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(54) Title: METHODS, KITS AND SYSTEMS FOR DETERMINING THE ER STATUS OF CANCER AND METHODS FOR
TREATING CANCER BASED ON SAME

(57) Abstract: The present disclosure includes, among other things, methods, kits, and systems for determining ER status of cancer,
e.g., a breast cancer. In various embodiments, the present disclosure relates to the use of one or more histone modifications, chromatin
accessibility, binding of one or more transcription factors, and/or DNA methylation that are characteristic of ER status of cancer.
In some embodiments, differential modifications and/or differential accessibility are detected and quantified at one or more genomic
loci of a biological sample, e.g., in cell-free DNA (cfDNA) from a liquid biopsy sample obtained or derived from a subject with cancer.
In various embodiments a determined ER status is useful, e.g., in selecting treatment for and/or treating a cancer, e.g., a breast cancer.



METHODS, KITS AND SYSTEMS FOR DETERMINING THE ER STATUS OF CANCER AND METHODS FOR TREATING CANCER BASED ON SAME

Cross-Reference to Related Applications

[0001] This application claims the benefit of U.S. Provisional Application No. 63/590,158, filed on 13 October 2023; and U.S. Provisional Application No. 63/650,860, filed on 22 May 2024; the entire contents of each application is incorporated herein in its entirety by this reference

BACKGROUND

[0002] It has long been recognized that some human breast cancers are hormone dependent. Estrogen regulates the differentiation and proliferation of breast epithelial cells and interacts with the estrogen receptor (ER) in the nucleus. Prolonged exposure of estrogen is an important risk factor for cancer. Progesterone receptor (PR) expression in normal breast epithelium is regulated by ER (Jensen, Cancer (1980) 46:2759-2761). Presence of ER, PR and human epidermal growth factor receptor-2 (HER2) status in invasive breast carcinoma is now routinely estimated as these markers are considered to be important prognostic factors. ER and PR status has been used for many years to determine a patient's suitability for treatment with endocrine therapy (*e.g.*, tamoxifen).

[0003] To determine if a cancer is ER-positive, medical practitioners currently order testing that is conducted on a tissue sample using immunohistochemistry (IHC). Samples are reviewed by a pathologist and typically reported as (a) the word positive or negative, (b) a percentage that tells you how many cells out of 100 stained positive for hormone receptors, *i.e.*, a number between 0% (none have receptors) and 100% (all have receptors), and/or (c) an Allred score between 0 and 8. The Allred scoring system looks at what percentage of cells test positive for hormone receptors, along with how well the receptors show up after staining, called intensity (Allred et al., Breast Cancer Res (2004) 6:240-245). This information is then combined to score the sample on a scale from 0 to 8 where, the higher the score, the more receptors were found and the easier they were to see in the sample.

[0004] ER-positive cancers can be treated with ER-targeted agents that lower estrogen levels or block estrogen receptors. Conversely, treatment with ER-targeted agents is not helpful

for ER-negative cancers. These cancers may instead be treated with one or more of surgery and/or radiation, HER2-targeted therapy (if HER2-positive), chemotherapy and immunotherapy.

[0005] Current methods are invasive and rely on a single tissue biopsy to characterize the ER status in metastatic breast cancer. Such methods focus only on a small region at a single tumor site at a given time and therefore do not accurately capture tumor heterogeneity or receptor evolution and therefore only partially characterize the relevant patient population. There remains a need in the art for more comprehensive and precise diagnostic methods for determining ER status including methods that are independent of IHC testing. Improved diagnostic methods would also better support future clinical trials that seek to identify subpopulations of patients that respond to ER-targeted agents. They would also expand our understanding of the underlying biology of ER-positive cancer and help identify new treatments.

SUMMARY

[0006] The present disclosure is based, at least in part, on the demonstration that the ER status of a cancer in a subject can be determined by detecting and quantifying the presence of histone modifications and/or DNA methylation at one or more genomic loci in cell-free DNA (cfDNA) from a liquid biopsy sample, *e.g.*, a plasma sample obtained or derived from the subject. The present disclosure also encompasses methods where chromatin accessibility and/or binding of one or more transcription factors are detected at the one or more genomic loci instead of (or in addition to) histone modifications and/or DNA methylation. The present disclosure is also based, at least in part, on the demonstration that genomic loci that are differentially modified based on different types of histone modifications (*e.g.*, histone methylation marks such as H3K4me3 and histone acetylation marks such as H3K27ac) and/or DNA methylation can be combined into multimodal classifiers to determine ER status. These new monomodal and multimodal classifiers provide minimally invasive ways of determining ER status that are more accurate, objective, and comprehensive than the current tissue-based approaches. No liquid biopsy platform to date has been able to provide actionable resolution on a transcriptionally regulated phenotype relevant for therapy such as ER status.

[0007] The present disclosure includes, among other things, technologies for the determination of ER status and for the detection, monitoring, and/or treatment of cancer (including, *e.g.*, breast, ovarian, or endometrial cancer) based on ER status. In various

embodiments, the present disclosure relates to the measurement of histone modifications in a sample obtained or derived from a subject to detect and/or treat cancer (including, *e.g.*, breast, ovarian, or endometrial cancer) based on ER status. The present disclosure includes, among other things, histone modification measurements in cell-free DNA (cfDNA) that are characteristic of cancer, and which in various embodiments are useful, *e.g.*, for detecting, monitoring, selecting treatment for, and/or treating cancer (including, *e.g.*, breast, ovarian, or endometrial cancer) based on ER status. The present disclosure includes, among other things, histone modification measurements in cfDNA that are characteristic of ER-positive and ER-negative cancers, which in various embodiments are useful, *e.g.*, in detecting, monitoring, selecting treatment for, and/or treating an ER-positive and ER-negative cancers. In some embodiments, histone modification measurements in cfDNA can be used to detect or determine resistance of a cancer (*e.g.*, breast, ovarian, or endometrial cancer) to a therapy or transformation of a cancer from one subtype to another. In various embodiments, the present disclosure includes exemplary genomic loci that are differentially modified in ER-positive vs. ER-negative cancer, *e.g.*, breast, ovarian, or endometrial cancer. In various embodiments, genomic loci differentially modified in cfDNA are or include one or more enhancers. In various embodiments, genomic loci differentially modified in cfDNA are or include one or more promoters.

[0008] In various embodiments, a genomic locus is differentially modified if it is characterized by increased or decreased histone modification as compared to a reference (*e.g.*, a sample from an ER-negative or healthy subject). Increased or decreased histone modification can be or include, *e.g.*, increased or decreased histone methylation (hypermethylation or hypomethylation, respectively) of one or more particular methylation marks, or a combination thereof; increased or decreased pan-methylation; increased or decreased histone acetylation (hyperacetylation or hypoacetylation, respectively) of one or more particular acetylation marks, or a combination thereof; and/or increased or decreased pan-acetylation (*e.g.*, pan-H3 acetylation). In various embodiments, histone methylation can be or include histone methylation marks selected from H3K4me1, H3K4me2, H3K4me3, or a combination thereof. In various embodiments, histone methylation can be or include H3K4me3. In various embodiments, histone acetylation can be or include histone acetylation marks selected from H3K9ac, H3K14ac, H3K18ac, H3K23ac, H3K27ac, or a combination thereof. In various embodiments, histone acetylation can be or include H3K27ac.

[0009] In various embodiments, the present disclosure relates to the measurement of DNA methylation in a sample obtained or derived from a subject to detect and/or treat cancer (including, *e.g.*, breast, ovarian, or endometrial cancer) based on ER status. The present disclosure includes, among other things, DNA methylation measurements in cell-free DNA (cfDNA) that are characteristic of cancer, and which in various embodiments are useful, *e.g.*, for detecting, monitoring, selecting treatment for, and/or treating cancer (including, *e.g.*, breast, ovarian, or endometrial cancer) based on ER status. In some embodiments, DNA methylation measurements in cfDNA can be used to detect or determine resistance of a cancer (*e.g.*, breast, ovarian, or endometrial cancer) to a therapy or transformation of a cancer from one subtype to another. In various embodiments, the present disclosure includes exemplary genomic loci that are differentially DNA methylated in ER-positive vs. ER-negative cancer, *e.g.*, breast, ovarian, or endometrial cancer. In various embodiments, a genomic locus is differentially modified if it is characterized by increased or decreased DNA methylation as compared to a reference (*e.g.*, a sample from an ER-negative or healthy subject). In various embodiments, genomic loci differentially modified in cfDNA are or include one or more enhancers. In various embodiments, genomic loci differentially modified in cfDNA are or include one or more promoters.

[0010] The present disclosure further relates, in various embodiments, to the measurement of chromatin accessibility in cell-free DNA (cfDNA) to determine ER status. The present disclosure includes, among other things, chromatin accessibility measurements in cfDNA that are characteristic of ER-positive cancers, which in various embodiments are useful, *e.g.*, in detecting, monitoring, selecting treatment for, and/or treating an ER-positive cancer. In some embodiments, chromatin accessibility measurements in cfDNA can be used to detect or determine resistance of a cancer (*e.g.*, breast, ovarian, or endometrial cancer) to a therapy or transformation of a cancer from one subtype to another. In various embodiments, the present disclosure includes genomic loci that are differentially accessible in ER-positive vs. ER-negative cancers. In various embodiments, genomic loci differentially accessible in cfDNA are or include one or more enhancers. In various embodiments, genomic loci differentially accessible in cfDNA are or include one or more promoters.

[0011] In various embodiments, without wishing to be bound by any particular scientific theory, histone methylation (*e.g.*, H3K4me3) corresponds and/or is correlated with chromatin accessibility. In various embodiments, without wishing to be bound by any particular scientific

theory, histone acetylation (*e.g.*, H3K27ac) corresponds and/or is correlated with chromatin accessibility. In various embodiments, without wishing to be bound by any particular scientific theory, DNA methylation corresponds and/or is correlated with chromatin accessibility.

[0012] In various embodiments, a genomic locus is differentially accessible if it is characterized by increased or decreased chromatin accessibility as compared to a reference (*e.g.*, a sample from an ER-negative or healthy subject). Increased or decreased histone modification can be or include, *e.g.*, increased or decreased accessibility as determined by various chromatin accessibility assays known in the art.

[0013] The present disclosure further relates, in various embodiments, to the measurement of transcription factor binding in cell-free DNA (cfDNA) to determine ER status. The present disclosure includes, among other things, transcription factor binding measurements in cfDNA that are characteristic of ER-positive cancers, which in various embodiments are useful, *e.g.*, in detecting, monitoring, selecting treatment for, and/or treating an ER-positive cancer. In some embodiments, transcription factor binding measurements in cfDNA can be used to detect or determine resistance of a cancer (*e.g.*, breast, ovarian, or endometrial cancer) to a therapy or transformation of a cancer from one subtype to another. In various embodiments, the present disclosure includes genomic loci that are differentially bound by transcription factors in ER-positive vs. ER-negative cancers. In various embodiments, genomic loci that are differentially bound by transcription factors in cfDNA are or include one or more enhancers. In various embodiments, genomic loci that are differentially bound by transcription factors in cfDNA are or include one or more promoters.

[0014] In various embodiments, without wishing to be bound by any particular scientific theory, histone methylation (*e.g.*, H3K4me3) corresponds and/or is correlated with transcription factor binding. In various embodiments, without wishing to be bound by any particular scientific theory, histone acetylation (*e.g.*, H3K27ac) corresponds and/or is correlated with transcription factor binding. In various embodiments, without wishing to be bound by any particular scientific theory, DNA methylation corresponds and/or is correlated with transcription factor binding.

[0015] In various embodiments, a genomic locus is differentially bound by transcription factors if it is characterized by increased or decreased transcription factor binding as compared to a reference (*e.g.*, a sample from an ER-negative or healthy subject). Increased or decreased

transcription factor binding can be or include, *e.g.*, increased or decreased transcription factor binding as determined by various transcription factor binding assays known in the art.

[0016] In one aspect, the present disclosure provides a method of determining the ER status of a cancer in a subject, the method comprising: quantifying, at one or more genomic loci in a biological sample, optionally in cell-free DNA (cfDNA) from a liquid biopsy sample, obtained or derived from the subject: (i) one or more histone modifications, (ii) chromatin accessibility, (iii) binding of one or more transcription factors, and/or (iv) DNA methylation.

[0017] In some embodiments, the one or more histone modifications are quantified using a histone modification assay that measures one or more of H3K9ac, H3K14ac, H3K18ac, H3K23ac, H3K27ac, H3K4me1, H3K4me2, H3K4me3, and pan-acetylation. In some embodiments, the histone modification assay detects H3K4me3 modifications. In some embodiments, the histone modification assay detects H3K27ac modifications. In some embodiments, the histone modification assay is selected from ChIP-seq (Chromatin ImmunoPrecipitation sequencing), CUT&RUN (Cleavage Under Targets and Release Using Nuclease) sequencing, and CUT&Tag (Cleavage Under Targets and Tagmentation) sequencing.

[0018] In some embodiments, chromatin accessibility is quantified using a chromatin accessibility assay selected from ATAC-seq (Assay of Transpose Accessible Chromatin sequencing), NOMe-seq (Nucleosome Occupancy and Methylome sequencing), FAIRE-seq (Formaldehyde-Assisted Isolation of Regulatory Elements sequencing), MNase-seq (Micrococcal Nuclease digestion with sequencing), and a DNase hypersensitivity assay.

[0019] In some embodiments, binding of one or more transcription factors is quantified using a transcription factor binding assay that detects binding of one or more of p300, mediator complex, cohesin complex, RNA pol II, FOXA1, ESR1, PR, MYC, EN1, FOXM1, KLF4, AP-2, RARα, or RUNX1. In some embodiments, the transcription factor binding assay is selected from ChIP-seq (Chromatin ImmunoPrecipitation sequencing), CUT&RUN (Cleavage Under Targets and Release Using Nuclease) sequencing, and CUT&Tag (Cleavage Under Targets and Tagmentation) sequencing.

[0020] In some embodiments, DNA methylation is quantified using Bisulfite sequencing (BS-Seq), Whole Genome Bisulfite Sequencing (WGBS), Methylated DNA ImmunoPrecipitation sequencing (MeDIP-seq), or Methyl-CpG-Binding Domain sequencing (MBD-seq).

[0021] In some embodiments, the method comprises quantifying two or more of the following, each at one or more genomic loci in cell-free DNA (cfDNA) from a liquid biopsy sample obtained or derived from the subject: (i) one or more histone modifications, (ii) chromatin accessibility, (iii) transcription factor binding, and/or (iv) DNA methylation. In some embodiments, the method comprises quantifying two or more histone modifications, *e.g.*, quantifying H3K4me3 and H3K27ac modifications. In some embodiments, the method comprises quantifying one or more histone modifications and DNA methylation, *e.g.*, quantifying H3K4me3 and/or H3K27ac modifications and DNA methylation. In some embodiments, the method comprises quantifying H3K4me3 modifications, H3K27ac modifications and DNA methylation.

[0022] In some embodiments, the biological sample is a liquid biopsy sample, *e.g.*, a plasma sample, serum sample, or urine sample.

[0023] In some embodiments, quantification of one or more histone modifications, chromatin accessibility, binding of one or more transcription factors, and/or DNA methylation at the one or more genomic loci as compared to a reference indicates that the subject has an ER-positive cancer.

[0024] In some embodiments, quantification of one or more histone modifications, chromatin accessibility, binding of one or more transcription factors, and/or DNA methylation at the one or more genomic loci as compared to a reference indicates that the subject has an ER-negative cancer.

[0025] In some embodiments, the cancer is breast cancer, ovarian cancer, or endometrial cancer. In some embodiments, the cancer is breast cancer.

[0026] In some embodiments, the reference is a predetermined threshold, a measurement from a liquid biopsy sample, and/or a normalized value, optionally wherein the reference is a measurement from a liquid biopsy sample obtained from a cohort of subjects who have previously been determined to have an ER-negative cancer or to be cancer free.

[0027] In some embodiments, a sample is a liquid biopsy sample comprising cfDNA, and a method comprises:

(a) quantifying H3K4me3 modifications at one or more genomic loci using an assay that comprises enriching for cfDNA comprising one or more H3K4me3 modifications and sequencing the cfDNA enriched for H3K4me3 modifications (*e.g.*, using a cfChIP-seq assay);

(b) quantifying H3K27ac modifications at one or more genomic loci using an assay that comprises enriching for cfDNA comprising one or more H3K27ac modifications and sequencing the cfDNA enriched for H3K27ac modifications (e.g., using a cfChIP-seq assay); and/or;

(c) quantifying methylated DNA using an assay that comprises enriching for methylated cfDNA and sequencing the enriched cfDNA to determine a count of sequences with one or more methylated nucleotides (e.g., using a MBD-seq assay).

[0028] In some embodiments,

[0029] (a) cfDNA comprising H3K4me3 modifications is enriched using a method that comprises incubating a sample with an agent (e.g., an antibody) that binds H3K4me3 modifications;

[0030] (b) cfDNA comprising H3K27ac modifications is enriched using a method that comprises incubating a sample with an agent (e.g., an antibody) that binds H3K27ac modifications; and/or

[0031] (c) methylated cfDNA is enriched using a method that comprises incubating a sample with an agent (e.g., an antibody or a methyl binding domain) that binds methylated DNA.

[0032] In some embodiments, an agent that binds H3K4me3 modifications, an agent that binds H3K27ac modifications, and/or an agent that binds methylated DNA can be attached (e.g., via a covalent or noncovalent bond) to a physical support (e.g., a bead, a magnetic bead, an agarose bead, or a magnetic epoxy bead) prior to incubating with a sample.

[0033] In embodiments where a method comprises incubating a sample with two or more of (a) an agent that binds H3K4 modifications, (b) an agent that binds H3K27ac modifications, and (c) an agent that binds methylated DNA, the sample is incubated with the two or more agents (1) in sequence, or (2) in parallel (e.g., wherein the sample is divided into fractions and each fraction is incubated with a different agent).

[0034] In some embodiments, sequencing is performed using a next generation sequencing method.

[0035] In some embodiments, a method comprises attaching (e.g., ligating) adapters to cfDNA obtained from the subject (e.g., attaching after cfDNA has been enriched for cfDNA

comprising one or more H3K4me3 modifications, cfDNA comprising one or more H3K27ac modifications, and/or methylated cfDNA).

[0036] In some embodiments, a plurality of converted DNA fragments are amplified after attaching adapters to the plurality of DNA fragments.

[0037] In some embodiments, sequence reads are mapped to a reference genome. In some embodiments, non-uniquely mapped and redundant sequence reads are discarded prior to quantifying one or more epigenetic biomarkers. In some embodiments, sequence reads are mapped to a reference genome, and one or more genomic loci correspond to sequence read peaks, wherein a sequence read peak corresponds to a region of the genome that has a higher number of sequence reads than the local background. In some embodiments, peaks in high noise regions are ignored when identifying genomic loci with a higher number of sequence reads than the local background. In some embodiments, peaks in regions likely to be artifactual are removed. In some embodiments, peaks that are less than 50 bp in length are removed. In some embodiments, peaks in regions with high levels of one or more epigenetic markers in white blood cells are removed.

[0038] In some embodiments, quantifying H3K4me3 modifications, H3K27ac modifications, and/or DNA methylation comprises summing the number of sequence reads having at least one nucleotide overlap one or more genomic loci. In some embodiments, sequence reads are adjusted on the basis of sequencing depth (e.g., quantile normalizing sequence reads to a common reference distribution) and/or ChIP quality prior to summing. In some embodiments, sequence counts are normalized to aggregate counts in a given sample across a set of regions (e.g., 10,000 regions) previously determined to have DNase hypersensitivity in most cell types. In some embodiments, an estimate of local background signal is subtracted from the sequence reads at each genomic loci prior to summing.

[0039] In some embodiments, a method comprises comparing a measure of one or more epigenetic biomarkers to a reference. In some embodiments, a reference is a predetermined threshold, a measurement from a liquid biopsy sample, a measurement from liquid biopsy samples obtained from a cohort of subjects, and/or a normalized value. In some embodiments, a predetermined threshold or a normalized value were previously shown to distinguish an ER-positive and an ER-negative cancer (e.g., distinguish with an AUROC of greater than 0.5). In

some embodiments, a reference is a measurement from a liquid biopsy sample obtained from a cohort of subjects who have previously been determined to have an ER-positive or ER-negative cancer. In some embodiments, a cohort of subjects has previously been determined to have cancer (e.g., breast cancer).

[0040] In some embodiments, a method comprises calculating a sequence read density at one or more genomic loci. In some embodiments, sequence read density can be calculated by a process comprising:

- (a) summing background adjusted sequence counts at each of one or more genomic loci and dividing by the sum of the kilobases of the one or more genomic loci; or
- (b) for each genomic loci, dividing background adjusted fragment count by the number of kilobases of the genomic loci, and then summing for each loci.

[0041] In some embodiments, one or more genomic loci include one or more genomic loci with an increased level of the one or more epigenetic biomarkers in (a) sample(s) obtained from a subject with an ER-positive cancer as compared to a sample obtained from a subject with an ER-negative cancer, and/or (b) sample(s) obtained from a subject with an ER-negative cancer as compared to a sample obtained from a subject with an ER-positive cancer.

[0042] In some embodiments, a method comprises calculating an ER-positive/ER-negative ratio score. In some embodiments, an ER-positive/ER-negative ratio score can be calculated by a method comprising:

- (a) calculating an ER-positive sequence read density by a method comprising summing background adjusted sequence counts at each of one or more genomic loci with an increased level of one or more epigenetic biomarkers in sample(s) obtained from subjects with an ER-positive cancer as compared to samples obtained from subjects with ER-negative cancer;
- (b) calculating an ER-negative sequence read density by a method comprising summing background adjusted sequence counts at each of one or more genomic loci with an increased level of one or more epigenetic biomarkers in sample(s) obtained from subjects with an ER-negative cancer as compared to samples obtained from subjects with an ER-positive cancer; and

(c) dividing the ER-positive sequence read density by the ER-negative sequence read density.

[0043] In some embodiments, a method comprises determining an ER-positive/ER-negative ratio score for one or more epigenetic biomarkers. In some embodiments, a method comprises:

- (a) determining an ER-positive/ER-negative ratio score for H3K4me3 modifications;
 - (b) determining an ER-positive/ER-negative ratio score for H3K27ac modifications;
- and/or
- (c) determining an ER-positive/ER-negative ratio score for methylated DNA.

[0044] In some embodiments, a method comprises determining an ER-positive/ER-negative ratio score for two or more epigenetic biomarkers. In some embodiments, a method comprises determining an ER-positive/ER-negative ratio score for two or more epigenetic biomarkers, wherein the ER-positive/ER-negative ratio scores are combined. In some embodiments, a method comprises determining an ER-positive/ER-negative ratio score each of H3K4me3 modifications, H3K27ac modifications, and methylated DNA, and combining the ratio scores. In some embodiments, two or more ratio scores can be combined using fitted values determined using a logistic regression.

[0045] In some embodiments, quantification of one or more histone modifications, chromatin accessibility, or binding of one or more transcription factors, or any combination thereof at the one or more genomic loci as compared to a reference indicates that the subject has an ER-positive cancer. In some embodiments, quantification of one or more histone modifications, chromatin accessibility, binding of one or more transcription factors, and/or DNA methylation at the one or more genomic loci as compared to a reference indicates that the subject has an ER-negative cancer.

[0046] In some embodiments, a method further comprises comparing one or more quantified epigenetic biomarkers to a reference, and wherein an increase or decrease in the one or more epigenetic markers as compared to the reference indicates that a subject has an ER-positive or an ER-negative cancer.

[0047] In some embodiments, a sample comprises a detectable amount of ctDNA (e.g., wherein estimated tumor fraction is >3% for the cfDNA, e.g., as determined by iChorCNA).

[0048] In some embodiments, the method comprises quantifying one or more histone modifications, chromatin accessibility, binding of one or more transcription factors, and/or DNA methylation at one or more genomic loci in Tables 1-3. In some embodiments, the method comprises quantifying H3K4me3 modifications for at least 5, 10, 20, 30, 40, or 50 genomic loci in Table 1. In some embodiments, the method comprises quantifying H3K27ac modifications for at least 5, 10, 20, 30, 40, or 50 genomic loci in Table 2. In some embodiments, the method comprises quantifying DNA methylation for at least 5, 10, 20, 30, 40, or 50 genomic loci in Table 3.

[0049] In some embodiments, the area under the receiver operating characteristic (AUROC) for determining if a subject has an ER-positive cancer vs. an ER-negative cancer is greater than 0.5 (e.g., greater than 0.55, greater than 0.6, greater than 0.65, greater than 0.7, greater than 0.75, greater than 0.8, greater than 0.85, greater than 0.9, or greater than 0.95).

[0050] In some embodiments, the ER-positive cancer is an ER-positive cancer based on IHC testing and the ER-negative cancer is an ER-negative cancer based on IHC testing. In some embodiments, the subject has previously been determined to have cancer. In some embodiments, a sample is obtained from a subject having cancer wherein a biopsy of the cancer is not possible and/or feasible.

[0051] In another aspect, the present disclosure provides a method of treating a subject having a cancer, the method comprising: administering a cancer therapy to the subject based on the ER status of the cancer, wherein the ER status of the cancer has been determined using any one of the aforementioned methods of determining ER status. In some embodiments, the method further comprises determining the ER status of the cancer using any one of the aforementioned methods of determining ER status. In some embodiments, the cancer has been determined to be ER-positive and the cancer therapy comprises an ER-targeted agent. In some embodiments, if a cancer has been determined to be ER-negative, the cancer therapy is one appropriate for an ER-negative cancer. In some embodiments, if the cancer has been determined to be ER-negative, the cancer therapy does not comprise administering an ER-targeted agent.

[0052] In another aspect, the present disclosure provides a method of treating a subject having a cancer, the method comprising: administering a cancer therapy to the subject based on

the ER status of the cancer, wherein the ER status of the cancer has been determined using any one of the aforementioned methods of determining ER status. In some embodiments, the method further comprises determining the ER status of the cancer using any one of the aforementioned methods of determining ER status. In some embodiments, if the cancer has been determined to be ER-positive, the cancer therapy comprises an ER-targeted agent. In some embodiments, if the cancer has been determined to be ER-negative, the cancer therapy does not comprise administering an ER-targeted agent.

[0053] In another aspect, the present disclosure provides a method of monitoring the ER status of a cancer in a subject, and optionally treating the cancer, the method comprising: determining the ER status of the cancer using any one of the aforementioned methods of determining ER status at first and second time points. In some embodiments, the subject has been administered an ER-targeted agent after the first time point and before the second time point. In some embodiments, the method further comprises administering a cancer therapy, optionally an ER-targeted agent, to the subject based on the ER status of the cancer at the second time point, optionally wherein the type, dose and/or frequency of administration of the cancer therapy is adjusted based on the ER status of the cancer at the second time point.

[0054] In another aspect, the present disclosure provides a method of treating a subject having a cancer, the method comprising: administering an ER-targeted agent to the subject if the subject has been determined to have a validated epigenetic profile indicative of an ER-positive cancer based on analysis of a biological sample, optionally of cell-free DNA (cfDNA) from a liquid biopsy sample, obtained or derived from the subject, and, if the subject has not been determined to a validated epigenetic profile indicative of an ER-positive cancer, not administering an ER-targeted agent, wherein the presence of the validated epigenetic profile has been determined using a validated classifier, wherein the validated classifier has been obtained by: (a) determining a genomic profile of one or more histone modifications, chromatin accessibility, binding of one or more transcription factors, and/or DNA methylation in (i) one or more ER-positive cell lines or (ii) biological samples obtained from a first cohort of subjects who have previously been determined to have an ER-positive cancer; (b) determining a genomic profile of one or more histone modifications, chromatin accessibility, binding of one or more transcription factors, and/or DNA methylation in (i) one or more ER-negative cell lines or (ii) biological samples obtained from a second cohort of healthy subjects or subjects who have

previously been determined to have an ER-negative cancer; (c) comparing the genomic profile determined in step (a) and the genomic profile determined in step (b), to identify genomic loci that have statistically different histone modification, chromatin accessibility, binding of transcription factor, and/or DNA methylation levels (“differential loci”); (d) training a classifier on histone modification, chromatin accessibility, binding of transcription factor, and/or DNA methylation levels in the differential loci to distinguish between (i) samples from one or more ER-positive cell lines or biological samples obtained from the first cohort, and (ii) samples from one or more ER-negative cell lines or biological samples obtained from the second cohort, to identify samples having a profile of histone modification, chromatin accessibility, binding of transcription factor, and/or DNA methylation levels (“epigenetic profile”) that indicates that the samples are likely obtained from an ER-positive cell line or from the first cohort; and (e) obtaining the validated classifier by validating the classifier from step (d) on a third cohort comprising an independent and group of subjects with ER-positive and ER-negative cancers and selecting a threshold such that the validated classifier predicts ER-positive cancers with an area under the receiver operating characteristic (AUROC) greater than 0.5 (*e.g.*, greater than 0.55, greater than 0.6, greater than 0.65, greater than 0.7, greater than 0.75, greater than 0.8, greater than 0.85, greater than 0.9, or greater than 0.95), wherein subjects falling within the group of predicted ER-positive cancers display the validated epigenetic profile and subjects that do not fall within the group of ER-positive cancers lack the validated epigenetic profile.

[0055] In some embodiments, the differential loci in step (c) were identified by comparing the genomic profile of one or more histone modifications and/or DNA methylation in (i) one or more ER-positive cell lines and (ii) one or more ER-negative cell lines.

[0056] In some embodiments, the classifier in step (d) was trained on histone modification, chromatin accessibility, binding of transcription factor, and/or DNA methylation levels in the differential loci that were obtained by *in silico* mixing sequence data from one or more ER-positive cell lines and sequence data obtained from liquid biopsy samples of healthy subjects.

[0057] In some embodiments, the validated classifier in step (e) was validated using liquid biopsy samples from the third cohort.

[0058] In some embodiments, the classifier in step (d) was trained on two or more histone modification levels in the differential loci. In some embodiments, the two or more histone modification levels comprise H3K4me3 and H3K27ac modification levels.

[0059] In some embodiments, the classifier in step (d) was trained on one or more histone modification levels and DNA methylation in the differential loci. In some embodiments, the one or more histone modification levels comprise H3K4me3 and/or H3K27ac modification levels. In some embodiments, the classifier in step (d) was trained using ridge regression, elastic-net regression, or lasso regression. In some embodiments, the one or more histone modification levels comprise H3K4me3 and H3K27ac modification levels. In some embodiments, the biological sample is a liquid biopsy sample, *e.g.*, a plasma sample, serum sample, or urine sample.

[0060] In another aspect, the present disclosure provides a kit comprising reagents for quantifying one or more histone modifications, chromatin accessibility, binding of one or more transcription factors, and/or DNA methylation at one or more genomic loci, wherein the one or more genomic loci are selected from Tables 1-3. In some embodiments, the kit comprises reagents for quantifying H3K4me3 for at least 5, 10, 20, 30, 40, or 50 genomic loci in Table 1. In some embodiments, the kit comprises reagents for quantifying H3K27ac for at least 5, 10, 20, 30, 40, or 50 genomic loci in Table 2. In some embodiments, the kit comprises reagents for quantifying DNA methylation for at least 5, 10, 20, 30, 40, or 50 genomic loci in Table 3.

[0061] In some embodiments, the kit comprises one or more antibodies for use in ChIP-seq, optionally wherein the one or more antibodies specifically bind H3K4me3- or H3K27ac-modified histones. In some embodiments, the kit comprises one or more methyl-binding domains for use in MBD-seq.

[0062] In some embodiments, the kit comprises reagents for isolation of cell-free DNA (cfDNA) from a liquid biopsy sample. In some embodiments, the kit comprises reagents for library preparation for sequencing. In some embodiments, the kit comprises reagents for sequencing. In some embodiments, the kit comprises instructions for determining if a subject has an ER-positive cancer.

[0063] In another aspect, the present disclosure provides a non-transitory computer readable storage medium encoded with a computer program, wherein the program comprises instructions that when executed by one or more processors cause the one or more processors to

perform operations to perform the method of any one of the aforementioned methods of determining ER status.

[0064] In another aspect, the present disclosure provides a computer system comprising a memory and one or more processors coupled to the memory, wherein the one or more processors are configured to perform operations to perform the method of any one of the aforementioned methods of determining ER.

[0065] In another aspect, the present disclosure provides a system for determining the ER status of a cancer in a subject, the system comprising a sequencer configured to generate a sequencing dataset from a sample; and a non-transitory computer readable storage medium of and/or a computer system of the present disclosure. In some embodiments, the sequencer is configured to generate a Whole Genome Sequencing (WGS) data set from the sample. In some embodiments, the system further comprises a sample preparation device. In some embodiments, the sample preparation device is configured to prepare the sample for sequencing from a biological sample, optionally a liquid biopsy sample. In some embodiments, the sample preparation device comprises reagents for quantifying one or more histone modifications, chromatin accessibility, binding of one or more transcription factors, and/or DNA methylation at one or more genomic loci in cell-free DNA (cfDNA) from the biological sample, optionally the liquid biopsy sample. In some embodiments, the one or more genomic loci are selected from Tables 1-3. In some embodiments, the device comprises reagents for quantifying H3K4me3, *e.g.*, for at least 5, 10, 20, 30, 40, or 50 genomic loci in Table 1. In some embodiments, the device comprises reagents for quantifying H3K27ac, *e.g.*, for at least 5, 10, 20, 30, 40, or 50 genomic loci in Table 2. In some embodiments, the device comprises reagents for quantifying DNA methylation, *e.g.*, for at least 5, 10, 20, 30, 40, or 50 genomic loci in Table 3. In some embodiments, the reagents comprise one or more antibodies for use in ChIP-seq, optionally wherein the one or more antibodies specifically bind H3K4me3- or H3K27ac-modified histones. In some embodiments, the reagents comprise one or more methyl-binding domains for use in MBD-seq. In some embodiments, the device comprises reagents for isolation of cell-free DNA (cfDNA) from the biological sample, optionally the liquid biopsy sample. In some embodiments, the device comprises reagents for library preparation for sequencing. In some embodiments, the sequencer comprises reagents for sequencing.

[0066] In some embodiments a method is for determining ER status of a cancer in a subject (c.g., patient). The method may include receiving (c.g., by a processor of a computing device) one or more genomic profiles of one or more histone modifications, chromatin accessibility, binding of one or more transcription factors, and/or DNA methylation for the subject. The method may further include determining whether the subject has an epigenetic profile indicative of an ER-positive cancer by classifying the genomic profile using an ER classifier.

[0067] In some embodiments, an ER classifier has been trained using one or more genomic profiles of one or more histone modifications, chromatin accessibility, binding of one or more transcription factors, and/or DNA methylation for (i) one or more ER-positive cell lines and one or more ER-negative cell lines and/or (ii) one or more biological samples obtained from one or more cohorts of subjects who have previously been determined to have an ER-positive cancer and one or more biological samples obtained from one or more cohorts of subjects who have previously been determined to have an ER-negative cancer. In some embodiments, genomic profiles correspond to samples that have been diluted *in silico* by mixing different proportions of sequencing fragments from healthy donor plasma samples and cell lines to achieve a simulated ctDNA percentage ranging from 0.5% to 50%.

[0068] In some embodiments, one or more genomic profiles are for differential genomic loci found to have statistically significant different levels of one or more histone modifications, chromatin accessibility, binding of one or more transcription factors, and/or DNA methylation levels between one or more ER-positive cell lines and one or more ER-negative cell lines and/or between one or more biological samples obtained from one or more cohorts of subjects who have previously been determined to have an ER-positive cancer and one or more biological samples obtained from one or more cohorts of subjects who have previously been determined to have an ER-negative cancer. In some embodiments, differential loci were identified by comparing the genomic profile of one or more histone modifications and/or DNA methylation in (i) one or more ER-positive cell lines and (ii) one or more ER-negative cell lines. In some embodiments, an ER classifier has been trained on histone modification, chromatin accessibility, binding of transcription factor, and/or DNA methylation levels in the differential loci that were obtained by *in silico* mixing sequence data from one or more ER-positive cell lines and sequence data obtained from liquid biopsy samples of healthy subjects.

[0069] In some embodiments, an ER classifier has been trained on two or more histone modification levels in the differential loci. In some embodiments, an ER classifier has been trained on one or more histone modification levels and DNA methylation levels in the differential loci. In some embodiments, a genomic profile of a subject used to classify comprises two or more histone modification levels. In some embodiments, two or more histone modification levels comprise H3K4me3 and H3K27ac modification levels. In some embodiments, a genomic profile of a subject used to classify comprises one or more histone modification levels and DNA methylation levels. In some embodiments, one or more histone modification levels comprise H3K4me3 and/or H3K27ac modification levels. In some embodiments, one or more histone modification levels comprise H3K4me3 and H3K27ac modification levels.

[0070] In some embodiments, an ER classifier has been trained with data derived from plasma. In some embodiments, an ER classifier has been trained with data derived from liquid biopsy samples.

[0071] In some embodiments, an ER classifier is a validated classifier. In some embodiments, an ER classifier has been validated by selecting a threshold such that the validated classifier predicts ER-positive cancers with an area under the receiver operating characteristic (AUROC) greater than 0.5 (*e.g.*, greater than 0.55, greater than 0.6, greater than 0.65, greater than 0.7, greater than 0.75, greater than 0.8, greater than 0.85, greater than 0.9, or greater than 0.95). In some embodiments, an ER classifier has been validated on a cohort of an independent group of subjects with ER-positive and ER-negative cancers, wherein subjects falling within a group of predicted ER-positive cancers display a validated epigenetic profile and subjects that do not fall within a group of ER-positive cancers lack the validated epigenetic profile. In some embodiments, an ER classifier has been validated using liquid biopsy sample data.

[0072] A non-transitory computer readable storage medium may be encoded with a computer program, where the program may comprise instructions that when executed by one or more processors cause the one or more processors to perform operations to perform a method for determining ER status of a cancer in a subject (*e.g.*, patient). A computer system may include a memory and one or more processors coupled to the memory, wherein the one or more processors are configured to perform operations to perform a method for determining ER status of a cancer in a subject (*e.g.*, patient).

[0073] In some embodiments, a method of treating a subject having a cancer includes administering an ER-targeted agent to the subject, wherein the subject has been determined to have a validated epigenetic profile indicative of an ER-positive cancer based on analysis of a biological sample, optionally of cell-free DNA (cfDNA) from a liquid biopsy sample, obtained or derived from the subject. In some embodiments, the presence of the validated epigenetic profile has been determined using a classifier (e.g., a validated classifier) according to a method for determining ER status of a cancer in a subject (e.g., patient).

BRIEF DESCRIPTION OF THE DRAWING

[0074] **Fig. 1** shows ROC curves for exemplary ER status classifiers that were generated in accordance with Example 2. As shown, different classifiers were generated using (i) ridge regression (all genomic loci from the relevant subset of genomic loci) ($\alpha = 0$); (ii) elastic-net regression (many genomic loci from the relevant subset of genomic loci) ($\alpha = 0.25$), or (iii) lasso regression (few genomic loci from the relevant subset of genomic loci) ($\alpha = 1$). As shown, different classifiers were generated with (a) genomic loci from Tables 1-3 for different modifications, namely (i) H3K4me3 modifications, (ii) H3K27ac modifications, (iii) DNA methylation (DNAm) or (iv) all of the above (All) and (b) using different subsets of genomic loci in Tables 1-3 for a particular modification, namely (i) all genomic loci with an absolute $\log_2(\text{fold-change}) \geq 0.5$, (ii) all genomic loci with an absolute $\log_2(\text{fold-change}) \geq 1$, (iii) all genomic loci with an absolute $\log_2(\text{fold-change}) \geq 2$, (iv) all genomic loci with an absolute $\log_2(\text{fold-change}) \geq 3$, and (v) all genomic loci with an absolute $\log_2(\text{fold-change}) \geq 4$.

[0075] **Fig. 2** shows representative, non-limiting graphs that demonstrate the accuracy of ER status (based on AUCROC) determination using the classifiers that were generated in accordance with Example 2.

[0076] **Fig. 3** (A) shows a heatmap representation of z-scored, ctDNA- and background-normalized counts at differential peaks (DE-seq, $\text{FDR} < 0.05$, $\log_2(\text{fold change}) > 1$) across ER +/- patients (status determined by IHC). Each row corresponds to signal observed in an individual patient, and each column represents an enhancer/promoter/MBD locus. (B) shows ROC curves for an exemplary ER status classifier generated in accordance with Example 3 and applied to plasma samples obtained from patients previously diagnosed with metastatic breast cancer. ROC curves assessing performance of a regularized logistic regression model to classify

ER IHC status (positive vs negative) in all samples collected (left curve), all samples with detectable ctDNA (as determined by iChor) (center curve), and samples with detectable ctDNA obtained from one particular source (right curve) are shown. Without wishing to be bound by theory, it is believed that the improved performance observed in samples obtained from the one particular source is due to higher quality of the samples and the pathology of the cancer. (C) shows the summed weights of the negative (left) and positive (right) coefficients in the ER model, stratified by analyte. Genes of known biological importance that were found proximal to enhancers/promoters are highlighted.

[0077] **Fig. 4** is a block diagram of an example network environment for use in the methods and systems described herein, according to illustrative embodiments of the present disclosure.

[0078] **Fig. 5** is a block diagram of an example computing device and an example mobile computing device, for use in illustrative embodiments of the present disclosure.

DETAILED DESCRIPTION

[0079] The present disclosure is based, at least in part, on the demonstration that the ER status of a cancer in a subject can be determined by detecting and quantifying the presence of histone modifications and/or DNA methylation at one or more genomic loci in cell-free DNA (cfDNA) from a liquid biopsy sample, *e.g.*, a plasma sample obtained or derived from the subject. The present disclosure also encompasses methods where chromatin accessibility and/or binding of one or more transcription factors are detected at the one or more genomic loci instead of (or in addition to) histone modifications and/or DNA methylation. The present disclosure is also based, at least in part, on the demonstration that genomic loci that are differentially modified based on different types of histone modifications (*e.g.*, histone methylation marks such as H3K4me3 and histone acetylation marks such as H3K27ac) and/or DNA methylation can be combined into multimodal classifiers to determine ER status. These new monomodal and multimodal classifiers provide minimally invasive ways of determining ER status that are more accurate, objective, and comprehensive than the current tissue-based approaches. No liquid biopsy platform to date has been able to provide actionable resolution on a transcriptionally regulated phenotype relevant for therapy such as ER status.

ER status and cancer

[0080] Estrogens are steroidal hormones that function as the primary female sex hormone. There are three major forms of estrogen, namely estrone (E1), estradiol (E2) and estriol (E3). Estradiol (E2) is the predominant estrogen in nonpregnant females, while estrone (E1) and estriol (E3) are primarily produced during pregnancy and following the onset of menopause, respectively. All estrogens are produced from androgens through actions of enzymes such as aromatase. Follicle-stimulating hormone and luteinizing hormone stimulate the synthesis of estrogen in the ovaries. However, some estrogens are also produced in smaller amounts by other tissues such as the liver, adrenal glands, and mammary gland. Studies have shown that estrogen is associated with mammary tumorigenesis, ovarian and endometrial carcinogenesis (Folkerd and Dowsett, *J Clin Oncol* (2010) 28:4038-4044). Also, mounting evidence suggests that estrogen and its target gene encoding progesterone receptor (PR) play critical roles in regulating breast cancer progression (Knutson et al., *J Hematol Oncol* (2017) 10:89).

[0081] The biological effects of estrogen are mostly mediated by its binding and activation of ER α and ER β , which are members of the nuclear receptor superfamily of transcription factors that are characterized by highly conserved DNA- and ligand-binding domains (Wang et al., *J Hematol Oncol* (2017) 10:168). The DNA binding domain, which is extremely well conserved between ER α and ER β (97% homology), contains two functionally distinct zinc finger motifs that are responsible for specific DNA binding, as well as mediating receptor dimerization (Hewitt and Korach, *Endocr Rev* (2018) 39(5):664-675). The unliganded ER has been shown to be present in a cytosolic complex with hsp90 and associated proteins, with ligand binding allowing dissociation from the hsp90 complex, receptor dimerization, nuclear localization and binding to estrogen response elements (EREs) in promoters of estrogen-regulated genes (Pratt and Toft, *Endocr Rev* (1997) 18:306-360). Genome-wide chromatin immunoprecipitation studies have confirmed that the majority of ER-binding sites in estrogen responsive genes conform well to this consensus sequence (Welboren et al., *EMBO J* (2009) 28:1418-1428). While ER α and ER β can bind to most ERE identically, the differences in ER α and ER β may lead to tethering differential transcription factors and then modulating different target genes. Thus, the activation of ER α or ER β can produce both unique and overlapping effects.

[0082] ER α has also been shown to modulate gene transcription through heterodimerizing with other transcription factors such as activating protein 1 (AP1) and nuclear factor kappa-light-chain-enhancer of activated B cells (NF- κ B). There is a large profile of estrogen-responsive genes, including pS2, cathepsin D, c-fos, c-jun, c-myc, TGF- α , retinoic acid receptor α 1, efp, progesterone receptor (PR), insulin-like growth factor 1 (IGF1) (Ikeda et al., *Acta Pharmacol Sin* (2015) 36:24-31). Many of these ER-regulated genes, including IGF1, cyclin D1, c-myc, and efp, are important for cell proliferation and survival. C-myc is a bona-fide oncogene that is amplified or overexpressed in a variety of human tumors. Efp is an ubiquitin ligase that promotes proteasomal degradation of 14-3-3 sigma thereby stimulating cellular proliferation. While PR is an estrogen-responsive gene, it may antagonize ER α action to inhibit tumor growth, particularly through interacting with RNA polymerase III and inhibiting tRNA transcription.

[0083] A pool of ER α are located in the plasma membrane and cytoplasm (Adlanmerini et al., *Proc Natl Acad Sci USA* (2014) 111:E283-290), where it binds to diverse membrane or cytoplasmic signaling molecules such as the p85 regulatory subunit of class I phosphoinositide 3-kinase, mitogen-activated protein kinase (MAPK) and Src (Omarjee et al., *Oncogene* (2017) 36:2503-2514). Activation of these signal transduction pathways by estrogen initiates cell survival and proliferation signals. Additionally, these signaling molecules are able to phosphorylate the ER α and its co-regulators to augment nuclear ER α signaling (Arnal et al., *Physiol Rev* (2017) 97:1045-1087). The genomic and non-genomic actions of ER α play a crucial role in breast epithelial cell proliferation and survival, as well as mammary tumorigenesis [28]. The purpose of this review is to decipher the complex mechanisms underlying the aberrant expression of ER α and ER β in human cancer.

