429_RF	AAATACAATTGAAATAAAAATAATCTTGTCGAAGCAAGGGCTTCCAGGTCATAGGTGGAT
6_149533510_149536508_149623404_149626512_RF	TGTTACTGGGCTCACCACAAGCTTAAAATCGAACGCTGCCAGCATTAGAACCTATTTGTT
17_73313347_73315473_73407153_73409693_FR	AAAAAGGCACTATGAAAAAACAACATGCTCGAACTCCTGACCTCAGATGATCCACACACC
1_198660142_198665086_198737979_198744955_RR	CAAACAAGAATAAAGAGTAGAGGGTGTTTCGAGAATCTTCAACTTTTTGTATCTTCTATT
1_171936106_171939290_171988822_171992948_RF	TCTCTTTGGAATGTCAGTTATTCAAATATCGAATAGCTCCTATTGTTATGGAGTGTAGCA
1_25106841_25109990_25142389_25144224_RF	TATCTCAGCTTTTGGCCTGTCTCAGCTTTCGACATAGTAGGTACTTGGTAAACATTTGTT

Table 42c ALS Probes - EpiSwitch™ markers to stratify ALS vs. healthy controls: Probes

Probe	Probe Location					4 kb Sequence Location				
	Chr	Start1	End1	Start2	End2	Chr	Start1	End1	Start2	End2
7_80060926_80068170_80299255_80301429_RF	7	80060926	80060955	80301398	80301429	7	80060926	80064925	80297430	80301429
6_149533510_149536508_149623404_149626512_RF	6	149533510	149533539	149626481	149626512	6	149533510	149537509	149622513	149626512
17_73313347_73315473_73407153_73409693_FR	17	73315444	73315473	73407154	73407183	17	73311474	73315473	73407154	73411153
1_198660142_198665086_198737979_198744955_RR	1	198660143	198660172	198737980	198738009	1	198660143	198664142	198737980	198741979
1_171936106_171939290_171988822_171992948_RF	1	171936106	171936135	171992917	171992948	1	171936106	171940105	171988949	171992948
1_25106841_25109990_25142389_25144224_RF	1	25106841	25106870	25144195	25144224	1	25106841	25110840	25140225	25144224

Table 42d

PCR Marker	Probe	GeneName	HyperG_Stats	P.Value	FC
ALS.61.63_8	7_80060926_80068170_80299255_80301429_RF	CD36	0.755369	0.00012	1.311151
NEALS.213.215_8	6_149533510_149536508_149623404_149626512_RF	TAB2	0.955552	0.00568	0.915476
NEALS.101.103_3	12_54983093_54985391_55002281_55007763_RR	GLYCAM1	0.058173	0.000625	0.765425
NEALS.249.251_4	17_73313347_73315473_73407153_73409693_FR	GRB2	0.979786	0.071514	0.946013
NEALS.45.47_8	6_112058283_112061400_112189648_112191961_RR	FYN	0.013161	0.000281	0.71137
ALS.49.51_4	1_198660142_198665086_198737979_198744955_RR	PTPRC	0.015074	0.000819	1.265845
NEALS.65.67_8	1_172053648_172060321_172083100_172087823_RR	DNM3	0.000673	0.000692	0.710146
NEALS.97.99_16	8_42121759_42128721_42138740_42142593_FR	IKBKB	0.046252	0.000338	0.752995
DNM3.5.7_16	1_171936106_171939290_171988822_171992948_RF	DNM3	0.000673	0.002108	1.354848
CLIC4 1.3_1	1_25106841_25109990_25142389_25144224_RF	CLIC4	0.616734	0.012406	1.389081

Table 43

Probe	GeneLocus	adj.P.Val	FC_1	LS	R/NR
IL15_4_142530356_142539177_142656375_142659066_RF	IL15	0.012659	1.789825	1	Responder
MYD88_3_38139864_38141788_38192489_38194027_RR	MYD88	0.044194	-1.43471	-1	BL NR
HLA-DQB1_6_32607972_32614493_32630138_32632737_RR	HLA-DQB1	0.047009	2.089555	1	BL R
IL12B_5_158737480_158738689_158781589_158783887_FF	IL12B	0.012659	-1.39097	-1	BL NR
PVRL1_11_119599998_119609544_119620830_119624585_FR	PVRL1	0.008848	-1.43039	-1	BL NR
PIK3R3_1_46633134_46639474_46678880_46685388_RF	PIK3R3	0.043255	1.197964	1	BL R
CD6_11_60744556_60751199_60768894_60771404_RR	CD6	0.009617	-1.40282	-1	BL NR
STAT5B_17_40403935_40406459_40464294_40468456_FR	STAT5B	0.031193	-1.43489	-1	12W R