[0084] Based on the ER status, breast tumors can be classified as ER-positive and ER-negative. About 75% of breast cancer cases are ER α positive at diagnosis (Allred et al., *Breast Cancer Res* (2004) 6:240-245). To determine if a cancer is ER-positive, medical practitioners currently order testing that is conducted on a tissue sample using immunohistochemistry (IHC). Samples are reviewed by a pathologist and typically reported as (a) the word positive or negative, (b) a percentage that tells you how many cells out of 100 stained positive for hormone receptors, *i.e.*, a number between 0% (none have receptors) and 100% (all have receptors), and/or (c) an Allred score between 0 and 8. The Allred scoring system looks at what percentage

of cells test positive for hormone receptors, along with how well the receptors show up after staining, called intensity (Allred et al., Breast Cancer Res (2004) 6:240-245). This information is then combined to score the sample on a scale from 0 to 8 where, the higher the score, the more receptors were found and the easier they were to see in the sample. The terms “ER-positive” and “ER-negative” as used herein can correspond to any of these traditional approaches for determining ER status.

[0085] ER-positive cancers can be treated with ER-targeted agents that lower estrogen levels or block estrogen receptors. ER-positive cancers tend to grow more slowly than those that are ER-negative. Women with hormone receptor-positive breast cancers tend to have a better outlook in the short-term, but these cancers can sometimes come back many years after treatment.

[0086] Treatment with ER-targeted agents is not helpful for ER-negative cancers. These cancers may instead be treated with one or more of surgery and/or radiation, HER2-targeted therapy (if HER2-positive), chemotherapy and immunotherapy. These cancers tend to grow faster than ER-positive cancers. If they come back after treatment, it is often in the first few years. ER-negative breast cancers are more common in women who have not yet gone through menopause.

ER-targeted agents

[0087] The introduction of ER-targeted agents has dramatically influenced the outcome of patients with ER-positive breast cancers. ER-targeted agents block or degrade estrogen receptors or lower estrogen levels. Many ER-targeted agents have already been approved and others are in development or being tested in clinical trials for ER-positive breast cancer and other ER-positive cancers.

Agents that block or degrade estrogen receptors (ER)

[0088] These agents stop estrogen from fueling breast cancer cells to grow. These agents work by preventing estrogen from activating estrogen receptors. They do this by blocking estrogen from binding to estrogen receptors or by degrading estrogen receptors. The former are called Selective Estrogen Receptor Modulators (SERMs) while the latter are called Selective Estrogen Receptor Degradors (SERDs).

Selective Estrogen Receptor Modulators (SERMs)

[0089] SERMs bind estrogen receptors and block them from binding to estrogen. These agents are pills, taken orally.

Tamoxifen

[0090] Tamoxifen can be used to treat women with breast cancer who have or have not gone through menopause. This agent can be used in several ways. In women at high risk of breast cancer, tamoxifen can be used to help lower the risk of developing breast cancer.

[0091] For women who have been treated with breast-conserving surgery for ductal carcinoma in situ (DCIS) that is ER-positive, taking tamoxifen for 5 years lowers the chance of the DCIS coming back in the same breast. It also lowers the chance of getting an invasive breast cancer or another DCIS in both breasts.

[0092] For women with ER-positive invasive breast cancer treated with surgery, tamoxifen can help lower the chances of the cancer coming back and improve the chances of living longer. It can also lower the risk of a new cancer developing in the other breast. Tamoxifen can be started either after (adjuvant) or before (neoadjuvant) surgery. When given after surgery, it is usually taken for 5 to 10 years. This drug is used mainly for women with early-stage breast cancer who have not yet gone through menopause. If the subject has gone through menopause, aromatase inhibitors (see below) are often used instead.

[0093] For women with ER-positive breast cancer that has spread to other parts of the body, tamoxifen can often help slow or stop the growth of the cancer and might even shrink some tumors.

Toremifene

[0094] Toremifene is a SERM that works in a similar way to tamoxifen, but it is used less often and is only approved to treat post-menopausal women with metastatic breast cancer. It is not likely to work if tamoxifen has already been used and has stopped working.

Selective estrogen receptor degraders (SERDs)

[0095] Like SERMs, these agents bind estrogen receptors but do so in a manner that causes them to be degraded. SERDs are used most often in post-menopausal women. When given to pre-menopausal women, they need to be combined with a luteinizing-hormone releasing hormone (LHRH) agonist to turn off the ovaries.

Fulvestrant

[0096] This ER-targeted agent can be used (i) alone to treat advanced breast cancer that has not been treated with other hormone therapy, (ii) alone to treat advanced breast cancer after other hormone drugs (like tamoxifen and often an aromatase inhibitor) have stopped working, or (iii) in combination with a CDK 4/6 inhibitor or PI3K inhibitor to treat metastatic breast cancer as initial hormone therapy or after other hormone treatments have been tried. It is given as two injections into the buttocks (bottom). For the first month, the two shots are given two weeks apart. After that, they are given once a month.

Elacestrant

[0097] This ER-targeted can be used to treat advanced, ER-positive, HER2-negative breast cancer when the cancer cells have an *ESR1* gene mutation, and the cancer has grown after at least one other type of hormone therapy. Elacestrant is taken daily as pills, orally.

Drugs that lower estrogen levels

[0098] Because estrogen stimulates ER-positive cancers to grow, lowering the estrogen level can help slow the cancer's growth or help prevent it from coming back.

Aromatase inhibitors (AIs)

[0099] Aromatase inhibitors (AIs) are drugs that stop most estrogen production in the body. Before menopause, most estrogen is made by the ovaries. But in women whose ovaries are not working, either because they have gone through menopause or because of certain treatments, estrogen is still made in body fat by an enzyme called aromatase. AIs work by preventing aromatase from making estrogen.

[0100] These drugs are useful for women who have gone through menopause, although they can also be used in pre-menopausal women when they are combined with ovarian

suppression. These AIs are pills taken orally every day to treat breast cancer and include letrozole, anastrozole, and exemestane.

Other ER-targeted agents and other cancers

[0101] While the sections above focus on FDA approved ER-targeted agents, many other ER-targeted agents are being developed and/or assessed in clinical trials. It is to be understood that these other ER-targeted agents can also be used in treatment methods of the present disclosure. In addition, while the sections above focus on the treatment of ER-positive breast cancer, many of these ER-targeted agents can also be used to treat other ER-positive cancers, *e.g.*, ovarian or endometrial ER-positive cancers.

Subjects and Samples

[0102] A sample analyzed using methods, kits and systems provided herein can be any biological sample including any processed sample that includes circulating tumor DNA (ctDNA) derived from a biological sample. In various embodiments, a sample analyzed using methods, kits and systems provided herein can be a sample obtained from a mammalian subject. In various embodiments, a sample analyzed using methods, kits and systems provided herein can be a sample obtained from a human subject.

[0103] In various instances, a human subject is a subject diagnosed or seeking diagnosis as having, diagnosed as, or seeking diagnosis as at risk of having, and/or diagnosed as or seeking diagnosis as at immediate risk of having, an ER-positive cancer, *e.g.*, ER-positive breast cancer, etc. In various instances, a human subject is a subject identified as needing ER status screening. In certain instances, a human subject is a subject identified as needing ER status screening by a medical practitioner.

[0104] The subject may not have undergone previous treatments for cancer, such as the treatments recited in this disclosure. In other embodiments, the subject has undergone previous treatments for cancer, such as the treatments recited in this disclosure.

[0105] In various embodiments a subject has one or more biomarkers and/or risk factors for cancer, *e.g.*, ER-positive cancer, *e.g.*, ER-positive breast cancer, etc. In certain embodiments, a human subject is identified as in need of ER status screening based on an initial cancer diagnosis, *e.g.*, a breast cancer, etc. diagnosis. In various instances, a human subject is a subject

not yet diagnosed as having, not at risk of having, not at immediate risk of having, not diagnosed as having, and/or not seeking diagnosis for a cancer. Genetic factors may also contribute to ER-positive cancer risk, as evidenced by individuals with a family history of ER-positive cancer.

[0106] In various embodiments, a sample from a subject, *e.g.*, a human can be obtained from a liquid biopsy. In certain embodiments, a sample and/or reference is obtained from serum, plasma, or urine. In certain embodiments, the sample is serum. In certain embodiments, a sample comprises circulating tumor DNA (ctDNA). In certain embodiments, a sample is derived from about 1 mL of blood obtained from the subject. In certain embodiments, a sample is derived from about 0.5-5 mL of blood obtained from the subject, *e.g.*, about 0.5 to about 2 mL, about 0.5 to 1.75 mL, about 0.5 to 1.5 mL, about 0.75 to 1.25 mL, about 0.9 to 1.1 mL, about 1 mL, about 2 mL, about 3 mL, about 4 mL, or about 5 mL of blood.

[0107] In various embodiments, a sample is a sample of cell-free DNA (cfDNA). cfDNA is typically found in human biofluids (*e.g.*, plasma, serum, or urine) in short, double-stranded fragments. The concentration of cfDNA is typically low, but can significantly increase under particular conditions, including without limitation pregnancy, autoimmune disorders, myocardial infarction, and cancer. Circulating tumor DNA (ctDNA) is the component of cell-free DNA specifically derived from cancer cells. ctDNA can be present in human biofluids bound to leukocytes and erythrocytes or not bound to leukocytes and erythrocytes. Various tests for detection of tumor-derived ctDNA are based on detection of genetic or epigenetic modifications that are characteristic of cancer (*e.g.*, of a relevant cancer). Genetic or epigenetic factors characteristic of cancer can include, without limitation, oncogenic or cancer-associated mutations in tumor-suppressor genes, activated oncogenes, chromosomal disorders, histone modifications (*e.g.*, histone methylation and/or histone acetylation), chromatin accessibility, binding of one or more transcription factors and/or DNA methylation.

[0108] In various embodiments, ctDNA comprises less than 30%, less than 20%, or less than 10% of the cfDNA in the liquid biopsy sample obtained from the subject, *e.g.*, less than 9%, 8%, 7%, 6%, 5%, 4%, 3%, 2% or less than 1% of the cfDNA in the sample. In some embodiments, the percentage of ctDNA in the liquid biopsy sample is assessed using ichorCNA which estimates the percentage of ctDNA in a sample probabilistically (see Adalsteinsson et al., Nat Commun (2017) 8(1):1324 the entire contents of which are incorporated herein by reference).

[0109] cfDNA and ctDNA can provide a real-time or nearly real time metric of status of a source tissue. cfDNA and ctDNA demonstrate a half-life in blood of about 2 hours, such that a sample taken at a given time provides a relatively timely reflection of the status of a source tissue.

[0110] In some embodiments, a method comprises isolating DNA (e.g., cfDNA) from a liquid biopsy sample (e.g., from 1, 2, 3, 4, or 5 mL of a liquid biopsy sample). Various methods of isolating nucleic acids from a sample (e.g., of isolating cfDNA from blood or plasma) are known in the art. Nucleic acids can be isolated using, without limitation, standard DNA purification techniques, by direct gene capture (e.g., by clarification of a sample to remove assay-inhibiting agents and capturing a target nucleic acid, if present, from the clarified sample with a capture agent to produce a capture complex and isolating the capture complex to recover the target nucleic acid).

[0111] Reagents and protocols for obtaining and analyzing cfDNA and ctDNA, such as circulating in blood or other tissue, are commercially available as described in the Examples and well-known in the art (see, for example, Anker et al., *Cancer and Metastasis Rev* (1999) 18:65-73; Wua et al., *Clin Chim Acta* (2002) 321:77-87; Fiegl et al., *Cancer Res* (2005) 15:1141-1145; Pathak et al., *Clin Chem* (2006) 52:1833-1842; Schwarzenbach et al., *Clin Cancer Res* (2009) 15:1032-1038; Schwarzenbach et al., *Nat Rev Cancer* (2011) 11:426-437) the contents of each of which is separately incorporated herein by reference in their entirety).

[0112] In various embodiments, samples can be collected from individuals repeatedly over a period of time (e.g., once daily, weekly, monthly, annually, biannually, etc.). In various embodiments, such samples can be used to verify results from earlier detections and/or to identify an alteration in biological pattern because of, for example, disease progression, resistance to therapy, treatment, remission, and the like. For example, subject samples can be taken and monitored every month, every two months, or combinations of one, two, or three-month intervals according to the present disclosure. In various embodiments, samples can be collected for monitoring over time beginning at or at certain clinically determined stages, such as at resistance to a therapy, before radiographic progression, after radiographic progression, and/or at tissue biopsy. In addition, the ER status obtained at different points in time can be conveniently compared with each other, as well as with those of normal controls during the

monitoring period, thereby providing the subject's own values, as an internal, or personal, control for long-term monitoring.

[0113] Samples include materials prepared by processes including, without limitation, steps such as concentration, dilution, adjustment of pH, removal of high abundance polypeptides (*e.g.*, albumin, gamma globulin, and transferrin, etc.), addition of preservatives, addition of calibrants, addition of protease inhibitors, addition of denaturants, desalting, concentration and/or extraction of sample nucleic acids, and/or amplification of sample nucleic acids (*e.g.*, by PCR or other nucleic acid amplification techniques). Samples also include materials prepared by techniques that isolate, *e.g.*, nucleosomes or transcription factors and/or nucleic acids associated with nucleosomes or transcription factors.

[0114] Removal from a sample of proteins that are not desirable for a relevant purpose or context (*e.g.*, high abundance, uninformative, or undetectable proteins) can be achieved using high affinity reagents, high molecular weight filters, ultracentrifugation and/or electrodialysis. High affinity reagents include antibodies or other reagents (*e.g.*, aptamers) that selectively bind to high abundance proteins. Sample preparation can also include ion exchange chromatography, metal ion affinity chromatography, gel filtration, hydrophobic chromatography, chromatofocusing, adsorption chromatography, isoelectric focusing and related techniques. Molecular weight filters include membranes that separate molecules based on size and molecular weight. Such filters may further employ reverse osmosis, nanofiltration, ultrafiltration and microfiltration. Ultracentrifugation is the centrifugation of a sample at about 15,000-60,000 rpm while monitoring with an optical system the sedimentation (or lack thereof) of particles. Electrodialysis is a procedure which uses an electromembrane or semipermeable membrane in a process in which ions are transported through semi-permeable membranes from one solution to another under the influence of a potential gradient. Since the membranes used in electrodialysis may have the ability to selectively transport ions having positive or negative charge, reject ions of the opposite charge, or to allow species to migrate through a semipermeable membrane based on size and charge, it renders electrodialysis useful for concentration, removal, or separation of electrolytes.

[0115] Separation and purification in the present disclosure may include any procedure known in the art, such as capillary electrophoresis (*e.g.*, in capillary or on-chip) or chromatography (*e.g.*, in capillary, column or on a chip). Electrophoresis is a method that can be

used to separate ionic molecules under the influence of an electric field. Electrophoresis can be conducted in a gel, capillary, or in a microchannel on a chip. Examples of gels used for electrophoresis include starch, acrylamide, polyethylene oxides, agarose, or combinations thereof. A gel can be modified by its cross-linking, addition of detergents, or denaturants, immobilization of enzymes or antibodies (affinity electrophoresis) or substrates (zymography) and incorporation of a pH gradient. Examples of capillaries used for electrophoresis include capillaries that interface with an electrospray.

[0116] Capillary electrophoresis (CE) is preferred for separating complex hydrophilic molecules and highly charged solutes. CE technology can also be implemented on microfluidic chips. Depending on the types of capillary and buffers used, CE can be further segmented into separation techniques such as capillary zone electrophoresis (CZE), capillary isoelectric focusing (CIEF), capillary isotachophoresis (CITP) and capillary electrochromatography (CEC). An embodiment to couple CE techniques to electrospray ionization involves the use of volatile solutions, for example, aqueous mixtures containing a volatile acid and/or base and an organic such as an alcohol or acetonitrile.

[0117] Capillary isotachophoresis (CITP) is a technique in which the analytes move through the capillary at a constant speed but are nevertheless separated by their respective mobilities. Capillary zone electrophoresis (CZE), also known as free-solution CE (FSCE), is based on differences in the electrophoretic mobility of the analytes, determined by the charge on the analytes, and the frictional resistance the analytes encounter during migration, which is often directly proportional to the size of the analytes. Capillary isoelectric focusing (CIEF) allows weakly-ionizable amphoteric molecules, to be separated by electrophoresis in a pH gradient. CEC is a hybrid technique between traditional high performance liquid chromatography (HPLC) and CE.

[0118] Separation and purification techniques used in the present disclosure can include any chromatography procedures known in the art. Chromatography can be based on the differential adsorption and elution of certain analytes or partitioning of analytes between mobile and stationary phases. Different examples of chromatography include, but not limited to, liquid chromatography (LC), gas chromatography (GC), high performance liquid chromatography (HPLC), etc.

[0119] In some embodiments, whole blood is collected from a subject, and a plasma layer is separated by centrifugation. cfDNA may be then extracted from the plasma using methods known in the art.

Histone Modifications, Chromatin Accessibility and Transcription Factor Binding

[0120] Histone methylation is understood to increase or decrease expression of associated coding sequences, depending on which histone residue is methylated. Histone methylation is an essential modification that can cause monomethylation (me1), dimethylation (me2), and trimethylation (me3) of several amino acids, thus directly affecting heterochromatin formation, gene imprinting, X chromosome inactivation, and gene transcriptional regulation. Histone methyltransferases promote monomethylation, dimethylation, or trimethylation of histones while histone demethylases promote demethylation of histones. In general, lysine (Lys or K), arginine (Arg or R), and rarely histidine (His or H) are the most common histone methyl acceptors. Histone methylation only occurs at specific lysine and arginine sites of histone H3 and H4. In histone H3, lysine 4, 9, 26, 27, 36, 56, and 79 and arginine 2, 8, and 17 can be methylated. By comparison, histone H4 has fewer methylation sites, in which only lysine 5, 12, and 20 and arginine 3 can be methylated. Histone methylation is often associated with transcriptional activation or inhibition of downstream genes. The methylation of histone H3K4, R8, R17, K26, K36, K79, H4R3, and K12 can activate gene transcription. However, the methylation of histone H3K9, K27, K56, H4K5, and K20 can inhibit gene transcription. Thus, for example, H3K4 methylation generally activates gene expression, while H3K27 methylation generally represses gene expression.

[0121] Histone acetylation occurs predominantly at lysine residues and is generally understood to increase expression of associated coding sequences. Without wishing to be bound by any theory, acetylation of lysine residues is thought to neutralize lysine's positive charge and thereby cause histones to drift away from DNA, which has a negative charge. The released structure facilitates access to transcriptional machinery such as transcription factors and RNA polymerase II. Histone acetylation and deacetylation are generally catalyzed by histone acetyltransferases (HATs) and HDACs, respectively. Acetyl-CoA can be a source and co-factor of acetylation. In regulatory regions, HATs can acetylate histones and recruit HAT-containing complexes to activate the transcriptional process. For instance, H3K9ac and H3K27ac levels can

be associated with promoter and enhancer activities. Furthermore, H3K27ac enhances not only the kinetics of transcriptional activation, but also accelerates the transition of RNA polymerase II from the initiation state to the elongation state.

[0122] Differential modification of a genomic locus (*e.g.*, differential histone methylation and/or differential histone acetylation) can refer to, or be determined by or detected as, a comparative difference or change in modification status of one or more genomic loci between a first sample, condition, disease, or state and a second or reference sample, condition, disease, or state. Those of skill in the art will appreciate that a reference is typically produced by measurement using a methodology identical, similar, or comparable to that by which a compared non-reference measurement was taken.

[0123] Chromatin accessibility can refer to the degree to which nuclear macromolecules are able to physically contact DNA and is determined in part by the occupancy and modification status of nucleosomes. Modified histones can regulate chromatin accessibility through a variety of mechanisms, such as altering transcription factor (TF) binding through steric hindrance and modulating nucleosome affinity for active chromatin remodelers. The topological organization of nucleosomes across the genome is non-uniform: while histones can be densely arranged within facultative and constitutive heterochromatin, histones can be depleted at regulatory loci, including within enhancers, insulators and transcribed gene bodies. Active regulatory elements of the genome are generally accessible.

[0124] Differential accessibility of a genomic locus can refer to, or be determined by or detected as, a comparative difference or change in modification status of one or more genomic loci between a first sample, condition, disease, or state and a second or reference sample, condition, disease, or state. Those of skill in the art will appreciate that a reference is typically produced by measurement using a methodology identical, similar, or comparable to that by which a compared non-reference measurement was taken.

[0125] A reference can be a value or set of values that are predetermined or derived from a sample or set of samples. A reference can be a sample or set of samples. A reference value can be a predetermined threshold value, a value that varies in accordance with circumstances (*e.g.*, according to patient subpopulation, age, weight, or other variables), or a ratio. Reference ratios can be ratios relating to the modification and/or accessibility of multiple loci within individual samples and/or references, or across or between samples and/or references. In various

embodiments, a reference can have or represent a normal, non-diseased state. In some embodiments, such as for staging of disease or for evaluating the efficacy of treatment, a reference can have or represent a diseased state, *e.g.*, a cancer, stage of cancer, or subtype of cancer, *e.g.*, ER-positive cancer or ER-negative cancer. In some embodiments, a reference can represent an ER+ cancer with an Allred score of 3, 4, 5, 6, 7 or 8 based on IHC testing or an ER+ cancer with an Allred score of at least 3, at least 4, at least 5, at least 6, at least 7 or 8 based on IHC testing. In some embodiments, a reference can represent an ER- cancer with an Allred score of 0, 1, or 2 based on IHC testing. In some embodiments, a reference can correspond to a subject having breast cancer and/or a breast cancer subtype, *e.g.*, ER-positive or ER-negative breast cancer.

[0126] In some embodiments, a reference is a predetermined threshold. In some embodiments, the predetermined threshold has previously been shown to be capable of distinguishing ER-positive and ER-negative cancers (*e.g.*, distinguish with an AUROC of greater than 0.5). In some embodiments, a reference is a measurement from a liquid biopsy sample. In some embodiments, a reference is a measurement from liquid biopsy samples obtained from a cohort of subjects. In some embodiments, a reference is a normalized sample. In some embodiments, a reference is a measurement obtained from liquid biopsy samples obtained from a cohort of subjects who have previously been determined to have an ER-positive or ER-negative cancer, including, *e.g.*, an ER-positive or ER-negative breast cancer.

[0127] In certain instances, a reference is a non-contemporaneous sample from the same source, *e.g.*, a prior sample from the same source, *e.g.*, from the same subject. In certain instances, a reference for the modification status of one or more genomic loci (*e.g.*, one or more differentially modified genomic loci) can be the modification status of the one or more genomic loci (*e.g.*, one or more differentially modified genomic loci) in a sample (*e.g.*, a sample from a subject), or a plurality of samples, known to represent a particular state (*e.g.*, an ER-positive cancer or ER-negative cancer). In certain instances, a reference for the accessibility status of one or more genomic loci (*e.g.*, one or more differentially accessible genomic loci) can be the accessibility status of the one or more genomic loci (*e.g.*, one or more differentially accessible genomic loci) in a sample (*e.g.*, a sample from a subject), or a plurality of samples, known to represent a particular state (*e.g.*, an ER-positive cancer or ER-negative cancer).

[0128] In some illustrative but non-limiting embodiments of the present disclosure differential modification or differential accessibility can refer to a differential (*e.g.*, between a sample and a reference) with an absolute $\log_2(\text{fold-change})$ that is greater than or equal to 0.5, 1.0, 1.5, 2.0, 2.5, 3.0, 3.5, 4.0 or more, or any range in between, inclusive, *e.g.*, as measured according to an assay provided herein. In Tables 1-3, the $\log_2(\text{fold-change})$ values are based on ratios of ER-positive to ER-negative reads, *i.e.*, positive $\log_2(\text{fold-change})$ values indicate that sequencing reads in a particular genomic locus are associated with an ER-positive status while a negative $\log_2(\text{fold-change})$ value indicates that sequencing reads in a particular genomic locus are associated with an ER-negative status.

[0129] Enhancers are genomic loci that can be differentially modified or differentially accessible in and/or between conditions, diseases, and other states. Enhancers are cis-acting DNA regulatory regions that are thought to bind trans-acting proteins that contribute to expression patterns of associated genes. Chromatin ImmunoPrecipitation sequencing (ChIP-seq) of histone modifications (*e.g.*, acetylation) have identified millions of enhancers in mammalian genomes. The number of active enhancers in any given cell type is estimated to be in the tens of thousands. Certain transcription factors (TFs), sometimes referred to as “master” transcription factors, associate with active enhancers with important impacts on gene expression and cell function. Certain such transcription factors preferentially associate with enhancers that regulate genes required for establishing cell identity and function, including enhancer domains known as “super-enhancers”. Moreover, master TFs can participate in inter-connected auto-regulatory circuitries or “cliques” that are self-reinforcing, show marked cell selectivity, and function to maintain cell state and/or cell survival.

Techniques for Detecting and Quantifying Histone Modifications and Transcription Factor Binding

[0130] Various techniques of molecular biology are well known in the art and/or disclosed in the present application for detecting and quantifying histone modifications and/or transcription factor binding. In some embodiments, the methods, kits and systems of present disclosure involve the detection and quantification of histone modifications and/or transcription factor binding in samples, *e.g.*, in liquid biopsy samples including cfDNA such as plasma samples including cfDNA. Chromatin ImmunoPrecipitation (ChIP) is one technique of

molecular biology useful in detecting and quantifying histone modifications and transcription factor binding in samples. CUT&RUN or CUT&Tag are other more recent techniques that can also be used to detect and quantify histone modifications and transcription factor binding sites. ChIP-chip, ChIP-exo, ChIP Re-ChIP, and ChIPmentation are other alternative techniques that could be used.

[0131] ChIP can involve various steps including one or more of fixation, sonication, immunoprecipitation, and analysis of the immunoprecipitated DNA. ChIP has become a very widely used tissue-based technique for determining the in vivo location of binding sites of various transcription factors and histones. Because the proteins are captured at the sites of their binding with DNA, ChIP helps to detect DNA-protein interactions that take place in living cells. More importantly, ChIP can be coupled to many commonly used molecular biology techniques such as PCR and real-time PCR, PCR with single-stranded conformational polymorphism, Southern blot analysis, Western blot analysis, cloning, and microarray. The resulting versatility has increased the potential of this technique.

[0132] ChIP of tissue samples usually involves cross-linking of the chromatin-bound proteins by formaldehyde, followed by sonication or nuclease treatment to obtain small DNA fragments. Immunoprecipitation can be then carried out using specific antibodies to the DNA-binding protein of interest. The DNA can be then released from the proteins and analyzed using various methods. ChIP has also been used to study RNA-protein interactions. X-ChIP methods utilize fixed chromatin fragmented by sonication, while the N-ChIP methods utilize native chromatin, which can be unfixed and nuclease digested.

[0133] The first step of the technique can be the cross-linking of DNA and proteins. Formaldehyde is one of the most used cross-linking agents. One advantage of using formaldehyde can be the ease of reversibility of the cross-links and its ability to form bonds that span approximately 2 angstroms. This means that formaldehyde can bind molecules in close association with each other. Generally, formaldehyde can be added to the medium in the cell culture flask or plate. It enters the cells through the cell membrane and cross-links the proteins to the chromatin. Formaldehyde fixation of tumor tissues has also been done. Other cross-linking agents that have been used include chemicals such as methylene blue and acridine orange, cisplatin, dimethylarsinic acid, potassium chromate, and ultraviolet (UV) light and lasers.

[0134] Harvested chromatin can be sonicated in one or more sonication cycles. DNA can be typically broken into to 100–500 bp fragments to pinpoint the location of the DNA sequence of interest. An alternative to sonication can be nuclease digestion of the chromatin, *e.g.*, in N-ChIP methods. Purification of chromatin can be achieved using a cesium chloride (CsCl) gradient centrifugation.

[0135] Chromatin can be enriched for a particular histone modification using an agent that binds the histone modification (*e.g.*, immunoprecipitating using one or more antibodies that bind a target epitope).

[0136] For example, an antibody used in ChIP can selectively bind a particular transcription factor or one or more particular histone modifications, such as one or more particular histone acetylation modifications or histone methylation modifications. In some embodiments, an antibody used to bind a target epitope can be a “pan” antibody (*e.g.*, a pan-acetylation antibody, a pan-methylation antibody, an antibody that binds a group of histone modifications associated with increased transcription activation, and/or an antibody that binds a group of histone modifications associated with increased transcription repression). The antibody against the protein of interest is allowed to bind to the protein-DNA complex, and the complex can be then precipitated. Immunosorbants commonly used to separate the antigen-antibody complex from the lysate include salmon sperm DNA-protein A-Sepharose®, protein G, magnetic beads, and other engineered immunoprecipitation systems known to those of skill in the art.

[0137] Immunoprecipitated DNA can be eluted. Once the DNA of interest is isolated, many detection and quantification methods can be used to study the isolated gene fragments. Commonly utilized methods include PCR, real-time PCR, slot blot hybridization, microarray techniques, and deep or next-generation sequencing. ChIP-seq combines chromatin immunoprecipitation (ChIP) with massively parallel DNA sequencing to identify the binding sites of DNA-associated proteins. ChIP-seq can be used to map DNA-binding proteins, *e.g.*, transcription factor binding sites and histone modifications in a genome-wide manner.

[0138] Cell-free Chromatin ImmunoPrecipitation sequencing (cfChIP-seq) involves applying ChIP-seq to samples that include cell-free DNA, *e.g.*, liquid biopsy samples including cfDNA such as plasma samples including cfDNA (*e.g.*, see Sadeh et al., Nat Biotechnol (2021) 39: 586–598 and Jang et al., Life Sci Alliance (2023) 6(12):e202302003 the entire contents of each of which are incorporated herein by reference). In some embodiments, cfChIP-seq uses

antibodies or antibody fragments that bind specific histone modifications (*e.g.*, H3K4me3 and/or H3K27ac) and/or transcription factors that are coupled (covalently or non-covalently) to beads, *e.g.*, magnetic beads such as Dynabeads® magnetic beads and incubated with a volume, *e.g.*, about 1 mL of thawed plasma obtained from a subject. Without limitation, exemplary antibodies that bind H3K4me3 include PA5-27029 (available from Thermo Fisher Scientific in Waltham, MA) and C15410003 (available from Diagenode in Denville, NJ) and exemplary antibodies that bind H3K27ac include ab21623 or ab4729 (both available from Abcam in Cambridge, UK) and C15210016 (available from Diagenode in Denville, NJ).

[0139] In some embodiments, the antibodies or antibody fragments can be covalently coupled to beads, *e.g.*, epoxy beads. In some embodiments, the antibodies or antibody fragments can be non-covalently coupled to beads, *e.g.*, Protein A or Protein G beads such as Dynabeads® Protein A or Dynabeads® Protein G beads. After washing, a cfDNA library is then typically prepared from the captured cfDNA. Library preparation can be done on-bead or after releasing the captured cfDNA by digestion of bound histones, *e.g.*, using proteinase K. The cfDNA library is then sequenced to generate reads of captured cfDNA sequences, *e.g.*, by next-generation sequencing (NGS) as is known in the art. The reads are then analyzed, *e.g.*, aligned and counted using standard bioinformatic techniques as is known in the art. A cfChIP-seq bioinformatic pipeline can include, *e.g.*, alignment of sequence reads to a reference genome with BWA or Bowtie2. Aligned reads can be used to call and quantify peaks as compared to a reference. In some embodiments, histone modifications at a given genomic loci can be quantified using sequencing data. *E.g.*, in some embodiments, histone modifications can be quantified by counting the number of sequence reads that fall within a genomic loci (*e.g.*, have at least one nucleotide overlapping with a genomic loci). In some embodiments, non-uniquely mapped and/or redundant sequence reads are discarded prior to quantifying histone modifications. In some embodiments, when quantifying histone modifications, sequence reads that fall within high noise regions of the genome are ignored.

[0140] In some embodiments, sequence reads are adjusted on the basis of sequencing depth prior to counting. Adjusting on the basis of sequencing depth can include, *e.g.*, quantile normalizing sequence reads to a common reference distribution. In some embodiments, sequence reads are adjusted on the basis of ChIP quality prior to counting. In some embodiments, sequence reads are normalized relative to aggregate counts across a set of regions (*e.g.*, 1,000, 2,000,

3,000, 4,000, 5,000, 6,000, 7,000, 8,000, 9,000, 10,000 or more regions) previously determined to have DNase hypersensitivity in most cell types. In some embodiments, an estimate of local background signal is subtracted from the count of sequence reads at each genomic loci.

[0141] CUT&Tag involves antibody-based binding of a target protein, *e.g.*, transcription factor or histone modification of interest, where antibody incubation is directly followed by the shearing of the chromatin and library preparation (see Kaya-Okur et al., Nat Comm (2019) 10:1930). CUT&Tag assays take advantage of a Tn5 transposase that is fused with Protein A to direct the enzyme to the antibody bound to its target on chromatin. Tn5 transposase is pre-loaded with sequencing adapters (generating the assembled pA-Tn5 adapter transposome) to carry out antibody-targeted tagmentation. In a typical CUT&Tag assay samples are incubated with an antibody immobilized on Concanavalin A-coated magnetic beads to facilitate subsequent washing steps. Cells can be incubated with a primary antibody specific for the target protein of interest followed by incubation with a secondary antibody. Samples can then be incubated with assembled transposomes, which consist of Protein A fused to the Tn5 transposase enzyme that is conjugated to NGS adapters. After incubation, unbound transposome can be washed away using stringent conditions. Tn5 is a Mg^{2+} -dependent enzyme so Mg^{2+} can be added to activate the reaction, which results in the chromatin being cut close to the protein binding site and simultaneous addition of the NGS adapter DNA sequences. Chromatin cleavage and library preparation can be achieved in one single step.

[0142] CUT&RUN is an epigenomic profiling strategy in which antibody-targeted controlled cleavage by micrococcal nuclease releases specific protein-DNA complexes into the supernatant for paired-end DNA sequencing (see Skene and Henikoff, Elife (2017) 6:1-35, Skene et al., Nat Protoc (2018) 13:1006-1019). As only targeted fragments enter into solution, and the vast majority of DNA is left behind, CUT&RUN has low background levels. In an example CUT&RUN assay, a sample is incubated with an antibody or antibody fragment that binds the target protein, *e.g.*, transcription factor or histone modification of interest. The sample is then incubated with Protein-A-MNase after which $CaCl_2$ can be added to initiate the calcium dependent nuclease activity of MNase to cleave the DNA around the target protein. The protein-A-MNase reaction can be quenched by adding chelating agents (EDTA and EGTA). Cleaved DNA fragments are then liberated, extracted, and used to construct a sequencing library.

[0143] A person of ordinary skill in the art is aware of suitable DNA sequencing technologies for use in methods described herein that comprise a sequencing step. Suitable DNA sequencing technologies include, e.g., next generation sequencing (NGS) approaches. Additional steps that are required to prepare DNA for sequencing via an appropriate sequencing approach can be incorporated into methods described herein. For example, in some embodiments, a method described herein comprises attaching (e.g., ligating) DNA adapters to cfDNA. In some embodiments, DNA adapters can be attached prior to, during, or after enrichment for a histone modification. In some embodiments, a method comprises amplifying cfDNA after attaching DNA adapters.

Techniques for Detecting and Quantifying Chromatin Accessibility

[0144] Various techniques of molecular biology are well known in the art and/or disclosed in the present application for detecting and quantifying chromatin accessibility. In some embodiments, the methods, kits and systems of the present disclosure involve the detection and quantification of chromatin accessibility in samples, *e.g.*, in liquid biopsy samples including cfDNA such as plasma samples including cfDNA. ATAC-seq (Assay of Transpose Accessible Chromatin sequencing), NOMe-seq (Nucleosome Occupancy and Methylome sequencing), FAIRE-seq (Formaldehyde-Assisted Isolation of Regulatory Elements sequencing), MNase-seq (Micrococcal Nuclease digestion with sequencing), and DNase hypersensitivity assays are exemplary techniques of molecular biology useful in detecting and quantifying chromatin accessibility in samples. Sono-Seq is another alternative method that could be used (see Auerbach et al., Proc Natl Acad USA (2009) 106(35):14926-14931).

[0145] DNase hypersensitivity assays can use the non-specific DNA endonuclease Deoxyribonuclease I (DNase I), which selectively digests accessible DNA regions. DNase I hypersensitivity sites (DHS) identified by DNase-seq include open chromatin regulatory regions. A typical DNase hypersensitivity assay can include a first step in which nuclei are isolated from cells using lysis buffer, and nuclei are digested using DNase I. DNA fragment sizes are measured to identify optimal digestion using gel electrophoresis. Biotinylated linkers can be ligated to the ends of digested DNA after polishing to make blunt ends, and the DNA can then be isolated. DNA with biotinylated linker can be digested by restriction endonuclease MmeI and captured by streptavidin coated Dynabeads® to generate short tags to which a second sequencing adaptor can

be ligated. A second linker can be ligated and amplified to generate a library for sequencing. A DNase-seq bioinformatic pipeline can include, *e.g.*, alignment of sequence reads to a reference genome with BWA or Bowtie2. Aligned reads can be used to call and quantify peaks as compared to a reference.

[0146] MNase-seq determines chromatin accessibility with micrococcal nuclease (MNase) that preferentially digests nucleosome-free, protein-unbound DNA. A typical MNase-seq assay can include a first step in which nuclei are isolated from either native or crosslinked chromatin and digested using MNase with titration. In vivo formaldehyde crosslinking step that is designed to capture the interaction between proteins and DNA. This crosslinking allows bound proteins to shield their associated DNA from digestion by MNase. Following crosslinking, samples are digested with MNase, which can be specifically activated by addition of Ca²⁺ to the buffer. Digestion can be halted by chelating the reaction, at which point the samples are RNase treated, crosslinks are reversed, and proteins are digested away from the chromatin. DNA can then be isolated via a phenol-chloroform extraction. Uncut DNA is purified and mononucleosome bands are isolated and excised through gel electrophoresis. Isolated DNA can be amplified by adding adapters to generate a library, and sequenced. MNase-seq primarily sequences regions of DNA bound by histones or other proteins. Therefore, it indirectly determines which regions of DNA are accessible by directly determining which regions are bound to nucleosomes or proteins.

[0147] FAIRE-seq is a method in which nucleosome-depleted regions of DNA (NDRs) are isolated from chromatin. A typical FAIRE-seq assay can include a first step in which cells are fixed using formaldehyde so that histones are crosslinked to interacting DNA. Crosslinked chromatin can then be sheared by sonication that generates protein-free DNA and protein-crosslinked DNA fragments. Protein-free DNA can be isolated using a phenol–chloroform extraction: DNA crosslinked with protein stays in organic phase, while protein-free DNA stays in aqueous phase. Highly crosslinked DNA remains in the organic phase and the non-crosslinked DNA is pulled to the aqueous phase. Non-crosslinked DNA from the aqueous phase can then be amplified and sequenced. Reads enriched in the sequencing pool tend to have lower nucleosome and transcription factor binding and are therefore inferred to come from accessible regions.

[0148] NOME-seq is a method to identify nucleosome-depleted regions of DNA (NDRs) with M.CviPI methyltransferase that methylates cytosine in GpC dinucleotides not protected by

nucleosomes or other proteins. Unlike C^mpG, GpC^m in the human genome does not occur naturally in most cell types. GpC^m levels at open chromatin regions can be compared to background signals and used to detect and quantify NDRs. A typical NOME-seq protocol can include a step in which samples are treated with M.CviPI and S-adenosylhomocysteine (SAM) to methylate accessible GpC sites. M.CviPI treated DNA can be sheared using a sonicator, so that DNA fragments can be sequenced. DNA is treated with bisulfite, which converts unmethylated cytosine to uracil using sodium bisulfite, while methylated cytosine is unaffected. A library is generated using adapters and sequenced. Accessible chromatin is expected to have high levels of GpC^m but low levels of C^mpG. Therefore, NOME-seq identifies NDRs using the two separate methylation analyses that serve as independent (but opposite) measures, providing matched chromatin designations for each regulatory element.

[0149] ATAC-seq uses hyperactive Tn5 transposase that preferentially cuts accessible chromatin regions and simultaneously inserts adapters to the fragmented region (Buenrostro et al., Nat Methods (2013) 10(12):1213-1218 the entirety of which is incorporated herein by reference). A typical ATAC-seq assay can include a first step in which samples are incubated with Tn5 transposase. DNA can then be isolated and purified. DNA fragmented and tagged by Tn5 transposase can be purified and then amplified to generate a library and sequenced for analysis.

Techniques for Detecting and Quantifying DNA Methylation

[0150] Various techniques of molecular biology are well known in the art and/or disclosed in the present application for detecting and quantifying DNA methylation. In some embodiments, the methods, kits and systems of the present disclosure involve the detection and quantification of chromatin accessibility in samples, *e.g.*, in liquid biopsy samples including cfDNA such as plasma samples including cfDNA. Bisulfite sequencing (BS-Seq), Whole Genome Bisulfite Sequencing (WGBS), Methylated DNA ImmunoPrecipitation sequencing (MeDIP-seq), or Methyl-CpG-Binding Domain sequencing (MBD-seq) are exemplary techniques of molecular biology useful in detecting and quantifying chromatin accessibility in samples. Reduced representation bisulfite sequencing (RRBS) is another alternative method that could be used (see Meissner et al., Nucleic Acids Res (2005) 33(18):5868-5877). Illumina Infinium arrays could also be used to detect and quantify DNA methylation.

[0151] DNA methylation typically refers to the methylation of the 5' position of cytosine (mC) by DNA methyltransferases (DNMT). It is a major epigenetic modification in humans and many other species. In mammals, most DNA methylations occur within the context of CpG dinucleotides. DNA methylation is thought to be a repressive chromatin modification. Aberrant methylation can lead to many diseases including cancers (Robertson, *Nat Rev Genet* (2005) 6:597–610 and Bergman and Cedar, *Nat Struct Mol Biol* (2013) 20:274–281).

[0152] Bisulfite sequencing (BS-Seq) or Whole-Genome Bisulfite Sequencing (WGBS) is a well-established protocol to detect methylated cytosines in genomic DNA. In this method, genomic DNA is treated with sodium bisulfite and then sequenced, providing single-base resolution of methylated cytosines in the genome. Upon bisulfite treatment, unmethylated cytosines are deaminated to uracil which, upon sequencing, are converted to thymidine. Simultaneously, methylated cytosines resist deamination and are read as cytosines. The location of the methylated cytosines can then be determined by comparing treated and untreated sequences.

[0153] In some embodiments, methylated DNA can be sequenced using a method that comprises enriching for cfDNA that comprises methylated DNA. Enrichment can be accomplished e.g., using an agent that selectively binds methylated DNA (e.g., an antibody as in MeDIP-seq or a methyl-CpG-Binding Domain (MBD), as in MBD-seq). In some embodiments, an agent that binds methylated DNA is attached (e.g., via a covalent or noncovalent bond) to a physical support (e.g., a bead, a magnetic bead, an agarose bead, or a magnetic epoxy bead), wherein the attaching can be prior to, during, or after incubation with a sample.

[0154] MeDIP-seq was first reported by Weber et al., *Nat Genet* (2005) 37:853–862. In a typical MeDIP-seq protocol, antibody or antibody-fragment that binds 5-methylcytidine (5mC) is used to enrich methylated DNA fragments, then these fragments are sequenced and analyzed. If using 5mC-specific antibodies or antibody fragments, methylated DNA is isolated from genomic DNA via immunoprecipitation. Anti-5mC antibodies are incubated with fragmented genomic DNA and precipitated, followed by DNA purification and sequencing.

[0155] Methyl-CpG-Binding Domain sequencing (MBD-seq) is similar to MeDIP-seq except that it uses methyl binding domain (MBD) proteins instead of antibodies or antibody fragments to bind methylated DNA. In a typical MBD-seq protocol, genomic DNA is first sonicated and incubated with tagged MBD proteins that can bind methylated cytosines. The protein-DNA

complex is then precipitated with antibody-conjugated beads that are specific to the MBD protein tag, followed by DNA purification and sequencing.

[0156] In some embodiments, DNA methylation at a given genomic loci can be quantified by sequencing methylated DNA. For example, in some embodiments, DNA methylation at a genomic loci can be quantified by counting the number of sequence reads that overlap with the genomic loci (e.g., comprise at least one nucleotide that overlaps with the genomic loci).

[0157] A person of skill in the art is aware of suitable DNA sequencing technologies for use in methods described herein that comprise a sequencing step. Suitable DNA sequencing technologies include, e.g., next generation sequencing (NGS) approaches. Additional steps that are required to prepare DNA for sequencing via an appropriate sequencing approach can be incorporated into methods described herein. For example, in some embodiments, a method described herein comprises attaching (e.g., ligating) DNA adapters to cfDNA. In some embodiments, DNA adapters can be attached prior to, during, or after enrichment for a histone modification.

Classifiers

[0158] In some embodiments, the present disclosure provides methods for obtaining a classifier, e.g., a validated classifier that can be used to determine ER status. In some embodiments, a subject is determined to have a validated epigenetic profile indicative of an ER-positive cancer based on analysis of a biological sample, optionally of cell-free DNA (cfDNA) from a liquid biopsy sample, obtained or derived from the subject, wherein the presence of the validated epigenetic profile has been determined using a validated classifier.