Table 44

Responder Versus Non Responder		
Array Interaction	PCR Primer 1 Sequence	PCR Primer 2 Sequence
>IL15_4_142530356_142539177_142656375_142659066_RF	TGAGTAACACAAAGCATCTG	AGTGACTGGCTATGTTCC
>MYD88_3_38139864_38141788_38192489_38194027_RR	CTGGTGATTTGTGTGACTTTG	AGGGAAGATGTGGAGGAG
>HLA-DQB1_6_32607972_32614493_32630138_32632737_RR	GTACGACTCCAGCCAAATG	GCTGTCTGTTACTAGATTGCAC
>IL12B_5_158737480_158738689_158781589_158783887_FF	ACCTTGCAAGAAGCACAG	ATGATACTTCCCAACTGACAC
>PVRL1_11_119599998_119609544_119620830_119624585_FR	AGGAGCATCCATATCAAGTG	CTGCCATGTCTGACTATCC
>PIK3R3_1_46633134_46639474_46678880_46685388_FR	CAGTGAAGAAGCCATCATCG	GCTTAGAGAAATACACCAGCAG
>CD6_11_60744556_60751199_60768894_60771404_RR	ATGGGCAGCATTTCTCAC	AGGGACGATTTATATGACTTGC

Responder Baseline Versus 12WKS		
Array Interaction	PCR Primer 1 Sequence	PCR Primer 2 Sequence
>STAT5B_17_40403935_40406459_40464294_40468456_FR	GTGCTGGTATGTACCTGTAATC	GAGGGTTGAGAAGCATCTTG

Table 45

Probe	GeneLocus	adj.P.Val	FC_1	LS	R/NR
IL15_4_142530356_142539177_142656375_142659066_RF	IL15	0.012658979	1.78982	1	R

Probe sequence
60 mer
TGTAAACTGTAATATCAAAAATTCAAAATCGAAGAGTTGATTTACTTATTAACATTAGAA

Probe Location					4 kb Sequence Location				
Chr	Start1	End1	Start2	End2	Chr	Start1	End1	Start2	End2
4	142530357	142530386	142659035	142659066	4	142530357	142534356	142655067	142659066

Table 46a

Probe	GeneName	Probe_Count_Total	Probe_Count_Sig	HyperG_Stats	FDR_HyperG	Percent_Sig	logFC
MYD88_3_38139864_38141788_38192489_38194027_RR	MYD88	18	10	0.009423624	0.173813506	55.56	-0.520757975
HLA-DQB1_6_32607972_32614493_32630138_32632737_RR	HLA-DQB1	12	8	0.004570722	0.126456634	66.67	1.063195633
IL12B_5_158737480_158738689_158781589_158783887_FF	IL12B	11	7	0.011584493	0.182699883	63.64	-0.476087861
PVRL1_11_119599998_119609544_119620830_119624585_FR	PVRL1	95	44	3.65E-05	0.003027108	46.32	-0.516406696
PIK3R3_1_46633134_46639474_46678880_46685388_RF	PIK3R3	55	24	0.005395839	0.137801433	43.64	0.260584827
CD6_11_60744556_60751199_60768894_60771404_RR	CD6	62	33	9.60E-06	0.001593482	53.23	-0.488334118
STAT5B_17_40403935_40406459_40464294_40468456_FR	STAT5B	20	9	0.025471082	0.255659576	45	-0.5209394

Table 46b.									
Probe	**AveExpr**	**t**	**P.Value**	**adj.P. Val**	**B**	**FC**	**FC_1**	**LS**	**Loop detected**
MYD88_3_38139864_38141788_38192489_38194027_RR	-0.52076	-3.83130	0.006090	0.04419	-2.25260	0.69701	-1.43471	-1	BL NR
HLA-DQB1_6_32607972_32614493_32630138_32632737_RR	1.063196	3.72400	0.007027	0.04701	-2.40073	2.08955	2.08955	1	BL R
IL12B_5_158737480_158738689_158781589_158783887_FF	-0.47609	-6.11480	0.000430	0.01266	0.48298	0.71892	-1.391-	-1	BL NR
PVRL1_11_119599998_119609544_119620830_119624585_FR	-0.51647	-8.79527	4.14E-05	0.00885	2.80036	0.69911	-1.43039	-1	BL NR
PIK3R3_1_46633134_46639474_46678880_46685388_RF	0.26059	3.86924	0.005792	0.04325	-2.20062	1.19796	1.19796	1	BL R
CD6_11_60744556_60751199_60768894_60771404_RR	-0.48834	-8.04736	7.46E-05	0.00962	2.2332	0.71285	-1.40282	-1	BL NR
STAT5B_17_40403935_40406459_40464294_40468456_FR	-0.52094	-4.11268	0.004912	0.03119	-1.91703	0.69692	-1.43489	-1	12W R