[0159] For illustration purposes and without limitation, in an exemplary embodiment of the present disclosure, the validated classifier may be obtained by:

[0160] (a) determining a genomic profile of one or more histone modifications, chromatin accessibility, binding of one or more transcription factors, and/or DNA methylation in (i) one or more ER-positive cell lines or (ii) biological samples obtained from a first cohort of subjects who have previously been determined to have an ER-positive cancer;

[0161] (b) determining a genomic profile of one or more histone modifications, chromatin accessibility, binding of one or more transcription factors, and/or DNA methylation in

(i) one or more ER-negative cell lines or (ii) biological samples obtained from a second cohort of healthy subjects or subjects who have previously been determined to have an ER-negative cancer;

[0162] (c) comparing the genomic profile determined in step (a) and the genomic profile determined in step (b), to identify genomic loci that have statistically different histone modification, chromatin accessibility, binding of transcription factor, and/or DNA methylation levels (“differential loci”);

[0163] (d) training a classifier on histone modification, chromatin accessibility, binding of transcription factor, and/or DNA methylation levels in the differential loci to distinguish between (i) samples from one or more ER-positive cell lines or biological samples obtained from the first cohort, and (ii) samples from one or more ER-negative cell lines or biological samples obtained from the second cohort, to identify samples having a profile of histone modification, chromatin accessibility, binding of transcription factor, and/or DNA methylation levels (“epigenetic profile”) that indicates that the samples are likely obtained from an ER-positive cell line or from the first cohort; and

[0164] (e) obtaining the validated classifier by validating the classifier from step (d) on a third cohort comprising an independent and group of subjects with ER-positive and ER-negative cancers and selecting a threshold such that the validated classifier predicts ER-positive cancers, with an area under the receiver operating characteristic (AUROC) greater than 0.5 (*e.g.*, greater than 0.55, greater than 0.6, greater than 0.65, greater than 0.7, greater than 0.75, greater than 0.8, greater than 0.85, greater than 0.9, or greater than 0.95), wherein subjects falling within the group of predicted ER-positive cancers display the validated epigenetic profile and subjects that do not fall within the group of ER-positive cancers lack the validated epigenetic profile.

[0165] A person of ordinary skill will appreciate that other methods can be used to obtain a classifier, *e.g.*, a validated classifier that can be used to determine ER status and that the present disclosure is not limited to classifiers obtained in accordance with this method.

Exemplary Genomic Loci

[0166] The present disclosure includes the identification of exemplary genomic loci that are differentially modified and/or differentially accessible in ER-positive vs. ER-negative cancer. See Tables 1-3 which show the chromosomal coordinates of each genomic locus and its observed

$\log_2(\text{fold-change})$ (ER-positive/ER-negative) which shows whether modification of a locus was correlated with ER-positive status ($\log_2(\text{FC}) > 0$) or correlated with ER-negative status ($\log_2(\text{FC}) < 0$). The genomic loci are sorted based on their chromosomal coordinates which are based on human genome build hg19.

[0167] The present disclosure is not limited to methods that use the exact same chromosomal coordinates that are recited in Tables 1-3. The present disclosure encompasses methods that use any of the genomic loci in Table 1-3 and also subregions thereof, *i.e.*, references herein to methods that involve detecting and/or quantifying one or more histone modifications, chromatin accessibility, binding of one or more transcription factors, and/or DNA methylation at one or more genomic loci of Table 1-3 encompasses methods that detect these marks anywhere within these genomic loci including within any subregions. For example, where Table 2 references chr1:901178-903765 as a genomic locus for detecting and/or quantifying H3K27ac modification, this encompasses methods that detect and/or quantify H3K27ac modification at any position or sub-region of chr1:901178-903765, *e.g.*, methods that detect and/or quantify H3K27ac modification within chr1:902178-903565, etc. In some embodiments, a subregion may span at least 100, 200, 300, 400, 500, 600, 700, 800, 900, 1000, 1500, 2000, 2500 or at least 3000 contiguous base pairs that are located between the lower and upper coordinates of a genomic locus recited in Tables 1-3. In some embodiments, a subregion may span less than 100, 200, 300, 400, 500, 600, 700, 800, 900, 1000, 1500, 2000, 2500 or at least 3000 contiguous base pairs that are located between the lower and upper coordinates of a genomic locus recited in Tables 1-3. In some embodiments, a subregion may have the same central coordinate as a genomic locus recited in Tables 1-3. In some embodiments, a subregion may have a different central coordinate as a genomic locus recited in Tables 1-3. It is also to be understood that the lower/upper coordinates of the genomic loci in Tables 1-3 are approximate and that the present disclosure encompasses methods where any one or more of the genomic loci are expanded by increasing the size of the genomic locus by 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40% or up to 50% in one or both directions.

[0168] In some embodiments a classifier is generated using a set of differentially modified and/or differentially accessible genomic loci that are correlated with ER-positive status and a set of differentially modified and/or differentially accessible loci that are correlated with ER-negative status. Sequence reads that fall into each selected genomic locus are analyzed and

counted, *e.g.*, as described herein including the Examples. In some embodiments, counts from genomic loci that are correlated with ER-positive status are aggregated and counts from genomic loci that are correlated with ER-negative status are aggregated. In some embodiments, a ratio of the aggregated ER-positive and ER-negative counts is used to determine ER status. Other ways of using the genomic loci and related sequencing data to generate and apply a classifier to determine ER status are described herein and known in the art, *e.g.*, without limitation, methods that use a learning statistical classifier system or a combination of learning statistical classifier systems.

[0169] In some embodiments, exemplary genomic loci from Table 1, 2 or 3 are used in a monomodal classifier, *e.g.*, a classifier that uses a single histone modification (*e.g.*, H3K4me3 or H3K27ac) or DNA methylation at one or more genomic loci for purposes of determining ER status. In some embodiments, exemplary genomic loci from Table 1, 2 and/or 3 are used in combination in a multimodal classifier, *e.g.*, a classifier that uses more than one histone modification (*e.g.*, H3K4me3 and H3K27ac) or one or more histone modifications (*e.g.*, H3K4me3 and/or H3K27ac) and DNA methylation at one or more genomic loci for purposes of determining ER status.

Differential H3K4me3 modification

[0170] Genomic loci demonstrating differential H3K4 methylation (in particular H3K4 trimethylation, H3K4me3) in ER-positive vs. ER-negative cancer are provided in Table 1 which shows the chromosomal coordinates of each genomic locus and its observed log₂(fold-change) (ER-positive/ER-negative). The genomic loci are sorted based on their chromosomal coordinates which are based on human genome build hg19.

[0171] A person of skill in the art will recognize that the methods disclosed herein do not require that every genomic locus listed in Table 1 be assessed for H3K4me3 modification. Instead, a subset of loci may be assessed for H3K4me3 modification. Subsets of the genomic loci of Table 1 can be selected (*e.g.*, for use in determining ER status) based on various performance criteria, *e.g.*, to select genomic loci that demonstrate differential modification with a particular level of statistical significance and/or a particular threshold of differential between relevant states (*e.g.*, a measured log₂(fold-change)). Subsets of the genomic loci may also be selected based on an algorithm, *e.g.*, during the process of obtaining a classifier. Those of skill in the art will

appreciate that such subsets of loci of Table 1, and loci included in such subsets, are together, individually, and/or in randomly selected subsets, at least as informative (*e.g.*, as statistically significant and/or reliable) for uses disclosed herein, *e.g.*, for determining ER status. See also the Examples of the present disclosure for experiments showing that informative classifiers can be generated using many different combinations of the loci. The present disclosure particularly includes, among other things, subsets of the genomic loci of Table 1, which have an absolute $\log_2(\text{fold-change})$ of 6.0 or higher, 5.5 or higher, 5.0 or higher, 4.5 or higher, 4.0 or higher, 3.5 or higher, 3.0 or higher, 2.5 or higher, 2.0 or higher, 1.9 or higher, 1.8 or higher, 1.7 or higher, 1.6 or higher, 1.5 or higher, 1.4 or higher, 1.3 or higher, 1.2 or higher, 1.1 or higher, 1.0 or higher, 0.9 or higher, 0.8 or higher, 0.7 or higher, 0.6 or higher, or 0.5 or higher. The present disclosure also includes subsets of the genomic loci of Table 1, which have an absolute $\log_2(\text{fold-change})$ of 6.0 or higher, 5.5 to less than 6.0, 5.0 to less than 5.5, 4.5 to less than 5.0, 4.0 to less than 4.5, 3.8 to less than 4.0, 3.6 to less than 3.8, 3.4 to less than 3.6, 3.2 to less than 3.4, 3.0 to less than 3.2, 2.8 to less than 3.0, 2.6 to less than 2.8, 2.4 to less than 2.6, 2.2 to less than 2.4, 2.0 to less than 2.2, 1.8 to less than 2.0, 1.6 to less than 1.8, 1.4 to less than 1.6, 1.2 to less than 1.4, 1.0 to less than 1.2, 0.8 to less than 1.0, or 0.6 to less than 0.8.

[0172] In various embodiments, a sample or subject from which the sample is obtained or derived, is determined to have a particular ER status (*e.g.*, ER-positive) if at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 150, 200, 250, 300, 350, 400, 450, 500, 750, 1000, 1500, 2000, 2500, or 3000 loci identified in Table 1 (or any subset thereof) are differentially H3K4me3 modified as compared to a reference (*e.g.*, a sample from an ER-negative or healthy subject). In certain embodiments, a subject from which the sample is obtained or derived, is determined to have a particular ER status (*e.g.*, ER-positive) if at least a number of loci identified in a Table 1 (or any subset thereof) having a lower bound selected from 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 150, 200, 250, or 300 and an upper bound selected from 10, 15, 20, 25, 50, 75, 100, 150, 200, 250, 300, 350, 400, 450, 500, 750, 1000, 1500, 2000, 2500, or 3000 is found to be differentially H3K4me3 modified as compared to a reference (*e.g.*, a sample from an ER-negative or healthy subject). In certain particular embodiments, a sample or subject from which the sample is obtained or derived, is determined to have a particular ER status (*e.g.*, ER-positive) if at least 1, 2, 3, 4, 5, 10, 20, 30, 40, or 50 loci identified in Table 1 (*e.g.*, about 1 to about 1,000,

about 5 to about 3,000, about 10 to about 1000, about 25 to about 200, about 5, about 10, about 20, or about 50 loci) are differentially H3K4me3 modified as compared to a reference (*e.g.*, a sample from an ER-negative or healthy subject). In various embodiments a sample or subject from which the sample is obtained or derived, is determined to have a particular ER status (*e.g.*, ER-positive) if at least 0.1%, 0.2%, 0.3%, 0.4%, 0.5%, 1%, 2%, 3%, 4%, 5%, 10%, 20%, 30%, 40%, 50%, 75%, or 100% of loci identified in Table 1 are differentially H3K4me3 modified as compared to a reference (*e.g.*, a sample from an ER-negative or healthy subject). In certain embodiments, a sample or subject from which the sample is obtained or derived, is determined to have a particular ER status (*e.g.*, ER-positive) if at least a percent of loci identified in Table 1 having a lower bound selected from 0.1%, 0.2%, 0.3%, 0.4%, 0.5%, 1%, 2%, 3%, 4%, 5%, or 10%, and an upper bound selected from 1%, 2%, 3%, 4%, 5%, 10%, 20%, 30%, 40%, 50%, 75%, or 100% is found to be differentially H3K4me3 modified as compared to a reference (*e.g.*, a sample from an ER-negative or healthy subject).

[0173] In various embodiments, a sample or subject from which the sample is derived, is determined to have a particular ER status (*e.g.*, ER-positive) if at least one (*e.g.*, at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, or at least 10) of the top 3, 5, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 150, 200, 250, 300, 350, 400, 450, 500, 750, 1000, 1500, 2000, 2500, or 3000 loci identified in Table 1 are differentially H3K4me3 modified as compared to a reference (*e.g.*, a sample from an ER-negative or healthy subject) (wherein, *e.g.*, the “top” 10 loci refers to the loci with 10 highest absolute log₂(fold-change) in Table 1). In some embodiments, a subject from which the sample is obtained or derived, is determined to have a particular ER status (*e.g.*, ER-positive) if at least one of the top 10 loci identified in Table 1 is differentially H3K4me3 modified as compared to a reference (*e.g.*, a sample from an ER-negative or healthy subject). In some embodiments, a subject from which the sample is obtained or derived, is determined to have a particular ER status (*e.g.*, ER-positive) if at least one of the top 25 loci identified in Table 1 is differentially H3K4me3 modified as compared to a reference (*e.g.*, a sample from an ER-negative or healthy subject). In some embodiments, a subject from which the sample is obtained or derived, is determined to have a particular ER status (*e.g.*, ER-positive) if at least one of the top 50 loci identified in Table 1 is differentially H3K4me3 modified as compared to a reference (*e.g.*, a sample from an ER-negative or healthy subject). In some embodiments, a subject from which the sample is obtained

or derived, is determined to have a particular ER status (*e.g.*, ER-positive) if at least five of the top 10 loci identified in Table 1 are differentially H3K4me3 modified as compared to a reference (*e.g.*, a sample from an ER-negative or healthy subject). In some embodiments, a subject from which the sample is obtained or derived, is determined to have a particular ER status (*e.g.*, ER-positive) if at least five of the top 25 loci identified in Table 1 are differentially H3K4me3 modified as compared to a reference (*e.g.*, a sample from an ER-negative or healthy subject). In some embodiments, a subject from which the sample is obtained or derived, is determined to have a particular ER status (*e.g.*, ER-positive) if at least five of the top 50 loci identified in Table 1 are differentially H3K4me3 modified as compared to a reference (*e.g.*, a sample from an ER-negative or healthy subject).

[0174] In various embodiments, a sample or subject from which the sample is derived, is determined to have a particular ER status (*e.g.*, ER-positive) if at least one of the top 10 loci (*e.g.*, at least 1, at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, or 10) identified in Table 1 and at least 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 150, 200, 250, 300, 350, 400, 450, 500, 750, 1000, 1500, 2000, 2500, or 3000 loci identified in Table 1 (or any subset thereof) in total are differentially H3K4me3 modified as compared to a reference (*e.g.*, a sample from an ER-negative or healthy subject). In various embodiments, a sample or subject from which the sample is derived, is determined to have a particular ER status (*e.g.*, ER-positive) if at least one of the top 25 loci identified in Table 1 (*e.g.*, at least 1, at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, or at least 10, at least 15, at least 20, or 25) and at least 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 150, 200, 250, 300, 350, 400, 450, 500, 750, 1000, 1500, 2000, 2500, or 3000 loci identified in Table 1 (or any subset thereof) in total are differentially H3K4me3 modified as compared to a reference (*e.g.*, a sample from an ER-negative or healthy subject). In various embodiments, a sample or subject from which the sample is derived, is determined to have a particular ER status (*e.g.*, ER-positive) if at least one of the top 50 loci (*e.g.*, at least 1, at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, or at least 10, at least 15, at least 20, or at least 25, at least 30, at least 35, at least 40, at least 45, or 50) identified in Table 1 and at least 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 150, 200, 250, 300, 350, 400, 450, 500, 750, 1000, 1500, 2000, 2500, or 3000 loci identified in Table 1 (or any subset thereof) in total are differentially H3K4me3 modified as compared to a reference (*e.g.*, a sample from an ER-

negative or healthy subject). In various embodiments, a sample or subject from which the sample is derived, is determined to have a particular ER status (*e.g.*, ER-positive) if at least five of the top 25 loci identified in Table 1 and at least 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 150, 200, 250, 300, 350, 400, 450, 500, 750, 1000, 1500, 2000, 2500, or 3000 loci identified in Table 1 (or any subset thereof) in total are differentially H3K4me3 modified as compared to a reference (*e.g.*, a sample from an ER-negative or healthy subject). In various embodiments, a sample or subject from which the sample is derived, is determined to have a particular ER status (*e.g.*, ER-positive) if at least five of the top 50 loci identified in Table 1 and at least 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 150, 200, 250, 300, 350, 400, 450, 500, 750, 1000, 1500, 2000, 2500, or 3000 loci identified in Table 1 (or any subset thereof) in total are differentially H3K4me3 modified as compared to a reference (*e.g.*, a sample from an ER-negative or healthy subject).

[0175] In various embodiments, differentially H3K4me3 modified refers to a methylation status characterized by an increase or decrease in a value measuring methylation (*e.g.*, of read counts and/or normalized read counts for a given genomic locus), and/or a mean, median and/or mode thereof, and/or a log thereof (*e.g.*, log base 2 (log₂)), of at least 1%, 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 75%, 100%, 2-fold, 3-fold, 4-fold, 5-fold, 6-fold, 7-fold, 8-fold, 9-fold, 10-fold, 15-fold, 20-fold, 25-fold, 30-fold, 35-fold, 40-fold, 45-fold, 50-fold, or greater, or any range in between, inclusive, such as 1% to 50%, 50% to 2-fold, 25% to 50-fold, 25% to 30-fold, 25% to 20-fold, 25% to 16-fold, 30% to 16-fold, 50% to 16-fold, 70% to 16-fold, 2-fold to 16-fold, 2.2-fold to 16-fold, 2.6-fold to 16-fold, 3-fold to 16-fold, 3.4-fold to 16-fold, 4-fold to 16-fold, 4.5-fold to 16-fold, 5.2-fold to 16-fold, 6-fold to 16-fold, 7-fold to 16-fold, or 8-fold to 16-fold, as compared to a reference, optionally where the statistical significance of the increase or decrease is at least 5e-2, 1e-2, 5e-3, 1e-3, 5e-4, 1e-4, 5e-5, 1e-5, 5e-6, or 1e-6. In various embodiments, an increase or decrease in a value measuring methylation can be, or is expressed as, a log₂(fold-change), *e.g.*, a log₂(fold-change) of at least 1%, 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 75%, 100%, 2-fold, 3-fold, 4-fold, 5-fold, 6-fold, 7-fold, 8-fold, 9-fold, 10-fold, 15-fold, 20-fold, or greater, or any range in between, inclusive, such as an increase or decrease of 0.1-fold to 10-fold, 0.2-fold to 5-fold, 0.2-fold to 4.0-fold, 0.4-4.0-fold, 0.4-fold to 4.0-fold, 0.6-fold to 4.0-fold, 0.8-fold to 4.0-fold, 1.0-fold to 4.0-fold, 1.2-fold to 4.0-fold, 1.4-fold to 4.0-fold, 1.6-fold to

4.0-fold, 1.8-fold to 4.0-fold, 2.0-fold to 4.0-fold, 2.2-fold to 4.0-fold, 2.4-fold to 4.0-fold, 2.6-fold to 4.0-fold, 2.8-fold to 4.0-fold, or 3.0-fold to 4.0-fold, optionally where the statistical significance of the increase or decrease is at least $5e-2$, $1e-2$, $5e-3$, $1e-3$, $5e-4$, $1e-4$, $5e-5$, $1e-5$, $5e-6$, or $1e-6$.

Differential H3K27ac modification

[0176] Genomic loci demonstrating differential H3K27ac modification in ER-positive vs. ER-negative cancer are provided in Table 2, which shows the chromosomal coordinates of each genomic locus and its observed $\log_2(\text{fold-change})$ (ER-positive/ER-negative). The genomic loci are sorted based on their chromosomal coordinates which are based on human genome build hg19.

[0177] A person of skill in the art will recognize that the methods disclosed herein do not require that every genomic locus listed in Table 2 be assessed for H3K27ac modification. Instead, a subset of loci may be assessed for H3K27ac modification. Subsets of the genomic loci of Table 2 can be selected (*e.g.*, for use in determining ER status) based on various performance criteria, *e.g.*, to select genomic loci that demonstrate differential modification with a particular level of statistical significance and/or a particular threshold of differential between relevant states (*e.g.*, a measured $\log_2(\text{fold-change})$). Subsets of the genomic loci may also be selected based on an algorithm, *e.g.*, during the process of obtaining a classifier. Those of skill in the art will appreciate that such subsets of loci of Table 2, and loci included in such subsets, are together, individually, and/or in randomly selected subsets, at least as informative (*e.g.*, as statistically significant and/or reliable) for uses disclosed herein, *e.g.*, for determining ER status. See also the Examples of the present disclosure for experiments showing that informative classifiers can be generated using many different combinations of the loci. The present disclosure particularly includes, among other things, subsets of the genomic loci of Table 2, which have an absolute $\log_2(\text{fold-change})$ of 6.0 or higher, 5.5 or higher, 5.0 or higher, 4.5 or higher, 4.0 or higher, 3.5 or higher, 3.0 or higher, 2.5 or higher, 2.0 or higher, 1.9 or higher, 1.8 or higher, 1.7 or higher, 1.6 or higher, 1.5 or higher, 1.4 or higher, 1.3 or higher, 1.2 or higher, 1.1 or higher, 1.0 or higher, 0.9 or higher, 0.8 or higher, 0.7 or higher, 0.6 or higher, or 0.5 or higher. The present disclosure also includes subsets of the genomic loci of Table 2, which have an absolute $\log_2(\text{fold-change})$ of 6.0 or higher, 5.5 to less than 6.0, 5.0 to less than 5.5, 4.5 to less than 5.0, 4.0 to less than 4.5, 3.8 to

less than 4.0, 3.6 to less than 3.8, 3.4 to less than 3.6, 3.2 to less than 3.4, 3.0 to less than 3.2, 2.8 to less than 3.0, 2.6 to less than 2.8, 2.4 to less than 2.6, 2.2 to less than 2.4, 2.0 to less than 2.2, 1.8 to less than 2.0, 1.6 to less than 1.8, 1.4 to less than 1.6, 1.2 to less than 1.4, 1.0 to less than 1.2, 0.8 to less than 1.0, or 0.6 to less than 0.8.

[0178] In various embodiments, a sample or subject from which the sample is obtained or derived, is determined to have a particular ER status (*e.g.*, ER-positive) if at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 150, 200, 250, 300, 350, 400, 450, 500, 750, 1000, 1500, 2000, 2500, or 3000 loci identified in Table 2 (or any subset thereof) are H3K27ac modified as compared to a reference (*e.g.*, a sample from an ER-negative or healthy subject). In certain embodiments, a subject from which the sample is obtained or derived, is determined to have a particular ER status (*e.g.*, ER-positive) if at least a number of loci identified in a Table 2 (or any subset thereof) having a lower bound selected from 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 150, 200, 250, or 300 and an upper bound selected from 10, 15, 20, 25, 50, 75, 100, 150, 200, 250, 300, 350, 400, 450, 500, 750, 1000, 1500, 2000, 2500, or 3000 is found to be H3K27ac modified as compared to a reference (*e.g.*, a sample from an ER-negative or healthy subject). In certain particular embodiments, a sample or subject from which the sample is obtained or derived, is determined to have a particular ER status (*e.g.*, ER-positive) if at least 1, 2, 3, 4, 5, 10, 20, 30, 40, or 50 loci identified in Table 2 (*e.g.*, about 1 to about 1,000, about 5 to about 3,000, about 10 to about 1000, about 25 to about 200, about 5, about 10, about 20, or about 50 loci) are H3K27ac modified as compared to a reference (*e.g.*, a sample from an ER-negative or healthy subject). In various embodiments a sample or subject from which the sample is obtained or derived, is determined to have a particular ER status (*e.g.*, ER-positive) if at least 0.1%, 0.2%, 0.3%, 0.4%, 0.5%, 1%, 2%, 3%, 4%, 5%, 10%, 20%, 30%, 40%, 50%, 75%, or 100% of loci identified in Table 2 are H3K27ac modified as compared to a reference (*e.g.*, a sample from an ER-negative or healthy subject). In certain embodiments, a sample or subject from which the sample is obtained or derived, is determined to have a particular ER status (*e.g.*, ER-positive) if at least a percent of loci identified in Table 2 having a lower bound selected from 0.1%, 0.2%, 0.3%, 0.4%, 0.5%, 1%, 2%, 3%, 4%, 5%, or 10%, and an upper bound selected from 1%, 2%, 3%, 4%, 5%, 10%, 20%, 30%, 40%, 50%, 75%, or 100% is found to be H3K27ac modified as compared to a reference (*e.g.*, a sample from an ER-negative or healthy subject).

[0179] In various embodiments, a sample or subject from which the sample is derived, is determined to have a particular ER status (*e.g.*, ER-positive) if at least one (*e.g.*, at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, or at least 10) of the top 3, 5, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 150, 200, 250, 300, 350, 400, 450, 500, 750, 1000, 1500, 2000, 2500, or 3000 loci identified in Table 2 are H3K27ac modified as compared to a reference (*e.g.*, a sample from an ER-negative or healthy subject) (wherein, *e.g.*, the “top” 10 loci refers to the loci with 10 highest absolute log₂(fold-change) in Table 2). In some embodiments, a subject from which the sample is obtained or derived, is determined to have a particular ER status (*e.g.*, ER-positive) if at least one of the top 10 loci identified in Table 2 is H3K27ac modified as compared to a reference (*e.g.*, a sample from an ER-negative or healthy subject). In some embodiments, a subject from which the sample is obtained or derived, is determined to have a particular ER status (*e.g.*, ER-positive) if at least one of the top 25 loci identified in Table 2 is H3K27ac modified as compared to a reference (*e.g.*, a sample from an ER-negative or healthy subject). In some embodiments, a subject from which the sample is obtained or derived, is determined to have a particular ER status (*e.g.*, ER-positive) if at least one of the top 50 loci identified in Table 2 is H3K27ac modified as compared to a reference (*e.g.*, a sample from an ER-negative or healthy subject). In some embodiments, a subject from which the sample is obtained or derived, is determined to have a particular ER status (*e.g.*, ER-positive) if at least five of the top 10 loci identified in Table 2 are H3K27ac modified as compared to a reference (*e.g.*, a sample from an ER-negative or healthy subject). In some embodiments, a subject from which the sample is obtained or derived, is determined to have a particular ER status (*e.g.*, ER-positive) if at least five of the top 25 loci identified in Table 2 are H3K27ac modified as compared to a reference (*e.g.*, a sample from an ER-negative or healthy subject). In some embodiments, a subject from which the sample is obtained or derived, is determined to have a particular ER status (*e.g.*, ER-positive) if at least five of the top 50 loci identified in Table 2 are H3K27ac modified as compared to a reference (*e.g.*, a sample from an ER-negative or healthy subject).

[0180] In various embodiments, a sample or subject from which the sample is derived, is determined to have a particular ER status (*e.g.*, ER-positive) if at least one of the top 10 loci (*e.g.*, at least 1, at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, or 10) identified in Table 2 and at least 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95,

100, 150, 200, 250, 300, 350, 400, 450, 500, 750, 1000, 1500, 2000, 2500, or 3000 loci identified in Table 2 (or any subset thereof) in total are H3K27ac modified as compared to a reference (*e.g.*, a sample from an ER-negative or healthy subject). In various embodiments, a sample or subject from which the sample is derived, is determined to have a particular ER status (*e.g.*, ER-positive) if at least one of the top 25 loci identified in Table 2 (*e.g.*, at least 1, at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, or at least 10, at least 15, at least 20, or 25) and at least 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 150, 200, 250, 300, 350, 400, 450, 500, 750, 1000, 1500, 2000, 2500, or 3000 loci identified in Table 2 (or any subset thereof) in total are H3K27ac modified as compared to a reference (*e.g.*, a sample from an ER-negative or healthy subject). In various embodiments, a sample or subject from which the sample is derived, is determined to have a particular ER status (*e.g.*, ER-positive) if at least one of the top 50 loci (*e.g.*, at least 1, at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, or at least 10, at least 15, at least 20, or at least 25, at least 30, at least 35, at least 40, at least 45, or 50) identified in Table 2 and at least 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 150, 200, 250, 300, 350, 400, 450, 500, 750, 1000, 1500, 2000, 2500, or 3000 loci identified in Table 2 (or any subset thereof) in total are H3K27ac modified as compared to a reference (*e.g.*, a sample from an ER-negative or healthy subject). In various embodiments, a sample or subject from which the sample is derived, is determined to have a particular ER status (*e.g.*, ER-positive) if at least five of the top 25 loci identified in Table 2 and at least 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 150, 200, 250, 300, 350, 400, 450, 500, 750, 1000, 1500, 2000, 2500, or 3000 loci identified in Table 2 (or any subset thereof) in total are H3K27ac modified as compared to a reference (*e.g.*, a sample from an ER-negative or healthy subject). In various embodiments, a sample or subject from which the sample is derived, is determined to have a particular ER status (*e.g.*, ER-positive) if at least five of the top 50 loci identified in Table 2 and at least 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 150, 200, 250, 300, 350, 400, 450, 500, 750, 1000, 1500, 2000, 2500, or 3000 loci identified in Table 2 (or any subset thereof) in total are H3K27ac modified as compared to a reference (*e.g.*, a sample from an ER-negative or healthy subject).

[0181] In various embodiments, differentially H3K27ac modified refers to an acetylation status characterized by an increase or decrease in a value measuring acetylation (*e.g.*, of read counts and/or normalized read counts for a given genomic locus), and/or a mean, median and/or

mode thereof, and/or a log thereof (*e.g.*, log base 2 ($\log_2$)), of at least 1%, 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 75%, 100%, 2-fold, 3-fold, 4-fold, 5-fold, 6-fold, 7-fold, 8-fold, 9-fold, 10-fold, 15-fold, 20-fold, 25-fold, 30-fold, 35-fold, 40-fold, 45-fold, 50-fold, or greater, or any range in between, inclusive, such as 1% to 50%, 50% to 2-fold, 25% to 50-fold, 25% to 30-fold, 25% to 20-fold, 25% to 16-fold, 30% to 16-fold, 50% to 16-fold, 70% to 16-fold, 2-fold to 16-fold, 2.2-fold to 16-fold, 2.6-fold to 16-fold, 3-fold to 16-fold, 3.4-fold to 16-fold, 4-fold to 16-fold, 4.5-fold to 16-fold, 5.2-fold to 16-fold, 6-fold to 16-fold, 7-fold to 16-fold, or 8-fold to 16-fold, as compared to a reference, optionally where the statistical significance of the increase or decrease is at least $5e-2$, $1e-2$, $5e-3$, $1e-3$, $5e-4$, $1e-4$, $5e-5$, $1e-5$, $5e-6$, or $1e-6$. In various embodiments, an increase or decrease in a value measuring acetylation can be, or is expressed as, a $\log_2(\text{fold-change})$, *e.g.*, a $\log_2(\text{fold-change})$ of at least 1%, 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 75%, 100%, 2-fold, 3-fold, 4-fold, 5-fold, 6-fold, 7-fold, 8-fold, 9-fold, 10-fold, 15-fold, 20-fold, or greater, or any range in between, inclusive, such as an increase or decrease of 0.1-fold to 10-fold, 0.2-fold to 5-fold, 0.2-fold to 4.0-fold, 0.4-4.0-fold, 0.4-fold to 4.0-fold, 0.6-fold to 4.0-fold, 0.8-fold to 4.0-fold, 1.0-fold to 4.0-fold, 1.2-fold to 4.0-fold, 1.4-fold to 4.0-fold, 1.6-fold to 4.0-fold, 1.8-fold to 4.0-fold, 2.0-fold to 4.0-fold, 2.2-fold to 4.0-fold, 2.4-fold to 4.0-fold, 2.6-fold to 4.0-fold, 2.8-fold to 4.0-fold, or 3.0-fold to 4.0-fold, optionally where the statistical significance of the increase or decrease is at least $5e-2$, $1e-2$, $5e-3$, $1e-3$, $5e-4$, $1e-4$, $5e-5$, $1e-5$, $5e-6$, or $1e-6$.

Differential DNA methylation

[0182] Genomic loci demonstrating differential DNA methylation in ER-positive vs. ER-negative cancer are provided in Table 3, which shows the chromosomal coordinates of each genomic locus and its observed $\log_2(\text{fold-change})$ (ER-positive/ER-negative). The genomic loci are sorted based on their chromosomal coordinates which are based on human genome build hg19.

[0183] A person of skill in the art will recognize that the methods disclosed herein do not require that every genomic locus listed in Table 3 be assessed for DNA methylation. Instead, a subset of loci may be assessed for DNA methylation. Subsets of the genomic loci of Table 3 can be selected (*e.g.*, for use in determining ER status) based on various performance criteria, *e.g.*, to

select genomic loci that demonstrate differential modification with a particular level of statistical significance and/or a particular threshold of differential between relevant states (*e.g.*, a measured $\log_2(\text{fold-change})$). Subsets of the genomic loci may also be selected based on an algorithm, *e.g.*, during the process of obtaining a classifier. Those of skill in the art will appreciate that such subsets of loci of Table 3, and loci included in such subsets, are together, individually, and/or in randomly selected subsets, at least as informative (*e.g.*, as statistically significant and/or reliable) for uses disclosed herein, *e.g.*, for determining ER status. See also the Examples of the present disclosure for experiments showing that informative classifiers can be generated using many different combinations of the loci. The present disclosure particularly includes, among other things, subsets of the genomic loci of Table 3, which have an absolute $\log_2(\text{fold-change})$ of 6.0 or higher, 5.5 or higher, 5.0 or higher, 4.5 or higher, 4.0 or higher, 3.5 or higher, 3.0 or higher, 2.5 or higher, 2.0 or higher, 1.9 or higher, 1.8 or higher, 1.7 or higher, 1.6 or higher, 1.5 or higher, 1.4 or higher, 1.3 or higher, 1.2 or higher, 1.1 or higher, 1.0 or higher, 0.9 or higher, 0.8 or higher, 0.7 or higher, 0.6 or higher, or 0.5 or higher. The present disclosure also includes subsets of the genomic loci of Table 3, which have an absolute $\log_2(\text{fold-change})$ of 6.0 or higher, 5.5 to less than 6.0, 5.0 to less than 5.5, 4.5 to less than 5.0, 4.0 to less than 4.5, 3.8 to less than 4.0, 3.6 to less than 3.8, 3.4 to less than 3.6, 3.2 to less than 3.4, 3.0 to less than 3.2, 2.8 to less than 3.0, 2.6 to less than 2.8, 2.4 to less than 2.6, 2.2 to less than 2.4, 2.0 to less than 2.2, 1.8 to less than 2.0, 1.6 to less than 1.8, 1.4 to less than 1.6, 1.2 to less than 1.4, 1.0 to less than 1.2, 0.8 to less than 1.0, or 0.6 to less than 0.8.

[0184] In various embodiments, a sample or subject from which the sample is obtained or derived, is determined to have a particular ER status (*e.g.*, ER-positive) if at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 150, 200, 250, 300, 350, 400, 450, 500, 750, 1000, 1500, 2000, 2500, or 3000 loci identified in Table 3 (or any subset thereof) are differentially DNA methylated as compared to a reference (*e.g.*, a sample from an ER-negative or healthy subject). In certain embodiments, a subject from which the sample is obtained or derived, is determined to have a particular ER status (*e.g.*, ER-positive) if at least a number of loci identified in a Table 3 (or any subset thereof) having a lower bound selected from 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 150, 200, 250, or 300 and an upper bound selected from 10, 15, 20, 25, 50, 75, 100, 150, 200, 250, 300, 350, 400, 450, 500, 750, 1000, 1500, 2000, 2500, or 3000 is found to be

differentially DNA methylated as compared to a reference (*e.g.*, a sample from an ER-negative or healthy subject). In certain particular embodiments, a sample or subject from which the sample is obtained or derived, is determined to have a particular ER status (*e.g.*, ER-positive) if at least 1, 2, 3, 4, 5, 10, 20, 30, 40, or 50 loci identified in Table 3 (*e.g.*, about 1 to about 1,000, about 5 to about 3,000, about 10 to about 1000, about 25 to about 200, about 5, about 10, about 20, or about 50 loci) are differentially DNA methylated as compared to a reference (*e.g.*, a sample from an ER-negative or healthy subject). In various embodiments a sample or subject from which the sample is obtained or derived, is determined to have a particular ER status (*e.g.*, ER-positive) if at least 0.1%, 0.2%, 0.3%, 0.4%, 0.5%, 1%, 2%, 3%, 4%, 5%, 10%, 20%, 30%, 40%, 50%, 75%, or 100% of loci identified in Table 3 are differentially DNA methylated as compared to a reference (*e.g.*, a sample from an ER-negative or healthy subject). In certain embodiments, a sample or subject from which the sample is obtained or derived, is determined to have a particular ER status (*e.g.*, ER-positive) if at least a percent of loci identified in Table 3 having a lower bound selected from 0.1%, 0.2%, 0.3%, 0.4%, 0.5%, 1%, 2%, 3%, 4%, 5%, or 10%, and an upper bound selected from 1%, 2%, 3%, 4%, 5%, 10%, 20%, 30%, 40%, 50%, 75%, or 100% is found to be differentially DNA methylated as compared to a reference (*e.g.*, a sample from an ER-negative or healthy subject).

[0185] In various embodiments, a sample or subject from which the sample is derived, is determined to have a particular ER status (*e.g.*, ER-positive) if at least one (*e.g.*, at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, or at least 10) of the top 3, 5, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 150, 200, 250, 300, 350, 400, 450, 500, 750, 1000, 1500, 2000, 2500, or 3000 loci identified in Table 3 are differentially DNA methylated as compared to a reference (*e.g.*, a sample from an ER-negative or healthy subject) (wherein, *e.g.*, the “top” 10 loci refers to the loci with 10 highest absolute log₂(fold-change) in Table 3). In some embodiments, a subject from which the sample is obtained or derived, is determined to have a particular ER status (*e.g.*, ER-positive) if at least one of the top 10 loci identified in Table 3 is differentially DNA methylated as compared to a reference (*e.g.*, a sample from an ER-negative or healthy subject). In some embodiments, a subject from which the sample is obtained or derived, is determined to have a particular ER status (*e.g.*, ER-positive) if at least one of the top 25 loci identified in Table 3 is differentially DNA methylated as compared to a reference (*e.g.*, a sample from an ER-negative or healthy subject). In some embodiments, a

subject from which the sample is obtained or derived, is determined to have a particular ER status (*e.g.*, ER-positive) if at least one of the top 50 loci identified in Table 3 is differentially DNA methylated as compared to a reference (*e.g.*, a sample from an ER-negative or healthy subject). In some embodiments, a subject from which the sample is obtained or derived, is determined to have a particular ER status (*e.g.*, ER-positive) if at least five of the top 10 loci identified in Table 3 are differentially DNA methylated as compared to a reference (*e.g.*, a sample from an ER-negative or healthy subject). In some embodiments, a subject from which the sample is obtained or derived, is determined to have a particular ER status (*e.g.*, ER-positive) if at least five of the top 25 loci identified in Table 3 are differentially DNA methylated as compared to a reference (*e.g.*, a sample from an ER-negative or healthy subject). In some embodiments, a subject from which the sample is obtained or derived, is determined to have a particular ER status (*e.g.*, ER-positive) if at least five of the top 50 loci identified in Table 3 are differentially DNA methylated as compared to a reference (*e.g.*, a sample from an ER-negative or healthy subject).

[0186] In various embodiments, a sample or subject from which the sample is derived, is determined to have a particular ER status (*e.g.*, ER-positive) if at least one of the top 10 loci (*e.g.*, at least 1, at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, or 10) identified in Table 3 and at least 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 150, 200, 250, 300, 350, 400, 450, 500, 750, 1000, 1500, 2000, 2500, or 3000 loci identified in Table 3 (or any subset thereof) in total are differentially DNA methylated as compared to a reference (*e.g.*, a sample from an ER-negative or healthy subject). In various embodiments, a sample or subject from which the sample is derived, is determined to have a particular ER status (*e.g.*, ER-positive) if at least one of the top 25 loci identified in Table 3 (*e.g.*, at least 1, at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, or at least 10, at least 15, at least 20, or 25) and at least 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 150, 200, 250, 300, 350, 400, 450, 500, 750, 1000, 1500, 2000, 2500, or 3000 loci identified in Table 3 (or any subset thereof) in total are differentially DNA methylated as compared to a reference (*e.g.*, a sample from an ER-negative or healthy subject). In various embodiments, a sample or subject from which the sample is derived, is determined to have a particular ER status (*e.g.*, ER-positive) if at least one of the top 50 loci (*e.g.*, at least 1, at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, or at least 10, at least 15, at least 20, or at least 25, at

least 30, at least 35, at least 40, at least 45, or 50) identified in Table 3 and at least 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 150, 200, 250, 300, 350, 400, 450, 500, 750, 1000, 1500, 2000, 2500, or 3000 loci identified in Table 3 (or any subset thereof) in total are differentially DNA methylated as compared to a reference (*e.g.*, a sample from an ER-negative or healthy subject). In various embodiments, a sample or subject from which the sample is derived, is determined to have a particular ER status (*e.g.*, ER-positive) if at least five of the top 25 loci identified in Table 3 and at least 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 150, 200, 250, 300, 350, 400, 450, 500, 750, 1000, 1500, 2000, 2500, or 3000 loci identified in Table 3 (or any subset thereof) in total are differentially DNA methylated as compared to a reference (*e.g.*, a sample from an ER-negative or healthy subject). In various embodiments, a sample or subject from which the sample is derived, is determined to have a particular ER status (*e.g.*, ER-positive) if at least five of the top 50 loci identified in Table 3 and at least 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 150, 200, 250, 300, 350, 400, 450, 500, 750, 1000, 1500, 2000, 2500, or 3000 loci identified in Table 3 (or any subset thereof) in total are differentially DNA methylated as compared to a reference (*e.g.*, a sample from an ER-negative or healthy subject).

[0187] In various embodiments, differentially DNA methylated refers to a methylation status characterized by an increase or decrease in a value measuring methylation (*e.g.*, of read counts and/or normalized read counts for a given genomic locus), and/or a mean, median and/or mode thereof, and/or a log thereof (*e.g.*, log base 2 ($\log_2$)), of at least 1%, 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 75%, 100%, 2-fold, 3-fold, 4-fold, 5-fold, 6-fold, 7-fold, 8-fold, 9-fold, 10-fold, 15-fold, 20-fold, 25-fold, 30-fold, 35-fold, 40-fold, 45-fold, 50-fold, or greater, or any range in between, inclusive, such as 1% to 50%, 50% to 2-fold, 25% to 50-fold, 25% to 30-fold, 25% to 20-fold, 25% to 16-fold, 30% to 16-fold, 50% to 16-fold, 70% to 16-fold, 2-fold to 16-fold, 2.2-fold to 16-fold, 2.6-fold to 16-fold, 3-fold to 16-fold, 3.4-fold to 16-fold, 4-fold to 16-fold, 4.5-fold to 16-fold, 5.2-fold to 16-fold, 6-fold to 16-fold, 7-fold to 16-fold, or 8-fold to 16-fold, as compared to a reference, optionally where the statistical significance of the increase or decrease is at least $5e-2$, $1e-2$, $5e-3$, $1e-3$, $5e-4$, $1e-4$, $5e-5$, $1e-5$, $5e-6$, or $1e-6$. In various embodiments, an increase or decrease in a value measuring methylation can be, or is expressed as, a $\log_2$ (fold-change), *e.g.*, a $\log_2$ (fold-change) of at least 1%, 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%,

75%, 100%, 2-fold, 3-fold, 4-fold, 5-fold, 6-fold, 7-fold, 8-fold, 9-fold, 10-fold, 15-fold, 20-fold, or greater, or any range in between, inclusive, such as an increase of 0.1-fold to 10-fold, 0.2-fold to 5-fold, 0.2-fold to 4.0-fold, 0.4-4.0-fold, 0.4-fold to 4.0-fold, 0.6-fold to 4.0-fold, 0.8-fold to 4.0-fold, 1.0-fold to 4.0-fold, 1.2-fold to 4.0-fold, 1.4-fold to 4.0-fold, 1.6-fold to 4.0-fold, 1.8-fold to 4.0-fold, 2.0-fold to 4.0-fold, 2.2-fold to 4.0-fold, 2.4-fold to 4.0-fold, 2.6-fold to 4.0-fold, 2.8-fold to 4.0-fold, or 3.0-fold to 4.0-fold, optionally where the statistical significance of the increase or decrease is at least $5e-2$, $1e-2$, $5e-3$, $1e-3$, $5e-4$, $1e-4$, $5e-5$, $1e-5$, $5e-6$, or $1e-6$.

Differential chromatin accessibility or transcription factor binding

[0188] Genomic loci provided in Tables 1-3 can also demonstrate differential chromatin accessibility or transcription factor binding in ER-positive cancer vs. ER-negative cancer.

[0189] In various embodiments, without wishing to be bound by any particular scientific theory, histone methylation (*e.g.*, H3K4me3) corresponds and/or is correlated with chromatin accessibility. In various embodiments, without wishing to be bound by any particular scientific theory, histone acetylation (*e.g.*, H3K27ac) corresponds and/or is correlated with chromatin accessibility. In various embodiments, without wishing to be bound by any particular scientific theory, DNA methylation corresponds and/or is correlated with chromatin accessibility.

[0190] In some embodiments, without wishing to be limited to any particular scientific theory, chromatin accessibility corresponds and/or is correlated with H3K4me3 modifications. As a result, in some embodiments, ER status may be determined by detecting and quantifying chromatin accessibility at one or more genomic loci in Table 1 in accordance with the section above discussing exemplary genomic loci with differential H3K4me3 modifications.

[0191] In some embodiments, without wishing to be limited to any particular scientific theory, chromatin accessibility corresponds and/or is correlated with H3K27ac modifications. As a result, in some embodiments, ER status may be determined by detecting and quantifying chromatin accessibility at one or more genomic loci in Table 2 in accordance with the section above discussing exemplary genomic loci with differential H3K27ac modifications.

[0192] In some embodiments, without wishing to be limited to any particular scientific theory, chromatin accessibility corresponds and/or is correlated with DNA methylation. As a result, in some embodiments, ER status may be determined by detecting and quantifying

chromatin accessibility at one or more genomic loci in Table 3 in accordance with the section above discussing exemplary genomic loci with differential DNA methylation.

[0193] In various embodiments, without wishing to be bound by any particular scientific theory, histone methylation (*e.g.*, H3K4me3) corresponds and/or is correlated with transcription factor binding. In various embodiments, without wishing to be bound by any particular scientific theory, histone acetylation (*e.g.*, H3K27ac) corresponds and/or is correlated with transcription factor binding. In various embodiments, without wishing to be bound by any particular scientific theory, DNA methylation corresponds and/or is correlated with transcription factor binding.

[0194] In some embodiments, without wishing to be limited to any particular scientific theory, binding of RNA pol II corresponds and/or is correlated with H3K4me3 modifications. As a result, in some embodiments, ER status may be determined by detecting and quantifying binding of RNA pol II at one or more genomic loci in Table 1 in accordance with the section above discussing exemplary genomic loci with differential H3K4me3 modifications.