Table 46c

Probes	60 mer
MYD88_3_38139864_38141788_38192489_38194027_RR	ACTTTTATAGTGAAAAGTGCCATTTGAGTCGACTGTGATTGAATGTAAAAGGTTTTAAAT
HLA-DQB1_6_32607972_32614493_32630138_32632737_RR	TACTGTAGTAAGTTCTCTGAGGAGGATATCGAAGTCTTGGATTAAGGTTCATTCAACAAA
IL12B_5_158737480_158738689_158781589_158783887_FF	TCCATTTGAAGGATGAGAAAACTGAGGCTCGAGGCTTAGAAAGTTTCATTTGGTTGCTCA
PVRL1_11_119599998_119609544_119620830_119624585_FR	TTTTAAACCCAGGTGCACACACAAGAGCTCGAAGCAGGAATCCTGGTTCTGTTCCCAGGC
PIK3R3_1_46633134_46639474_46678880_46685388_RF	CCACTCCCCCAGGCTTACCTGCGAGCCATCGAGGTGGGCCTGGGTTCTCGTGGAGGGAGA
CD6_11_60744556_60751199_60768894_60771404_RR	TCACTCATTCTAGATCCCTCTGTAAAGTTCGAACTCTGGACCTTGTGATCCACCCACCTT
STAT5B_17_40403935_40406459_40464294_40468456_FR	TTCCATAGATTACTTTTCAAATCATCCTTCGAAGCTGGCGGCTGAGGGCCCGGCGCCAAG

Table 46d

Probes	Chr	Start1	End1	Start2	End2	Chr	Start1	End1	Start2	End2
MYD88_3_38139864_38141788_38192489_38194027_RR	3	38139865	38139894	38192490	38192519	3	38139865	38143864	38192490	38196489
HLA_DQB1_6_32607972_32614493_32630138_32632737_RR	6	32607973	32608002	32630139	32630168	6	32607973	32611972	32630139	32634138
IL12B_5_158737480_158738689_158781589_158783887_FF	5	1.59E+08	1.59E+08	1.59E+08	1.59E+08	5	1.59E+08	1.59E+08	1.59E+08	1.59E+08
PVRL1_11_119599998_119609544_119620830_119624585_FR	11	1.2E+08	1.2E+08	1.2E+08	1.2E+08	11	1.2E+08	1.2E+08	1.2E+08	1.2E+08
PIK3R3_1_46633134_46639474_46678880_46685388_RF	1	46633135	46633164	46685359	46685388	1	46633135	46637134	46681389	46685388
CD6_11_60744556_60751199_60768894_60771404_RR	11	60744557	60744586	60768895	60768924	11	60744557	60748556	60768895	60772894
STAT5B_17_40403935_40406459_40464294_40468456_FR	17	40406430	40406459	40464295	40464324	17	40402460	40406459	40464295	40468294

Table 47

Table 47. Patients	IL15-69/71-1	PVRL1-13/15_2	IL12B-29/31_1	STAT5B-317/75-2	STAT5B-73/75_2	HLA-DQB1-85/87_1	MYD88-9/11_1
Benign_Thryoid_1	0	1	1	0	0	0	0
Benign_Thryoid_2	0	1	0	1	1	0	1
Benign_Thryoid_3	0	1	0	0	1	1	0
Benign_Thryoid_4	0	1	0	0	0	0	0
Benign_Thryoid_5	1	1	0	0	1	0	0
Malignant_Thryoid_1	0	1	1	1	0	0	0
Malignant_Thryoid_2	1	1	1	0	1	0	0
Malignant_Thryoid_3	1	1	1	0	0	0	1
Malignant_Thryoid_4	0	0	1	0	1	0	0
Malignant_Thryoid_5	0	0	1	0	0	0	0
DLBCL_ABC_1	0	1	1	0	1	0	0

Table 47. Patients	IL15-69/71-1	PVRL1-13/15_2	IL12B-29/31_1	STAT5B-317/75-2	STAT5B-73/75_2	HLA-DQB1-85/87_1	MYD88-9/11_1
DLBCL_ABC_2	0	1	1	0	0	0	1
DLBCL_ABC_3	1	1	1	0	1	0	0
DLBCL_ABC_4	1	1	1	1	0	0	0
DLBCL_ABC_5	1	1	1	0	0	0	0
DLBCL_ABC_6	1	1	1	0	1	1	1
DLBCL_ABC_7	0	1	1	0	0	0	1
DLBCL_ABC_8	0	0	1	1	0	0	1
DLBCL_ABC_9	1	1	1	0	1	0	1
DLBCL_ABC_10	1	1	0	1	0	0	0
DLBCL_GBC_1	1	1	1	0	1	0	1
DLBCL_GBC_2	1	1	1	1	1	1	1
DLBCL_GBC_3	1	1	1	0	1	0	0
DLBCL_GBC_4	1	1	0	0	1	0	1
DLBCL_GBC_5	0	1	0	0	0	0	0
DLBCL_GBC_6	1	1	1	0	0	0	0
DLBCL_GBC_7	1	1	1	0	0	1	0
DLBCL_GBC_8	1	1	1	0	1	1	0
DLBCL_GBC_9	0	1	1	0	0	0	0
DLBCL_GBC_10	1	1	1	0	0	0	1
HCC_HEPB_1	0	0	1	1	1	0	1
HCC_HEPB_2	0	1	0	0	0	0	1
HCC_HEPB_3	0	0	1	0	0	0	0
HCC_HEPC_1	1	1	1	1	1	0	0
HCC_HEPC_2	1	1	1	1	1	0	1
HCC_HEPC_3	0	1	0	0	0	0	0
HCC_1	0	0	0	1	0	0	0
HCC_2	1	1	1	1	1	0	1
HCC_3	0	1	1	1	0	0	0

Table 47. Patients	IL15-69/71-1	PVRL1-13/15_2	IL12B-29/31_1	STAT5B-317/75-2	STAT5B-73/75_2	HLA-DQB1-85/87_1	MYD88-9/11_1
HEPB+R_1	0	1	1	1	0	0	1
Pca_Class3_1	0	0	1	0	0	0	1
Pca_Class3_2	0	1	1	0	1	0	1
Pca_Class3_3	0	1	0	1	1	0	1
Pca_Class3_4	1	1	1	0	0	1	1
Pca_Class2_1	1	1	1	0	1	0	1
Pca_Class2_2	0	1	0	0	0	0	1
Pca_Class2_3	1	1	1	0	0	0	1
Pca_Class1_1	0	1	1	0	1	1	0
Pca_Class1_2	1	1	1	1	1	0	1
Pca_Class1_3	1	1	1	0	1	1	1
BrCa_Stg4_1	1	0	1	0	0	0	1
BrCa_Stg4_2	1	1	1	1	0	0	0
BrCa_Stg4_3	1	1	1	0	0	0	0
BrCa_Stg3B_1	0	1	1	0	0	0	0
BrCa_Stg3B_2	1	1	1	0	1	0	1
BrCa_Stg2A_1	1	1	1	1	1	0	1
BrCa_Stg2B_1	1	1	1	1	0	0	0
BrCa_Stg1A_1	0	0	1	0	0	0	0
BrCa_Stg1A_2	0	1	1	1	1	0	0
BrCa_Stg1_1	0	1	1	0	0	0	0
PD_1_R_Melanoma	1	0	0	0	1	1	1
PD_1_NR_Melanoma	0	1	1	1	0	0	0