[0195] In some embodiments, without wishing to be limited to any particular scientific theory, binding of p300, mediator complex, cohesin complex or RNA pol II corresponds and/or is correlated with H3K27ac modifications. As a result, in some embodiments, ER status may be determined by detecting and quantifying binding of p300, mediator complex, cohesin complex or RNA pol II at one or more genomic loci in Table 2 in accordance with the section above discussing exemplary genomic loci with differential H3K27ac modifications.

[0196] In some embodiments, without wishing to be limited to any particular scientific theory, binding of FOXA1, ESR1, PR, MYC, EN1, FOXM1, KLF4, AP-2, RARa, or RUNX1 corresponds and/or is correlated with histone methylation (*e.g.*, H3K4me3), histone acetylation (*e.g.*, H3K27ac) or DNA methylation. As a result, in some embodiments, ER status may be determined by detecting and quantifying binding of FOXA1, ESR1, PR, MYC, EN1, FOXM1, KLF4, AP-2, RARa, RUNX1 at one or more genomic loci in Tables 1-3 in accordance with the sections above discussing exemplary genomic loci with differential histone methylation (*e.g.*, H3K4me3), histone acetylation (*e.g.*, H3K27ac) or DNA methylation.

Applications

[0197] Methods, kits and systems of the present disclosure include analysis of differentially modified and/or differentially accessible genomic loci to determine the ER status of

a cancer. Methods, kits and systems of the present disclosure can be used in any of a variety of applications. For example, methods, kits and systems of the present disclosure can be used in detecting and/or treating cancers based on ER status. Methods, kits and systems of the present disclosure can also be used to detect or determine resistance of a cancer, *e.g.*, breast, ovarian, or endometrial cancer to a therapy or transformation from one cancer subtype to another.

[0198] In various embodiments, methods, kits and systems of the present disclosure can be applied to an asymptomatic human subject. As used herein, a subject can be referred to as “asymptomatic” if the subject does not report, and/or demonstrate by non-invasively observable indicia (*e.g.*, without one, several, or all of device-based probing, tissue sample analysis, bodily fluid analysis, surgery, or cancer screening), sufficient characteristics of cancer to support a medically reasonable suspicion that the subject is likely suffering from cancer, *e.g.*, breast, ovarian, or endometrial cancer. Detection of early-stage cancer can be achieved using methods, kits and systems of the present disclosure, with attendant medical benefits including potential for early treatment and attendant improvement in therapeutic outcomes.

[0199] In various embodiments, methods, kits, and systems of the present disclosure can be applied to a human subject that has increased susceptibility for cancer (including breast cancer).

[0200] In various embodiments, methods, kits and systems of the present disclosure can be applied to a symptomatic human subject. As used herein, a subject can be referred to as “symptomatic” if the subject report, and/or demonstrates by non-invasively observable indicia (*e.g.*, without one, several, or all of device-based probing, tissue sample analysis, bodily fluid analysis, surgery, or cancer screening), sufficient characteristics of cancer to support a medically reasonable suspicion that the subject is likely suffering from cancer, *e.g.*, breast, ovarian, or endometrial cancer. For example, in various embodiments a sample from a subject, optionally where the subject has a cancer that is of unknown ER status, can be assayed according to one or more embodiments of the present disclosure to determine if the cancer is ER-positive or ER-negative. In various embodiments a sample from a subject, where the subject has a cancer that is known or suspected of being ER-positive (or ER-negative), can be assayed according to one or more embodiments of the present disclosure to determine if the cancer is in fact ER-positive (or ER-negative).

[0201] In some embodiments, methods, kits and systems of the present disclosure can be used to determine that a subject has an ER-positive cancer, optionally an ER-positive cancer that correlates with an ER+ Allred score of 3, 4, 5, 6, 7 or 8 based on IHC testing. In some embodiments, methods, kits and systems of the present disclosure can be used to determine that a subject has an ER-positive cancer, optionally an ER-positive cancer that correlates with an ER+ Allred score of at least 3, at least 4, at least 5, at least 6, at least 7 or 8 based on IHC testing. In some embodiments, methods, kits and systems of the present disclosure can be used to determine that a subject has an ER-negative cancer, optionally an ER-negative cancer that correlates with ER- Allred score of 0, 1, or 2 based on IHC testing.

[0202] In some embodiments, methods, kits and systems of the present disclosure can be used to validate or confirm a prior determination that a subject has an ER-positive cancer, optionally an ER-positive cancer that correlates with an ER+ Allred score of 3, 4, 5, 6, 7 or 8 based on IHC testing. In some embodiments, methods, kits and systems of the present disclosure can be used to validate or confirm a prior determination that a subject has an ER-positive cancer, optionally an ER-positive cancer that correlates with an ER+ Allred score of at least 3, at least 4, at least 5, at least 6, at least 7 or 8 based on IHC testing. In some embodiments, methods, kits and systems of the present disclosure can be used to validate or confirm a prior determination that a subject has an ER-negative cancer, optionally an ER-negative cancer that correlates with ER- Allred score of 0, 1, or 2 based on IHC testing.

[0203] In some embodiments, methods, kits and systems of the present disclosure are used to identify and detect new ER related categories that are independent of IHC or ISH scoring. For example, instead of training the classifier on samples from cohorts that were defined based on ER IHC or ISH testing, classifiers are trained on samples from cohorts that are defined based on whether they respond or do not respond to a particular ER-targeted agent. The resulting classifiers are then used to identify subjects that are more likely to respond to the particular ER-targeted agent independent of any IHC or ISH scoring. It is therefore to be understood that the term “ER status” as used herein is not limited to ER-positive and ER-negative or the traditional ER scoring based on IHC or ISH testing but can encompass any ER related categories including whether a subject will or will not respond to a particular ER-targeted agent.

[0204] Those of skill in the art will appreciate that regular, preventative, and/or prophylactic screening to determine ER status improves diagnosis of cancer, including and/or

particularly early-stage cancer. Thus, the present disclosure provides, among other things, methods, kits and systems particularly useful for the diagnosis and treatment of early-stage cancer. Generally, and particularly in embodiments in which ER-positive cancer detection in accordance with the present disclosure is carried out annually, and/or in which a subject is asymptomatic at time of detecting, methods, kits and systems of the present disclosure are especially likely to detect early-stage ER-positive cancer. In various embodiments, detecting in accordance with methods, kits and systems of the present disclosure reduces cancer mortality, *e.g.*, by early cancer diagnosis.

[0205] In various embodiments ER status determination in accordance with the present disclosure is performed once for a given subject or multiple times for a given subject. In various embodiments, ER status determination in accordance with the present disclosure is performed on a regular basis, *e.g.*, every six months, annually, every two years, every three years, every four years, every five years, or every ten years.

[0206] In various embodiments, methods, kits and systems disclosed herein provide a determination of ER status. In other instances, methods, kits and systems disclosed herein will be indicative of ER status but not definitive for ER status. In various instances in which methods, kits and systems of the present disclosure are used to determine ER status, the same can be followed by a further confirmatory assay, which further assay can confirm, support, undermine, or reject a determination resulting from a prior determination, *e.g.*, a determination in accordance with the present disclosure. As used herein, a confirmatory assay can be an ER test that is currently recognized by medical practitioners, *e.g.*, ER scoring based on IHC or ISH testing.

[0207] In various embodiments, ER status determination according to one or more methods, kits and/or systems disclosed herein is followed by treatment of cancer. In various embodiments, treatment of cancer includes administration of a therapeutic regimen including one or more cancer therapies provided herein, including without limitation one or more of ER targeted therapy, surgery, radiation, endocrine therapy, chemotherapy, and/or immunotherapy. In various embodiments, treatment of cancer includes administration of a therapeutic regimen including one or more treatments provided herein as available, appropriate, and/or preferred for a particular ER status.

[0208] In various embodiments, methods, kits and systems can be used to determine whether a particular subject and/or cancer is likely to be and/or is characterized as responsive to

ER targeted therapy. In some such embodiments, methods, kits and systems can be followed by treatment of the subject with an ER targeted therapy.

[0209] In various embodiments, methods, kits and systems can be used to determine whether a particular subject and/or cancer is likely to be and/or is characterized as resistant to, non-responsive to, or not recommended treatment with to ER targeted therapy. In some such embodiments, methods, kits and systems can be followed by treatment with one or more of surgery and/or radiation, a HER2-targeted agent (if HER2-positive), chemotherapy and immunotherapy instead of ER targeted therapy.

[0210] Responsiveness can refer to the ability or likelihood of a therapy to cause a reduction in tumor size or inhibit tumor growth or metastasis. Responsiveness can refer to improvement in prognosis (*e.g.*, increased time to cancer recurrence or increased life expectancy, *e.g.*, overall survival, recurrence-free survival, metastasis-free survival, or disease-free survival). Responsiveness can refer to achievement of a treatment benefit, including *e.g.*, improvement in one or more symptoms of cancer, *e.g.*, breast, ovarian, or endometrial cancer. Responsiveness can be measured quantitatively (*e.g.*, as in the case of tumor size; as in the case of measurement of histone modification, chromatin accessibility, transcription factor binding, or DNA methylation at one or more genomic loci; or as in the calculation of clinical benefit (CBR)), or qualitatively (*e.g.*, by measures such as “pathological complete response” (pCR), “clinical complete remission” (cCR), “clinical partial remission” (cPR), “clinical stable disease” (cSD), “clinical progressive disease” (cPD), or other qualitative criteria). Resistance can refer to the inability or unlikelihood of a therapy to achieve a desired therapeutic effect (*e.g.*, a reduction in tumor size, improvement in prognosis, or other treatment benefit such as, *e.g.*, improvement in one or more symptoms of cancer) in a subject and/or cancer. Resistance includes both acquired and natural resistance. In certain embodiments, resistance includes the extent to which one or more desired therapeutic benefits results from administration of a therapy to a subject and/or cancer is less than that expected and/or achieved in a reference (*e.g.*, less than 90%, 80%, 70%, 60%, 50%, 40%, 30%, 20%, or 10% of benefit achieved in a reference).

[0211] In various embodiments, methods, kits and systems can be used to detect the clinical efficacy of a course of therapy for cancer, *e.g.*, breast, ovarian, or endometrial cancer. For example, methods and/or compositions of the present disclosure could be used to determine the presence, absence, or ER status of a cancer in a subject over the course of treatment. Methods

and/or compositions of the present disclosure could be used in conjunction with, or confirmed by, other means of determining the presence, absence, or ER status of a cancer including, for example measurements of tumor size or character by techniques such as CT, PET, mammogram, ultrasound, palpation, histology, caliper measurement after biopsy or surgical resection, or by various qualitative, quantitative, or semi quantitative scoring systems including without limitation based on IHC or ISH testing, residual cancer burden (Symmans et al., J Clin Oncol (2007) 25:4414-4422, incorporated by reference herein in its entirety) or Miller-Payne score (Ogston et al., Breast (2003) 12:320-327, incorporated by reference herein in its entirety) in a qualitative fashion like “pathological complete response” (pCR), “clinical complete remission” (cCR), “clinical partial remission” (cPR), “clinical stable disease” (cSD), or “clinical progressive disease” (cPD).

[0212] In some embodiments, methods, kits, and systems described herein can be used to monitor progression of disease in a subject. In some embodiments, monitoring progression entails obtaining and characterizing samples from a subject at at least a first and a second time point. In some embodiments, at the first time point, a subject has already been diagnosed with lung cancer (e.g., an ER-negative cancer or ER-positive cancer). In some embodiments, at a first time point, a subject has been determined to have cancer and therapy is administered before or close to (e.g., the same day as) the first time point or between the first time point and the second time point; in such embodiments, determination of ER status at at least the first and the second time points can be used to monitor treatment efficacy and/or determine when a change in therapy should be made. For example, in some embodiments, a subject has previously been diagnosed with an ER-positive at the first time point, an ER-positive therapy is being or will be administered to the subject, and disease status can be monitored, which can be useful, e.g., for determining whether a change in therapy should be made. In some embodiments, treatment efficacy can be monitored, e.g., by using a method described herein to determine a decrease or increase in disease state signal, which can be useful, e.g., for determining whether an administered therapy is effective and/or whether a change in therapy should be made. In some embodiments, at the first time point, a cancer has gone into remission for a subject (e.g., the subject has minimal residual disease). In embodiments where a cancer has gone into remission, methods, kits, and systems described herein can be useful, e.g., for detecting reoccurrence of

cancer, and can be faster, less expensive, and/or less invasive than, e.g., approaches that rely on tissue biopsies and/or imaging techniques.

[0213] In some embodiments, methods, kits and systems for ER status determination provided herein can inform treatment and/or payment (*e.g.*, reimbursement for or reduction of cost of medical care, such as detecting or treatment) decisions and/or actions, *e.g.*, by individuals, healthcare facilities, healthcare practitioners, health insurance providers, governmental bodies, or other parties interested in healthcare cost.

[0214] In some embodiments, methods, kits and systems for ER status determination provided herein can inform decision making relating to whether health insurance providers reimburse a healthcare cost payer or recipient (or not), *e.g.*, for (1) ER status determination itself (*e.g.*, reimbursement for detecting otherwise unavailable, available only for periodic/regular detecting, or available only for temporally- and/or incidentally- motivated detecting); and/or for (2) treatment, including initiating, maintaining, and/or altering therapy, *e.g.*, based on the determined ER status. For example, in some embodiments, methods, kits and systems for ER status determination provided herein are used as the basis for, to contribute to, or support a determination as to whether a reimbursement or cost reduction will be provided to a healthcare cost payer or recipient. In some instances, a party seeking reimbursement or cost reduction can provide results of ER status determination conducted in accordance with the present disclosure together with a request for such reimbursement or reduction of a healthcare cost. In some instances, a party making a determination as to whether or not to provide a reimbursement or reduction of a healthcare cost will reach a determination based in whole or in part upon receipt and/or review of results of ER status determination conducted in accordance with the present disclosure.

[0215] In various embodiments, ER status determination using methods, kits and systems disclosed herein can be used in classifying subjects, samples, and/or tumors (*e.g.*, breast cancer subjects, samples, and/or tumors). In various embodiments, methods, kits and systems disclosed herein can be used to generate a set of subjects, samples, and/or tumors identified according to the present methods, kits and systems each classified as corresponding to a particular ER status, and optionally using two or more of such classified subjects, samples, and/or tumors to identify biomarkers that distinguish the classes (*i.e.*, distinguish the subjects, samples, and/or tumors according to their class, *e.g.*, according to their ER status).

[0216] For illustration purposes and without limitation, in an exemplary assay of the present disclosure, one or more samples obtained from a subject (*e.g.*, a liquid biopsy sample including cfDNA, *e.g.*, a plasma sample including cfDNA) are analyzed by a method comprising enriching for cfDNA comprising a particular histone modification, wherein enriching is performed by a method that comprises incubating the sample with a reagent that specifically binds the histone modification being enriched for, and sequencing the enriched cfDNA. One example of such an assay is ChIP-seq for a histone modification (*e.g.*, H3K4me3 and/or H3K27ac). Sequence reads (*e.g.*, ChIP-seq sequence reads) can be aligned to human genome build hg19, *e.g.*, using the Burrows-Wheeler Aligner (BWA). Non-uniquely mapping and redundant reads are optionally discarded.

[0217] To provide one example of peak calling, MACS v2.1.1.20140616 can be used for sequence (*e.g.*, ChIP-seq) peak calling with a q-value (FDR) threshold of 0.01. Sequence (*e.g.*, ChIP-seq) data quality can optionally be evaluated by any of one or more of a variety of measures, including total peak number, FRiP (fraction of reads in peak) score, number of high-confidence peaks (*e.g.*, enriched > ten-fold over background), and percent of peak overlap with “blacklist” DHS peaks derived from the ENCODE project (Amemiya et al., Sci Rep (2019) 9(1):9354). If the sequence (*e.g.*, ChIP-seq) data quality is below a particular threshold, the data may be discarded and the assay repeated. Sequence (*e.g.*, ChIP-seq) peaks that overlap with selected genomic loci that are differentially modified as provided herein for the relevant histone modification (Tables 1-2) can then be used to determine ER status. The number of reads overlapping the selected genomic loci for the relevant histone modification can be summed, *e.g.*, in some embodiments all the genomic loci that are differentially modified with an absolute $\log_2(\text{fold-change}) \geq 4.0$ are selected. In some embodiments, the average number of reads in the local background of each ChIP-seq peak is subtracted to improve signal to noise. In some embodiments, a sequence read density for one or more histone modifications can be calculated by a method that comprises (1) summing background adjusted sequence counts at at one or more genomic loci and dividing the resulting sum by the total number of kilobases of the one or more genomic loci, or (2) for each genomic loci, determining the ratio of background adjusted fragment counts to the number of kilobases of the genomic loci, and then summing the ratios for each loci. In some embodiments, a method comprises determining an ER-positive/ ER-negative ratio score, *e.g.*, by a method that comprises (a) calculating an ER-positive sequence read

density, calculating an ER-negative sequence read density, and dividing the ER-positive sequence read density by the ER-negative sequence read density. In some embodiments, an ER-positive sequence read density can be determined by a method that comprises calculating sequence read density using one or more genomic loci with an increased level of one or more epigenetic biomarkers in sample(s) obtained from one or more subjects with an ER -positive cancer as compared to one or more sample(s) obtained from subjects with an ER-negative cancer. In some embodiments, an ER -negative sequence read density can be determined by a method that comprises calculating sequence read density using one or more genomic loci with an increased level of one or more epigenetic biomarkers in sample(s) obtained from one or more subjects with an ER-negative cancer as compared to one or more sample(s) obtained from subjects with an ER-positive cancer. An ER-positive/ ER-negative ratio score is determined for one or more histone modifications. In some embodiments an ER-positive/ER-negative ratio score is determined for H3K4me3 modifications. In some embodiments, an ER-positive/ER-negative ratio score is determined for H3K27ac modifications. In some embodiments, an ER-positive/ER-negative ratio score is determined for methylated DNA. In some embodiments, an ER-positive/ER-negative ratio score is determined for H3K4me3 modifications and H3K27ac modifications, H3K4me3 and methylated DNA, or H3K27ac and methylated DNA. In some embodiments, an ER-positive/ER-negative ratio score is determined for each of H3K4me3 modifications, H3K27ac modifications, and methylated DNA. In some embodiments, two or more ER-positive/ER-negative ratio scores for different epigenetic biomarkers can be combined. In some embodiments, each ratio score can be combined using fitted values that have been determined using a logistic regression.

[0218] The data can then be log₂-transformed and quantile normalized to match the distribution of the data used to train a classifier. Normalized data can be used as input into a classifier that was trained using the same histone modification(s) and selected genomic loci. The classifier can then use inputted data to determine ER status of a subject's cancer. It will be appreciated that this or similar approaches can be applied to assays of the present disclosure that quantify chromatin accessibility, transcription factor binding and/or DNA methylation.

[0219] In some embodiments, multiple epigenetic biomarkers (e.g., one or more histone modifications, chromatin accessibility, binding of one or more transcription factors, and/or DNA methylation) can be quantified for a single sample. In such embodiments, two or more assays for

assessing the epigenetic biomarkers can be performed in sequence (meaning a single sample can be probed for each modification in sequence) or in parallel (meaning that a single sample can be divided into multiple fractions, and then each fraction analyzed to quantifying an epigenetic biomarker). In some embodiments, H3K4me3 and H3K27ac histone modifications; H3K4me3 modifications and DNA methylation; H3K27ac modifications and DNA methylation; or H3K4me3 modifications, H3K27ac histone modifications, and DNA methylation are quantified in a single sample.

[0220] For the avoidance of any doubt, those of skill in the art will appreciate from the present disclosure that methods, kits and systems for ER status determination of the present disclosure are at least for *in vitro* use. Accordingly, all aspects and embodiments of the present disclosure can be performed and/or used at least *in vitro*.

[0221] Those of skill in the art will also appreciate that, in certain embodiments, methods of the present disclosure can be implemented on and/or in conjunction with a computer program and computer system. In some embodiments, methods of the present disclosure can be implemented on and/or in conjunction with a non-transitory computer readable storage medium encoded with the computer program, wherein the program comprises instructions that when executed by one or more processors cause the one or more processors to perform operations to perform the method. A computer system can also store and manipulate data generated by methods of the present disclosure that comprise a plurality of genomic locus modification status and/or accessibility status changes/profiles, which data can be used by a computer system in implementing methods disclosed herein. In certain embodiments, a computer system (i) receives modification status and/or accessibility status data; (ii) stores the data; and (iii) compares the data in any number of ways described herein (*e.g.*, analysis relative to appropriate references), *e.g.*, to determine ER status. In certain embodiments, a computer system (i) compares the genomic locus modification and/or accessibility status to a reference; and (ii) outputs an indication of whether the modification status and/or accessibility status of the genomic locus is significantly different from the reference and/or provides a determination regarding ER status.

[0222] Numerous types of computer systems can be used to implement methods of the present disclosure according to knowledge possessed by a skilled artisan in the bioinformatics and/or computer arts. Several software components can be loaded into memory during operation of such a computer system. The software components can comprise both software components

that are standard in the art and components that are special to the present disclosure (*e.g.*, dCHIP software described in Lin et al., *Bioinformatics* (2004) 20:1233-1240, incorporated herein by reference in its entirety; radial basis machine learning algorithms (RBM) known in the art). Methods of the present disclosure can also be programmed or modeled in mathematical software packages that allow symbolic entry of equations and high-level specification of processing, including specific algorithms to be used, thereby freeing a user of the need to procedurally program individual equations and algorithms. Such packages include, *e.g.*, Matlab from Mathworks (Natick, MA), Mathematica from Wolfram Research (Champaign, IL), S-Plus from MathSoft (Seattle, WA), R from R Foundation for Statistical Computing (Vienna, Austria), Python from Python Software Foundation (Wilmington, DE), or Perl from Perl Foundation (Holland, MI). In certain embodiments, a computer system comprises a database for storage of genomic locus modification status and/or accessibility status data. Such stored profiles can be accessed and used to perform comparisons of interest at a later point in time. In addition to the exemplary program structures and computer systems described herein, other, alternative program structures and computer systems will be readily apparent to the skilled artisan.

[0223] As demonstrated in the Examples, various algorithms can be applied to the comparison, between samples and references, of the modification status and/or accessibility status of genomic loci that are differentially modified in different ER states. In various embodiments, an algorithm can be a single learning statistical classifier system. Other suitable statistical algorithms are well known to those of skill in the art. For example, learning statistical classifier systems include a machine learning algorithmic technique capable of adapting to complex datasets (*e.g.*, a panel of genomic loci of interest) and making decisions based upon such datasets. In some embodiments, a single learning statistical classifier system such as a classification tree (*e.g.*, random forest) is used. In other embodiments, a combination of 2, 3, 4, 5, 6, 7, 8, 9, 10, or more learning statistical classifier systems are used, preferably in tandem. Examples of learning statistical classifier systems include, but are not limited to, those described in the Examples and also those using inductive learning (*e.g.*, decision/classification trees such as random forests, classification and regression trees (C&RT), boosted trees, etc.), Probably Approximately Correct (PAC) learning, connectionist learning (*e.g.*, neural networks (NN), artificial neural networks (ANN), neuro fuzzy networks (NFN), network structures, perceptrons such as multi-layer perceptrons, multi-layer feed-forward networks, applications of neural

networks, Bayesian learning in belief networks, etc.), reinforcement learning (*e.g.*, passive learning in a known environment such as naive learning, adaptive dynamic learning, and temporal difference learning, passive learning in an unknown environment, active learning in an unknown environment, learning action-value functions, applications of reinforcement learning, etc.), and genetic algorithms and evolutionary programming. Other learning statistical classifier systems include support vector machines (*e.g.*, Kernel methods), multivariate adaptive regression splines (MARS), Levenberg-Marquardt algorithms, Gauss-Newton algorithms, mixtures of Gaussians, gradient descent algorithms, and learning vector quantization (LVQ). In certain embodiments, methods of the present disclosure can include sending classification results to a medical practitioner, *e.g.*, an oncologist.

[0224] In various embodiments, the area under the receiver operating characteristic (AUROC) for determining if a subject has a particular ER cancer status (*e.g.*, an ER-positive cancer vs. an ER-negative cancer) is greater than 0.5 (*e.g.*, greater than 0.55, greater than 0.6, greater than 0.65, greater than 0.7, greater than 0.75, greater than 0.8, greater than 0.85, greater than 0.9, or greater than 0.95).

Formulation and Administration of Therapeutic Agents

[0225] The present disclosure includes methods where a therapeutic agent or regimen is administered to a subject based on the ER status of a cancer (*e.g.*, breast cancer, ovarian cancer, or endometrial cancer). In general, the therapeutic agent or regimen provided herein will be available, appropriate, and/or preferred for the determined ER status. Those of skill in the art will be aware of recommended and/or governmentally approved formulations and/or dosages for various therapeutic agents provided herein.

[0226] The present disclosure includes pharmaceutical compositions for delivery of one or more therapeutic agents to a subject. As disclosed herein, a pharmaceutical composition may be in any form known in the art, including formulations for administration according to any route known in the art. A suitable means of administration can be selected based on the age and condition of a subject.

[0227] Pharmaceutical composition forms of the present disclosure can include, *e.g.*, liquid, semi-solid and solid dosage forms. Pharmaceutical composition forms of the present disclosure can include, *e.g.*, liquid solutions (*e.g.*, injectable and infusible solutions), dispersions

or suspensions, tablets, pills, powders, and liposomes. Selection or use of any particular form may depend, in part, on the intended mode of administration and therapeutic application.

Accordingly, the compositions can be formulated for administration by a parenteral mode (*e.g.*, intravenous, subcutaneous, intraperitoneal, or intramuscular injection) or a non-parenteral mode.

As used herein, parenteral administration refers to modes of administration other than enteral and topical administration, usually by injection or infusion.

[0228] In some embodiments, the compositions provided herein are present in unit dosage form, which unit dosage form can be suitable for self-administration. Such a unit dosage form may be provided within a container, *e.g.*, a pill, vial, cartridge, prefilled syringe, or disposable pen.

[0229] A pharmaceutical composition of the present disclosure can be in an injectable or infusible form. For example, the present disclosure includes sterile formulations for injection or infusion, which can be formulated in accordance with conventional pharmaceutical practices. Sterile solutions can be prepared by incorporating a composition described herein in the required amount in an appropriate solvent with one or a combination of ingredients enumerated above, as required, followed by filter sterilization. Solutions can be formulated, *e.g.*, using distilled water, physiological saline, or an isotonic solution containing glucose and other supplements such as D-sorbitol, D-mannose, D-mannitol, or sodium chloride as an aqueous solution for injection, optionally in combination with a suitable solubilizing agent, for example, an alcohol such as ethanol and/or a polyalcohol such as propylene glycol or polyethylene glycol, and/or a nonionic surfactant such as polysorbate 80™ or HCO-50, and the like. In the case of sterile powders for the preparation of sterile injectable solutions, methods for preparation include vacuum drying and freeze-drying that yield a powder of a composition described herein plus any additional desired ingredient (see below) from a previously sterile-filtered solution thereof. The proper fluidity of a solution can be maintained, for example, by the use of a coating such as lecithin, by the maintenance of the required particle size in the case of dispersion and by the use of surfactants. Prolonged absorption of injectable compositions can be brought about by including in the composition a reagent that delays absorption, for example, monostearate salts, and gelatin. In particular instances, a pharmaceutical composition can be formulated, for example, as a buffered solution at a suitable concentration and suitable for storage, *e.g.*, at 2-8°C (*e.g.*, 4°C).

[0230] In various embodiments, a pharmaceutical composition of the present disclosure can be formulated as a solution, microemulsion, dispersion, liposome, or other ordered structure suitable for stable storage at high concentration. Generally, dispersions are prepared by incorporating a composition described herein into a sterile vehicle that contains a basic dispersion medium and the required other ingredients from those enumerated above.

[0231] In various instances, a pharmaceutical composition can be formulated to include a pharmaceutically acceptable carrier or excipient. Examples of pharmaceutically acceptable carriers include, without limitation, any and all solvents, dispersion media, coatings, antibacterial and antifungal agents, isotonic and absorption delaying agents, and the like that are physiologically compatible.

[0232] In certain embodiments, compositions can be formulated with a carrier that will protect the therapeutic agent against rapid release, such as a controlled release formulation, including implants and microencapsulated delivery systems. Biodegradable, biocompatible polymers can be used, such as ethylene vinyl acetate, polyanhydrides, polyglycolic acid, collagen, polyorthoesters, and polylactic acid. Many methods for the preparation of such formulations are known in the art. See, *e.g.*, J. R. Robinson (1978) "Sustained and Controlled Release Drug Delivery Systems," Marcel Dekker, Inc., New York.

[0233] Route of administration can be parenteral, for example, administration by injection. Administration by injection can be by intravenous injection, intramuscular injection, intraperitoneal injection, subcutaneous injection. Administration can be systemic or local. In certain embodiments, a composition described herein can be therapeutically delivered to a subject by way of local administration. As used herein, "local administration" or "local delivery," can refer to delivery that does not rely upon transport of the composition or therapeutic agent to its intended target tissue or site via the vascular system. For example, the composition may be delivered by injection or implantation of the composition or therapeutic agent or by injection or implantation of a device containing the composition or therapeutic agent. In certain embodiments, following local administration in the vicinity of a target tissue or site, the composition or therapeutic agent, or one or more components thereof, may diffuse to an intended target tissue or site that is not the site of administration.

[0234] A pharmaceutical composition can be administered parenterally in the form of an injectable formulation comprising a sterile solution or suspension in water or another

pharmaceutically acceptable liquid. For example, a pharmaceutical composition can be formulated by suitably combining the therapeutic molecule with pharmaceutically acceptable vehicles or media, such as sterile water and physiological saline, vegetable oil, emulsifier, suspension agent, surfactant, stabilizer, flavoring excipient, diluent, vehicle, preservative, binder, followed by mixing in a unit dose form required for generally accepted pharmaceutical practices. Examples of oily liquid include sesame oil and soybean oil, and it may be combined with benzyl benzoate or benzyl alcohol as a solubilizing agent. Other items that may be included are a buffer such as a phosphate buffer, or sodium acetate buffer, a soothing agent such as procaine hydrochloride, a stabilizer such as benzyl alcohol or phenol, and an antioxidant. The formulated injection can be packaged in a suitable ampule.

[0235] In various embodiments, subcutaneous administration can be accomplished by means of a device, such as a syringe, a prefilled syringe, an auto-injector (*e.g.*, disposable or reusable), a pen injector, a patch injector, a wearable injector, an ambulatory syringe infusion pump with subcutaneous infusion sets, or other device for combining with a therapeutic agent for subcutaneous injection.

[0236] An injection system of the present disclosure may employ a delivery pen as described in U.S. Pat. No. 5,308,341. Pen devices, most commonly used for self-delivery of insulin to patients with diabetes, are well known in the art. Such devices can include at least one injection needle, are typically pre-filled with one or more therapeutic unit doses of a solution that includes the therapeutic agent and are useful for rapidly delivering solution to a subject with as little pain as possible. One medication delivery pen includes a vial holder into which a vial of a therapeutic or other medication may be received. The pen may be an entirely mechanical device or it may be combined with electronic circuitry to accurately set and/or indicate the dosage of medication that is injected into the user. See, *e.g.*, U.S. Pat. No. 6,192,891. In some embodiments, the needle of the pen device is disposable and the kits include one or more disposable replacement needles. Pen devices suitable for delivery of any one of the presently featured compositions are also described in, *e.g.*, U.S. Pat. Nos. 6,277,099; 6,200,296; and 6,146,361, the disclosures of each of which are incorporated herein by reference in their entirety. A microneedle-based pen device is described in, *e.g.*, U.S. Pat. No. 7,556,615, the disclosure of which is incorporated herein by reference in its entirety. See also the Precision Pen Injector (PPI) device, MOLLY™, manufactured by Scandinavian Health Ltd.

[0237] In certain embodiments, administration of a therapeutic agent as described herein is achieved by administering to a subject a nucleic acid encoding a therapeutic agent described herein. Nucleic acids encoding a therapeutic agent described herein can be incorporated into a gene construct to be used as a part of a gene therapy protocol to deliver nucleic acids that can be used to express and produce therapeutic agent within cells. Expression constructs of such components may be administered in any therapeutically effective carrier, *e.g.*, any formulation or composition capable of effectively delivering the component gene to cells *in vivo*. Approaches include insertion of the subject gene in viral vectors including recombinant retroviruses, adenovirus, adeno-associated virus, lentivirus, and herpes simplex virus-1 (HSV-1), or recombinant bacterial or eukaryotic plasmids. Viral vectors can transfect cells directly; plasmid DNA can be delivered with the help of, for example, cationic liposomes (lipofectin) or derivatized, polylysine conjugates, gramicidin S, artificial viral envelopes or other such intracellular carriers, as well as direct injection of the gene construct or CaPO₄ precipitation. Examples of suitable retroviruses include adenovirus-derived vectors, adeno-associated virus (AAV), pLJ, pZIP, pWE, and pEM which are known to those skilled in the art.

[0238] In some embodiments, a composition can be formulated for storage at a temperature below 0°C (*e.g.*, -20°C or -80°C). In some embodiments, the composition can be formulated for storage for up to 2 years (*e.g.*, one month, two months, three months, four months, five months, six months, seven months, eight months, nine months, 10 months, 11 months, 1 year, or 2 years) at 2-8°C (*e.g.*, 4°C). Thus, in some embodiments, the compositions described herein are stable in storage for at least 1 year at 2-8°C (*e.g.*, 4°C).

[0239] A pharmaceutical composition can include a therapeutically effective amount of a therapeutic agent described herein. Such effective amounts can be readily determined by one of ordinary skill in the art. A therapeutically effective amount can be an amount at which any toxic or detrimental effects of the composition are outweighed by therapeutically beneficial effects. In some embodiments, a dose can also be chosen to reduce or avoid production of antibodies or other host immune responses against a therapeutic agent. Those of skill in the art will appreciate that data obtained from cell culture assays and animal studies can be used in formulating a range of dosage for use in humans. In various embodiments, the amount of active ingredient included in a pharmaceutical composition is such that a suitable dose within the designated range can be administered to subjects. The dose and method of administration can vary depending on weight,

age, condition, and other characteristics of a patient, and can be suitably selected as needed by those skilled in the art.

[0240] Pharmaceutical compositions including certain therapeutic agents, *e.g.*, therapeutic antibodies, can be administered as a fixed dose, or in a milligram per kilogram (mg/kg) dose. While in no way intended to be limiting, an exemplary single dose of certain pharmaceutical compositions described herein can include certain therapeutic agents as described herein in an amount equal to, *e.g.*, 0.001 to 1000 mg/kg, 1-1000 mg/kg, 1-100 mg/kg, 0.5-50 mg/kg, 0.1-100 mg/kg, 0.5-25 mg/kg, 1-20 mg/kg, and 1-10 mg/kg body weight. Exemplary dosages of a composition described herein include, without limitation, 0.1 mg/kg, 0.5 mg/kg, 1 mg/kg, 2 mg/kg, 4 mg/kg, 8 mg/kg, or 20 mg/kg. The present disclosure is not limited to such ranges or dosages.

[0241] The present disclosure further includes methods of preparing pharmaceutical compositions of the present disclosure and kits including pharmaceutical compositions of the present disclosure.

[0242] In various embodiments, therapeutic agents of the present disclosure can be administered to a subject in a course of treatment that further includes administration of one or more additional therapeutic agents or therapies that are not therapeutic agents (*e.g.*, surgery or radiation). Combination therapies of the present disclosure can include simultaneous exposure of a subject to therapeutic agents of two or more therapeutic regimens.

[0243] In certain embodiments, a therapeutic agent as described herein can be administered together with (*e.g.*, at the same time and/or in the same composition as) an additional agent or therapy. In certain embodiments, a therapeutic agent of the present disclosure can be administered separately from an additional therapeutic agent or therapy (*e.g.*, at a different time and/or in a different composition than the additional therapeutic agent or therapy). Dosing regimens of a therapeutic agent and one or more additional therapeutic agents with which it is administered in combination can be coordinated or independently determined. In various embodiments, an additional therapeutic agent or therapy administered in combination with a therapeutic agent as described herein can be administered at the same time as therapeutic agent, on the same day as therapeutic agent, or in the same week as therapeutic agent. In various embodiments, an additional therapeutic agent or therapy administered in combination with a therapeutic agent as described herein can be administered such that administration of the

therapeutic agent and the additional therapeutic agent or therapy are separated by one or more hours before or after, one or more days before or after, one or more weeks before or after, or one or more months before or after administration of the therapeutic agent. In various embodiments, the administration frequency and/or dosage of one or more additional therapeutic agents can be the same as, similar to, or different from the administration frequency of a therapeutic agent. In some embodiments, the two or more regimens can be administered simultaneously; in some embodiments, such regimens can be administered sequentially (*e.g.*, all “doses” of a first regimen are administered prior to administration of any doses of a second regimen); in some embodiments, such therapeutic agents are administered in overlapping dosing regimens.

[0244] In certain embodiments, administration of a therapeutic agent can be to a subject having previously received, scheduled to receive, or in the course of a treatment regimen including an additional cancer therapy. Administration of a therapeutic agent can, in some instances, improve delivery or efficacy of another therapeutic agent or therapy with which it is administered in combination.

[0245] It is contemplated that therapeutic agent combination therapies can demonstrate synergy and/or greater-than-additive effects between a therapeutic agent and one or more additional therapeutic agents with which it is administered in combination. A therapeutic agent can be administered in any effective amount as determined independently or as determined by the joint action of therapeutic agent and any of one or more additional therapeutic agents or therapies administered. Administration of the therapeutic agent may, in some embodiments, reduce the therapeutically effective dosage, required dosage, or administered dosage of the additional therapeutic agent or therapy relative to a reference regimen for administration of additional therapeutic agent or therapy or therapy absent the therapeutic agent. In certain embodiment, a composition described herein can replace or augment other previously or currently administered therapy. For example, upon treating with therapeutic agent, administration of one or more additional therapeutic agents or therapies can cease or diminish, *e.g.*, be administered at lower levels.

Kits

[0246] The present disclosure includes kits for detecting modification and/or accessibility of one or more genomic loci. In some embodiments, the present disclosure provides kits for

quantifying one or more histone modifications, chromatin accessibility, binding of one or more transcription factors, and/or DNA methylation at one or more genomic loci. Kits of the present disclosure can include, *e.g.*, reagents such as buffers and/or antibodies useful in the detection and quantification of histone modifications. In certain embodiments, a kit of the present disclosure can include at least one antibody that selective binds a histone modification selected from H3K9ac, H3K14ac, H3K18ac, H3K23ac, H3K27ac, H3K4me1, H3K4me2, or H3K4me3, or pan acetylation. In certain embodiments, a kit of the present disclosure can include at least one antibody that selective binds H3K4me3 modifications. In certain embodiments, a kit of the present disclosure can include at least one antibody that selective binds H3K27ac modifications. A kit of the present disclosure can include instructional materials disclosing or describing the use of the kit in a method of determining ER status and/or treatment disclosed herein. In various embodiments, a kit of the present disclosure can include one or more therapeutic agents useful in the treatment of cancer, *e.g.*, as disclosed herein, optionally in combination with instruction materials for treatment of cancer, *e.g.*, breast cancer, ovarian cancer, or endometrial cancer based on ER status.

[0247] In some embodiments, a kit of the present disclosure comprises reagents for quantifying one or more histone modifications, chromatin accessibility, binding of one or more transcription factors, and/or DNA methylation at one or more genomic loci, wherein the one or more genomic loci are selected from Tabled 1-3.

[0248] In some embodiments, the kit comprises reagents for quantifying H3K4me3 for at least 5, 10, 20, 30, 40, or 50 genomic loci in Table 1. In some embodiments, the kit comprises reagents for quantifying H3K27ac for at least 5, 10, 20, 30, 40, or 50 genomic loci in Table 2. In some embodiments, the kit comprises one or more antibodies for use in ChIP-seq, optionally wherein the one or more antibodies specifically bind H3K4me3- or H3K27ac-modified histones.

[0249] In some embodiments, the kit comprises reagents for quantifying DNA methylation for at least 5, 10, 20, 30, 40, or 50 genomic loci in Table 3. In some embodiments, the kit comprises one or more methyl-binding domains for use in MBD-seq. In some embodiments, the kit comprises one or more antibodies that can bind methylated DNA (*e.g.*, for use in MeDIP).

[0250] In some embodiments, the kit comprises reagents for isolation of cell-free DNA (cfDNA) from a liquid biopsy sample. In some embodiments, the kit comprises reagents for

library preparation for sequencing. In some embodiments, the kit comprises reagents for sequencing. In some embodiments, the kit comprises instructions for determining if a subject has an ER-positive cancer.

Systems

[0251] The present disclosure includes systems for detecting modification and/or accessibility of one or more genomic loci. In some embodiments, the present disclosure provides systems for quantifying one or more histone modifications, chromatin accessibility, binding of one or more transcription factors, and/or DNA methylation at one or more genomic loci. Systems of the present disclosure can include a sequencer configured to generate a sequencing dataset from a sample; and a non-transitory computer readable storage medium and/or a computer system.

[0252] In some embodiments, the non-transitory computer readable storage medium is encoded with a computer program, wherein the program comprises instructions that when executed by one or more processors cause the one or more processors to perform operations to perform a method of the present disclosure.

[0253] In some embodiments, the computer system comprises a memory and one or more processors coupled to the memory, wherein the one or more processors are configured to perform a method of the present disclosure.

[0254] In some embodiments, the sequencer is configured to generate a Whole Genome Sequencing (WGS) dataset from the sample. In some embodiments, the system also includes a sample preparation device configured to prepare the sample for sequencing from a biological sample, optionally a liquid biopsy sample. The sample preparation device may include reagents for quantifying one or more histone modifications, chromatin accessibility, binding of one or more transcription factors, and/or DNA methylation at one or more genomic loci in cell-free DNA (cfDNA) from the biological sample, optionally the liquid biopsy sample.

[0255] Systems of the present disclosure can include, *e.g.*, reagents such as buffers and/or antibodies useful in the detection and quantification of histone modifications. In certain embodiments, a system of the present disclosure can include at least one antibody that selective binds a histone modification selected from H3K9ac, H3K14ac, H3K18ac, H3K23ac, H3K27ac, H3K4me1, H3K4me2, or H3K4me3, or pan acetylation. In certain embodiments, a system of the

present disclosure can include at least one antibody that selective binds H3K4me3 modifications. In certain embodiments, a system of the present disclosure can include at least one antibody that selective binds H3K27ac modifications. A system of the present disclosure can include instructional materials disclosing or describing the use of the system in a method of determining ER status and/or treatment disclosed herein.

[0256] In some embodiments, a system of the present disclosure comprises reagents for quantifying one or more histone modifications, chromatin accessibility, binding of one or more transcription factors, and/or DNA methylation at one or more genomic loci, wherein the one or more genomic loci are selected from Tabled 1-3.

[0257] In some embodiments, the system comprises reagents for quantifying H3K4me3 for at least 5, 10, 20, 30, 40, or 50 genomic loci in Table 1. In some embodiments, the system comprises reagents for quantifying H3K27ac for at least 5, 10, 20, 30, 40, or 50 genomic loci in Table 2. In some embodiments, the system comprises one or more antibodies for use in ChIP-seq, optionally wherein the one or more antibodies specifically bind H3K4me3- or H3K27ac-modified histones.

[0258] In some embodiments, the system comprises reagents for quantifying DNA methylation for at least 5, 10, 20, 30, 40, or 50 genomic loci in Table 3. In some embodiments, the system comprises one or more methyl-binding domains for use in MBD-seq.

[0259] In some embodiments, the system comprises reagents for isolation of cell-free DNA (cfDNA) from a liquid biopsy sample. In some embodiments, the sequencer comprises reagents for library preparation for sequencing. In some embodiments, the sequencer comprises reagents for sequencing. In some embodiments, the system comprises instructions for determining if a subject has an ER-positive cancer.

[0260] Illustrative embodiments of systems and methods disclosed herein were described above with reference to computations performed locally by a computing device. However, computations performed over a network are also contemplated. Fig. 4 shows an illustrative network environment 400 for use in the methods and systems described herein. In brief overview, referring now to Fig. 4, a block diagram of an illustrative cloud computing environment 400 is shown and described. The cloud computing environment 400 may include one or more resource providers 402a, 402b, 402c (collectively, 402). Each resource provider 402 may include computing resources. In some implementations, computing resources may include any hardware and/or

software used to process data. For example, computing resources may include hardware and/or software capable of executing algorithms, computer programs, and/or computer applications. In some implementations, illustrative computing resources may include application servers and/or databases with storage and retrieval capabilities. Each resource provider 402 may be connected to any other resource provider 402 in the cloud computing environment 400. In some implementations, the resource providers 402 may be connected over a computer network 408. Each resource provider 402 may be connected to one or more computing device 404a, 404b, 404c (collectively, 404), over the computer network 408.

[0261] The cloud computing environment 400 may include a resource manager 406. The resource manager 406 may be connected to the resource providers 402 and the computing devices 404 over the computer network 408. In some implementations, the resource manager 406 may facilitate the provision of computing resources by one or more resource providers 402 to one or more computing devices 404. The resource manager 406 may receive a request for a computing resource from a particular computing device 404. The resource manager 406 may identify one or more resource providers 402 capable of providing the computing resource requested by the computing device 404. The resource manager 406 may select a resource provider 402 to provide the computing resource. The resource manager 406 may facilitate a connection between the resource provider 402 and a particular computing device 404. In some implementations, the resource manager 406 may establish a connection between a particular resource provider 402 and a particular computing device 404. In some implementations, the resource manager 406 may redirect a particular computing device 404 to a particular resource provider 402 with the requested computing resource.

[0262] Fig. 5 shows an example of a computing device 500 and a mobile computing device 550 that can be used in the methods and systems described in this disclosure. The computing device 500 is intended to represent various forms of digital computers, such as laptops, desktops, workstations, personal digital assistants, servers, blade servers, mainframes, and other appropriate computers. The mobile computing device 550 is intended to represent various forms of mobile devices, such as personal digital assistants, cellular telephones, smart-phones, and other similar computing devices. The components shown here, their connections and relationships, and their functions, are meant to be examples only, and are not meant to be limiting.

[0263] The computing device 500 includes a processor 502, a memory 504, a storage device 506, a high-speed interface 508 connecting to the memory 504 and multiple high-speed expansion ports 510, and a low-speed interface 512 connecting to a low-speed expansion port 514 and the storage device 506. Each of the processor 502, the memory 504, the storage device 506, the high-speed interface 508, the high-speed expansion ports 510, and the low-speed interface 512, are interconnected using various busses, and may be mounted on a common motherboard or in other manners as appropriate. The processor 502 can process instructions for execution within the computing device 500, including instructions stored in the memory 504 or on the storage device 506 to display graphical information for a GUI on an external input/output device, such as a display 516 coupled to the high-speed interface 508. In other implementations, multiple processors and/or multiple buses may be used, as appropriate, along with multiple memories and types of memory. Also, multiple computing devices may be connected, with each device providing portions of the necessary operations (e.g., as a server bank, a group of blade servers, or a multi-processor system). Also, multiple computing devices may be connected, with each device providing portions of the necessary operations (e.g., as a server bank, a group of blade servers, or a multi-processor system). Thus, as the term is used herein, where a plurality of functions are described as being performed by “a processor”, this encompasses embodiments wherein the plurality of functions are performed by any number of processors (e.g., one or more processors) of any number of computing devices (e.g., one or more computing devices). Furthermore, where a function is described as being performed by “a processor”, this encompasses embodiments wherein the function is performed by any number of processors (e.g., one or more processors) of any number of computing devices (e.g., one or more computing devices) (e.g., in a distributed computing system).

[0264] The memory 504 stores information within the computing device 500. In some implementations, the memory 504 is a volatile memory unit or units. In some implementations, the memory 504 is a non-volatile memory unit or units. The memory 504 may also be another form of computer-readable medium, such as a magnetic or optical disk.

[0265] The storage device 506 is capable of providing mass storage for the computing device 500. In some implementations, the storage device 506 may be or contain a computer-readable medium, such as a hard disk device, an optical disk device, a flash memory or other similar solid state memory device, or an array of devices, including devices in a storage area network or other configurations. Instructions can be stored in an information carrier. The

instructions, when executed by one or more processing devices (for example, processor 502), perform one or more methods, such as those described above. The instructions can also be stored by one or more storage devices such as computer- or machine-readable mediums (for example, the memory 504, the storage device 506, or memory on the processor 502).

[0266] The high-speed interface 508 manages bandwidth-intensive operations for the computing device 500, while the low-speed interface 512 manages lower bandwidth-intensive operations. Such allocation of functions is an example only. In some implementations, the high-speed interface 508 is coupled to the memory 504, the display 516 (e.g., through a graphics processor or accelerator), and to the high-speed expansion ports 510, which may accept various expansion cards (not shown). In the implementation, the low-speed interface 512 is coupled to the storage device 506 and the low-speed expansion port 514. The low-speed expansion port 514, which may include various communication ports (e.g., USB, Bluetooth®, Ethernet, wireless Ethernet) may be coupled to one or more input/output devices, such as a keyboard, a pointing device, a scanner, or a networking device such as a switch or router, e.g., through a network adapter.

[0267] The computing device 500 may be implemented in a number of different forms, as shown in the figure. For example, it may be implemented as a standard server 520, or multiple times in a group of such servers. In addition, it may be implemented in a personal computer such as a laptop computer 522. It may also be implemented as part of a rack server system 524. Alternatively, components from the computing device 500 may be combined with other components in a mobile device (not shown), such as a mobile computing device 550. Each of such devices may contain one or more of the computing device 500 and the mobile computing device 550, and an entire system may be made up of multiple computing devices communicating with each other.

[0268] The mobile computing device 550 includes a processor 552, a memory 564, an input/output device such as a display 554, a communication interface 566, and a transceiver 568, among other components. The mobile computing device 550 may also be provided with a storage device, such as a micro-drive or other device, to provide additional storage. Each of the processor 552, the memory 564, the display 554, the communication interface 566, and the transceiver 568, are interconnected using various buses, and several of the components may be mounted on a common motherboard or in other manners as appropriate.

[0269] The processor 552 can execute instructions within the mobile computing device 550, including instructions stored in the memory 564. The processor 552 may be implemented as a chipset of chips that include separate and multiple analog and digital processors. The processor 552 may provide, for example, for coordination of the other components of the mobile computing device 550, such as control of user interfaces, applications run by the mobile computing device 550, and wireless communication by the mobile computing device 550.

[0270] The processor 552 may communicate with a user through a control interface 558 and a display interface 556 coupled to the display 554. The display 554 may be, for example, a TFT (Thin-Film-Transistor Liquid Crystal Display) display or an OLED (Organic Light Emitting Diode) display, or other appropriate display technology. The display interface 556 may comprise appropriate circuitry for driving the display 554 to present graphical and other information to a user. The control interface 558 may receive commands from a user and convert them for submission to the processor 552. In addition, an external interface 562 may provide communication with the processor 552, so as to enable near area communication of the mobile computing device 550 with other devices. The external interface 562 may provide, for example, for wired communication in some implementations, or for wireless communication in other implementations, and multiple interfaces may also be used.

[0271] The memory 564 stores information within the mobile computing device 550. The memory 564 can be implemented as one or more of a computer-readable medium or media, a volatile memory unit or units, or a non-volatile memory unit or units. An expansion memory 574 may also be provided and connected to the mobile computing device 550 through an expansion interface 572, which may include, for example, a SIMM (Single In Line Memory Module) card interface. The expansion memory 574 may provide extra storage space for the mobile computing device 550, or may also store applications or other information for the mobile computing device 550. Specifically, the expansion memory 574 may include instructions to carry out or supplement the processes described above, and may include secure information also. Thus, for example, the expansion memory 574 may be provided as a security module for the mobile computing device 550, and may be programmed with instructions that permit secure use of the mobile computing device 550. In addition, secure applications may be provided via the SIMM cards, along with additional information, such as placing identifying information on the SIMM card in a non-hackable manner.

[0272] The memory may include, for example, flash memory and/or NVRAM memory (non-volatile random access memory), as discussed below. In some implementations, instructions are stored in an information carrier and, when executed by one or more processing devices (for example, processor 552), perform one or more methods, such as those described above. The instructions can also be stored by one or more storage devices, such as one or more computer- or machine-readable mediums (for example, the memory 564, the expansion memory 574, or memory on the processor 552). In some implementations, the instructions can be received in a propagated signal, for example, over the transceiver 568 or the external interface 562.

[0273] The mobile computing device 550 may communicate wirelessly through the communication interface 566, which may include digital signal processing circuitry where necessary. The communication interface 566 may provide for communications under various modes or protocols, such as GSM voice calls (Global System for Mobile communications), SMS (Short Message Service), EMS (Enhanced Messaging Service), or MMS messaging (Multimedia Messaging Service), CDMA (code division multiple access), TDMA (time division multiple access), PDC (Personal Digital Cellular), WCDMA (Wideband Code Division Multiple Access), CDMA2000, or GPRS (General Packet Radio Service), among others. Such communication may occur, for example, through the transceiver 568 using a radio-frequency. In addition, short-range communication may occur, such as using a Bluetooth®, Wi-Fi™, or other such transceiver (not shown). In addition, a GPS (Global Positioning System) receiver module 570 may provide additional navigation- and location-related wireless data to the mobile computing device 550, which may be used as appropriate by applications running on the mobile computing device 550.

[0274] The mobile computing device 550 may also communicate audibly using an audio codec 560, which may receive spoken information from a user and convert it to usable digital information. The audio codec 560 may likewise generate audible sound for a user, such as through a speaker, e.g., in a handset of the mobile computing device 550. Such sound may include sound from voice telephone calls, may include recorded sound (e.g., voice messages, music files, etc.) and may also include sound generated by applications operating on the mobile computing device 550.

[0275] The mobile computing device 550 may be implemented in a number of different forms, as shown in the figure. For example, it may be implemented as a cellular telephone 580. It

may also be implemented as part of a smart-phone 582, personal digital assistant, or other similar mobile device.

[0276] Various implementations of the systems and techniques described here can be realized in digital electronic circuitry, integrated circuitry, specially designed ASICs (application specific integrated circuits), computer hardware, firmware, software, and/or combinations thereof. These various implementations can include implementation in one or more computer programs that are executable and/or interpretable on a programmable system including at least one programmable processor, which may be special or general purpose, coupled to receive data and instructions from, and to transmit data and instructions to, a storage system, at least one input device, and at least one output device.

[0277] These computer programs (also known as programs, software, software applications or code) include machine instructions for a programmable processor, and can be implemented in a high-level procedural and/or object-oriented programming language, and/or in assembly/machine language. As used herein, the terms machine-readable medium and computer-readable medium refer to any computer program product, apparatus and/or device (e.g., magnetic discs, optical disks, memory, Programmable Logic Devices (PLDs)) used to provide machine instructions and/or data to a programmable processor, including a machine-readable medium that receives machine instructions as a machine-readable signal. The term machine-readable signal refers to any signal used to provide machine instructions and/or data to a programmable processor.

[0278] To provide for interaction with a user, the systems and techniques described here can be implemented on a computer having a display device (e.g., a CRT (cathode ray tube) or LCD (liquid crystal display) monitor) for displaying information to the user and a keyboard and a pointing device (e.g., a mouse or a trackball) by which the user can provide input to the computer. Other kinds of devices can be used to provide for interaction with a user as well; for example, feedback provided to the user can be any form of sensory feedback (e.g., visual feedback, auditory feedback, or tactile feedback); and input from the user can be received in any form, including acoustic, speech, or tactile input.

[0279] Systems and techniques described here can be implemented in a computing system that includes a back end component (e.g., as a data server), or that includes a middleware component (e.g., an application server), or that includes a front end component (e.g., a client computer having a graphical user interface or a Web browser through which a user can interact

with an implementation of the systems and techniques described here), or any combination of such back end, middleware, or front end components. The components of the system can be interconnected by any form or medium of digital data communication (e.g., a communication network). Examples of communication networks include a local area network (LAN), a wide area network (WAN), and the Internet.

[0280] The computing system can include clients and servers. A client and server are generally remote from each other and typically interact through a communication network. The relationship of client and server arises by virtue of computer programs running on the respective computers and having a client-server relationship to each other.

[0281] Certain embodiments described herein make use of computer algorithms in the form of software instructions executed by a computer processor, for example in a classifier. In certain embodiments, the software instructions include a machine learning (ML) module, for example as a classifier. As used herein, a machine learning module refers to a computer implemented process (e.g., a software function) that implements one or more specific machine learning techniques, e.g., artificial neural networks (ANNs), e.g., convolutional neural networks (CNNs), random forest, decision trees, support vector machines, and the like, in order to determine, for a given input, one or more output values. In certain embodiments, the input comprises image data and/or alphanumeric data which can include 2D and/or 3D datasets, numbers, words, phrases, or lengthier strings, for example. In certain embodiments, the one or more output values comprise image data (e.g. 2D and/or 3D datasets) and/or values representing numeric values, words, phrases, or other alphanumeric strings.

[0282] In certain embodiments, machine learning modules implementing machine learning techniques are trained, for example, using datasets that include categories of data described herein. Such training may be used to determine various parameters of machine learning algorithms implemented by a machine learning module, such as weights associated with layers in neural networks. In certain embodiments, once a machine learning module is trained, e.g., to accomplish a specific task such as identifying certain response strings, values of determined parameters are fixed and the (e.g., unchanging, static) machine learning module is used to process new data (e.g., different from the training data) and accomplish its trained task without further updates to its parameters (e.g., the machine learning module does not receive feedback and/or updates). In certain embodiments, available input data includes training data and validation data, e.g., where

the validation data is separate and non-overlapping with the training data. For example, in certain embodiments, training data is used during the training process to optimize a model, whereas validation data is used to check the accuracy of the model while operating on previously unseen data. In certain embodiments, training data is divided into batches (e.g., portions) that is sequentially used (e.g., in random order) as sets of inputs to train a model. In certain embodiments, a model is trained multiple times (e.g., epochs) on the entire set of training data. In certain embodiments, machine learning modules may receive feedback, e.g., based on user review of accuracy, and such feedback may be used as additional training data, to dynamically update the machine learning module. In certain embodiments, two or more machine learning modules may be combined and implemented as a single module and/or a single software application. In certain embodiments, two or more machine learning modules may also be implemented separately, e.g., as separate software applications. A machine learning module may be software and/or hardware. For example, a machine learning module may be implemented entirely as software, or certain functions of a ANN module may be carried out via specialized hardware (e.g., via an application specific integrated circuit (ASIC) and/or field programmable gate arrays (FPGAs)).

[0283] In certain embodiments, machine learning modules implementing machine learning techniques may be composed of individual nodes (e.g. units, neurons). A node may receive a set of inputs that may include at least a portion of a given input data for the machine learning module and/or at least one output of another node. A node may have at least one parameter to apply and/or a set of instructions to perform (e.g., mathematical functions to execute) over the set of inputs. In certain embodiments, node instructions may include a step to provide various relative importance to the set of inputs using various parameters, such as weights. The weights may be applied by performing scalar multiplication (e.g., or other mathematical function) between a set of inputs values and the parameters, resulting in a set of weighted inputs. In certain embodiments, a node may have a transfer function to combine the set of weighted inputs into one output value. A transfer function may be implemented by a summation of all the weighted inputs and the addition of an offset (e.g., bias) value. In certain embodiments, a node may have an activation function to introduce non-linearity into the output value. Non-limiting examples of the activation function include Rectified Linear Activation (ReLU), logistic (e.g., sigmoid), hyperbolic tangent (tanh), and softmax. In certain embodiments, a node may have a capability of remembering previous states

(e.g., recurrent nodes). Previous states may be applied to the input and output values using a set of learning parameters.

[0284] In certain embodiments, the machine learning module comprises a deep learning architecture composed of nodes organized into layers. For example, a layer is a set of nodes that receives data input (e.g., weighted or non-weighted input), transforms it (e.g., by carrying out instructions, e.g., applying a set of functions e.g., linear and/or non-linear functions), and passes transformed values as output (e.g., to the next layer). In certain embodiments, the set of nodes in a particular layer may share the same parameters and instructions without interacting with each other. A machine learning module may be composed of at least one layer (e.g., ordered). Examples of types of layers include convolutional layers (e.g., layers with a kernel, a matrix of parameters that is slid across an input to be multiplied with multiple input values to reduce them to a single output value); fully connected (FC) layers (e.g. all nodes are connected to all outputs of the previous layer); recurrent layers, long/short term memory (LSTM) layers, gated recurrent unit (GRU) layers (e.g., nodes with the various abilities to memorize and apply their previous inputs and/or outputs); batch normalization (BN) layers (e.g., layers that normalize a set of outputs from another layer, allowing for more independent learning of individual layers); activation layers (e.g., layers with nodes that only contain an activation function); and/or (un)pooling layers [e.g., layers that reduce (increase) dimensions of an input by summarizing (splitting) input values in defined patches).

[0285] In certain embodiments, the performance of a machine learning module may be characterized by its ability to produce an output data with specific accuracy. To achieve specific accuracy, a training process is performed to find optimal parameters, such as weights, for each node in each layer of the machine learning module. In certain embodiments, the training process of a machine learning module may involve using output data to calculate an objective function (e.g., cost function, loss function, error function) that needs to be optimized (e.g., minimized, maximized). For example, a machine learning objective function may be a combination of a loss function and regularization parameter. The loss function is related to how well the output is able to predict the input. The loss function may take various forms, like mean squared error, mean absolute error, binary cross-entropy, categorical cross-entropy, for example. The regularization term may be needed to prevent overfitting and improve generalization of the training process. Examples of regularization techniques include L1 Regularization or Lasso Regression, L2

Regularization or Ridge Regression, and Dropout (e.g., dropping layer outputs at random during training process).

[0286] In certain embodiments, objective function optimization of a machine learning module may involve finding at least one (e.g., all) of the present global optima (e.g., as opposed to local optima). In certain embodiments, the algorithm for objective function optimization follows principles of mathematical optimization for a multi-variable function and relies on achieving specific accuracy of the process. Examples of objective function optimization algorithms include gradient descent, nonlinear conjugate gradient, random search, Levenberg-Marquardt algorithm, limited-memory Broyden-Fletcher-Goldfarb-Shanno algorithm, pattern search, basin hopping method, Krylov method, Adam method, genetic algorithm, particle swarm optimization, surrogate optimization, and simulated annealing.

[0287] Methods disclosed herein may utilize one or more machine-learned models as a classifier. A machine-learned model may be or include an artificial neural network. A machine-learned model may employ, for example, an attention-based model (e.g., a transformer model, such as, for example, a vision transformer), a transformer model (e.g., a vision transformer), a regression-based model (e.g., a logistic regression model), a regularization-based model (e.g., an elastic net model or a ridge regression model), an instance-based model (e.g., a support vector machine or a k-nearest neighbor model), a Bayesian-based model (e.g., a naive-based model or a Gaussian naive-based model), a clustering-based model (e.g., an expectation maximization model), an ensemble-based model (e.g., an adaptive boosting model, a random forest model, a bootstrap-aggregation model, or a gradient boosting machine model), or a neural-network-based model (e.g., a convolutional neural network, a recurrent neural network, autoencoder, a back propagation network, or a stochastic gradient descent network).

[0288] In some embodiments, a machine-learned model used as a classifier is or is derived from a decision tree methodology, a neural boosted methodology, a bootstrap forest methodology, a boosted tree methodology, a k nearest neighbors methodology, a generalized regression forward selection methodology, a generalized regression pruned forward selection methodology, a fit stepwise methodology, a generalized regression lasso methodology, a generalized regression elastic net methodology, a generalized regression ridge methodology, a nominal logistic methodology, a support vector machines methodology, a discriminant methodology, a naïve Bayes methodology, or a combination thereof. In some embodiments, a machine-learned model is or is

derived from a decision tree methodology, a neural boosted methodology, a bootstrap forest methodology, a boosted tree methodology, a generalized regression lasso methodology, a generalized regression elastic net methodology, a generalized regression ridge methodology, a nominal logistic methodology, a support vector machines methodology, a discriminant methodology, or a combination thereof. In some embodiments, a machine-learned model is or is derived from a decision tree methodology, a neural boosted methodology, a bootstrap forest methodology, a boosted tree methodology, a support vector machines methodology, or a combination thereof.

Definitions

[0289] “A” or “An”: The articles “a” and “an” are used herein to refer to one or to more than one (*i.e.*, to at least one) of the grammatical object of the article. By way of example, “an element” refers to one element or more than one element.

[0290] *About:* The term “about”, when used herein in reference to a value, refers to a value that is similar, in context, to the referenced value. In general, those skilled in the art, familiar with the context, will appreciate the relevant degree of variance encompassed by “about” in that context. For example, in some embodiments, the term “about” can encompass a range of values that within 25%, 20%, 19%, 18%, 17%, 16%, 15%, 14%, 13%, 12%, 11%, 10%, 9%, 8%, 7%, 6%, 5%, 4%, 3%, 2%, 1%, or within a fraction of a percent, of the referenced value.

[0291] “Accessibility Status” or “Chromatin Accessibility Status”: As used herein, “accessibility status” or “chromatin accessibility status” of a genomic locus refers to the frequency with which DNA sequences corresponding to the genomic locus are identified in an assay for detection of accessible chromatin. Accessibility status can be determined by various assays known in the art, including without limitation ChIP-seq as one example. Where two samples are separately analyzed by the same assay or comparable assays for detection of accessible DNA sequences, differences in chromatin accessibility status of genomic loci can be detected. Accessibility status can be compared to a standard or reference. A sample that has an accessibility status that differs in accessibility status from a standard or reference can be referred to as differentially modified. Suitable assays for determining chromatin accessibility are known in the art. Exemplary assays include ATAC-seq (Assay of Transpose Accessible Chromatin

sequencing), NOME-seq (Nucleosome Occupancy and Methylome sequencing), FAIRE-seq (Formaldehyde-Assisted Isolation of Regulatory Elements sequencing), MNase-seq (Micrococcal Nuclease digestion with sequencing), and/or a DNase hypersensitivity assay.

[0292] Administration: As used herein, the term “administration” typically refers to the administration of a disease appropriate (*e.g.*, ER-positive cancer appropriate) treatment. In some embodiments, the disease appropriate treatment may comprise administering a composition to a subject, for example to achieve delivery of an agent that is, is included in, or is otherwise delivered by, the composition. In some embodiments, the disease appropriate treatment may comprise administering an appropriate surgical procedure or radiological procedure, optionally in combination with administration of a composition.

[0293] Agent: As used herein, the term “agent” may refer to any chemical or physical entity, including without limitation any of one or more of an atom, *e.g.*, a radioactive atom, molecule, compound, conjugate, polypeptide, polynucleotide, polysaccharide, lipid, cell, or combination or complex thereof.

[0294] Antibody: As used herein, the term “antibody” refers to a polypeptide that includes one or more canonical immunoglobulin sequence elements sufficient to confer specific binding to a particular antigen (*e.g.*, a heavy chain variable domain, a light chain variable domain, and/or one or more CDRs). Thus, the term antibody includes, without limitation, human antibodies, non-human antibodies, synthetic and/or engineered antibodies, fragments thereof, and agents including the same. Antibodies can be naturally occurring immunoglobulins (*e.g.*, generated by an organism reacting to an antigen). Synthetic, non-naturally occurring, or engineered antibodies can be produced by recombinant engineering, chemical synthesis, or other artificial systems or methodologies known to those of skill in the art.

[0295] As is well known in the art, typical human immunoglobulins are approximately 150 kD tetrameric agents that include two identical heavy (H) chain polypeptides (about 50 kD each) and two identical light (L) chain polypeptides (about 25 kD each) that associate with each other to form a structure commonly referred to as a “Y-shaped” structure. Typically, each heavy chain includes a heavy chain variable domain (VH) and a heavy chain constant domain (CH). The heavy chain constant domain includes three CH domains: CH1, CH2 and CH3. A short region, known as the “switch”, connects the heavy chain variable and constant regions. The “hinge” connects CH2 and CH3 domains to the rest of the immunoglobulin. Each light chain

includes a light chain variable domain (VL) and a light chain constant domain (CL), separated from one another by another “switch.” Each variable domain contains three hypervariable loops known as “complement determining regions” (CDR1, CDR2, and CDR3) and four somewhat invariant “framework” regions (FR1, FR2, FR3, and FR4). In each VH and VL, the three CDRs and four FRs are arranged from amino-terminus to carboxy-terminus in the following order: FR1, CDR1, FR2, CDR2, FR3, CDR3, and FR4. The variable regions of a heavy and/or a light chain are typically understood to provide a binding moiety that can interact with an antigen. Constant domains can mediate binding of an antibody to various immune system cells (*e.g.*, effector cells and/or cells that mediate cytotoxicity), receptors, and elements of the complement system. Heavy and light chains are linked to one another by a single disulfide bond, and two other disulfide bonds connect the heavy chain hinge regions to one another, so that the dimers are connected to one another and the tetramer is formed. When natural immunoglobulins fold, the FR regions form the beta sheets that provide the structural framework for the domains, and the CDR loop regions from both the heavy and light chains are brought together in three-dimensional space so that they create a single hypervariable antigen binding site located at the tip of the Y structure.

[0296] In some embodiments, an antibody is a polyclonal, monoclonal, monospecific, or multispecific antibody (*e.g.*, a bispecific antibody). In some embodiments, an antibody includes at least one light chain monomer or dimer, at least one heavy chain monomer or dimer, at least one heavy chain-light chain dimer, or a tetramer that includes two heavy chain monomers and two light chain monomers. Moreover, the term “antibody” can include (unless otherwise stated or clear from context) any art-known constructs or formats utilizing antibody structural and/or functional features including without limitation intrabodies, domain antibodies, antibody mimetics, Zybodies®, Fab fragments, Fab’ fragments, F(ab’)2 fragments, Fd’ fragments, Fd fragments, isolated CDRs or sets thereof, single chain antibodies, single-chain Fvs (scFvs), disulfide-linked Fvs (sdFv), polypeptide-Fc fusions, single domain antibodies (*e.g.*, shark single domain antibodies such as IgNAR or fragments thereof), cameloid antibodies, camelized antibodies, masked antibodies (*e.g.*, Probodies®), affybodies, anti-idiotypic (anti-Id) antibodies (including, *e.g.*, anti-anti-Id antibodies), Small Modular ImmunoPharmaceuticals (SMIPs), single chain or Tandem diabodies (TandAb®), VHHs, Anticalins®, Nanobodies®, minibodies, BiTE®s, ankyrin repeat proteins or DARPINs®, Avimers®, DARTs, TCR-like antibodies,

Adnectins®, Affilins®, Trans-bodies®, Affibodies®, TrimerX®, MicroProteins, Fynomers®, Centyrins®, KALBITOR®, chimeric antigen receptors (CARs), engineered T-cell receptors (TCRs), and antigen-binding fragments of any of the above.

[0297] In various embodiments, an antibody includes one or more structural elements recognized by those skilled in the art as a complementarity determining region (CDR) or variable domain. In some embodiments, an antibody can be a covalently modified (“conjugated”) antibody (*e.g.*, an antibody that includes a polypeptide including one or more canonical immunoglobulin sequence elements sufficient to confer specific binding to a particular antigen, where the polypeptide is covalently linked with one or more of a therapeutic agent, a detectable moiety, another polypeptide, a glycan, or a polyethylene glycol molecule). In some embodiments, antibody sequence elements are humanized, primatized, chimeric, etc., as is known in the art.

[0298] An antibody including a heavy chain constant domain can be, without limitation, an antibody of any known class, including but not limited to, IgA, secretory IgA, IgG, IgE and IgM, based on heavy chain constant domain amino acid sequence (*e.g.*, alpha (α), delta (δ), epsilon (ϵ), gamma (γ) and mu (μ)). IgG subclasses are also well known to those in the art and include but are not limited to human IgG1, IgG2, IgG3 and IgG4. “Isotype” refers to the Ab class or subclass (*e.g.*, IgM or IgG1) that is encoded by the heavy chain constant region genes. As used herein, a “light chain” can be of a distinct type, *e.g.*, kappa (κ) or lambda (λ), based on the amino acid sequence of the light chain constant domain. In some embodiments, an antibody has constant region sequences that are characteristic of mouse, rabbit, primate, or human immunoglobulins. Naturally produced immunoglobulins are glycosylated, typically on the CH2 domain. As is known in the art, affinity and/or other binding attributes of Fc regions for Fc receptors can be modulated through glycosylation or other modification. In some embodiments, an antibody may lack a covalent modification (*e.g.*, attachment of a glycan) that it would have if produced naturally. In some embodiments, antibodies produced and/or utilized in accordance with the present disclosure include glycosylated Fc domains, including Fc domains with modified or engineered glycosylation.

[0299] In some embodiments, an antibody can be specific for a particular histone modification (*e.g.*, an antibody can bind one histone modification, *e.g.*, H3K27ac with a higher affinity than other histone modifications, under conditions that are commonly used in ChIP-seq

experiments). In some embodiments, an antibody is specific for an H3K9ac, H3K14ac, H3K18ac, H3K23ac, H3K27ac, H3K4me1, H3K4me2, or H3K4me3 modification. In some embodiments, an antibody is specific for an H3K27ac modification. In some embodiments, an antibody is specific for an H3K4me3 modification.

[0300] In some embodiments, an antibody is a “pan” antibody. As used herein, the term pan antibody refers to an antibody that can bind a group of histone modifications having one or more features that are similar. In some embodiments, a pan antibody is a pan-methylation antibody (*e.g.*, an antibody that can bind a histone, *e.g.*, H3 that comprises at least one methylated lysine, wherein the at least one methylated lysine can be at any one of a plurality of amino acid positions, *e.g.*, in some embodiments, a pan-methylation antibody can bind an H3 protein comprising a methylated lysine at any position). In some embodiments, a pan antibody is a pan-acetylation antibody (*e.g.*, an antibody that can bind a histone, *e.g.*, H3 that comprises at least one acetylated lysine, wherein the at least one acetylated lysine can be at any one of a plurality of amino acid positions, *e.g.*, a pan-acetylation antibody can bind an H3 protein comprising an acetylated lysine at any position). In some embodiments, a pan antibody can bind one or more histone modifications that are associated with transcription activation. In some embodiments, a pan antibody can bind one or more histone modifications that are associated with transcription silencing.

[0301] *Antibody fragment:* As used herein, an “antibody fragment” refers to a portion of an antibody or antibody agent as described herein, and typically refers to a portion that includes an antigen-binding portion or variable region thereof. An antibody fragment can be produced by any means. For example, in some embodiments, an antibody fragment can be enzymatically or chemically produced by fragmentation of an intact antibody or antibody agent. Alternatively, in some embodiments, an antibody fragment can be recombinantly produced, *i.e.*, by expression of an engineered nucleic acid sequence. In some embodiments, an antibody fragment can be wholly or partially synthetically produced. In some embodiments, an antibody fragment (particularly an antigen-binding antibody fragment) can have a length of at least about 50, 60, 70, 80, 90, 100, 110, 120, 130, 140, 150, 160, 170, 180, 190 amino acids or more, in some embodiments at least about 200 amino acids.

[0302] *Associated with:* Two events or entities are “associated” with one another, as that term is used herein, if the presence, level and/or form of one is correlated with that of the other.

For example, a particular entity (*e.g.*, an epigenetic profile comprising one or more histone modifications at a set of genomic loci, etc.) is considered to be associated with a particular disease, disorder, or condition, if its presence, level and/or form correlates with incidence of and/or susceptibility to the disease, disorder, or condition (*e.g.*, across a relevant population). In some embodiments, two or more entities are physically “associated” with one another if they interact, directly or indirectly, so that they are and/or remain in physical proximity with one another. In some embodiments, two or more entities that are physically associated with one another are covalently linked to one another; in some embodiments, two or more entities that are physically associated with one another are not covalently linked to one another but are non-covalently associated, for example by means of hydrogen bonds, van der Waals interaction, hydrophobic interactions, magnetism, or a combination thereof.

[0303] “Between” or “From”: As used herein, the term “between” refers to content that falls between indicated upper and lower, or first and second, boundaries, inclusive of the boundaries. Similarly, the term “from”, when used in the context of a range of values, indicates that the range includes content that falls between indicated upper and lower, or first and second, boundaries, inclusive of the boundaries.

[0304] Biological Sample: As used herein, the term “biological sample” typically refers to a sample obtained or derived from a biological source (*e.g.*, a tissue or organism or cell) of interest, as described herein. In some embodiments, a biological source is or includes an organism, such as a human subject. In some embodiments, a biological sample is or includes a biological tissue or fluid. In some embodiments, a biological sample can be or include cells, tissue, or bodily fluid. “Bodily fluids” refer to fluids that are excreted or secreted from the body as well as fluids that are normally not (*e.g.*, blood, serum, plasma, Cowper’s fluid or pre-ejaculate fluid, chyle, chyme, stool, interstitial fluid, intracellular fluid, lymph, menses, saliva, sebum, semen, serum, sweat, synovial fluid, tears, urine, vitreous humor, vomit). In some embodiments, a biological sample can be or include blood, blood components, cell-free DNA (cfDNA), circulating-tumor DNA (ctDNA), ascites, biopsy samples, surgical specimens, cell-containing body fluids, sputum, saliva, feces, urine, cerebrospinal fluid, peritoneal fluid, pleural fluid, lymph, gynecological fluids, secretions, excretions, skin swabs, vaginal swabs, oral swabs, nasal swabs, washings or lavages such as a ductal lavages or bronchoalveolar lavages, aspirates, scrapings, or bone marrow. In some embodiments, a biological sample is a liquid biopsy sample

obtained from a bodily fluid. In some embodiments, a biological sample is or includes DNA obtained from a single subject or from a plurality of subjects. A biological sample can be a “primary sample” obtained directly from a biological source or can be a “processed sample”, *i.e.*, a sample that was derived from a primary sample, *e.g.*, via dilution, purification, mixing with one or more reagents, or any other processing step(s) as described herein. A biological sample can also be referred to as a “sample.”

[0305] *Blood component:* As used herein, the term “blood component” refers to any component of whole blood, including red blood cells, white blood cells, plasma, platelets, endothelial cells, mesothelial cells, epithelial cells, cell-free DNA (cfDNA), and circulating-tumor DNA (ctDNA). Blood components also include the components of plasma, including proteins, metabolites, lipids, nucleic acids, and carbohydrates, and any other cells that can be present in blood, *e.g.*, due to pregnancy, organ transplant, infection, injury, or disease.

[0306] *Cancer:* As used herein, the terms “cancer,” “malignancy,” “tumor,” and “carcinoma,” are used interchangeably to refer to a disease, disorder, or condition in which cells exhibit or exhibited relatively abnormal, uncontrolled, and/or autonomous growth, so that they display or displayed an abnormally elevated proliferation rate and/or aberrant growth phenotype. In some embodiments, a cancer can include one or more tumors. In some embodiments, a cancer can be or include cells that are precancerous (*e.g.*, benign), malignant, pre-metastatic, metastatic, and/or non-metastatic. In some embodiments, a cancer can be or include a solid tumor. In some embodiments, a cancer be associated with ER-positive status, *e.g.*, an ER-positive breast cancer, etc.

[0307] *Combination therapy:* As used herein, the term “combination therapy” refers to administration to a subject of two or more therapeutic agents or therapeutic regimens such that the two or more therapeutic agents or therapeutic regimens together treat a disease, condition, or disorder of the subject. In some embodiments, the two or more therapeutic agents or therapeutic regimens can be administered simultaneously, sequentially, or in overlapping dosing regimens. Those of skill in the art will appreciate that combination therapy includes but does not require that the two therapeutic agents or therapeutic regimens be administered together in a single composition, nor at the same time.

[0308] *Corresponding to:* As used herein, the term “corresponding to” may be used to designate the position/identity of a structural element in a compound or composition through

comparison with an appropriate reference compound or composition. For example, in some embodiments, a monomeric residue in a polymer (*e.g.*, an amino acid residue in a polypeptide or a nucleic acid residue in a polynucleotide) may be identified as “corresponding to” a residue in an appropriate reference polymer. For example, those of skill in the art appreciate that residues in a provided polypeptide or polynucleotide sequence are often designated (*e.g.*, numbered or labeled) according to the scheme of a related reference sequence (even if, *e.g.*, such designation does not reflect literal numbering of the provided sequence). By way of illustration, if a reference sequence includes a particular amino acid motif at positions 100-110, and a second related sequence includes the same motif at positions 110-120, the motif positions of the second related sequence can be said to “correspond to” positions 100-110 of the reference sequence. Those of skill in the art appreciate that corresponding positions can be readily identified, *e.g.*, by alignment of sequences, and that such alignment is commonly accomplished by any of a variety of known tools, strategies, and/or algorithms, including without limitation software programs such as, for example, BLAST, CS-BLAST, CUDASW++, DIAMOND, FASTA, GGSEARCH/GLSEARCH, Genoogle, HMMER, HHpred/HHsearch, IDF, Infernal, KLAST, USEARCH, parasail, PSI-BLAST, PSI-Search, ScalaBLAST, Sequilab, SAM, SSEARCH, SWAPHI, SWAPHI-LS, SWIMM, or SWIPE. Two sequences can be identified as corresponding if they are identical or if they share substantial identity, *e.g.*, at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity, *e.g.*, over a length of at least 10, 20, 30, 40, 50, 60, 70, 80, 90, 100, 200, 300, 400, 500 or more residues. In various embodiments, a nucleic acid sequence can correspond to a sequence that is identical or substantially identical (*e.g.*, at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical) to the complement of the nucleic acid sequence, *e.g.*, over a length of at least 10, 20, 30, 40, 50, 60, 70, 80, 90, 100, 200, 300, 400, 500 or more nucleic acid residues.

[0309] **“Diagnosing”, “Detecting”, “Determining” or “Screening for”:** As used herein, “diagnosing”, “detecting”, “determining”, “screening for” the presence of a condition or disease (*e.g.*, ER-positive cancer), or a related state (*e.g.*, responsiveness of an ER-positive cancer to one or more ER-targeted therapies) includes the act, process, and/or outcome of determining whether, and/or the qualitative or quantitative probability that, a subject has or will develop the condition, disease, or related state. In some instances, diagnosing can include a determination relating to

prognosis and/or likely response to one or more general or particular therapeutic agents or regimens.

[0310] *Differentially accessible:* As used herein, the term “differentially accessible” describes a genomic locus for which chromatin accessibility status differs between a first condition or sample and a second condition or sample (*e.g.*, a standard or reference). A differentially accessible genomic locus can include a greater or smaller measured accessibility under a selected condition of interest, such as ER-positive state, as compared to a reference state, such as ER-negative state.

[0311] *Differentially modified:* As used herein, the term “differentially modified” describes a genomic locus for which histone modification status and/or DNA methylation status differs between a first condition or sample and a second condition or sample (*e.g.*, a standard or reference). A differentially modified genomic locus can include a greater or smaller number or frequency of histone modification and/or DNA methylations under a selected condition of interest, such as ER-positive state, as compared to a reference state, such as ER-negative state.

[0312] *Epigenetic modification:* As used herein, the term “epigenetic modifications” refers to heritable alterations to the genome that are not due to changes in DNA sequence. Epigenetic modifications include chemical modifications such as, *e.g.*, DNA methylation and histone modification. In some embodiments, epigenetic modifications can cause a change in chromatin structure, DNA accessibility, and/or transcription factor binding. In some embodiments, epigenetic modifications can be detected or measured directly (*e.g.*, by using an agent that binds an epigenetic modification (*e.g.*, an antibody that binds H3K4me3 or H3K27ac)). In some embodiments, epigenetic modifications can be measured indirectly, *e.g.*, by measuring or detecting one or more attributes, changes in which are indicative of changes in epigenetic modifications. For example, in some embodiments, chromatin accessibility and/or transcription factor binding can be used as a measure of epigenetic modifications at a given locus. As used herein, the term “epigenetic marker” refers to an indicator of epigenetic state, and includes, *e.g.*, epigenetic modifications (*e.g.*, histone modifications and DNA methylation, transcription factor binding, chromatin accessibility. As used herein, the term “epigenetic biomarker” refers to an epigenetic marker that can be used in the detection of a disease or condition.

[0313] *Identity:* As used herein, the term “identity” refers to the overall relatedness between polymeric molecules, *e.g.*, between nucleic acid molecules (*e.g.*, DNA molecules) and/or between polypeptide molecules. Methods for the calculation of a percent identity as between two provided sequences are known in the art. The term “% sequence identity” refers to a relationship between two or more sequences, as determined by comparing the sequences. In the art, “identity” also means the degree of sequence relatedness between protein and nucleic acid sequences as determined by the match between strings of such sequences. “Identity” (often referred to as “similarity”) can be readily calculated by known methods, including those described in: Computational Molecular Biology (Lesk, A. M. ed.) Oxford University Press, NY (1988); Biocomputing: Informatics and Genome Projects (Smith, D. W. ed.) Academic Press, NY (1994); Computer Analysis of Sequence Data, Part I (Griffin, A. M. and Griffin, H. G. eds.) Humana Press, NJ (1994); Sequence Analysis in Molecular Biology (Von Heijne, G. ed.) Academic Press (1987); and Sequence Analysis Primer (Gribskov, M. and Devereux, J. eds.) Oxford University Press, NY (1992), each of which are separately incorporated by reference in their entirety. Preferred methods to determine identity are designed to give the best match between the sequences tested. Methods to determine identity and similarity are codified in publicly available computer programs. For example, calculation of the percent identity of two nucleic acid or polypeptide sequences can be performed by aligning the two sequences (or the complement of one or both sequences) for optimal comparison purposes (*e.g.*, gaps can be introduced in one or both of a first and a second sequences for optimal alignment and non-identical sequences can be disregarded for comparison purposes). The nucleotides or amino acids at corresponding positions are then compared. When a position in the first sequence is occupied by the same residue (*e.g.*, nucleotide or amino acid) as the corresponding position in the second sequence, then the molecules are identical at that position. The percent identity between the two sequences is a function of the number of identical positions shared by the sequences, optionally accounting for the number of gaps, and the length of each gap, which may need to be introduced for optimal alignment of the two sequences. The comparison of sequences and determination of percent identity between two sequences can be accomplished using a computational algorithm, such as BLAST (basic local alignment search tool). Sequence alignments and percent identity calculations may be performed using the Megalign program of the LASERGENE bioinformatics computing suite (DNASTAR, Inc., Madison, Wisconsin). Multiple alignment of the sequences

can also be performed using the Clustal method of alignment (Higgins and Sharp, *Comp Appl Biosci* (1989) 5(2):151-153), incorporated by reference herein in its entirety, with default parameters (GAP PENALTY=10, GAP LENGTH PENALTY=10). Relevant programs also include the GCG suite of programs (Wisconsin Package Version 9.0, Genetics Computer Group (GCG), Madison, Wisconsin); BLASTP, BLASTN, BLASTX (Altschul et al., *J Mol Biol* (1990) 215:403-410); DNASTAR (DNASTAR, Inc., Madison, Wisconsin); and the FASTA program incorporating the Smith-Waterman algorithm (Pearson, *Comput Methods Genome Res [Proc Int Symp]* (1994), Meeting Date 1992, 111-120. Eds. Suhai, Sandor. Plenum, New York, NY (the contents of each of which is separately incorporated herein by reference in its entirety). Within the context of this disclosure, it will be understood that where sequence analysis software is used for analysis, the results of the analysis are based on the “default values” of the program referenced. “Default values” will mean any set of values or parameters, which originally load with the software when first initialized.

[0314] “Improve,” “increase,” “inhibit,” or “reduce”: As used herein, the terms “improve”, “increase”, “inhibit”, and “reduce”, and grammatical equivalents thereof, indicate qualitative or quantitative difference from a reference.

[0315] *Methylation Status:* As used herein, “methylation status” of a genomic locus refers to the frequency with which DNA sequences corresponding to the genomic locus are identified in an assay for detection of DNA methylated sequences and/or the density (*e.g.*, the measured density) of DNA methylation corresponding to the genomic locus. Methylation status can be determined by various assays known in the art, including without limitation Bisulfite sequencing (BS-Seq), Whole Genome Bisulfite Sequencing (WGBS), Methylated DNA ImmunoPrecipitation sequencing (MeDIP-seq), or Methyl-CpG-Binding Domain sequencing (MBD-seq). Where two samples are separately analyzed by the same assay or comparable assays for detection of DNA methylated sequences, differences in methylation status of genomic loci can be detected. Methylation status can be compared to a standard or reference. A sample that has a methylation status that differs from a standard or reference can be referred to as differentially modified.

[0316] “Modification Status” or “Histone Modification Status”: As used herein, “modification status” or “histone modification status” of a genomic locus refers to the frequency with which DNA sequences corresponding to the genomic locus are identified in an assay for

detection of DNA sequences associated with histones bearing one or more histone modifications (*e.g.*, one or more particular histone modifications) and/or the density (*e.g.*, the measured density) of histone modifications (*e.g.*, one or more particular histone modifications) corresponding to the genomic locus. Modification status can be determined by various assays known in the art, including without limitation ChIP-seq as one example. Other well-known assays include CUT&RUN (Cleavage Under Targets and Release Using Nuclease) sequencing and CUT&Tag (Cleavage Under Targets and Tagmentation). Where two samples are separately analyzed by the same assay or comparable assays for detection of DNA sequences associated with histones bearing one or more histone modifications (*e.g.*, one or more particular histone modifications), differences in modification status of genomic loci can be detected. Modification status can be compared to a standard or reference. A sample that has a modification status that differs in modification status or histone modification status from a standard or reference can be referred to as differentially modified.

[0317] *Regulatory sequence:* As used herein in the context of expression of a nucleic acid coding sequence, a regulatory sequence is a nucleic acid sequence that controls expression of a coding sequence, *e.g.*, a promoter sequence or an enhancer sequence. In some embodiments, a regulatory sequence can control or impact one or more aspects of gene expression (*e.g.*, cell-type-specific expression, inducible expression, etc.).

[0318] *Subject:* As used herein, the term “subject” refers to an organism, typically a mammal (*e.g.*, a human). In some embodiments, a subject is suffering from a disease, disorder or condition (*e.g.*, ER-positive cancer, *e.g.*, ER-positive breast cancer, etc.). In some embodiments, a subject is susceptible to a disease, disorder, or condition. In some embodiments, a subject displays one or more symptoms or characteristics of a disease, disorder or condition. In some embodiments, a subject is not suffering from a disease, disorder or condition. In some embodiments, a subject does not display any symptom or characteristic of a disease, disorder, or condition. In some embodiments, a subject has one or more features characteristic of susceptibility to or risk of a disease, disorder, or condition. In some embodiments, a subject is a subject that has been tested for a disease, disorder, or condition, and/or to whom therapy has been administered. In some instances, a human subject can be interchangeably referred to as a “patient” or “individual”.

[0319] *Therapeutic agent:* As used herein, the term “therapeutic agent” refers to any agent that elicits a desired pharmacological effect when administered to a subject. In some embodiments, an agent is considered to be a therapeutic agent if it demonstrates a statistically significant effect across an appropriate population. In some embodiments, the appropriate population can be a population of model organisms or a human population. In some embodiments, an appropriate population can be defined by various criteria, such as a certain age group, gender, genetic background, preexisting clinical conditions, etc. In some embodiments, a therapeutic agent is a substance that can be used for treatment of a disease, disorder, or condition (*e.g.*, ER-positive cancer, *e.g.*, ER-positive breast cancer, etc.). In some embodiments, a therapeutic agent is an agent that has been or is required to be approved by a government agency before it can be marketed for administration to humans. In some embodiments, a therapeutic agent is an agent for which a medical prescription is required for administration to humans.