Table 48. P-values

	Condition	No	Top range	Mid range	Bottom	Top range	Mid range	Bottom	Range boundaries
		All/gp	P-value			Adj-P			
Table 18	ALS	61/20	0.0058-0.0013	0.0013-0.0004	0.0004 - 0.00011	0.067-0.046	0.046-0.045	0.045-0.044	0.0013; 0.0004
Table 19	preT2 DM	50/17	0.0083-0.0013	0.0013-0.0004	0.0004-0.00006	0.008	0.055-0.046	0.046-0.036	0.0013; 0.0004
Table 20	T2DM	50/17	0.011-0.0043	0.0043-0.001	0.001-0.00006	0.0986-0.087	0.087-0.085141	0.085141	0.0043; 0.001
Table 21	T1DM	50/17	0.0059-0.0006	0.00039-0.0001	0.0001-2.7x10-6	0.0641-0.0232	0.0199-0.01084	0.0097-0.0025	0.0005; 0.0001
Table 22	UC	50/17	0.0034-0.00040	0.00038-0.0001	9.9x10-5–8x10-6	0.026-0.012	0.0118-0.009	0.0087-0.0048	0.0004; 0.00001
Table 23	SLE	50/17	0.0077-0.0031	0.0028-0.001	0.001-6x10-5	0.049-0.038	0.0378-0.03651	0.036258	0.003; 0.001
Table 24	MSRR	50/17	0.0075-0.00306	0.0029-0.00082	0.000567-2x10-5	0.26-0.228	0.213-0.100	0.985-0.0165	0.003;0.0006
Table 25	IFN-B R	50/17	0.0061-0.00068	0.0005-2.6x10-5	1.9x10-5-2x10-7	0.0598-0.0214	0.0119-0.0051	0.0042- 0.0013	0.0005;0.00002
Table 6	RA-MTX	50/17	0.021-0.0103(17)	0.0096-0.0024(35)	0.0018-0.00011				0.01; 0.002
Table 36e	antiPD1NR	25/8	0.0061-0.0004	0.00018-0.000107	7.46x10-5 - 2x10-5				0.0002; 0.0001 up to 0.0004; 0.0001
Table 27	ALS	97/33	0.298-0.21 (28)	0.19-0.102 (66)	0.097-9.7x10-5				0.2; 0.1
Table 28	preT2 DM	39/13	0.204-0.059 (13)	0.04-0.0097 (26)	0.00578-3x10-5				0.04; 0.006
Table 29	T2 DM	89/33	0.28-0.14 (27)	0.126-0.017 (66)	0.0147-1.5x10-5				0.13;0.015
Table 30	T1 DM	70/23	0.26-0.144 (22)	0.138-0.052 (47)	0.038-0.0007				0.14; 0.04
Table 31	UC	75/25	0.273-0.183 (22)	0.167-0.079(48)	0.065-0.0001				0.17; 0.07
Table 32	SLE	73/24	0.2965-0.17 (23)	0.163-0.083 (49)	0.079-0.0002				0.17, 0.08
Table 33	MSRR	58/19	0.28-0.1807(19)	0.165-0.079 (38)	0.0698-1.3x10-5				0.18, 0.07
Table 34	IFN-B R	89/30	0.29-0.203 (29)	0.187-0.064(59)	0.055-5x10-5				0.2; 0.06
Table 35	NeurFib	63/21	0.289-0.171 (20)	0.163-0.065 (43)	0.057-7x10-5				0.17; 0.06

Table 49 Data for additional anti-PD1 probe

Probe				Sequence					
STAT5B_17_40388884_40391941_40464294_40468456_RR				TACAGTCTTTGTAGATGCAGAGTAGCGTTCGAAGCTGGCGGCTGAGGGCCCGGCGCCAAG					
logFC	AveExpr	t	P.Value	adj.P.Val	B	FC	FC_1	LS	Chi_Square
0.5443091	0.5443091	6.64801232	0.00025533	0.01131185	1.01165877	1.45832179	1.45832179	1	0.138
PCR Probe	STAT5B-317/75-2		Gene Locus	STAT5B					
Primer	Primer Sequence								
STAT5B-317	CTGCCCGTAAATAAGCAGAAG								
STAT5B-75	GAGGGTTGAGAAGCATCTTG								

CLAIMS

1. A companion diagnostic assay method which determines which subgroup a person is in for a characteristic relevant to treatment and/or prophylaxis which method comprises:

(i) detecting the presence or absence of at least 10 epigenetic chromosome interactions represented by the probes disclosed in Table 19 to identify a pre-diabetic state, or

(ii) detecting the presence or absence of at least 10 epigenetic chromosome interactions represented by the probes disclosed in Table 20 to identify predisposition to type-2 diabetes, or

(iii) detecting the presence or absence of at least 10 epigenetic chromosome interactions represented by the probes disclosed in Table 21 to identify predisposition to type-1 diabetes.

2. A method according to claim 1 wherein the presence or absence of 20 to 300 epigenetic chromosome interactions is detected.

3. A method according to claim 2 wherein the presence or absence of 50 to 100 epigenetic chromosome interactions is detected.