[0320] *Therapeutically effective amount:* As used herein, “therapeutically effective amount” refers to an amount that produces the desired effect for which it is administered. In some embodiments, the term refers to an amount that is sufficient, when administered to a population suffering from or susceptible to a disease, disorder, and/or condition (*e.g.*, ER-positive cancer, *e.g.*, ER-positive breast cancer, etc.) in accordance with a therapeutic dosing regimen, to treat the disease, disorder, and/or condition. In some embodiments, a therapeutically effective amount is one that reduces the incidence and/or severity of, and/or delays onset of, one or more symptoms of the disease, disorder, and/or condition. Those of ordinary skill in the art will appreciate that the term “therapeutically effective amount” does not in fact require successful treatment be achieved in a particular individual. Rather, a therapeutically effective amount may be that amount that provides a particular desired pharmacological response in a significant number of subjects when administered to patients in need of such treatment. In some embodiments, reference to a therapeutically effective amount may be a reference to an amount as measured in one or more specific tissues (*e.g.*, a tissue affected by the disease, disorder or condition) or fluids (*e.g.*, blood, saliva, serum, sweat, tears, urine, etc.). Those of ordinary skill in the art will appreciate that, in some embodiments, a therapeutically effective amount of a particular agent or therapy may be formulated and/or administered in a single dose. In some embodiments, a therapeutically effective amount of a particular agent or therapy may be formulated and/or administered in a plurality of doses, for example, as part of a dosing regimen.

[0321] **Treatment:** As used herein, the term “treatment” (also “treat” or “treating”) refers to administration of a therapy that partially or completely alleviates, ameliorates, relieves, inhibits, delays onset of, reduces severity of, and/or reduces incidence of one or more symptoms, features, and/or causes of a particular disease, disorder, or condition, or is administered for the purpose of achieving any such result. In some embodiments, such treatment can be of a subject who does not exhibit signs of the relevant disease, disorder, or condition and/or of a subject who exhibits only early signs of the disease, disorder, or condition (*e.g.*, ER-positive cancer, *e.g.*, ER-positive breast cancer, etc.). Alternatively, or additionally, such treatment can be of a subject who exhibits one or more established signs of the relevant disease, disorder and/or condition. In some embodiments, treatment can be of a subject who has been diagnosed as suffering from the relevant disease, disorder, and/or condition. In some embodiments, treatment can be of a subject known to have one or more susceptibility factors that are statistically correlated with increased risk of development of the relevant disease, disorder, or condition. A “prophylactic treatment” includes a treatment administered to a subject who does not display signs or symptoms of a condition to be treated or displays only early signs or symptoms of the condition to be treated such that treatment is administered for the purpose of diminishing, preventing, or decreasing the risk of developing the condition. Thus, a prophylactic treatment functions as a preventative treatment against a condition. A “therapeutic treatment” includes a treatment administered to a subject who displays symptoms or signs of a condition and is administered to the subject for the purpose of reducing the severity or progression of the condition.

Certain Exemplary Embodiments

1. A method of determining the ER status of a cancer in a subject, the method comprising: quantifying, at one or more genomic loci in a biological sample, optionally in cell-free DNA (cfDNA) from a liquid biopsy sample, obtained or derived from the subject one or more epigenetic biomarkers, wherein the one or more epigenetic biomarkers comprise:

- (i) one or more histone modifications,
- (ii) chromatin accessibility,
- (iii) binding of one or more transcription factors, and/or
- (iv) DNA methylation.

2. The method of embodiment 1, wherein the one or more histone modifications are quantified using a histone modification assay that measures one or more of H3K9ac, H3K14ac, H3K18ac, H3K23ac, H3K27ac, H3K4me1, H3K4me2, H3K4me3, and pan-acetylation.
3. The method of embodiment 2, wherein the histone modification assay detects H3K4me3 modifications.
4. The method of embodiment 2, wherein the histone modification assay detects H3K27ac modifications.
5. The method of any one of embodiments 2-4, wherein the histone modification assay is selected from ChIP-seq (Chromatin ImmunoPrecipitation sequencing), CUT&RUN (Cleavage Under Targets and Release Using Nuclease) sequencing, and CUT&Tag (Cleavage Under Targets and Tagmentation) sequencing.
6. The method of any one of embodiments 1-5, wherein chromatin accessibility is quantified using a chromatin accessibility assay selected from ATAC-seq (Assay of Transpose Accessible Chromatin sequencing), NOMe-seq (Nucleosome Occupancy and Methylome sequencing), FAIRE-seq (Formaldehyde-Assisted Isolation of Regulatory Elements sequencing), MNase-seq (Micrococcal Nuclease digestion with sequencing), and a DNase hypersensitivity assay.
7. The method of any one of embodiments 1-6, wherein the binding of one or more transcription factors is quantified using a transcription factor binding assay that detects binding of one or more of p300, mediator complex, cohesin complex, RNA pol II, FOXA1, ESR1, PR, MYC, EN1, FOXM1, KLF4, AP-2, RARa, or RUNX1.
8. The method of embodiment 7, wherein the transcription factor binding assay is selected from ChIP-seq (Chromatin ImmunoPrecipitation sequencing), CUT&RUN (Cleavage Under Targets and Release Using Nuclease) sequencing, and CUT&Tag (Cleavage Under Targets and Tagmentation) sequencing.
9. The method of any one of embodiments 1-8, wherein DNA methylation is quantified using Bisulfite sequencing (BS-Seq), Whole Genome Bisulfite Sequencing (WGBS), Methylated DNA ImmunoPrecipitation sequencing (MeDIP-seq), or Methyl-CpG-Binding Domain sequencing (MBD-seq).

10. The method of any one of embodiments 1-9, comprising quantifying two or more of the epigenetic biomarkers, each at one or more genomic loci in cell-free DNA (cfDNA) from a liquid biopsy sample obtained or derived from the subject.
11. The method of embodiment 10, comprising quantifying two or more histone modifications.
12. The method of embodiment 11, comprising quantifying H3K4me3 and H3K27ac modifications.
13. The method of embodiment 10, comprising quantifying one or more histone modifications and DNA methylation.
14. The method of embodiment 13, comprising quantifying H3K4me3 and/or H3K27ac modifications and DNA methylation.
15. The method of embodiment 14, comprising quantifying H3K4me3 modifications, H3K27ac modifications and DNA methylation.
16. The method of any one of embodiments 1-15, wherein the liquid biopsy sample is a plasma sample, serum sample, or urine sample.
17. The method of any one of embodiments 1-16, wherein the method comprises isolating DNA (e.g., cfDNA) from 1, 2, 3, 4, or 5 mL of the liquid biopsy sample (e.g., plasma sample).
18. The method of any one of embodiments 1-17, wherein the sample is a liquid biopsy sample comprising cfDNA, and the method comprises:
 - (a) quantifying H3K4me3 modifications at one or more genomic loci using an assay that comprises enriching for cfDNA comprising one or more H3K4me3 modifications and sequencing the cfDNA enriched for H3K4me3 modifications (e.g., using a cfChIP-seq assay);
 - (b) quantifying H3K27ac modifications at one or more genomic loci using an assay that comprises enriching for cfDNA comprising one or more H3K27ac modifications and sequencing the cfDNA enriched for H3K27ac modifications (e.g., using a cfChIP-seq assay); and/or;
 - (c) quantifying methylated DNA using an assay that comprises enriching for methylated cfDNA and sequencing the enriched cfDNA to determine a count of sequences with one or more methylated nucleotides (e.g., using a MBD-seq assay).
19. The method of embodiment 18, wherein:

(a) the cfDNA comprising H3K4me3 modifications is enriched using a method that comprises incubating the sample with an agent (e.g., an antibody) that binds H3K4me3 modifications;

(b) the cfDNA comprising H3K27ac modifications is enriched using a method that comprises incubating the sample with an agent (e.g., an antibody) that binds H3K27ac modifications; and/or

(c) methylated cfDNA is enriched using a method that comprises incubating the sample with an agent (e.g., an antibody or a methyl binding domain) that binds methylated DNA.

20. The method of embodiment 19, wherein the agent that binds H3K4me3 modifications, the agent that binds H3K27ac modifications, and/or the agent that binds methylated DNA are attached (e.g., via a covalent or noncovalent bond) to a physical support (e.g., a bead, a magnetic bead, an agarose bead, or a magnetic epoxy bead) prior to incubating with the sample.

21. The method of embodiment 19 or 20, wherein, if the method comprises incubating with two or more of the agent that binds H3K4 modifications, the agent that binds H3K27ac modifications, and the agent that binds methylated DNA, the sample is incubated with the two or more agents (a) in sequence, or (b) in parallel (e.g., wherein the sample is divided into fractions and each fraction is incubated with a different agent).

22. The method of any one of embodiments 18-21, wherein the sequencing is performed using a next generation sequencing method.

23. The method of any one of embodiments 18-22, wherein the method comprises attaching (e.g., ligating) adapters to cfDNA obtained from the subject (e.g., attaching after cfDNA has been enriched for cfDNA comprising one or more H3K4me3 modifications, cfDNA comprising one or more H3K27ac modifications, and/or methylated cfDNA).

24. The method of embodiment 23, wherein the method comprises amplifying the plurality of converted DNA fragments after attaching adapters to the plurality of DNA fragments.

25. The method of any one of embodiments 18-24, comprising mapping sequence reads to a reference genome.

26. The method of any one of embodiments 18-25, wherein non-uniquely mapped and redundant sequence reads are discarded.

27. The method of any one of embodiments 18-26, wherein the sequence reads are mapped to a reference genome, wherein the one or more genomic loci correspond to sequence read peaks,

wherein a sequence read peak corresponds to a region of the genome that has a higher number of sequence reads than the local background.

28. The method of embodiment 27, wherein peaks in high noise regions are removed and/or where peaks in regions that having increased levels of one or more epigenetic markers in white blood cells are removed.

29. The method of embodiments 27 or 28, wherein peaks in regions likely to be artifactual are removed.

30. The method of any one of embodiments 27-29, wherein peaks that are less than 50 bp in length are removed.

31. The method of any one of embodiments 18-30, wherein quantifying H3K4me3 modifications, H3K27ac modifications, and/or DNA methylation comprises summing the number of sequence reads having at least one nucleotide overlap the one or more genomic loci.

32. The method of embodiment 31, wherein sequence reads are adjusting on the basis of sequencing depth (e.g., quantile normalizing sequence reads to a common reference distribution) and/or ChIP quality prior to summing.

33. The method of embodiment 31 or 32, wherein sequence counts are normalized to aggregate counts in a given sample across a set of regions (e.g., 10,000 regions) previously determined to have DNase hypersensitivity in most cell types.

34. The method of any one of embodiments 31-33, wherein an estimate of local background signal is subtracted from the sequence reads at each genomic loci prior to summing.

35. The method of any one of embodiments 1-34, further comprising comparing the measure of the one or more epigenetic biomarkers to a reference.

36. The method of embodiment 35, wherein the reference is a predetermined threshold, a measurement from a liquid biopsy sample, a measurement from liquid biopsy samples obtained from a cohort of subjects, and/or a normalized value, optionally wherein:

the predetermined threshold and the normalized value were previously shown to distinguish an ER-positive cancer and an ER-negative cancer (e.g., distinguish with an AUROC of greater than 0.5);

the reference is a measurement from a liquid biopsy sample obtained from a cohort of subjects who have previously been determined to have an ER-positive cancer or an ER-negative cancer.

37. The method of any one of embodiments 18-36, comprising calculating sequence read density at the one or more genomic loci, optionally wherein sequence read density is calculated by:

- (a) summing background adjusted sequence counts at each of the one or more genomic loci and dividing by the sum of the kilobases of the one or more genomic loci; or
- (b) for each genomic loci, dividing background adjusted fragment count by the number of kilobases of the genomic loci, and then summing for each loci.

38. The method of embodiment 37, wherein the one or more genomic loci include one or more genomic loci with an increased level of the one or more epigenetic biomarkers in (a) sample(s) obtained from a subject with an ER-positive cancer as compared to a sample obtained from a subject with an ER-negative cancer, and/or (b) sample(s) obtained from a subject with an ER-negative cancer as compared to a sample obtained from a subject with an ER-positive cancer.

39. The method of embodiment 38, comprising calculating an ER-positive/ER-negative ratio score, by a method comprising:

- (a) calculating an ER-positive sequence read density by a method comprising summing background adjusted sequence counts at each of the one or more genomic loci with an increased level of one or more epigenetic biomarkers in sample(s) obtained from subjects with an ER-positive cancer as compared to samples obtained from subjects with ER-negative cancer;
- (b) calculating an ER-negative sequence read density by a method comprising summing background adjusted sequence counts at each of the one or more genomic loci with an increased level of the one or more epigenetic biomarkers in sample(s) obtained from subjects with an ER-negative cancer as compared to samples obtained from subjects with an ER-positive cancer; and
- (c) dividing the ER-positive sequence read density by the ER-negative sequence read density.

40. The method of embodiment 39, comprising:

- (a) determining an ER-positive/ER-negative ratio score for H3K4me3 modifications;
 - (b) determining an ER-positive/ER-negative ratio score for H3K27ac modifications;
- and/or
- (c) determining an ER-positive/ER-negative ratio score for methylated DNA.

41. The method of embodiment 40, comprising performing each of (a)-(c), and combining each of the ratio scores.
42. The method of embodiment 41, where the ratio scores are combined using fitted values determined using a logistic regression.
43. The method of any one of embodiments 1-42, wherein the method further comprises comparing the one or more quantified genomic markers to a reference, and wherein an increase or decrease in the one or more genomic markers as compared to the reference indicates that the subject has an ER-positive or an ER-negative cancer.
44. The method of any one of embodiments 35-43, wherein the reference is a predetermined threshold, a measurement from a liquid biopsy sample, and/or a normalized value, optionally wherein:
- the reference is a measurement from liquid biopsy samples obtained from a cohort of subjects who have previously been determined to have an ER-negative cancer or to be cancer free;
 - the predetermined threshold and the normalized value were previously shown to distinguish ER-positive and ER-negative cancers (e.g., to provide an AUROC value of at least 0.5); or
 - the cohort of subjects had previously been determined to have a cancer (e.g., an ER-positive or ER-negative cancer).
45. The method of any one of embodiments 1-44, wherein the method comprises quantifying one or more of the epigenetic biomarkers at one or more genomic loci in Tables 1-3.
46. The method of embodiment 45, wherein the method comprises:
- (a) quantifying H3K4me3 modifications for at least 5, 10, 20, 30, 40, or 50 genomic loci listed in Table 1;
 - (b) quantifying H3K27ac modifications for at least 5, 10, 20, 30, 40, or 50 genomic loci listed in Table 2; and/or
 - (c) quantifying DNA methylation for at least 5, 10, 20, 30, 40, or 50 genomic loci listed in Table 3.
47. The method of any one of embodiments 1-46, wherein the method provides an area under the receiver operating characteristic (AUROC) for determining if a subject has an ER-positive cancer vs. an ER-negative cancer of greater than 0.5 (e.g., greater than 0.55, greater than 0.6,

greater than 0.65, greater than 0.7, greater than 0.75, greater than 0.8, greater than 0.85, greater than 0.9, or greater than 0.95).

48. The method of any one of embodiments 1-46, wherein the ER-positive cancer is an ER-positive cancer based on IHC testing and the ER-negative cancer is an ER-negative cancer based on IHC testing.

49. The method of any one of embodiments 1-48, wherein the sample comprises a detectable amount of ctDNA (e.g., wherein estimated tumor fraction is $>3\%$ for the cfDNA, e.g., as determined by iChorCNA).

50. The method of any one of embodiments 1-49, wherein the subject has previously been determined to have cancer, the subject has an increased susceptibility to cancer, and/or the method further comprises determining whether the subject has a cancer.

51. The method of any one of embodiments 1-50, wherein the cancer is breast cancer (e.g., metastatic breast cancer), ovarian cancer, or endometrial cancer.

52. The method of embodiment 51, wherein the cancer is breast cancer.

53. A method of treating a subject having a cancer, the method comprising:
administering a cancer therapy to the subject based on the ER status of the cancer, wherein the ER status of the cancer has been determined using the method of any one of embodiments 1-52.

54. The method of embodiment 53, further comprising determining the ER status of the cancer using the method of any one of embodiments 1-52.

55. The method of embodiment 54 or 55, wherein, if the cancer has been determined to be ER-positive, the cancer therapy administered is an ER-targeted agent.

56. The method of embodiment 54 or 55, wherein, if the cancer has been determined to be ER-negative, the cancer therapy administered is an ER-targeted agent.

57. The method of embodiment 56, wherein, if the cancer has been determined to be ER-negative, the cancer therapy is one appropriate for an ER-negative cancer (e.g., a therapy that comprises surgery, and/or radiation therapy).

58. A method of monitoring the ER status of a cancer in a subject, and optionally treating the cancer, the method comprising:

determining the ER status of the cancer using the method of any one of embodiments 1-52 at first and second time points.

59. The method of embodiment 58, wherein the subject has been administered an ER-targeted agent after the first time point and before the second time point.

60. The method of embodiment 58 or 59, further comprising administering a cancer therapy, optionally an ER-targeted agent, to the subject based on the ER status of the cancer at the second time point, optionally wherein the type, dose and/or frequency of administration of the cancer therapy is adjusted based on the ER status of the cancer at the second time point.

61. A method of treating a subject having a cancer, the method comprising:

administering an ER-targeted agent to the subject if the subject has been determined to have a validated epigenetic profile indicative of an ER-positive cancer based on analysis of a biological sample, optionally of cell-free DNA (cfDNA) from a liquid biopsy sample, obtained or derived from the subject, and, if the subject has not been determined to have a validated epigenetic profile indicative of an ER-positive cancer, not administering an ER-targeted agent,

wherein the presence of the validated epigenetic profile has been determined using a validated classifier,

wherein the validated classifier has been obtained by:

(a) determining a genomic profile of one or more histone modifications, chromatin accessibility, binding of one or more transcription factors, and/or DNA methylation in (i) one or more ER-positive cell lines or (ii) biological samples obtained from a first cohort of subjects who have previously been determined to have an ER-positive cancer;

(b) determining a genomic profile of one or more histone modifications, chromatin accessibility, binding of one or more transcription factors, and/or DNA methylation in (i) one or more ER-negative cell lines or (ii) biological samples obtained from a second cohort of healthy subjects or subjects who have previously been determined to have an ER-negative cancer;

(c) comparing the genomic profile determined in step (a) and the genomic profile determined in step (b), to identify genomic loci that have statistically different histone modification, chromatin accessibility, binding of transcription factor, and/or DNA methylation levels ("differential loci");

(d) training a classifier on histone modification, chromatin accessibility, binding of transcription factor, and/or DNA methylation levels in the differential loci to

distinguish between (i) samples from one or more ER-positive cell lines or biological samples obtained from the first cohort, and (ii) samples from one or more ER-negative cell lines or biological samples obtained from the second cohort, to identify samples having a profile of histone modification, chromatin accessibility, binding of transcription factor, and/or DNA methylation levels (“epigenetic profile”) that indicates that the samples are likely obtained from an ER-positive cell line or from the first cohort; and

(e) obtaining the validated classifier by validating the classifier from step (d) on a third cohort comprising an independent group of subjects with ER-positive and ER-negative cancers and selecting a threshold such that the validated classifier predicts ER-positive cancers, with an area under the receiver operating characteristic (AUROC) greater than 0.5 (*e.g.*, greater than 0.55, greater than 0.6, greater than 0.65, greater than 0.7, greater than 0.75, greater than 0.8, greater than 0.85, greater than 0.9, or greater than 0.95), wherein subjects falling within the group of predicted ER-positive cancers display the validated epigenetic profile and subjects that do not fall within the group of ER-positive cancers lack the validated epigenetic profile.

62. The method of embodiment 61, wherein the differential loci in step (c) were identified by comparing the genomic profile of one or more histone modifications and/or DNA methylation in (i) one or more ER-positive cell lines and (ii) one or more ER-negative cell lines.

63. The method of embodiment 61 or 62, wherein the classifier in step (d) was trained on histone modification, chromatin accessibility, binding of transcription factor, and/or DNA methylation levels in the differential loci that were obtained by *in silico* mixing sequence data from one or more ER-positive cell lines and sequence data obtained from liquid biopsy samples of healthy subjects.

64. The method of any one of embodiments 61-63, wherein the validated classifier in step (e) was validated using liquid biopsy samples from the third cohort.

65. The method of any one of embodiments 61-64, wherein the classifier in step (d) was trained on two or more histone modification levels in the differential loci.

66. The method of embodiment 65, wherein the two or more histone modification levels comprise H3K4me3 and H3K27ac modification levels.

67. The method of any one of embodiments 61-66, wherein the classifier in step (d) was trained on one or more histone modification levels and DNA methylation in the differential loci.

68. The method of any one of embodiments 61-66, wherein the classifier in step (d) was trained using ridge regression, elastic-net regression, or lasso regression.
69. The method of embodiment 61 or 62, wherein the one or more histone modification levels comprise H3K4me3 and/or H3K27ac modification levels.
70. The method of any one of embodiments 61-69, wherein the liquid biopsy sample is a plasma sample, serum sample, or urine sample.
71. A kit comprising reagents for quantifying one or more histone modifications, chromatin accessibility, binding of one or more transcription factors, and/or DNA methylation at one or more genomic loci, wherein the one or more genomic loci are selected from Tables 1-3.
72. The kit of embodiment 71, wherein the kit comprises reagents for:
- (a) quantifying H3K4me3 modifications for at least 5, 10, 20, 30, 40, or 50 genomic loci in Table 1;
 - (b) quantifying H3K27ac modifications for at least 5, 10, 20, 30, 40, or 50 genomic loci in Table 2;
 - (c) quantifying DNA methylation for at least 5, 10, 20, 30, 40, or 50 genomic loci in Table 3;
 - (d) any combination of (a)-(c).
73. The kit of embodiment 71 or 72, wherein the kit comprises one or more antibodies for use in ChIP-seq, optionally wherein the one or more antibodies specifically bind H3K4me3- or H3K27ac-modified histones.
74. The kit of any one of embodiments 71-73, wherein the kit comprises one or more methyl-binding domains for use in MBD-seq or wherein the kit comprises one or more antibodies that bind methylated DNA for use in MeDIP-seq.
75. The kit of any one of embodiments 71-74, wherein the kit comprises reagents for isolation of cell-free DNA (cfDNA) from a liquid biopsy sample.
76. The kit of any one of embodiments 71-75, wherein the kit comprises reagents for library preparation for sequencing.
77. The kit of any one of embodiments 71-76, wherein the kit comprises reagents for sequencing.
78. The kit of any one of embodiments 71-77, wherein the kit comprises instructions for determining if a subject has an ER-positive cancer.

79. A non-transitory computer readable storage medium encoded with a computer program, wherein the program comprises instructions that when executed by one or more processors cause the one or more processors to perform operations to perform the method of any one of embodiments 1-70.

80. A computer system comprising a memory and one or more processors coupled to the memory, wherein the one or more processors are configured to perform operations to perform the method of any one of embodiments 1-70.

81. A system for determining the ER status of a cancer in a subject, the system comprising a sequencer configured to generate a sequencing dataset from a sample; and a non-transitory computer readable storage medium of embodiment 79 and/or a computer system of embodiment 80.

82. The system of embodiment 81, wherein the sequencer is configured to generate a Whole Genome Sequencing (WGS) dataset from the sample.

83. The system of embodiment 81 or 82 further comprising a sample preparation device configured to prepare the sample for sequencing from a biological sample, optionally a liquid biopsy sample.

84. The system of embodiment 83, wherein the sample preparation device comprises reagents for quantifying one or more histone modifications, chromatin accessibility, binding of one or more transcription factors, and/or DNA methylation at one or more genomic loci in cell-free DNA (cfDNA) from the biological sample, optionally the liquid biopsy sample.

85. The system of embodiment 84, wherein the one or more genomic loci are selected from Tables 1-3.

86. The system of any one of embodiments 83-85, wherein the device comprises reagents for quantifying:

- (a) H3K4me3, *e.g.*, for at least 5, 10, 20, 30, 40, or 50 genomic loci in Table 1;
- (b) H3K27ac, *e.g.*, for at least 5, 10, 20, 30, 40, or 50 genomic loci in Table 2;
- (c) DNA methylation, *e.g.*, for at least 5, 10, 20, 30, 40, or 50 genomic loci in Table 3; or
- (d) any combination of (a)-(c).

87. The system of embodiment 85 or 86, wherein the reagents comprise one or more antibodies for use in ChIP-seq, optionally wherein the one or more antibodies specifically bind H3K4me3- or H3K27ac-modified histones.
88. The system of embodiment 86 or 87, wherein the reagents comprise one or more methyl-binding domains for use in MBD-seq.
89. The system of any one of embodiments 83-88, wherein the device comprises reagents for isolation of cell-free DNA (cfDNA) from the biological sample, optionally the liquid biopsy sample.
90. The system of any one of embodiments 81-89, wherein the device comprises reagents for library preparation for sequencing.
91. The system of any one of embodiments 81-90, wherein the sequencer comprises reagents for sequencing.
92. A method of determining the ER status of a cancer in a subject (e.g., patient), the method comprising:
- receiving (e.g., by a processor of a computing device) one or more genomic profiles of one or more histone modifications, chromatin accessibility, binding of one or more transcription factors, and/or DNA methylation for the subject; and
 - determining whether the subject has an epigenetic profile indicative of an ER-positive cancer by classifying (e.g., by the processor) the genomic profile using the ER classifier.
93. The method of embodiment 92, wherein the ER classifier has been trained using one or more genomic profiles of one or more histone modifications, chromatin accessibility, binding of one or more transcription factors, and/or DNA methylation for (i) one or more ER-positive cell lines and one or more ER-negative cell lines and/or (ii) one or more biological samples obtained from one or more cohorts of subjects who have previously been determined to have an ER-positive cancer and one or more biological samples obtained from one or more cohorts of subjects who have previously been determined to have an ER-negative cancer.
94. The method of embodiment 93, wherein the one or more genomic profiles used to train the ER classifier comprise one or more genomic profiles generated by *in silico* diluting sequence data from ER-positive or ER-negative cell lines with sequence data obtained from healthy donor plasma samples so as to achieve a simulated ctDNA percentage ranging from 0.5% to 50%.

95. The method of embodiment 2 or 3, wherein the one or more genomic profiles used to train the ER classifier are for differential loci having statistically significant differences in levels of one or more histone modifications, chromatin accessibility, binding of one or more transcription factors, and/or DNA methylation levels in (a) one or more ER-positive cell lines as compared to one or more ER-negative cell lines and/or (b) one or more biological samples obtained from one or more cohorts of subjects who have previously been determined to have an ER-positive cancer and one or more biological samples obtained from one or more cohorts of subjects who have previously been determined to have an ER-negative cancer.
96. The method of embodiment 95, wherein the differential loci were identified by comparing genomic profiles of one or more histone modifications and/or DNA methylation in (i) one or more ER-positive cell lines and (ii) one or more ER-negative cell lines.
97. The method of embodiment 95 or 96, wherein the ER classifier has been trained on the levels of one or more histone modifications, chromatin accessibility, binding of one or more transcription factors, and/or DNA methylation in the differential loci for the genomic profiles that were generated by *in silico* diluting sequence data from one or more ER-positive cell lines and sequence data obtained from liquid biopsy samples of healthy subjects.
98. The method of any one of embodiments 95-97, wherein the ER classifier has been trained on two or more histone modification levels in the differential loci.
99. The method of any one of embodiments 95-98, wherein the ER classifier has been trained on one or more histone modification levels and DNA methylation levels in the differential loci.
100. The method of any one of embodiments 92-99, comprising receiving one or more genomic profiles of two or more histone modification levels.
101. The method of embodiment 98 or 100, wherein the two or more histone modifications comprise H3K4me3 and H3K27ac modifications.
102. The method of any one of embodiments 92-101, comprising receiving one or more genomic profiles of one or more histone modifications and DNA methylation.
103. The method of embodiment 99 or 102, wherein the one or more histone modifications comprise H3K4me3 and/or H3K27ac modifications.
104. The method of embodiment 99 or embodiment 102, wherein the one or more histone modifications comprise H3K4me3 and H3K27ac modifications.

105. The method of any one of embodiments 92-104, wherein the ER classifier has been trained with sequence data derived from plasma samples.
106. The method of any one of embodiments 92-105, wherein the ER classifier has been trained with data derived from liquid biopsy samples.
107. The method of any one of embodiments 92-106, wherein the ER classifier is a validated classifier.
108. The method of embodiment 107, wherein the ER classifier has been validated by selecting a threshold such that the validated classifier predicts ER-positive cancers with an area under the receiver operating characteristic (AUROC) greater than 0.5 (*e.g.*, greater than 0.55, greater than 0.6, greater than 0.65, greater than 0.7, greater than 0.75, greater than 0.8, greater than 0.85, greater than 0.9, or greater than 0.95).
109. The method of embodiment 107 or 108, wherein the ER classifier has been validated on a group of subjects with ER-positive or ER-negative cancers, wherein subjects falling within a group of predicted ER-positive cancers display a validated epigenetic profile and subjects that do not fall within a group of ER-positive cancers lack the validated epigenetic profile.
110. The method of any one of embodiments 107-109 wherein the ER classifier has been validated using liquid biopsy sample data.
111. A non-transitory computer readable storage medium encoded with a computer program, wherein the program comprises instructions that when executed by one or more processors cause the one or more processors to perform operations to perform the method of any one of embodiments 92-110.
112. A computer system comprising a memory and one or more processors coupled to the memory, wherein the one or more processors are configured to perform operations to perform the method of any one of embodiments 92-110.
113. A method of treating a subject having a cancer, the method comprising:
administering an ER-targeted agent to the subject, wherein the subject has been determined to have a validated epigenetic profile indicative of an ER-positive cancer based on analysis of a biological sample, optionally of cell-free DNA (cfDNA) from a liquid biopsy sample, obtained or derived from the subject,
wherein the presence of the validated epigenetic profile has been determined using a classifier (*e.g.*, a validated classifier) according to a method of any one of embodiments 92-110.

EXAMPLES

[0322] The present Examples demonstrate the identification and use of differentially modified and/or differentially accessible genomic loci in ER-positive and ER-negative cell lines and/or from cfDNA in plasma samples obtained from subjects with ER-positive and ER-negative breast cancers. The present Examples show that differentially modified and/or differentially accessible genomic loci of the present disclosure can be used to determine ER status from cfDNA in plasma samples obtained from subjects with ER-positive and ER-negative cancers.

Example 1: Materials and Methods

[0323] This Example describes the materials and methods that were used to generate sequencing data that was then used in Examples 2 and 3 to create ER status classifiers.

Materials

Cell lines

[0324] The following ER-positive cell lines were used: ZR751, ZR7530, BT483, T47D, BT474, CAMA1, MCF7, HCC1428, and HCC1500. The following ER-negative cell lines were used: BT549, DU4475, HS578T, BT20, UACC893, HCC38, HCC70, HCC202, HCC1143, HCC1187, HCC1419, HCC1599, HCC1806, HCC1954, HCC2157, HCC2218, and SKBR3.

Plasma samples

[0325] Plasma samples were prepared from whole blood collected in EDTA blood collection tubes or Streck cell-free DNA BCT with 4-6 hours of collection and plasma was stored at -80°C until use. Whole blood was obtained from breast cancer patients under a protocol approved by an IRB. Breast cancer patients had previously been determined to be ER-positive or ER-negative. Informed consent was obtained in each case and samples were de-identified.

Methods

Chromatin immunoprecipitation (ChIP)

[0326] Chromatin immunoprecipitation (ChIP) for histone marks (H3K4me3 and H3K27ac) in cell lines was performed using methods similar to those previously described in Schones et al., Cell (2008) 132(5):887-898, which is incorporated by reference herein in its entirety. Briefly, the cells were lysed and the chromatin was MNase digested to generate approximately 80% mononucleosomes. Nucleosomes were then incubated with antibodies that bind H3K4me3 modifications or H3K27ac modifications that were previously conjugated to magnetic epoxy beads (Invitrogen) with constant mild shaking overnight. The beads were then washed and rinsed. Sequencing libraries were generated from purified immunoprecipitated sample DNA and then sequenced.

[0327] Chromatin immunoprecipitation (ChIP) for histone marks (H3K4me3 and H3K27ac) in plasma samples was performed using methods similar to those previously described in Sadeh et al., Nat Biotechnol (2021) 39: 586-598 and Jang et al., Life Sci Alliance (2023) 6(12):e202302003. Briefly, about 1 mL frozen plasma was thawed and then prepared for ChIP. The thawed plasma was incubated with antibodies that bind H3K4me3 modifications or H3K27ac modifications that were previously conjugated to magnetic epoxy beads (Invitrogen) with constant mild shaking overnight. The beads were then washed and rinsed. Sequencing libraries were generated from purified immunoprecipitated sample DNA and then sequenced.

Methylated DNA enrichment

[0328] Enrichment of DNA methylation was performed on DNA extracted from cell lines and human plasma samples using the EpiMark® Methylated DNA Enrichment Kit (E2600S, available from New England Biolabs) following the manufacturer's protocol. Briefly, cfDNA libraries were prepared and adaptors ligated. Then, the EpiMark® capture reagent was applied to each library sample following the manufacturer's protocol. Enriched DNA libraries were amplified and sequenced.

ChIP-seq and DNA methylation data analysis

[0329] ChIP-sequencing reads and MeDIP-sequencing reads were aligned to the human genome build hg19 using the Burrows-Wheeler Aligner (BWA) version 0.7.15. Non-uniquely mapping and redundant reads were discarded. MACS v2.2.7.1 was used for peak calling with a q-value (FDR) threshold of 0.01. Data quality was evaluated by a variety of measures, including

total peak number, FrIP (fraction of reads in peak) score, number of high-confidence peaks (enriched > ten-fold over background), and percent of peak overlap with “blacklist” DHS peaks derived from the ENCODE project (Amemiya et al., Sci Rep (2019) 9(1):9354). Peaks were assessed for overlap with gene features and CpG islands using annotatr. IGV was used to visualize normalized read counts at specific genomic loci. Overlap of peaks was assessed using BEDTools and the GenomicRanges package in Bioconductor. Peaks were considered overlapping if they shared one or more nucleotide.

Example 2: ER status classifiers based on complex modeling of signals across different subsets of individual genomic loci that are differentiated based on ER-positive and ER-negative status

[0330] To construct an ER status classifier, genomic loci likely to differentiate ER-positive and ER-negative samples based on H3K4me3 modification, H3K27ac modification or DNA methylation were first identified. To accomplish this, for each analyte, union peak maps were created by merging peak coordinates for all of the cell lines, removing regions likely to be artifactual (the ENCODE “blacklist” regions, see Amemiya et al., Sci Rep (2019) 9(1):9354) and discarding all peaks less than 50 bp in length. The number of sequencing fragments overlapping each peak (by at least 1 bp) were quantified for each analyte, local background signal was subtracted to improve signal-to-noise, the result was log2-transformed, and quantile normalized across the entire dataset (for each analyte separately). Genomic loci that had differential analyte signal between ER-positive and ER-negative cell lines were determined using DESeq2 (Love et al., Genome Biol (2014) 15(12):550), with an FDR cutoff of 5%. These differential loci are shown in Table 1 (H3K4me3), Table 2 (H3K27ac) and Table 3 (DNA methylation).

[0331] Next, a simulated dataset was built for each analyte to train an ER status classifier. This dataset was constructed for each analyte by mixing different proportions of sequencing fragments from healthy donor plasma samples and the cell lines to achieve simulated ctDNA percentages ranging from 0.5% to 50%. Sequencing fragments overlapping the union cell line maps for each simulated dataset were then quantified as described above. Quantifications for all genomic loci were then used with a given absolute log2-fold-change cutoff and for a given analyte (or combination of analytes) from the simulated dataset as input to train a regularized logistic regression. More specifically, models were trained on the ER status of the cell lines from

which the simulated datasets were constructed, using glmnet (Engelbrechtsen and Bohlin, Clin Epigenetics (2019) 11(1):123). Models were trained with different alpha values ranging from 1 (lasso) to 0 (ridge) in order to demonstrate the robustness of the approach.

[0332] **Fig. 1** shows ROC curves for exemplary ER status classifiers that were generated in accordance with this method. As shown, different classifiers were generated using (i) ridge regression (all features from the relevant subset of genomic loci) ($\alpha = 0$); (ii) elastic-net regression (many features from the relevant subset of genomic loci) ($\alpha = 0.25$), or (iii) lasso regression (few features from the relevant subset of genomic loci) ($\alpha = 1$). As shown, different classifiers were generated with (a) genomic loci from Tables 1-3 for different modifications, namely (i) H3K4me3 modifications, (ii) H3K27ac modifications, (iii) DNA methylation (DNAm) or (iv) all of the above (All) and (b) using different subsets of genomic loci in Tables 1-3 for a particular modification, namely (i) all genomic loci with an absolute $\log_2(\text{fold-change}) \geq 0.5$, (ii) all genomic loci with an absolute $\log_2(\text{fold-change}) \geq 1$, (iii) all genomic loci with an absolute $\log_2(\text{fold-change}) \geq 2$, (iv) all genomic loci with an absolute $\log_2(\text{fold-change}) \geq 3$, and (v) all genomic loci with an absolute $\log_2(\text{fold-change}) \geq 4$.

[0333] **Fig. 2** shows a representative, non-limiting graphs that demonstrates the accuracy of ER status (based on AUCROC) determination using the classifiers that were generated in accordance with this Example.

Example 3: ER Status Determination in Plasma Samples

[0334] The present example provides data demonstrating that technologies provided in the present disclosure can be used to determine ER status in a subject having cancer, using samples comprising cfDNA. In the present example, plasma samples from patients diagnosed with metastatic breast cancer were characterized.

[0335] Plasma samples were obtained from 91 subjects. Of these samples, 43 were obtained from subjects having associated clinical data, 80 provided high quality datasets across all analytes (promoter, enhancer, DNAm), and 49 had ctDNA that could be measured by copy number variation analysis ($>3\%$ ctDNA as quantified by ichorCNA (see, e.g., Adalsteinsson et al., Nat Comm., 2017, the contents of which are incorporated by reference herein in their entirety). 41 samples were obtained from subjects having HER2- breast cancer and 12 samples were obtained from subjects having HER2+ breast cancer. 28 samples were obtained from

subjects having an ER- breast cancer and 25 were obtained from subjects having an ER+ breast cancer. Samples were collected in accordance with the method provided in Example 1. Blood samples were collected within 6 weeks of tumor biopsy, with ER status determined using immunohistochemistry (IHC).

[0336] A multianalyte, liquid biopsy assay performed in accordance with the approaches described herein (e.g., as described in Example 1) was applied to capture genome-wide epigenomic signals, and to map enhancers, promoters, and DNA methylation data from 1 mL of plasma. A logistic regression model was applied to infer ER status from plasma-based epigenomic profiles.

Results

[0337] The ER status classifier was applied to 19 of 44 samples determined to have detectable ctDNA. 11 of the 19 (58%) samples were from subjects having an ER+ cancer as determined by IHC (ER IHC range was 80-95% for these subjects). Overall, 18 of the 19 samples were correctly classified as ER+ or ER- by the ER classifier (AUC=1). 3 of the 19 samples were collected from patients who were ER+ at primary diagnosis and ER- at the time of tissue sampling. For each of these samples, the ER classifier correctly predicted ER- status.

[0338] AUC plots are shown in Fig. 3(A). As shown in the plots, the classifiers provided herein are capable of accurately distinguishing subjects having ER+ vs ER- cancers using plasma samples (even for samples without detectable ctDNA). For samples with detectable ctDNA (e.g., ctDNA > 3%), accuracy increased. As shown in Fig. 3(A), accuracy further improved when characterizing samples from a particular source (see right plot, showing an accuracy that was virtually the same as IHC). Fig. 3(A) demonstrates that technologies provided herein are capable of accurately determining ER status of different cancers.

[0339] As shown in Fig. 3(B), classifiers described herein detected analyte features that were previously associated with ER+ and ER- status. This data demonstrates that methods provided herein can detect genes that are biologically relevant, and accurately reflect ER status of a cancer.

[0340] Table 4 shows genes that were determined to be associated with ER status using the disclosed classifiers. As indicated below, genes previously associated with ER status (left column); genes previously shown to have a biological link, but not directly associated with ER

activity (middle column); and genes not previously shown to be associated with ER status (right column) were all found to be associated with ER status. The below table demonstrates that classifiers provided herein can detect biologically relevant features (indicating that they accurately reflect ER status) and can also discover new genes and pathways that may play a role in ER expression. In some embodiments, an ER classifier described herein measures an epigenomic marker (e.g., promoter, enhancer, or DNA methylation marker) associated with one or more of the genes listed in Table 4.

[0341] **Table 4:** Selected Genes Incorporated in Certain ER Status Classifiers

Genes Previously Associated with ER Status	Genes Previously Linked with ER status	Genes Not Previously Associated or Linked with ER status
PCGF2	TBX2	PLEKHA5
BCAS3	E2F6	PYY2
ZNF703		MEIOSIN
RDH16		ACACA
DCK17		PIP4K2B
		ANKFN1

TABLES

[0342] The following Tables identify exemplary genomic loci that are differentially modified and/or differentially accessible in ER-positive vs. ER-negative cancer. Table 1 is based on differential H3K4me3 modifications. Table 2 is based on differential H3K27ac modifications. Table 3 is based on differential DNA methylation.

Table 1: Exemplary genomic loci that are differentially H3K4me3 modified in ER-positive vs. ER-negative cancer.

Index	Genomic locus	log2(FC)	Index	Genomic locus	log2(FC)
1	chr1:793725-794444	-1.41	676	chr13:99710786-99710933	1.60
2	chr1:893310-896975	-0.66	677	chr13:100085058-100085407	-2.00
3	chr1:948208-950545	-1.22	678	chr13:100310028-100311435	-3.08
4	chr1:1078012-1080755	-2.11	679	chr13:100547110-100548163	-2.44
5	chr1:1092571-1094235	-0.85	680	chr13:101452369-101453452	1.72
6	chr1:1181806-1184230	-2.19	681	chr13:107818517-107818763	1.59
7	chr1:1352710-1354673	-2.45	682	chr13:109752798-109753486	-2.20
8	chr1:1368525-1372363	-0.73	683	chr13:109917811-109918302	-2.87
9	chr1:1607548-1608305	2.29	684	chr13:109919919-109920279	-3.23
10	chr1:1857963-1858833	-2.23	685	chr13:110430718-110430921	-1.80
11	chr1:2091766-2092896	-2.31	686	chr13:110532689-110533742	-1.91
12	chr1:2460030-2462599	-1.63	687	chr13:110583246-110584049	-2.59
13	chr1:2486982-2489006	-1.94	688	chr13:110775500-110776228	-1.86
14	chr1:2542510-2543400	-1.82	689	chr13:110972342-110973169	-1.95
15	chr1:3086862-3087876	-1.88	690	chr13:111039733-111041489	-1.91
16	chr1:3089565-3090529	-2.39	691	chr13:111199448-111200204	-1.73
17	chr1:3229631-3230883	-1.69	692	chr13:112597570-112599676	1.54
18	chr1:3339843-3340100	-1.75	693	chr13:112867429-112868559	1.61
19	chr1:3580709-3581442	-2.33	694	chr13:113806643-113809068	-1.02
20	chr1:3589806-3590224	-2.39	695	chr13:114064332-114066266	-1.75
21	chr1:3600599-3601078	-2.55	696	chr13:114523674-114524813	-1.86
22	chr1:5585742-5586942	-2.42	697	chr14:20571849-20572534	1.66
23	chr1:6171464-6172015	-2.05	698	chr14:20703750-20704421	1.85
24	chr1:6309173-6310083	-1.99	699	chr14:21182788-21184219	-2.12
25	chr1:6478386-6480670	-1.27	700	chr14:21372528-21373895	-1.76
26	chr1:6506755-6509496	-3.76	701	chr14:26253363-26254045	1.72
27	chr1:6941150-6942498	-2.35	702	chr14:26674199-26674655	-2.40
28	chr1:7447495-7447664	1.23	703	chr14:34179071-34179912	2.12
29	chr1:7522797-7523990	-2.42	704	chr14:35507381-35508708	-3.27
30	chr1:7763761-7765942	-0.84	705	chr14:37325246-37326091	2.01
31	chr1:7945368-7947025	-2.15	706	chr14:38063075-38065737	0.62
32	chr1:8481899-8485036	-0.88	707	chr14:38314605-38314851	1.65
33	chr1:9258111-9259053	-2.59	708	chr14:39571716-39573482	0.57
34	chr1:9377876-9378547	-2.21	709	chr14:39735475-39737787	0.55
35	chr1:9473354-9473909	-1.88	710	chr14:39828158-39828600	1.54
36	chr1:9554998-9555854	-1.03	711	chr14:40817303-40818002	2.30
37	chr1:9686453-9687674	-0.99	712	chr14:41378968-41379467	1.55
38	chr1:9747249-9750386	-1.18	713	chr14:44119264-44121350	2.62
39	chr1:9775318-9778154	-2.67	714	chr14:45266939-45268370	-2.35
40	chr1:9894644-9896970	-1.75	715	chr14:46357708-46358411	2.02
41	chr1:10475004-10475635	-2.29	716	chr14:46977785-46978299	1.96
42	chr1:10588334-10588989	-2.11	717	chr14:47289420-47289908	2.14
43	chr1:10701760-10703821	-2.76	718	chr14:52117301-52119929	0.51
44	chr1:10752245-10756070	-0.84	719	chr14:52211337-52212145	2.39
45	chr1:11035778-11036418	-2.23	720	chr14:53161365-53162869	0.62

Index	Genomic locus	log2(FC)	Index	Genomic locus	log2(FC)
46	chr1:11761594-11762165	-2.11	721	chr14:55543845-55544874	-2.13
47	chr1:12004546-12004908	-1.87	722	chr14:55764423-55766166	-1.58
48	chr1:12674913-12679947	-1.04	723	chr14:56695388-56696005	1.62
49	chr1:15221576-15222178	-2.17	724	chr14:58763753-58766860	0.51
50	chr1:15271601-15272720	-1.68	725	chr14:61613657-61615378	-2.58
51	chr1:15497526-15499491	-1.93	726	chr14:62026099-62027207	1.86
52	chr1:15710719-15711560	-2.39	727	chr14:62068281-62069807	-2.39
53	chr1:16082808-16086331	-1.31	728	chr14:67944873-67945531	2.77
54	chr1:16420058-16420387	1.26	729	chr14:67946559-67947478	1.89
55	chr1:16479155-16482845	-0.86	730	chr14:67958507-67959427	2.13
56	chr1:16713118-16714443	-2.18	731	chr14:68013880-68014396	1.51
57	chr1:17895642-17896457	-2.12	732	chr14:69073881-69074227	1.38
58	chr1:19043262-19044067	-2.37	733	chr14:69103522-69103667	1.33
59	chr1:19048794-19049346	1.77	734	chr14:69125665-69126330	1.70
60	chr1:19889963-19890682	-2.51	735	chr14:69320288-69321086	1.53
61	chr1:20915257-20916128	-2.51	736	chr14:69823912-69824746	1.35
62	chr1:21660741-21662455	-1.22	737	chr14:70345821-70347140	-1.63
63	chr1:21754197-21755329	-3.39	738	chr14:71734074-71734762	-2.07
64	chr1:21835329-21837321	-1.72	739	chr14:75077152-75079804	-0.66
65	chr1:21877154-21878561	1.63	740	chr14:75420926-75422717	-1.00
66	chr1:22915335-22915881	-1.90	741	chr14:77294198-77294881	-2.14
67	chr1:22926739-22927851	-2.39	742	chr14:87826600-87827112	1.87
68	chr1:23279499-23280438	-2.62	743	chr14:91631097-91631343	1.42
69	chr1:23763218-23763663	-2.43	744	chr14:93153055-93154581	1.08
70	chr1:23953876-23955013	-2.30	745	chr14:93346935-93347929	1.12
71	chr1:24229142-24229746	-2.49	746	chr14:94179303-94179870	-1.96
72	chr1:24377849-24378435	-1.91	747	chr14:95241730-95242316	1.73
73	chr1:24446335-24447459	-1.81	748	chr14:95273215-95273520	1.55
74	chr1:24512972-24514742	-0.76	749	chr14:96561977-96562770	1.48
75	chr1:24717995-24719221	-2.31	750	chr14:96661252-96662137	1.50
76	chr1:25255220-25257426	-2.44	751	chr14:96828285-96830797	0.52
77	chr1:25348663-25349777	-2.29	752	chr14:96967473-96969714	0.52
78	chr1:26686401-26687014	-2.48	753	chr14:97082602-97083392	-2.21
79	chr1:26872032-26872992	-2.06	754	chr14:97207480-97208332	0.79
80	chr1:27049519-27050598	-2.30	755	chr14:97572652-97573278	2.33
81	chr1:27143998-27144142	-2.27	756	chr14:98243189-98243868	1.73
82	chr1:27328220-27328908	-2.16	757	chr14:98651057-98651753	2.19
83	chr1:27383844-27387900	-2.44	758	chr14:98840404-98840921	1.82
84	chr1:28632940-28633432	1.73	759	chr14:99502050-99503210	-2.01
85	chr1:29460023-29461217	-2.41	760	chr14:99718898-99720058	-2.60
86	chr1:30417094-30418011	1.56	761	chr14:100125723-100126558	-2.31
87	chr1:31319926-31320491	-1.73	762	chr14:100149257-100151188	0.54
88	chr1:32041069-32043850	-3.43	763	chr14:100305108-100305256	1.82
89	chr1:32054199-32055093	-3.68	764	chr14:100485560-100488348	2.77
90	chr1:32180174-32181630	-1.89	765	chr14:100513660-100513843	1.70
91	chr1:32226118-32226897	-3.14	766	chr14:100622943-100623287	2.27

Index	Genomic locus	log2(FC)	Index	Genomic locus	log2(FC)
92	chr1:32665518-32667241	-0.91	767	chr14:100624667-100626493	0.85
93	chr1:32936339-32937033	-1.94	768	chr14:101138744-101139982	1.47
94	chr1:33102687-33103651	-1.75	769	chr14:101169915-101170924	1.79
95	chr1:33347009-33348212	-2.24	770	chr14:101539138-101540206	1.04
96	chr1:33772195-33773181	-2.41	771	chr14:102171939-102172903	-2.27
97	chr1:35290867-35291541	1.86	772	chr14:102716603-102717993	-2.29
98	chr1:36334905-36336221	-3.02	773	chr14:103045917-103046612	-2.83
99	chr1:36574663-36575172	-1.81	774	chr14:103617512-103618214	-2.35
100	chr1:36626404-36627073	-1.90	775	chr14:103978852-103979975	-1.85
101	chr1:36816452-36817074	-2.11	776	chr14:104060124-104062107	-3.40
102	chr1:38200773-38201279	-2.52	777	chr14:104201800-104203190	1.42
103	chr1:39025172-39025621	-1.91	778	chr14:104582493-104584772	0.76
104	chr1:39974587-39975695	-2.71	779	chr14:104668440-104669013	1.75
105	chr1:40366291-40368434	-0.53	780	chr14:104895638-104896124	1.66
106	chr1:40408701-40410152	-2.45	781	chr14:104977128-104977721	-1.98
107	chr1:41405265-41405593	-2.06	782	chr14:105056939-105057600	-2.50
108	chr1:41444678-41446884	-0.55	783	chr14:106551250-106551401	2.11
109	chr1:41846431-41849213	-2.48	784	chr14:106610292-106610634	1.79
110	chr1:42091721-42092427	-1.62	785	chr15:23617330-23618024	-2.20
111	chr1:42204491-42205152	-1.99	786	chr15:24671998-24672484	1.56
112	chr1:43250853-43251278	-2.05	787	chr15:29076904-29078248	-2.89
113	chr1:43472618-43474398	-2.18	788	chr15:30355785-30358052	-1.66
114	chr1:44444319-44446477	-0.63	789	chr15:31115542-31117142	-2.74
115	chr1:45645423-45646366	2.59	790	chr15:31890835-31891349	1.74
116	chr1:46357713-46359001	-1.91	791	chr15:33153875-33154528	-2.91
117	chr1:46632265-46633145	-3.26	792	chr15:35292208-35292885	-1.68
118	chr1:47654513-47656434	-3.30	793	chr15:37402382-37403696	-3.01
119	chr1:47881902-47882866	-3.08	794	chr15:39579712-39579987	-1.99
120	chr1:47910133-47911036	-4.11	795	chr15:40629594-40633390	-1.14
121	chr1:50886665-50887068	-2.28	796	chr15:40874880-40876545	-1.89
122	chr1:52641956-52642766	1.96	797	chr15:41060974-41063700	-1.85
123	chr1:53067701-53068609	-2.83	798	chr15:41803045-41804711	-2.58
124	chr1:53527540-53528737	-2.76	799	chr15:42170136-42170609	1.31
125	chr1:53611778-53611906	-2.12	800	chr15:45103818-45104707	1.35
126	chr1:55265413-55267824	-2.71	801	chr15:45421212-45422826	-2.56
127	chr1:55388477-55389169	-1.78	802	chr15:50075960-50076379	1.59
128	chr1:56842298-56842851	-2.35	803	chr15:51861042-51861753	2.59
129	chr1:58898404-58899380	-1.88	804	chr15:54270388-54271181	1.63
130	chr1:59340135-59341747	-1.96	805	chr15:57842023-57844442	-1.47
131	chr1:60139044-60140771	-2.14	806	chr15:58551911-58553189	-1.58
132	chr1:62775424-62776360	-1.61	807	chr15:58782307-58783393	-2.04
133	chr1:62792815-62793742	-2.15	808	chr15:59586813-59588405	-2.92
134	chr1:64127494-64128584	-1.75	809	chr15:59748303-59748976	1.24
135	chr1:64312498-64313568	-2.70	810	chr15:63050207-63051144	-2.47
136	chr1:64412340-64413499	-2.24	811	chr15:63305342-63306236	-2.82
137	chr1:65062912-65064248	-2.77	812	chr15:63671362-63674618	0.91

Index	Genomic locus	log2(FC)	Index	Genomic locus	log2(FC)
138	chr1:65731098-65732136	-3.33	813	chr15:63969997-63970618	2.09
139	chr1:68606902-68607998	-2.44	814	chr15:65115982-65119854	-0.67
140	chr1:75080036-75080341	-2.44	815	chr15:66903413-66904101	-1.78
141	chr1:76187987-76188318	-2.02	816	chr15:66914241-66914900	-2.24
142	chr1:78353970-78355123	-3.16	817	chr15:67325766-67326361	-2.25
143	chr1:78511478-78512637	-2.92	818	chr15:68119065-68119789	-2.58
144	chr1:84503223-84504607	-2.17	819	chr15:69152716-69153642	-2.56
145	chr1:85724216-85725946	-0.64	820	chr15:69612126-69612579	1.82
146	chr1:85872463-85873919	-2.73	821	chr15:70660617-70660970	1.40
147	chr1:86859904-86862604	-0.98	822	chr15:71036103-71036935	-2.73
148	chr1:87169349-87172082	-0.63	823	chr15:72529033-72530371	-2.19
149	chr1:87222733-87224167	-2.55	824	chr15:72754297-72754800	-2.29
150	chr1:87617111-87618074	-2.13	825	chr15:74466030-74467819	-2.35
151	chr1:88807547-88808278	-1.91	826	chr15:74528334-74529468	-2.03
152	chr1:89148618-89151263	-0.59	827	chr15:77448215-77448967	2.63
153	chr1:89356260-89359194	-1.00	828	chr15:77905590-77908773	-3.08
154	chr1:89470928-89472099	-2.00	829	chr15:79295242-79297045	-1.72
155	chr1:89593678-89595188	-2.87	830	chr15:81989450-81990259	2.13
156	chr1:89989595-89992128	-0.57	831	chr15:82089750-82090890	2.96
157	chr1:90017338-90018535	-2.10	832	chr15:88020872-88021732	1.47
158	chr1:90098078-90100145	-0.68	833	chr15:88827759-88828161	1.87
159	chr1:90203708-90205711	-1.91	834	chr15:89437600-89438900	-2.02
160	chr1:90286023-90288414	-0.51	835	chr15:89583900-89585730	-2.53
161	chr1:90355326-90357145	-2.15	836	chr15:90692384-90693353	1.47
162	chr1:90420118-90423292	-2.65	837	chr15:91103004-91104575	-2.18
163	chr1:90439552-90441448	-2.57	838	chr15:91427279-91428470	-2.48
164	chr1:90459862-90462567	-0.63	839	chr15:91806703-91807876	-1.92
165	chr1:90528144-90529037	-2.38	840	chr15:92115315-92115609	1.52
166	chr1:90539657-90540933	-2.16	841	chr15:92409560-92411446	-2.18
167	chr1:91176260-91176973	-2.54	842	chr15:92462195-92462896	-2.15
168	chr1:91183081-91184594	-2.89	843	chr15:93695496-93696671	-1.71
169	chr1:91965719-91967977	-0.75	844	chr15:96724750-96725483	-1.88
170	chr1:92269297-92270521	-1.97	845	chr15:97961752-97962636	1.66
171	chr1:92948050-92952470	-1.71	846	chr15:99352246-99353553	-2.51
172	chr1:94453690-94455834	-2.14	847	chr15:100047995-100048711	-2.29
173	chr1:94520569-94521406	-1.85	848	chr15:101258251-101259329	-2.23
174	chr1:95692890-95693860	-2.76	849	chr15:101418381-101422885	-1.05
175	chr1:96562030-96563247	-2.07	850	chr16:1196487-1196853	-1.90
176	chr1:100374321-100375103	-1.88	851	chr16:1771476-1772562	-1.88
177	chr1:100511825-100513480	-2.51	852	chr16:1843690-1844871	1.61
178	chr1:104678778-104679651	-1.78	853	chr16:2171653-2175503	-2.70
179	chr1:109809463-109810157	-2.40	854	chr16:4042335-4043722	-2.45
180	chr1:110174984-110175879	-2.08	855	chr16:4114840-4115530	-2.38
181	chr1:110230015-110231264	-4.23	856	chr16:4151573-4151941	1.92
182	chr1:110335904-110336492	-1.93	857	chr16:4201861-4202745	2.70
183	chr1:110419699-110420555	-2.17	858	chr16:5665932-5666536	1.66

Index	Genomic locus	log2(FC)	Index	Genomic locus	log2(FC)
184	chr1:111735041-111736290	-2.18	859	chr16:5699949-5700420	1.70
185	chr1:112902423-112903371	-2.54	860	chr16:6623260-6624052	1.91
186	chr1:113286184-113287056	-2.33	861	chr16:8767820-8769962	0.77
187	chr1:113397082-113397711	-3.89	862	chr16:9082857-9083701	-1.67
188	chr1:115604702-115605618	-1.76	863	chr16:11587440-11588094	-1.98
189	chr1:115656594-115657201	-1.95	864	chr16:11800201-11800351	1.41
190	chr1:116021533-116022420	-2.11	865	chr16:12241387-12242427	-1.86
191	chr1:117236658-117237723	-1.68	866	chr16:13203903-13204949	-2.09
192	chr1:119522364-119522740	-2.44	867	chr16:16451486-16452930	-2.35
193	chr1:119542970-119543479	-2.37	868	chr16:17498683-17499716	-1.89
194	chr1:119549171-119549917	-2.26	869	chr16:17827055-17827583	1.57
195	chr1:145562078-145563442	-2.03	870	chr16:19768793-19769998	-2.42
196	chr1:150033253-150034178	-2.05	871	chr16:19815788-19816413	-1.75
197	chr1:150700821-150702962	-4.95	872	chr16:20009210-20009477	1.63
198	chr1:151098157-151098925	2.07	873	chr16:20083994-20085753	3.00
199	chr1:151571475-151573528	-3.11	874	chr16:21371279-21371749	1.74
200	chr1:151653085-151653436	-1.67	875	chr16:21831345-21832227	-3.07
201	chr1:151693764-151694361	-2.03	876	chr16:23503100-23504375	-2.41
202	chr1:153462530-153463966	-1.88	877	chr16:24990655-24992172	-1.70
203	chr1:153479352-153479873	-1.91	878	chr16:26761373-26761612	1.82
204	chr1:154425586-154426651	-2.29	879	chr16:27931728-27932195	1.56
205	chr1:154763817-154764768	-1.59	880	chr16:28754436-28755293	-2.23
206	chr1:156585793-156586693	1.27	881	chr16:29196083-29197109	-1.92
207	chr1:157986405-157986990	-1.84	882	chr16:29393452-29393704	2.24
208	chr1:158979786-158980138	-2.94	883	chr16:29394276-29394580	1.96
209	chr1:159930668-159932322	-2.59	884	chr16:30631731-30635509	2.07
210	chr1:160693862-160694636	-2.44	885	chr16:31465619-31465749	-2.19
211	chr1:161348822-161349172	2.12	886	chr16:33483181-33483715	1.96
212	chr1:162602209-162603530	-2.63	887	chr16:46683118-46683916	-3.37
213	chr1:164964853-164965056	1.59	888	chr16:49053079-49053263	1.41
214	chr1:165414019-165414702	2.12	889	chr16:49486041-49486763	-1.86
215	chr1:167236977-167238077	-1.81	890	chr16:50300275-50300801	-2.39
216	chr1:169818247-169818943	1.64	891	chr16:53545039-53545805	1.67
217	chr1:170223808-170224547	1.95	892	chr16:54057460-54057628	1.97
218	chr1:170426741-170426982	1.56	893	chr16:54128322-54128987	3.17
219	chr1:172024999-172025723	2.29	894	chr16:54543188-54543740	1.89
220	chr1:172956020-172956455	2.69	895	chr16:54688279-54689835	-2.63
221	chr1:173219623-173219865	1.69	896	chr16:56650853-56652590	-2.48
222	chr1:175615482-175616254	1.49	897	chr16:56701498-56702299	-2.62
223	chr1:178029642-178030733	-2.11	898	chr16:57550378-57550519	1.63
224	chr1:182615359-182616036	1.59	899	chr16:57972734-57973605	-2.58
225	chr1:182640891-182641257	1.31	900	chr16:58018301-58019527	-1.87
226	chr1:182921723-182922416	-2.36	901	chr16:59026689-59027185	1.68
227	chr1:183066420-183067880	-2.12	902	chr16:59130374-59131068	2.08
228	chr1:183149191-183150089	-2.47	903	chr16:59598470-59599193	2.66
229	chr1:184449714-184450077	1.30	904	chr16:60010422-60011037	2.23

Index	Genomic locus	log2(FC)	Index	Genomic locus	log2(FC)
230	chr1:185381520-185382485	-2.57	905	chr16:64070755-64070916	1.52
231	chr1:195561050-195561943	-2.12	906	chr16:66331185-66331677	1.42
232	chr1:196960896-196961756	1.63	907	chr16:66442443-66442879	-1.56
233	chr1:197589721-197590304	1.81	908	chr16:67678520-67679744	-2.92
234	chr1:198684276-198684555	1.61	909	chr16:68015998-68016586	-3.01
235	chr1:200119907-200120408	1.92	910	chr16:70466706-70467399	1.81
236	chr1:201350066-201350856	1.30	911	chr16:70812946-70813140	1.56
237	chr1:202168422-202168577	-1.85	912	chr16:70974627-70974927	1.75
238	chr1:202237069-202237785	1.47	913	chr16:71416181-71417703	-2.04
239	chr1:202266595-202267533	-1.82	914	chr16:71558893-71561081	-2.48
240	chr1:203225832-203226213	1.63	915	chr16:73204317-73205572	1.63
241	chr1:203251134-203251702	1.88	916	chr16:74774675-74775165	-2.31
242	chr1:204117873-204122094	0.80	917	chr16:75174362-75175459	-3.23
243	chr1:204224923-204225083	1.60	918	chr16:75528466-75529529	-2.10
244	chr1:204346165-204347691	0.68	919	chr16:79415216-79415634	1.81
245	chr1:204893425-204893770	1.96	920	chr16:79685205-79685784	-2.53
246	chr1:205215922-205217457	-2.21	921	chr16:81086845-81087742	1.89
247	chr1:205752156-205753516	-2.27	922	chr16:81894458-81896350	-2.35
248	chr1:207021075-207021258	1.44	923	chr16:81961702-81963201	-2.09
249	chr1:207817950-207819077	-2.24	924	chr16:82171532-82173314	1.99
250	chr1:208132198-208133040	-2.86	925	chr16:83980287-83981164	1.57
251	chr1:208259802-208260428	-2.19	926	chr16:84560554-84561843	-2.30
252	chr1:208649740-208650711	2.08	927	chr16:86156350-86156837	-1.93
253	chr1:208704810-208705154	1.72	928	chr16:86332201-86332479	1.68
254	chr1:209212744-209213509	-2.06	929	chr16:86600433-86602711	-2.83
255	chr1:209719411-209720299	1.70	930	chr16:86658588-86659020	2.20
256	chr1:210443791-210444155	2.08	931	chr16:86750084-86751773	-2.41
257	chr1:214223895-214224193	1.43	932	chr16:87551202-87553025	-3.11
258	chr1:214280698-214281581	-1.95	933	chr16:87574680-87576555	-2.22
259	chr1:215571188-215571441	1.36	934	chr16:88184223-88185409	-2.66
260	chr1:218524745-218525114	-2.04	935	chr16:88828291-88828728	1.44
261	chr1:218844919-218845267	1.50	936	chr16:88947264-88948043	-3.79
262	chr1:223168369-223169390	-2.15	937	chr16:89034680-89034941	-2.01
263	chr1:224099457-224101519	-2.59	938	chr16:89328091-89328976	-2.48
264	chr1:225668361-225669694	-1.56	939	chr16:89497248-89497898	1.77
265	chr1:225887191-225888847	-1.74	940	chr16:89900176-89900353	1.94
266	chr1:225896252-225897643	-2.01	941	chr17:180783-183272	-2.56
267	chr1:225934265-225934982	-2.31	942	chr17:854769-855133	-2.28
268	chr1:227634952-227635825	-2.13	943	chr17:981176-982461	-2.47
269	chr1:229705616-229707055	-2.60	944	chr17:983328-984694	-2.56
270	chr1:229714228-229715485	-2.69	945	chr17:1029523-1030651	-2.23
271	chr1:230593998-230595794	-2.46	946	chr17:1201716-1202260	-1.86
272	chr1:231884661-231884923	1.50	947	chr17:1477522-1479285	-2.41
273	chr1:231935688-231936974	-2.19	948	chr17:1810941-1812237	-1.58
274	chr1:233476807-233478073	-2.16	949	chr17:1905067-1906736	-1.97
275	chr1:234573370-234573827	1.53	950	chr17:2238826-2241949	-0.67

Index	Genomic locus	log2(FC)	Index	Genomic locus	log2(FC)
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277	chr1:238401977-238402635	1.61	952	chr17:2440931-2441546	-2.33
278	chr1:240020912-240022110	-2.18	953	chr17:2626714-2628637	-2.20
279	chr1:240815932-240816353	1.67	954	chr17:3438640-3439187	-2.62
280	chr1:241193178-241193512	1.65	955	chr17:3791566-3792400	-2.15
281	chr1:245378455-245380792	-2.05	956	chr17:4379350-4380299	-1.71
282	chr1:245651712-245652502	1.85	957	chr17:4401170-4404396	-0.84
283	chr1:245772591-245773253	2.15	958	chr17:4612282-4614999	-0.69
284	chr1:245966240-245966762	2.04	959	chr17:4958502-4959044	-2.08
285	chr1:246746176-246746478	1.48	960	chr17:5025381-5027058	-2.41
286	chr1:246960778-246961521	1.72	961	chr17:5487542-5488238	-2.40
287	chr1:247614755-247614914	1.38	962	chr17:5522509-5523082	-2.36
288	chr1:248416243-248416601	1.73	963	chr17:6458275-6460567	-0.76
289	chr10:821213-821954	-1.87	964	chr17:6615684-6617107	-2.51
290	chr10:989239-990876	-2.34	965	chr17:6658795-6660845	-2.70
291	chr10:3268676-3270414	-2.53	966	chr17:7348238-7349336	-2.11
292	chr10:3365101-3367379	-2.56	967	chr17:7491959-7493033	-3.16
293	chr10:3389411-3390634	-2.23	968	chr17:7826080-7826673	-2.21
294	chr10:3677413-3679570	-3.44	969	chr17:7906111-7906813	-2.22
295	chr10:3851745-3854300	-1.74	970	chr17:8229972-8230776	-3.15
296	chr10:4395960-4397258	-2.54	971	chr17:8311564-8312878	-2.22
297	chr10:4713050-4714791	-2.45	972	chr17:9136061-9136654	-2.02
298	chr10:4728383-4729238	-2.26	973	chr17:10705943-10707404	-2.68
299	chr10:5538352-5541865	-2.04	974	chr17:12876940-12877891	-3.71
300	chr10:5670212-5670950	-2.60	975	chr17:15847729-15850992	-1.28
301	chr10:6316943-6317915	-1.91	976	chr17:15851344-15851595	-1.81
302	chr10:6778340-6782203	-1.94	977	chr17:15862034-15863372	-1.72
303	chr10:7252547-7252813	1.52	978	chr17:16570354-16570878	-2.72
304	chr10:8103235-8104124	1.89	979	chr17:16747440-16748763	-2.13
305	chr10:8104693-8104851	1.79	980	chr17:17316697-17317949	-2.93
306	chr10:8445807-8446878	-2.07	981	chr17:17528474-17530522	-2.31
307	chr10:9271504-9271978	2.28	982	chr17:17531953-17532272	-1.74
308	chr10:11593571-11594868	-2.51	983	chr17:17641325-17645574	-1.65
309	chr10:12447175-12448528	1.96	984	chr17:18128363-18130086	-0.78
310	chr10:13845719-13846455	1.64	985	chr17:18538021-18538510	-2.46
311	chr10:13889141-13889806	1.70	986	chr17:19398548-19398809	-2.02
312	chr10:15078998-15080157	-2.55	987	chr17:20420205-20421075	-2.49
313	chr10:16874319-16875251	-2.00	988	chr17:20623653-20623791	-1.81
314	chr10:17256549-17258253	-2.76	989	chr17:20744021-20744723	-3.20
315	chr10:19499732-19500066	1.67	990	chr17:21279534-21280993	-1.58
316	chr10:20163332-20164616	-2.86	991	chr17:21477474-21477842	-2.09
317	chr10:20210396-20211988	-2.86	992	chr17:25553803-25555284	1.86
318	chr10:20219661-20220778	-1.81	993	chr17:25957910-25959619	-1.61
319	chr10:21423814-21425021	-1.98	994	chr17:26851902-26852790	1.69
320	chr10:26680623-26681435	-2.15	995	chr17:28112553-28113210	2.31
321	chr10:28467069-28467662	-1.58	996	chr17:29835240-29836406	2.14

Index	Genomic locus	log2(FC)	Index	Genomic locus	log2(FC)
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323	chr10:28623883-28624297	1.82	998	chr17:30878149-30878900	-2.16
324	chr10:29300137-29301549	-2.37	999	chr17:33868064-33868240	-1.73
325	chr10:29678736-29679512	-2.12	1000	chr17:35504195-35504618	2.55
326	chr10:29875791-29876747	-2.01	1001	chr17:36442427-36443136	1.58
327	chr10:29921639-29923861	-3.21	1002	chr17:36747522-36748754	1.75
328	chr10:29949631-29950957	-2.09	1003	chr17:36908200-36909701	1.23
329	chr10:30046342-30047547	-2.40	1004	chr17:37036152-37036477	1.65
330	chr10:31072825-31074595	-2.08	1005	chr17:37158494-37159728	1.86
331	chr10:31758174-31758664	2.05	1006	chr17:37320398-37321555	-1.75
332	chr10:31985726-31986964	-1.87	1007	chr17:37394116-37395232	-1.87
333	chr10:33622647-33626227	-0.80	1008	chr17:37709614-37710254	-2.29
334	chr10:35255241-35256875	-1.84	1009	chr17:37753662-37756365	-2.42
335	chr10:37115535-37117150	-2.62	1010	chr17:37787559-37789520	-3.68
336	chr10:43436598-43437417	1.43	1011	chr17:37964492-37965245	-2.41
337	chr10:44162753-44163036	-1.98	1012	chr17:38100027-38101313	-2.90
338	chr10:44669086-44670349	2.95	1013	chr17:38346967-38348353	-2.61
339	chr10:46992491-46994271	-2.16	1014	chr17:39767046-39769564	-1.97
340	chr10:47746842-47748289	-3.73	1015	chr17:40480566-40482642	-2.04
341	chr10:48438393-48439487	-2.37	1016	chr17:40561259-40562470	-2.28
342	chr10:49198899-49200008	-2.66	1017	chr17:42897518-42899508	-2.44
343	chr10:49734352-49734807	-1.69	1018	chr17:45949501-45950372	-2.15
344	chr10:60580602-60581559	-2.07	1019	chr17:46064635-46065797	1.94
345	chr10:61750948-61752423	-1.66	1020	chr17:46225509-46226128	2.17
346	chr10:63683360-63683708	1.42	1021	chr17:47393055-47394847	2.03
347	chr10:64693537-64694549	-1.99	1022	chr17:47817090-47817507	1.62
348	chr10:65558086-65559605	-2.12	1023	chr17:49770189-49770656	2.18
349	chr10:65571580-65572704	-2.84	1024	chr17:50486463-50487170	1.74
350	chr10:66201375-66202226	3.19	1025	chr17:51228265-51228608	1.48
351	chr10:69366322-69367168	-2.15	1026	chr17:51417278-51418020	2.25
352	chr10:71085350-71086244	-1.61	1027	chr17:51900136-51900812	2.33
353	chr10:71398893-71399836	-1.68	1028	chr17:52977061-52979111	0.83
354	chr10:71671246-71673114	-2.28	1029	chr17:53044882-53046931	0.82
355	chr10:72015506-72016608	-1.90	1030	chr17:53315379-53316761	1.04
356	chr10:72200318-72201436	-2.66	1031	chr17:53362779-53363276	1.50
357	chr10:73323802-73324597	-2.18	1032	chr17:53421896-53422240	1.69
358	chr10:73565279-73566110	-1.87	1033	chr17:53498119-53499853	0.74
359	chr10:73735054-73736249	-2.15	1034	chr17:53535676-53536207	2.17
360	chr10:73740425-73741414	-1.89	1035	chr17:53712564-53713094	1.73
361	chr10:73768374-73770674	-2.59	1036	chr17:53747008-53747189	1.44
362	chr10:73932837-73933988	-2.17	1037	chr17:53783210-53783350	2.13
363	chr10:75312592-75314185	-2.40	1038	chr17:53784342-53784914	2.03
364	chr10:77871836-77872532	2.37	1039	chr17:54776359-54777642	1.36
365	chr10:80274798-80275193	1.44	1040	chr17:55049661-55049812	1.36
366	chr10:81895752-81896865	-2.18	1041	chr17:55057888-55058787	-2.66
367	chr10:81966679-81967968	-2.79	1042	chr17:55418237-55418552	1.60

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370	chr10:88304839-88305168	1.47	1045	chr17:56764325-56764720	1.89
371	chr10:88316250-88317146	1.37	1046	chr17:56769583-56770840	0.97
372	chr10:88839306-88840393	-2.00	1047	chr17:57183017-57185892	1.04
373	chr10:94822308-94823268	-2.28	1048	chr17:57286268-57288534	0.81
374	chr10:95522681-95523311	1.70	1049	chr17:57407837-57410694	0.73
375	chr10:97068755-97069832	-1.85	1050	chr17:57425381-57425958	1.38
376	chr10:97153989-97154654	-1.90	1051	chr17:57695721-57698575	0.82
377	chr10:97174983-97175857	-2.21	1052	chr17:57947823-57948225	1.68
378	chr10:97573654-97574458	-2.02	1053	chr17:58419708-58420259	2.16
379	chr10:97880881-97881868	-2.39	1054	chr17:58707736-58708743	2.60
380	chr10:98129578-98130291	-1.91	1055	chr17:59296598-59297205	2.26
381	chr10:99288805-99289869	-2.40	1056	chr17:59527483-59528112	2.43
382	chr10:99534483-99535161	-1.68	1057	chr17:61336372-61336719	1.75
383	chr10:102329476-102330643	-2.28	1058	chr17:62097353-62098322	-2.56
384	chr10:102643083-102643555	2.13	1059	chr17:62195430-62196358	-2.28
385	chr10:105036576-105037992	-2.57	1060	chr17:65250114-65250957	-3.18
386	chr10:105344090-105344866	-2.69	1061	chr17:66437222-66438080	1.76
387	chr10:105419551-105421991	-2.75	1062	chr17:66981018-66981277	1.66
388	chr10:105599607-105600637	-2.00	1063	chr17:67496664-67498961	-2.19
389	chr10:105630253-105631123	-1.99	1064	chr17:67613441-67614105	1.56
390	chr10:106086907-106088789	-2.00	1065	chr17:67728841-67730389	-2.59
391	chr10:106390471-106391016	1.55	1066	chr17:68573556-68574073	2.26
392	chr10:107495356-107496038	1.80	1067	chr17:69463993-69464558	-2.38
393	chr10:110075115-110075850	1.89	1068	chr17:69970762-69972637	-1.99
394	chr10:110983366-110983962	1.78	1069	chr17:70301826-70302672	-2.14
395	chr10:112095505-112096719	-2.39	1070	chr17:70406819-70409137	-2.69
396	chr10:113343740-113344416	1.92	1071	chr17:70593135-70594213	-2.39
397	chr10:114135567-114136750	-2.83	1072	chr17:70630853-70631503	1.33
398	chr10:114817950-114819635	-2.90	1073	chr17:70712218-70713102	-2.36
399	chr10:116039560-116040259	1.38	1074	chr17:71502261-71503953	2.30
400	chr10:117332377-117333006	1.71	1075	chr17:73245330-73247112	-2.79
401	chr10:122756123-122756599	1.86	1076	chr17:73439809-73441536	-2.30
402	chr10:123340077-123340847	2.16	1077	chr17:73749548-73750186	-2.15
403	chr10:124898702-124900024	-3.25	1078	chr17:73822945-73824319	-2.12
404	chr10:125649795-125651559	-3.75	1079	chr17:74310797-74311184	1.76
405	chr10:125823886-125824025	1.44	1080	chr17:74964795-74965902	-2.19
406	chr10:126277231-126278866	-2.19	1081	chr17:75260830-75261232	2.43
407	chr10:126881225-126881371	1.31	1082	chr17:75315208-75319650	-2.54
408	chr10:127381529-127382449	-2.00	1083	chr17:75387944-75389346	-2.20
409	chr10:128128424-128129545	-2.57	1084	chr17:75390251-75392086	-2.80
410	chr10:131320607-131320922	1.40	1085	chr17:75938340-75939215	-2.72
411	chr10:131492202-131493178	-2.11	1086	chr17:76227701-76228352	-2.46
412	chr10:131555039-131556651	-2.65	1087	chr17:76365961-76366137	1.75
413	chr10:133558815-133559096	-2.58	1088	chr17:76498488-76499112	2.03

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416	chr11:318193-321164	-1.17	1091	chr17:78165436-78166825	-2.51
417	chr11:710583-711149	-2.68	1092	chr17:78474921-78475713	-1.84
418	chr11:823678-824874	-2.19	1093	chr17:80196392-80197124	1.75
419	chr11:1035340-1037053	-2.48	1094	chr17:80328371-80328812	-2.50
420	chr11:1077952-1078809	-2.08	1095	chr17:80645218-80645974	-2.37
421	chr11:1255707-1257069	-2.22	1096	chr17:80744159-80745908	-3.57
422	chr11:2846607-2847646	-2.00	1097	chr17:80872400-80872624	1.80
423	chr11:2883404-2884633	-2.54	1098	chr17:81054494-81055040	1.32
424	chr11:3002201-3003598	-2.16	1099	chr17:81099458-81099753	1.57
425	chr11:3190620-3192921	-1.81	1100	chr17:81128999-81129123	1.80
426	chr11:3253063-3253990	-1.81	1101	chr18:2292253-2294366	-1.68
427	chr11:5710755-5712637	-2.90	1102	chr18:2905620-2907580	-1.28
428	chr11:5949872-5951064	-2.29	1103	chr18:2979786-2980820	-1.95
429	chr11:6340100-6342876	-3.06	1104	chr18:3036685-3037866	-2.03
430	chr11:8183088-8183993	-2.04	1105	chr18:3305377-3306624	-2.29
431	chr11:8410704-8411670	-1.75	1106	chr18:3349283-3351539	-2.49
432	chr11:8861308-8862504	-1.87	1107	chr18:3411614-3413098	-3.77
433	chr11:8998826-8999257	-1.96	1108	chr18:3526652-3527323	-2.05
434	chr11:9554537-9555065	1.52	1109	chr18:3836502-3837793	-2.08
435	chr11:9567159-9567868	1.86	1110	chr18:5004040-5004683	1.78
436	chr11:10765148-10765580	1.92	1111	chr18:5890144-5891279	-2.64
437	chr11:11678787-11679508	-1.89	1112	chr18:6404761-6406004	-2.18
438	chr11:12387631-12388092	1.56	1113	chr18:6413746-6415549	-2.60
439	chr11:12451951-12452811	-2.35	1114	chr18:6539857-6541776	-2.18
440	chr11:13229082-13229807	-2.29	1115	chr18:6781053-6782046	-2.07
441	chr11:13237768-13238293	-1.86	1116	chr18:9016707-9018033	-1.77
442	chr11:13983950-13986448	-1.55	1117	chr18:9722212-9723295	-1.81
443	chr11:16902416-16903429	-1.81	1118	chr18:9734142-9734716	-1.70
444	chr11:17071637-17071992	-2.02	1119	chr18:9757972-9758379	1.59
445	chr11:19701511-19702278	-1.82	1120	chr18:10353617-10354780	-2.11
446	chr11:20569245-20569760	-2.32	1121	chr18:11857204-11858204	-2.69
447	chr11:24850208-24850854	1.60	1122	chr18:11858863-11860003	-2.24
448	chr11:26472685-26473218	2.10	1123	chr18:12896810-12897196	-2.69
449	chr11:30078102-30078773	2.69	1124	chr18:13176685-13177456	-2.77
450	chr11:30695220-30695867	1.72	1125	chr18:13381747-13382094	-2.29
451	chr11:31960859-31961191	1.89	1126	chr18:13862584-13863583	1.69
452	chr11:32460486-32460985	2.01	1127	chr18:13868476-13869277	-2.20
453	chr11:35402214-35402459	1.43	1128	chr18:14784958-14786399	2.76
454	chr11:35544883-355446148	-1.72	1129	chr18:19664118-19665154	-2.24
455	chr11:36476999-36478095	-1.91	1130	chr18:22239788-22240797	-3.06
456	chr11:39776640-39777342	2.28	1131	chr18:28620995-28623240	-2.33
457	chr11:40050516-40051329	1.75	1132	chr18:29026243-29030262	-4.33
458	chr11:40743203-40743520	1.89	1133	chr18:29031995-29032399	-1.98
459	chr11:41681372-41682119	1.99	1134	chr18:33332974-33334165	-1.99

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462	chr11:43183241-43183963	1.67	1137	chr18:42179334-42180280	-1.89
463	chr11:43577935-43579550	1.85	1138	chr18:48663311-48664460	-2.29
464	chr11:45354189-45355364	1.97	1139	chr18:49018115-49018409	2.04
465	chr11:46581883-46582807	-2.12	1140	chr18:51209509-51210379	-2.34
466	chr11:47952408-47953324	-3.09	1141	chr18:52988669-52990786	-2.15
467	chr11:48008991-48009805	-1.96	1142	chr18:55248517-55248901	1.34
468	chr11:48313986-48314756	2.14	1143	chr18:55914190-55915148	-2.47
469	chr11:48555042-48555583	1.68	1144	chr18:60649850-60650058	1.56
470	chr11:50288881-50289575	1.98	1145	chr18:60892798-60893631	3.30
471	chr11:55987037-55987691	2.01	1146	chr18:68048361-68049637	-2.36
472	chr11:56099326-56099957	2.42	1147	chr18:70632743-70633089	1.72
473	chr11:57036714-57037425	-1.81	1148	chr18:70930512-70932058	-2.27
474	chr11:58441717-58443152	-2.73	1149	chr18:71936381-71937378	1.55
475	chr11:58667945-58668688	1.65	1150	chr18:72191258-72191749	-2.18
476	chr11:60524351-60525271	2.39	1151	chr18:74162469-74164204	-3.36
477	chr11:61722348-61723800	-1.64	1152	chr18:74240593-74241203	1.59
478	chr11:62037623-62039079	2.22	1153	chr18:74276805-74277742	1.57
479	chr11:62162501-62163090	-1.40	1154	chr18:74300531-74301262	1.96
480	chr11:66221537-66222443	-2.01	1155	chr18:74567708-74569610	2.76
481	chr11:66649831-66650933	-1.90	1156	chr18:74755399-74755561	1.44
482	chr11:67651730-67652916	-2.72	1157	chr18:74812629-74814233	-1.94
483	chr11:68472406-68472750	-2.26	1158	chr18:76822746-76823365	1.48
484	chr11:68530345-68531504	1.65	1159	chr18:77244732-77246596	-2.38
485	chr11:68600156-68600888	1.78	1160	chr18:77320365-77321162	-2.27
486	chr11:68622083-68623441	-3.39	1161	chr18:77348572-77350099	-2.03
487	chr11:68933811-68935046	-2.02	1162	chr18:77555562-77556206	-1.82
488	chr11:69330070-69330397	1.76	1163	chr19:373352-375090	1.56
489	chr11:69785552-69786250	1.68	1164	chr19:491419-491615	-2.46
490	chr11:69962833-69962971	1.83	1165	chr19:616264-617387	-2.29
491	chr11:70058194-70058939	1.31	1166	chr19:1130927-1132875	-3.38
492	chr11:70243463-70246114	0.84	1167	chr19:1225960-1228249	-2.48
493	chr11:70449267-70450591	2.30	1168	chr19:2670219-2670635	1.62
494	chr11:70672126-70673703	-2.59	1169	chr19:3135991-3136890	-2.08
495	chr11:70759673-70760590	-2.19	1170	chr19:3481873-3483637	-2.38
496	chr11:70823589-70824422	2.40	1171	chr19:3818261-3819349	-2.32
497	chr11:70849615-70852270	-2.15	1172	chr19:4130792-4132157	-3.31
498	chr11:71144105-71146173	-2.08	1173	chr19:4726373-4726875	-2.46
499	chr11:71976561-71977728	-2.65	1174	chr19:5370133-5370808	1.71
500	chr11:72975430-72976666	-3.12	1175	chr19:6719202-6720971	-2.78
501	chr11:75077599-75078198	1.62	1176	chr19:7922619-7923629	-2.82
502	chr11:75132596-75133982	2.00	1177	chr19:7965306-7965740	-2.46
503	chr11:76293469-76294598	-2.71	1178	chr19:8207779-8208237	-2.12
504	chr11:77867506-77867957	1.39	1179	chr19:8407425-8408552	-1.60
505	chr11:77907321-77908240	-2.30	1180	chr19:8488238-8489427	-1.70

Index	Genomic locus	log2(FC)	Index	Genomic locus	log2(FC)
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507	chr11:85820259-85821755	-2.44	1182	chr19:9119523-9121572	-2.20
508	chr11:91760097-91760561	1.90	1183	chr19:12978031-12978941	-3.60
509	chr11:93063179-93064231	-2.95	1184	chr19:13112530-13114224	-3.32
510	chr11:93275358-93277181	-0.70	1185	chr19:13121477-13122456	-2.68
511	chr11:93505394-93505978	-1.92	1186	chr19:13123235-13125768	-4.04
512	chr11:94276808-94278892	-1.05	1187	chr19:13142169-13143134	-2.62
513	chr11:94371137-94372443	-2.00	1188	chr19:13164008-13167292	-2.26
514	chr11:94799853-94802020	-0.73	1189	chr19:13198726-13199195	-2.11
515	chr11:94962602-94965757	-1.09	1190	chr19:13317804-13319477	-3.83
516	chr11:95054119-95055424	-3.30	1191	chr19:13813266-13813871	-2.96
517	chr11:95186704-95187692	-1.71	1192	chr19:14043513-14044375	-2.21
518	chr11:95901535-95903079	-1.71	1193	chr19:14088724-14090329	-2.56
519	chr11:95961306-95962122	-1.97	1194	chr19:14222624-14225010	-1.52
520	chr11:96039563-96041291	-2.09	1195	chr19:14260082-14261755	-2.05
521	chr11:96072240-96076945	-1.55	1196	chr19:14473743-14474888	-1.54
522	chr11:96159135-96160829	-2.06	1197	chr19:15661840-15662500	-2.85
523	chr11:100904940-100905309	2.04	1198	chr19:16403974-16404350	-2.03
524	chr11:102430998-102431992	-2.23	1199	chr19:16449280-16450291	-2.45
525	chr11:104905222-104906155	-2.58	1200	chr19:16574025-16575245	1.93
526	chr11:104980787-104981483	-2.58	1201	chr19:16844501-16845653	-2.44
527	chr11:111780283-111784633	-2.21	1202	chr19:17365842-17366563	-1.86
528	chr11:111868080-111868319	-2.31	1203	chr19:17861924-17862740	-2.46
529	chr11:112394128-112394679	-1.75	1204	chr19:18108927-18109280	-2.20
530	chr11:112483264-112484936	-2.02	1205	chr19:18197574-18198012	-1.90
531	chr11:113575333-113577372	-2.32	1206	chr19:18811080-18812568	-3.25
532	chr11:117666504-117668075	1.66	1207	chr19:19747992-19748621	-2.20
533	chr11:118415427-118415675	1.56	1208	chr19:22320529-22321100	2.60
534	chr11:120004981-120009244	-2.76	1209	chr19:22397667-22398641	2.94
535	chr11:120018075-120019257	-2.07	1210	chr19:23015058-23015542	2.26
536	chr11:120271470-120272296	-1.72	1211	chr19:32063156-32064512	2.01
537	chr11:122426893-122427732	-2.66	1212	chr19:32274467-32274960	1.53
538	chr11:124940941-124942055	-1.64	1213	chr19:34150869-34151581	-1.92
539	chr11:126187599-126189058	-2.63	1214	chr19:35135773-35136486	1.63
540	chr11:126455380-126456534	-1.48	1215	chr19:35395628-35396406	-2.11
541	chr11:128366100-128368079	-2.19	1216	chr19:35644494-35647193	-1.28
542	chr11:128456785-128457729	-2.08	1217	chr19:35783917-35784734	-1.63
543	chr11:129085007-129086560	-2.41	1218	chr19:35991419-35991930	1.53
544	chr11:129481925-129483048	-2.19	1219	chr19:36346948-36348414	-1.62
545	chr11:131766603-131767245	1.94	1220	chr19:38886156-38887051	-2.58
546	chr11:132189073-132189771	2.13	1221	chr19:40653348-40654306	-3.27
547	chr11:133402011-133402347	1.74	1222	chr19:40728978-40731266	-2.22
548	chr11:133465898-133466403	1.87	1223	chr19:40871355-40872116	-2.17
549	chr11:133787798-133790521	-2.64	1224	chr19:40904349-40904821	-2.14
550	chr11:133903559-133905082	1.32	1225	chr19:41304051-41308279	0.66
551	chr12:593233-593814	1.71	1226	chr19:41472417-41473253	-2.76

Index	Genomic locus	log2(FC)	Index	Genomic locus	log2(FC)
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553	chr12:1552652-1554083	-3.37	1228	chr19:41909109-41909790	2.07
554	chr12:1583038-1584316	-2.20	1229	chr19:42292727-42293197	1.67
555	chr12:1699858-1700037	-1.79	1230	chr19:42984893-42985140	1.72
556	chr12:3960398-3961216	1.77	1231	chr19:43820853-43821306	1.57
557	chr12:4378389-4379169	-2.40	1232	chr19:44155995-44156598	2.40
558	chr12:4524335-4524709	1.58	1233	chr19:44281643-44285442	-1.39
559	chr12:7780789-7781700	-2.59	1234	chr19:44324191-44325175	-2.49
560	chr12:11964739-11966563	-1.92	1235	chr19:46056670-46057379	-2.48
561	chr12:12393251-12394389	-1.97	1236	chr19:46443337-46443950	-2.62
562	chr12:15650481-15651371	-2.55	1237	chr19:47835106-47837386	2.37
563	chr12:17151345-17152004	2.10	1238	chr19:47840053-47840485	1.95
564	chr12:18008537-18009059	2.22	1239	chr19:48900177-48903997	-1.53
565	chr12:18198573-18199414	2.01	1240	chr19:49699694-49700449	-2.22
566	chr12:19184860-19186000	2.36	1241	chr19:49711087-49711727	-2.42
567	chr12:20094130-20094444	1.93	1242	chr19:49784691-49785026	-2.79
568	chr12:20960224-20961067	2.46	1243	chr19:50030665-50032333	-4.50
569	chr12:21240981-21241543	2.15	1244	chr19:50073721-50074147	1.54
570	chr12:21513384-21513929	1.83	1245	chr19:51454834-51456793	-3.17
571	chr12:21571980-21572676	2.10	1246	chr19:52956389-52957412	-2.42
572	chr12:23228822-23229551	2.08	1247	chr19:54931343-54932219	-2.06
573	chr12:25557729-25558327	1.98	1248	chr19:55597941-55598899	-3.08
574	chr12:25876529-25877701	-2.02	1249	chr2:795689-797266	-1.72
575	chr12:26920882-26922492	1.88	1250	chr2:1724152-1726592	-3.33
576	chr12:27707353-27708596	-2.17	1251	chr2:3280208-3281284	-2.31
577	chr12:28210520-28211621	-2.22	1252	chr2:3285856-3287164	-2.28
578	chr12:29564929-29565355	1.59	1253	chr2:3583360-3584180	-3.40
579	chr12:30741358-30742032	1.79	1254	chr2:3642200-3644594	-2.70
580	chr12:34263344-34264143	1.63	1255	chr2:4205437-4206173	2.26
581	chr12:34278705-34279528	-1.59	1256	chr2:6341961-6343648	-2.31
582	chr12:40285975-40286195	1.59	1257	chr2:9132854-9135225	-2.76
583	chr12:41239550-41240440	1.65	1258	chr2:9455268-9456013	-2.19
584	chr12:42361563-42362653	-2.26	1259	chr2:9526580-9527548	-3.12
585	chr12:45661962-45663443	-2.02	1260	chr2:9878943-9880049	-3.20
586	chr12:46464103-46464874	-1.89	1261	chr2:10081037-10082579	-2.04
587	chr12:46887308-46887449	1.43	1262	chr2:11055721-11056382	1.70
588	chr12:47385660-47386330	2.18	1263	chr2:11087041-11087949	-2.14
589	chr12:48337257-48337901	1.32	1264	chr2:11676190-11676354	1.61
590	chr12:48868082-48868885	1.76	1265	chr2:11679380-11680755	1.91
591	chr12:48947389-48948040	1.80	1266	chr2:11681465-11683234	3.30
592	chr12:51328337-51329519	-2.04	1267	chr2:11854750-11857430	-1.75
593	chr12:52249647-52249999	-1.97	1268	chr2:12245772-12246809	-2.06
594	chr12:52672253-52674126	1.11	1269	chr2:12727952-12728952	-1.91
595	chr12:52679753-52682635	-2.48	1270	chr2:15814056-15814315	-1.72
596	chr12:52912472-52914529	-3.36	1271	chr2:16408013-16409451	-1.83
597	chr12:53342416-53346207	0.64	1272	chr2:17622363-17623321	-1.72

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600	chr12:63144468-63145826	-2.55	1275	chr2:20740137-20740758	-1.75
601	chr12:64237199-64239834	0.72	1276	chr2:23603554-23604056	-2.33
602	chr12:64845090-64847160	0.55	1277	chr2:23755150-23755953	-2.05
603	chr12:64993353-64994148	1.71	1278	chr2:23779538-23780659	-2.02
604	chr12:65002174-65005920	0.56	1279	chr2:23851732-23852522	-2.47
605	chr12:65152243-65154395	0.65	1280	chr2:24232485-24233495	-2.77
606	chr12:67477568-67477892	1.69	1281	chr2:24398473-24398699	-2.00
607	chr12:67862341-67862860	1.41	1282	chr2:25054886-25055694	-1.93
608	chr12:68221730-68222104	-2.78	1283	chr2:25555429-25555881	-1.68
609	chr12:69198641-69199113	3.57	1284	chr2:26395441-26397084	-1.01
610	chr12:71057704-71058716	-2.48	1285	chr2:26407398-26408713	-2.52
611	chr12:72125723-72126182	2.30	1286	chr2:27668170-27669944	-2.16
612	chr12:72913705-72914407	2.36	1287	chr2:27781589-27782254	-2.83
613	chr12:77458565-77460018	0.56	1288	chr2:28447932-28448626	-1.97
614	chr12:77572743-77573115	-2.11	1289	chr2:29287739-29288887	-2.85
615	chr12:80083025-80085815	0.57	1290	chr2:29352953-29353506	-2.12
616	chr12:80327277-80329860	0.57	1291	chr2:29537595-29538415	-2.17
617	chr12:80871335-80872051	2.27	1292	chr2:33747185-33748333	-2.07
618	chr12:81318896-81319812	1.54	1293	chr2:37603053-37604664	-2.81
619	chr12:83079458-83082207	0.53	1294	chr2:39186937-39188018	-3.37
620	chr12:83145979-83146260	1.55	1295	chr2:39812364-39812931	-2.40
621	chr12:87157688-87158487	2.11	1296	chr2:40738679-40739753	-2.92
622	chr12:89744581-89748959	0.57	1297	chr2:41562576-41563157	-2.80
623	chr12:92734774-92735406	2.11	1298	chr2:41942267-41943134	-2.64
624	chr12:93293053-93294162	-2.26	1299	chr2:43018975-43020289	-4.59
625	chr12:95941888-95942910	-2.58	1300	chr2:43191401-43192117	-1.99
626	chr12:100535461-100537298	0.59	1301	chr2:43259034-43260544	-1.73
627	chr12:100838894-100839821	-2.12	1302	chr2:43313503-43314405	-1.79
628	chr12:101188241-101189204	1.67	1303	chr2:43385099-43387076	-2.20
629	chr12:102217676-102218816	-2.05	1304	chr2:43746625-43748497	-2.49
630	chr12:102643703-102643900	1.57	1305	chr2:44805753-44807326	-2.99
631	chr12:105368053-105369583	-2.36	1306	chr2:45003818-45006240	-2.46
632	chr12:106977150-106977895	-1.85	1307	chr2:45155124-45157487	-2.95
633	chr12:108516859-108517462	1.76	1308	chr2:45168162-45171962	-1.30
634	chr12:110160948-110161878	-2.00	1309	chr2:45931995-45933922	-2.15
635	chr12:112431789-112432971	1.88	1310	chr2:46078856-46079575	-1.59
636	chr12:113223926-113224425	1.39	1311	chr2:46716593-46718132	-1.67
637	chr12:114135469-114136210	1.50	1312	chr2:47006918-47008962	-2.00
638	chr12:114203872-114204571	-1.53	1313	chr2:47561646-47562156	-1.57
639	chr12:115844925-115845304	1.45	1314	chr2:51179715-51180237	-1.97
640	chr12:115945803-115946360	-1.86	1315	chr2:51819970-51820251	1.52
641	chr12:118589965-118590197	1.63	1316	chr2:53161014-53162563	-2.88
642	chr12:119418358-119419913	2.59	1317	chr2:53739074-53740670	-2.23
643	chr12:119619636-119619952	2.68	1318	chr2:54892995-54894687	-2.85

Index	Genomic locus	log2(FC)	Index	Genomic locus	log2(FC)
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645	chr12:121377719-121378752	-2.42	1320	chr2:54935676-54937002	-3.08
646	chr12:122601063-122602226	-2.23	1321	chr2:55947552-55947736	-1.77
647	chr12:122622267-122622724	1.48	1322	chr2:58706730-58707173	1.69
648	chr12:123428879-123429841	-1.47	1323	chr2:60521920-60523172	-2.41
649	chr12:124701804-124703270	1.55	1324	chr2:60610380-60611445	-1.88
650	chr12:125517103-125517900	2.12	1325	chr2:60705450-60707419	-2.21
651	chr12:125563731-125565711	-2.25	1326	chr2:60757296-60759165	-2.20
652	chr12:125798808-125799202	1.69	1327	chr2:62144234-62145121	-2.69
653	chr13:21606546-21608877	-2.16	1328	chr2:63286715-63288048	-3.05
654	chr13:22103980-22105112	2.06	1329	chr2:64096930-64099774	-2.44
655	chr13:24121043-24121910	-2.44	1330	chr2:64630823-64632099	-2.26
656	chr13:24162994-24163260	2.21	1331	chr2:64954996-64955568	1.75
657	chr13:24269877-24270146	-2.04	1332	chr2:65258419-65259843	-2.01
658	chr13:24612271-24613763	-2.43	1333	chr2:65889407-65890345	-2.69
659	chr13:24845792-24847502	-2.23	1334	chr2:65927550-65928753	-2.14
660	chr13:28549851-28550226	-2.64	1335	chr2:66927094-66928111	-1.81
661	chr13:28551636-28552878	-2.82	1336	chr2:69533561-69534936	-1.72
662	chr13:29025560-29026656	-3.64	1337	chr2:70025054-70026463	-3.00
663	chr13:31019476-31020370	-3.05	1338	chr2:70342333-70344328	-2.15
664	chr13:31489965-31490747	2.05	1339	chr2:70768539-70769820	-2.41
665	chr13:33867047-33867205	-1.77	1340	chr2:71133950-71135190	-2.44
666	chr13:43148178-43149388	-2.28	1341	chr2:71204148-71206169	-1.27
667	chr13:44879890-44881305	-2.23	1342	chr2:71319521-71320627	-2.89
668	chr13:51251518-51253490	-2.18	1343	chr2:71329940-71331416	-2.12
669	chr13:51330122-51331626	-1.46	1344	chr2:71387545-71388353	-1.88
670	chr13:52207112-52207693	-2.01	1345	chr2:71770499-71771125	-2.44
671	chr13:80163082-80164680	-2.10	1346	chr2:71787497-71788022	-1.91
672	chr13:80911301-80911968	-2.33	1347	chr2:71822890-71823804	-2.05
673	chr13:86334992-86335335	1.64	1348	chr2:72370185-72370949	-2.01
674	chr13:97619350-97620262	-2.38	1349	chr2:72373911-72375095	-1.99
675	chr13:99217859-99218895	-1.65	1350	chr2:73122898-73123367	-1.85

Index	Genomic locus	log2(FC)	Index	Genomic locus	log2(FC)
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1352	chr2:76148013-76148969	-3.12	2027	chr5:103224521-103224986	2.34
1353	chr2:79396553-79397349	2.12	2028	chr5:105016583-105016878	1.83
1354	chr2:86038217-86038594	-1.86	2029	chr5:106015837-106017320	-1.91
1355	chr2:87016646-87018200	-2.16	2030	chr5:106115923-106116691	1.52
1356	chr2:95719139-95719949	1.56	2031	chr5:111326993-111327772	2.19
1357	chr2:97151523-97152399	-2.81	2032	chr5:111725754-111726612	1.85
1358	chr2:97651711-97652663	-1.99	2033	chr5:111839154-111840057	1.44
1359	chr2:99439041-99439460	-2.54	2034	chr5:113498446-113499002	2.15
1360	chr2:100170811-100171280	-2.19	2035	chr5:114180246-114180747	1.53
1361	chr2:100496653-100497502	-1.86	2036	chr5:118774354-118775508	1.99
1362	chr2:101396619-101397545	-2.56	2037	chr5:119517318-119517829	1.88
1363	chr2:101679796-101681837	-2.29	2038	chr5:121498881-121500262	-1.92
1364	chr2:102368203-102369790	-2.32	2039	chr5:121517808-121519514	-2.66
1365	chr2:102867054-102868215	-2.21	2040	chr5:121718670-121719218	2.63
1366	chr2:105478425-105479188	-1.95	2041	chr5:122765312-122766730	-2.28
1367	chr2:106162757-106163342	1.65	2042	chr5:124078875-124080402	-2.50
1368	chr2:108160797-108161672	2.43	2043	chr5:127088085-127088815	2.17
1369	chr2:109787894-109788869	-2.09	2044	chr5:127573080-127573493	1.63
1370	chr2:109934351-109935688	-2.46	2045	chr5:131592883-131595475	-2.45
1371	chr2:110871302-110874105	-1.25	2046	chr5:131714183-131714683	1.97
1372	chr2:112133947-112135712	-2.15	2047	chr5:133394445-133395664	-2.18
1373	chr2:112688089-112689233	-1.82	2048	chr5:134827261-134827656	1.55
1374	chr2:113379404-113380189	-2.28	2049	chr5:137390431-137391346	-1.75
1375	chr2:116562437-116563462	1.97	2050	chr5:137727003-137728231	-2.01
1376	chr2:118981025-118982979	-3.30	2051	chr5:138288447-138289492	-1.78
1377	chr2:119067280-119068885	-1.98	2052	chr5:138443510-138444514	-2.43
1378	chr2:119495753-119496865	-2.40	2053	chr5:139531777-139532257	1.53
1379	chr2:119598879-119599690	-3.48	2054	chr5:140456842-140457302	-2.48
1380	chr2:119600342-119608782	-2.14	2055	chr5:140479784-140481003	2.15
1381	chr2:119610228-119613897	-1.42	2056	chr5:142024308-142025272	-2.27
1382	chr2:120601828-120603158	-2.60	2057	chr5:145235616-145236449	-2.17
1383	chr2:121036258-121037073	2.56	2058	chr5:147284858-147286476	-2.71
1384	chr2:121077689-121078498	-1.76	2059	chr5:148529407-148529806	2.10
1385	chr2:121106911-121108054	-2.26	2060	chr5:149189883-149190313	1.67
1386	chr2:121344168-121345435	-2.59	2061	chr5:149400526-149402890	-3.08
1387	chr2:121427996-121429020	-2.54	2062	chr5:149681773-149682749	-2.51
1388	chr2:121684325-121685154	-2.06	2063	chr5:154460367-154461089	1.85
1389	chr2:121932400-121933772	-1.98	2064	chr5:160434731-160435109	1.40
1390	chr2:121953945-121955564	-1.70	2065	chr5:163971300-163972001	1.64
1391	chr2:124951242-124951883	2.03	2066	chr5:167591853-167593194	-2.42
1392	chr2:127412837-127415932	-2.43	2067	chr5:168097921-168098452	1.46
1393	chr2:127862975-127865574	-0.71	2068	chr5:169322527-169323333	-1.67
1394	chr2:128420640-128422481	-2.27	2069	chr5:170735506-170737246	-2.99
1395	chr2:128438722-128439350	-2.55	2070	chr5:170877492-170878952	-2.95

Index	Genomic locus	log2(FC)	Index	Genomic locus	log2(FC)
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1397	chr2:129352480-129353083	1.30	2072	chr5:171530113-171530609	-1.90
1398	chr2:130997369-130997802	1.96	2073	chr5:171537944-171538626	-2.08
1399	chr2:131009114-131011295	-2.82	2074	chr5:171985908-171986551	-2.41
1400	chr2:131085257-131085766	-2.23	2075	chr5:173069207-173069625	1.55
1401	chr2:132088609-132089039	-2.13	2076	chr5:179243928-179244391	-2.38
1402	chr2:132152819-132153227	-1.78	2077	chr6:604022-604924	-2.18
1403	chr2:132191816-132192121	2.23	2078	chr6:1136252-1137299	-2.42
1404	chr2:134930755-134931759	-1.85	2079	chr6:1604426-1606026	-1.27
1405	chr2:137084668-137085394	1.92	2080	chr6:1614188-1615813	-2.58
1406	chr2:149645314-149646067	-2.26	2081	chr6:2141486-2142938	-2.23
1407	chr2:151091073-151092023	-1.98	2082	chr6:2891278-2892308	-2.57
1408	chr2:151457507-151458773	-1.85	2083	chr6:3389213-3390852	-2.10
1409	chr2:153325629-153326126	-2.11	2084	chr6:3750311-3753054	-1.05
1410	chr2:160971071-160971877	1.87	2085	chr6:4351668-4352684	-1.90
1411	chr2:161223724-161224814	-2.35	2086	chr6:5851254-5852003	-2.42
1412	chr2:161522785-161523554	-1.93	2087	chr6:6003640-6005069	-3.29
1413	chr2:162279869-162280833	-3.16	2088	chr6:7519569-7520162	1.58
1414	chr2:166813431-166814125	-2.50	2089	chr6:9225649-9226402	-1.64
1415	chr2:170186165-170187117	1.92	2090	chr6:10268348-10269495	-2.08
1416	chr2:173204444-173205652	-2.04	2091	chr6:10451742-10452567	-1.91
1417	chr2:173223218-173224367	-2.01	2092	chr6:10517594-10518638	-1.98
1418	chr2:174855563-174857381	-1.50	2093	chr6:10520700-10524972	-1.47
1419	chr2:175190800-175192107	-3.40	2094	chr6:10659552-10660589	-3.94
1420	chr2:175196960-175197710	-2.27	2095	chr6:11194974-11196062	-2.09
1421	chr2:175743195-175743929	-1.94	2096	chr6:11330539-11330967	-2.27
1422	chr2:177329757-177330123	1.75	2097	chr6:11770486-11771226	-2.91
1423	chr2:177354872-177355543	-2.20	2098	chr6:13398171-13399212	-2.73
1424	chr2:180886477-180887233	1.56	2099	chr6:13427681-13430022	-2.34
1425	chr2:182258331-182258885	-1.90	2100	chr6:13860003-13860803	-2.90
1426	chr2:187816321-187817112	1.98	2101	chr6:14017621-14018712	-3.67
1427	chr2:191295846-191297604	-2.14	2102	chr6:15221398-15224633	-1.42
1428	chr2:191684105-191685072	-2.15	2103	chr6:16320138-16321112	-2.62
1429	chr2:192492756-192494231	-1.89	2104	chr6:17417548-17419086	-1.95
1430	chr2:198243375-198244073	-1.73	2105	chr6:17580002-17581462	-1.22
1431	chr2:198492430-198493614	-2.21	2106	chr6:17907566-17908088	-2.05
1432	chr2:198557694-198558617	-2.91	2107	chr6:21033536-21034528	-1.96
1433	chr2:202483570-202483849	-2.02	2108	chr6:21996353-21997562	-1.88
1434	chr2:202657866-202658130	1.63	2109	chr6:26016339-26018539	-4.16
1435	chr2:202798591-202799986	-1.64	2110	chr6:26614137-26614875	-2.40
1436	chr2:202814026-202814592	1.98	2111	chr6:27197075-27199780	-1.97
1437	chr2:202977753-202978779	1.53	2112	chr6:27462757-27463521	-2.51
1438	chr2:203113533-203114982	-1.72	2113	chr6:27506845-27507519	-2.44
1439	chr2:206611055-206611833	-1.86	2114	chr6:28320886-28321931	-3.81
1440	chr2:206895803-206897182	-2.33	2115	chr6:28410476-28411668	-2.48
1441	chr2:208199152-208200161	-2.41	2116	chr6:28917309-28920279	-2.34

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1443	chr2:209223483-209225998	-2.85	2118	chr6:30651453-30655759	-0.70
1444	chr2:210798376-210799572	-2.00	2119	chr6:31153053-31154837	-3.59
1445	chr2:211046245-211046559	1.50	2120	chr6:31899506-31901975	-2.75
1446	chr2:212300095-212300505	2.24	2121	chr6:31913156-31914648	-2.03
1447	chr2:212630982-212631835	1.30	2122	chr6:33738765-33740064	-2.04
1448	chr2:213710258-213711149	-2.13	2123	chr6:33849519-33850698	-2.25
1449	chr2:215274921-215275253	1.43	2124	chr6:37045580-37045899	-2.06
1450	chr2:218112623-218113630	1.36	2125	chr6:37515404-37516116	-1.70
1451	chr2:219471853-219473731	1.23	2126	chr6:39016174-39017396	-2.68
1452	chr2:219609137-219612367	-2.39	2127	chr6:39281168-39282174	-2.59
1453	chr2:219710493-219712837	-2.08	2128	chr6:41604442-41606612	-1.44
1454	chr2:220107965-220108835	-2.33	2129	chr6:41690987-41691633	-2.04
1455	chr2:220316070-220319020	-2.19	2130	chr6:41773414-41774701	-3.22
1456	chr2:220941553-220941841	1.42	2131	chr6:43252682-43253245	-2.52
1457	chr2:222332197-222332555	-2.08	2132	chr6:45534353-45535069	-2.08
1458	chr2:222506577-222507024	-2.00	2133	chr6:47007864-47010335	-2.96
1459	chr2:223232881-223233383	1.90	2134	chr6:47408063-47409200	-2.32
1460	chr2:227860397-227860867	1.42	2135	chr6:49681015-49682135	-2.62
1461	chr2:228172475-228174407	-2.15	2136	chr6:55022327-55022455	1.45
1462	chr2:228682687-228683824	-2.01	2137	chr6:55733509-55735146	-1.88
1463	chr2:229290164-229290701	2.56	2138	chr6:64354388-64355329	-1.80
1464	chr2:229463700-229464192	1.67	2139	chr6:70500875-70501492	-1.99
1465	chr2:230153580-230154007	1.77	2140	chr6:74159479-74162279	-0.89
1466	chr2:230309457-230311225	-1.93	2141	chr6:76151269-76152618	-2.24
1467	chr2:231206477-231207190	2.44	2142	chr6:79338919-79339430	-2.02
1468	chr2:232492548-232493008	-1.85	2143	chr6:79861825-79862545	-2.13
1469	chr2:233230536-233231523	-2.36	2144	chr6:83278104-83278254	1.50
1470	chr2:233251192-233251986	-2.14	2145	chr6:85471990-85474272	-2.35
1471	chr2:233312472-233315158	-2.83	2146	chr6:88717685-88718861	-1.87
1472	chr2:233734473-233737723	-2.42	2147	chr6:89744528-89745948	-2.05
1473	chr2:234296310-234297291	-1.61	2148	chr6:90020670-90022815	-1.31
1474	chr2:235237820-235238433	-1.85	2149	chr6:100911592-100913491	-3.75
1475	chr2:235872239-235873148	-1.73	2150	chr6:105388268-105390043	-2.13
1476	chr2:236430181-236431134	-2.43	2151	chr6:105875712-105876752	-1.84
1477	chr2:237072939-237073379	-2.91	2152	chr6:106245676-106246258	-2.10
1478	chr2:238064820-238065486	-2.25	2153	chr6:106967117-106968351	-2.11
1479	chr2:238263025-238264720	-2.10	2154	chr6:107562287-107563153	-1.67
1480	chr2:238320874-238322942	-3.22	2155	chr6:107979028-107980647	-1.83
1481	chr2:239129186-239130245	-2.33	2156	chr6:108436071-108437093	-2.26
1482	chr2:239800381-239801105	-1.95	2157	chr6:108489842-108490054	-1.93
1483	chr2:240143228-240146457	-2.11	2158	chr6:110678736-110679838	-3.73
1484	chr2:240248494-240249468	-1.90	2159	chr6:110720651-110721597	-2.67
1485	chr2:240727802-240729610	-1.92	2160	chr6:110797262-110798208	-2.41
1486	chr20:259054-260178	-2.56	2161	chr6:116203135-116204273	-2.71
1487	chr20:516487-517472	-2.05	2162	chr6:117770793-117771422	-1.53

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1489	chr20:644082-644691	-2.48	2164	chr6:128799098-128801952	-2.26
1490	chr20:750709-751073	-1.77	2165	chr6:128899809-128902422	-3.83
1491	chr20:948365-948865	-2.37	2166	chr6:132488897-132490016	-2.57
1492	chr20:1277451-1277996	-1.96	2167	chr6:134321849-134322228	-1.87
1493	chr20:1293752-1294499	-2.46	2168	chr6:134323954-134324770	-1.82
1494	chr20:1298143-1298782	-1.95	2169	chr6:134438532-134439062	2.29
1495	chr20:1782751-1784617	-2.25	2170	chr6:134668729-134670441	-2.49
1496	chr20:1822030-1822518	-1.94	2171	chr6:134838011-134839545	-2.19
1497	chr20:1918233-1918424	-1.94	2172	chr6:135229613-135230725	-1.92
1498	chr20:1927430-1928210	-2.52	2173	chr6:136389030-136389729	-1.89
1499	chr20:2245201-2246072	1.97	2174	chr6:137103006-137103879	-1.75
1500	chr20:2781020-2782597	-1.73	2175	chr6:138914144-138914949	-2.94
1501	chr20:3073269-3073929	-3.49	2176	chr6:139003784-139004609	-2.53
1502	chr20:3640728-3642118	-2.26	2177	chr6:139307214-139310037	-0.62
1503	chr20:4012251-4013504	-2.50	2178	chr6:142863798-142864369	-2.10
1504	chr20:4018024-4019463	-1.91	2179	chr6:143947276-143948010	-2.43
1505	chr20:4594069-4595306	-2.48	2180	chr6:144996186-144997076	-1.88
1506	chr20:5295714-5298179	-2.44	2181	chr6:146134826-146136932	-0.54
1507	chr20:6032393-6033651	-2.79	2182	chr6:148498978-148501338	-2.54
1508	chr20:9496306-9497467	-2.10	2183	chr6:148662939-148666140	-0.83
1509	chr20:9869986-9870442	-1.86	2184	chr6:149082024-149083084	-1.74
1510	chr20:10501652-10502214	-1.77	2185	chr6:150463311-150465467	-1.19
1511	chr20:11432299-11433350	-2.09	2186	chr6:150525121-150526486	-2.01
1512	chr20:11656304-11658728	-2.41	2187	chr6:150813645-150814835	-3.04
1513	chr20:17626594-17627082	1.43	2188	chr6:151178041-151179425	-2.27
1514	chr20:17673848-17674903	-2.19	2189	chr6:151937271-151938018	2.29
1515	chr20:20180289-20181504	1.91	2190	chr6:154730976-154732643	-1.92
1516	chr20:20187817-20188349	1.51	2191	chr6:154769163-154770584	-2.00
1517	chr20:20421125-20422333	2.10	2192	chr6:154795625-154796891	-1.67
1518	chr20:21499037-21499438	1.71	2193	chr6:155509348-155511150	-2.37
1519	chr20:21642269-21642659	2.07	2194	chr6:155540326-155542092	-2.84
1520	chr20:21748266-21748854	1.70	2195	chr6:155769840-155771408	-1.75
1521	chr20:24792832-24793290	1.78	2196	chr6:155967173-155968926	-2.79
1522	chr20:30709414-30710861	-2.92	2197	chr6:157625526-157626779	-1.99
1523	chr20:30762812-30764279	-3.17	2198	chr6:158090624-158091271	-1.54
1524	chr20:32458765-32459575	-1.95	2199	chr6:158447009-158447982	-1.74
1525	chr20:33741496-33742483	-3.08	2200	chr6:159074461-159075934	-1.80
1526	chr20:34025741-34026491	-2.04	2201	chr6:159458867-159460625	-2.19
1527	chr20:35697166-35698386	-2.79	2202	chr6:159998447-160000358	-2.08
1528	chr20:36888281-36889666	-2.13	2203	chr6:160397920-160399945	-1.56
1529	chr20:37089855-37091549	-3.07	2204	chr6:160404163-160405105	-1.95
1530	chr20:37561296-37561839	-1.83	2205	chr6:161694271-161695806	-1.37
1531	chr20:43880832-43883542	-2.16	2206	chr6:161739154-161740411	-2.06
1532	chr20:44539344-44541106	-1.99	2207	chr6:161855206-161856677	-2.47
1533	chr20:44728186-44728652	-2.19	2208	chr6:163812763-163813972	-1.87

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1537	chr20:46116366-46116603	2.02	2212	chr6:167039701-167042256	-0.70
1538	chr20:46129568-46132521	0.86	2213	chr6:167834557-167835236	-2.52
1539	chr20:46540903-46541258	2.16	2214	chr6:168099955-168100630	-2.11
1540	chr20:46613340-46613493	1.63	2215	chr6:168133966-168135256	-1.90
1541	chr20:46855160-46855823	1.76	2216	chr6:168233495-168234985	-2.02
1542	chr20:47088981-47089912	2.24	2217	chr6:168551319-168551923	1.40
1543	chr20:47321645-47322033	1.93	2218	chr6:169224822-169227043	-2.24
1544	chr20:47480755-47481721	2.17	2219	chr6:169435234-169435906	-2.02
1545	chr20:48183831-48185593	-2.06	2220	chr6:169557583-169558907	-2.59
1546	chr20:48258721-48259919	-2.33	2221	chr6:169629346-169630648	-3.22
1547	chr20:48313622-48314088	-1.80	2222	chr6:169651642-169654258	-2.98
1548	chr20:48364102-48364987	-1.93	2223	chr7:640825-642913	-2.49
1549	chr20:48388519-48390930	-2.37	2224	chr7:1481233-1483069	-2.44
1550	chr20:48626215-48626844	-3.31	2225	chr7:1687797-1688333	-1.87
1551	chr20:48671450-48671999	-2.12	2226	chr7:1967720-1968753	1.64
1552	chr20:48936445-48938666	-2.18	2227	chr7:2148485-2151476	-2.34
1553	chr20:48955021-48956379	-1.97	2228	chr7:2738608-2739353	-1.94
1554	chr20:49453897-49454805	-2.36	2229	chr7:2933922-2934674	-2.36
1555	chr20:49464965-49466198	-2.18	2230	chr7:3033310-3033787	-1.97
1556	chr20:50040080-50041297	-2.45	2231	chr7:3220873-3221610	-2.64
1557	chr20:50104100-50104873	-3.01	2232	chr7:3794607-3795108	1.51
1558	chr20:50142432-50143211	1.89	2233	chr7:4652698-4653831	-2.81
1559	chr20:50578522-50579489	2.37	2234	chr7:4707242-4708320	-2.64
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1561	chr20:51159442-51160154	1.59	2236	chr7:4959656-4960052	-1.79
1562	chr20:51962255-51963200	2.15	2237	chr7:6575974-6576865	-2.69
1563	chr20:52367485-52367877	1.53	2238	chr7:6703456-6704304	-2.33
1564	chr20:52375591-52376475	1.64	2239	chr7:6989771-6990493	-2.74
1565	chr20:52385582-52386224	1.80	2240	chr7:7030723-7031569	-2.36
1566	chr20:52531649-52532712	1.57	2241	chr7:8279204-8279842	1.87
1567	chr20:52560342-52560986	2.05	2242	chr7:12342076-12343410	-1.88
1568	chr20:52811962-52812780	2.08	2243	chr7:16503248-16506012	-2.95
1569	chr20:53096394-53097021	2.05	2244	chr7:18497393-18498421	-2.55
1570	chr20:53399028-53399649	2.62	2245	chr7:18548066-18549396	-2.42
1571	chr20:53405180-53405567	1.64	2246	chr7:20179427-20180128	1.71
1572	chr20:53443875-53444084	1.73	2247	chr7:21826216-21826400	1.72
1573	chr20:53509294-53509806	2.19	2248	chr7:23245368-23246352	-2.40
1574	chr20:53530515-53530840	1.76	2249	chr7:23283129-23283529	-2.16
1575	chr20:53535559-53536029	1.95	2250	chr7:23286299-23288285	-1.77
1576	chr20:53546610-53546745	1.79	2251	chr7:23507432-23509613	-2.26
1577	chr20:53571992-53572727	1.81	2252	chr7:23513173-23514609	-2.40
1578	chr20:53676813-53677350	1.93	2253	chr7:26191453-26193934	-0.66
1579	chr20:53710984-53711652	2.43	2254	chr7:26282962-26284494	-3.14

Index	Genomic locus	log2(FC)	Index	Genomic locus	log2(FC)
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1581	chr20:54079717-54080016	1.89	2256	chr7:27238296-27240442	-1.17
1582	chr20:54244548-54245129	2.12	2257	chr7:27264924-27265704	-2.26
1583	chr20:54269675-54270206	1.80	2258	chr7:27278961-27279513	-2.29
1584	chr20:54480702-54481427	1.91	2259	chr7:31923238-31923860	-1.63
1585	chr20:55033382-55033994	2.55	2260	chr7:32802436-32803077	-1.95
1586	chr20:55340019-55340982	-2.15	2261	chr7:33080439-33080788	-2.73
1587	chr20:55355926-55358569	-3.11	2262	chr7:35958984-35959722	-1.88
1588	chr20:55562628-55563562	2.26	2263	chr7:36195728-36196083	-1.86
1589	chr20:55600145-55600302	1.74	2264	chr7:36438775-36438929	1.55
1590	chr20:55734377-55734991	2.22	2265	chr7:36513145-36514102	-1.78
1591	chr20:55827366-55828149	1.79	2266	chr7:41739084-41741216	-2.91
1592	chr20:56554926-56556208	1.67	2267	chr7:43686741-43688298	-2.71
1593	chr20:56704814-56706741	-2.96	2268	chr7:44360383-44360719	1.58
1594	chr20:56869686-56870229	2.57	2269	chr7:44933037-44933824	-1.71
1595	chr20:57443575-57444198	-2.14	2270	chr7:45243334-45244665	-1.52
1596	chr20:57974051-57974728	2.35	2271	chr7:47008431-47009820	-2.88
1597	chr20:58112134-58113011	2.60	2272	chr7:47366609-47368438	-1.96
1598	chr20:58235310-58235594	2.20	2273	chr7:47783537-47783970	1.94
1599	chr20:58325709-58327928	2.30	2274	chr7:51189589-51190229	1.89
1600	chr20:58410641-58411783	-2.40	2275	chr7:55120981-55122004	-2.19
1601	chr20:59173666-59174737	1.88	2276	chr7:55153785-55154925	-3.10
1602	chr20:59335878-59336260	1.98	2277	chr7:55195286-55195953	-2.06
1603	chr20:59443374-59444432	2.33	2278	chr7:55280434-55281389	-2.38
1604	chr20:59711029-59711387	1.66	2279	chr7:62726695-62727016	1.71
1605	chr20:59836919-59837367	1.79	2280	chr7:65746696-65747703	-2.84
1606	chr20:60025652-60025999	2.05	2281	chr7:66074842-66075224	-2.31
1607	chr20:61401993-61405363	-2.20	2282	chr7:70003957-70005536	-2.15
1608	chr20:61560329-61560998	-3.13	2283	chr7:70596065-70598112	-2.57
1609	chr20:61747778-61748289	2.05	2284	chr7:72837933-72839084	-2.05
1610	chr20:62031982-62032655	2.09	2285	chr7:72980252-72980688	-1.88
1611	chr20:62383110-62383485	-2.14	2286	chr7:73406230-73406989	-2.11
1612	chr21:15353853-15354243	-2.18	2287	chr7:78490114-78490603	1.51
1613	chr21:17108303-17108883	-1.80	2288	chr7:80789423-80790740	-2.04
1614	chr21:17680183-17681085	-2.87	2289	chr7:86720917-86721346	1.66
1615	chr21:18665022-18665748	-1.99	2290	chr7:87094272-87095028	2.13
1616	chr21:18983244-18985851	-1.07	2291	chr7:88632198-88632615	-2.00
1617	chr21:19060948-19064352	-1.73	2292	chr7:89347873-89348749	1.55
1618	chr21:19114394-19114649	-2.48	2293	chr7:92262768-92263528	-1.91
1619	chr21:19272715-19275222	-2.43	2294	chr7:92264191-92265065	-1.88
1620	chr21:20131943-20132684	-2.56	2295	chr7:93997513-93998581	-2.28
1621	chr21:27944851-27945803	-3.33	2296	chr7:94106306-94107346	1.74
1622	chr21:28558629-28559204	1.71	2297	chr7:96693745-96694448	-2.31
1623	chr21:32726341-32727429	-1.54	2298	chr7:98198387-98199654	-2.51
1624	chr21:34493326-34494812	-2.04	2299	chr7:99457150-99458967	-2.39
1625	chr21:35633873-35635726	-2.03	2300	chr7:99540950-99542708	-2.88

Index	Genomic locus	log2(FC)	Index	Genomic locus	log2(FC)
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1627	chr21:37110279-37111682	-1.92	2302	chr7:100317848-100319513	-2.18
1628	chr21:37377295-37378843	-2.46	2303	chr7:100844838-100845712	-2.35
1629	chr21:37826326-37826740	-1.73	2304	chr7:104851090-104851987	-1.98
1630	chr21:38091245-38092355	-2.66	2305	chr7:104950208-104950727	1.77
1631	chr21:38579252-38581561	-2.28	2306	chr7:105280387-105280837	1.73
1632	chr21:39003640-39004651	-2.71	2307	chr7:106741694-106742104	1.68
1633	chr21:40405862-40407042	-2.05	2308	chr7:107333587-107335047	-1.59
1634	chr21:40951371-40952170	1.88	2309	chr7:107743363-107743840	1.66
1635	chr21:41690351-41692662	3.29	2310	chr7:112206248-112207763	-2.31
1636	chr21:41710742-41711298	2.76	2311	chr7:112506433-112507372	-2.19
1637	chr21:42579467-42580199	-1.93	2312	chr7:116314663-116314966	-1.77
1638	chr21:42733690-42734843	-2.54	2313	chr7:116712688-116713133	-2.01
1639	chr21:43071439-43072275	-1.91	2314	chr7:121951862-121952219	-2.00
1640	chr21:44598384-44599459	-2.06	2315	chr7:127399998-127400155	1.76
1641	chr21:44608647-44609574	-1.87	2316	chr7:127743458-127744463	-2.06
1642	chr21:44726672-44727419	-1.59	2317	chr7:127841191-127841848	-2.29
1643	chr21:44865470-44867616	-2.20	2318	chr7:128808145-128809524	-2.95
1644	chr21:44998525-44998912	1.43	2319	chr7:128934848-128935417	-1.78
1645	chr21:45151503-45152495	-2.60	2320	chr7:129947957-129948662	1.97
1646	chr21:45176580-45179210	-3.36	2321	chr7:129990026-129991352	-1.92
1647	chr21:45230204-45232804	-1.46	2322	chr7:129995673-129997451	-1.72
1648	chr21:45602164-45602830	1.51	2323	chr7:130418204-130419572	-1.22
1649	chr21:46020441-46020777	-1.60	2324	chr7:130593988-130598703	-2.27
1650	chr21:46142786-46144357	-2.47	2325	chr7:130605058-130607787	-2.38
1651	chr21:47572977-47573659	-1.71	2326	chr7:132066511-132067261	1.78
1652	chr22:18530905-18531472	1.70	2327	chr7:132867550-132868645	1.95
1653	chr22:19136960-19138013	-2.01	2328	chr7:134212182-134213217	-1.96
1654	chr22:19738496-19739069	1.37	2329	chr7:134233448-134234494	-2.50
1655	chr22:21024673-21025629	-2.54	2330	chr7:134593179-134593810	-1.94
1656	chr22:21367818-21370148	-1.88	2331	chr7:134617334-134618739	-2.02
1657	chr22:23317312-23317444	1.77	2332	chr7:135433330-135434333	-1.69
1658	chr22:23623831-23625131	-2.35	2333	chr7:137928293-137928460	1.79
1659	chr22:24684722-24686632	-1.99	2334	chr7:139226448-139227945	-2.34
1660	chr22:24862373-24864325	-2.00	2335	chr7:140185093-140186477	-2.19
1661	chr22:25081702-25082197	-2.18	2336	chr7:140225335-140226036	-1.50
1662	chr22:25515855-25518407	-1.90	2337	chr7:140753341-140753842	-1.73
1663	chr22:27043567-27044461	-1.73	2338	chr7:142785448-142785952	1.67
1664	chr22:28216912-28217974	-2.23	2339	chr7:143582058-143582701	2.91
1665	chr22:28838142-28839601	-2.34	2340	chr7:144938446-144939129	2.15
1666	chr22:30254846-30255090	-1.93	2341	chr7:148611205-148611979	-2.50
1667	chr22:32438672-32441438	-2.37	2342	chr7:150600710-150601610	-1.97
1668	chr22:32975986-32976141	1.86	2343	chr7:150665778-150666650	-2.02
1669	chr22:33141310-33142540	-2.78	2344	chr7:150822565-150823591	-3.65
1670	chr22:35531085-35532209	-2.18	2345	chr7:151136638-151137850	-2.16
1671	chr22:35552555-35553103	-2.01	2346	chr7:151422988-151423768	-1.79

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1674	chr22:37324923-37325564	-1.98	2349	chr7:153568300-153568842	2.04
1675	chr22:37767923-37769725	-2.32	2350	chr7:154705685-154706555	-1.79
1676	chr22:37955603-37960039	-0.73	2351	chr7:154777069-154777477	2.45
1677	chr22:38035117-38037579	-0.88	2352	chr7:155108177-155108991	1.82
1678	chr22:38301575-38303948	-0.66	2353	chr7:156347287-156348007	1.82
1679	chr22:38377471-38380554	-3.92	2354	chr7:156452664-156452826	1.60
1680	chr22:38395604-38396767	-1.84	2355	chr7:156696144-156696672	-1.84
1681	chr22:38412058-38413717	-1.60	2356	chr7:157102272-157103901	-2.05
1682	chr22:38434446-38436274	-2.10	2357	chr7:157138678-157140645	-2.05
1683	chr22:38476871-38478661	-2.49	2358	chr7:158293326-158293744	-2.02
1684	chr22:38483985-38485566	-2.38	2359	chr7:158603722-158604925	-2.43
1685	chr22:38863506-38865359	-0.82	2360	chr7:158605835-158606914	-2.83
1686	chr22:38900083-38903155	-0.67	2361	chr8:6398057-6398722	-2.44
1687	chr22:39277352-39278278	-2.00	2362	chr8:6758319-6759049	-1.86
1688	chr22:39409881-39411178	-3.23	2363	chr8:8168016-8169264	-1.69
1689	chr22:39859799-39860639	-1.81	2364	chr8:8492416-8492660	-1.94
1690	chr22:40042373-40043352	-2.63	2365	chr8:9947184-9947824	-2.16
1691	chr22:40342392-40344011	-2.47	2366	chr8:10547984-10549018	-1.92
1692	chr22:40672081-40673037	-2.07	2367	chr8:10587319-10588706	-2.78
1693	chr22:41577428-41579470	-2.25	2368	chr8:11057126-11059443	-2.52
1694	chr22:42083655-42085684	-0.63	2369	chr8:12953394-12954384	-2.30
1695	chr22:42709290-42710885	-2.58	2370	chr8:17356171-17356639	1.97
1696	chr22:42763531-42765850	-0.84	2371	chr8:18835402-18837125	-2.41
1697	chr22:42827110-42828052	-2.44	2372	chr8:19613554-19615981	-1.11
1698	chr22:42835805-42837421	-3.54	2373	chr8:20125760-20126857	-2.01
1699	chr22:43003133-43005644	-3.50	2374	chr8:22085254-22085386	-2.23
1700	chr22:43926419-43927007	-2.38	2375	chr8:22249819-22251386	-2.27
1701	chr22:44576783-44577996	-3.39	2376	chr8:23017834-23021925	-1.62
1702	chr22:44724944-44725881	-2.57	2377	chr8:23564473-23565261	-2.38
1703	chr22:44759078-44759985	-1.83	2378	chr8:26047646-26048394	-2.83
1704	chr22:44946281-44947325	-2.47	2379	chr8:28515335-28515829	-1.92
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1706	chr22:45054001-45055595	-2.31	2381	chr8:29970379-29971358	-3.01
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1709	chr22:45593276-45594452	2.49	2384	chr8:36347270-36348364	1.93
1710	chr22:46273402-46274656	-2.30	2385	chr8:36583081-36584012	2.26
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1712	chr22:46448665-46452408	-0.70	2387	chr8:37010541-37011118	2.19
1713	chr22:46457129-46458087	-3.15	2388	chr8:37017852-37018055	1.57
1714	chr22:46545370-46547845	-1.03	2389	chr8:37031718-37032537	2.20
1715	chr22:46567341-46568727	-2.35	2390	chr8:37041305-37042039	2.68
1716	chr22:46786051-46787891	-1.66	2391	chr8:37159625-37161497	1.66
1717	chr22:46812352-46813569	-2.25	2392	chr8:37240987-37241291	2.07

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1720	chr22:48576018-48578950	-2.07	2395	chr8:37419694-37420212	2.07
1721	chr22:49046797-49050687	-2.27	2396	chr8:37448181-37449309	2.15
1722	chr22:50521376-50522070	-2.02	2397	chr8:37454597-37456939	2.29
1723	chr3:4927121-4929183	2.14	2398	chr8:37460675-37461077	2.36
1724	chr3:6108463-6109205	1.87	2399	chr8:37549074-37549255	2.44
1725	chr3:9245824-9246470	1.44	2400	chr8:37556892-37557429	1.92
1726	chr3:9358412-9359207	-2.84	2401	chr8:37593619-37595668	1.68
1727	chr3:10035609-10037243	-2.18	2402	chr8:37604863-37606167	2.70
1728	chr3:10391770-10392391	-1.82	2403	chr8:37619576-37621235	1.52
1729	chr3:11056564-11057251	-1.98	2404	chr8:37688775-37689222	1.94
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1732	chr3:11600074-11601250	-2.14	2407	chr8:37713901-37714991	3.11
1733	chr3:11609417-11611033	-2.38	2408	chr8:37721321-37723077	2.88
1734	chr3:11679688-11681212	-2.56	2409	chr8:37728699-37729870	2.49
1735	chr3:11806105-11807092	-2.04	2410	chr8:37754721-37757431	1.68
1736	chr3:12045030-12046700	-2.73	2411	chr8:37761121-37762488	2.62
1737	chr3:13245616-13246226	-3.00	2412	chr8:37781743-37783208	2.91
1738	chr3:14058218-14060307	-2.83	2413	chr8:37828585-37828804	2.08
1739	chr3:16924092-16925313	-2.50	2414	chr8:37887330-37889839	1.23
1740	chr3:17686513-17687328	-1.82	2415	chr8:37921710-37922032	1.70
1741	chr3:18168326-18168482	1.38	2416	chr8:38367172-38368779	1.59
1742	chr3:19417399-19418093	2.14	2417	chr8:38569845-38570894	-2.71
1743	chr3:28060635-28061172	1.68	2418	chr8:39938870-39939463	1.79
1744	chr3:29153144-29153576	1.94	2419	chr8:40148112-40148247	1.67
1745	chr3:31917331-31918545	-2.23	2420	chr8:40386850-40387579	2.68
1746	chr3:32009600-32011090	-1.75	2421	chr8:40672940-40673793	1.86
1747	chr3:34460215-34460648	1.74	2422	chr8:40706529-40706784	1.57
1748	chr3:36805268-36806262	-2.34	2423	chr8:40754139-40755647	1.84
1749	chr3:37976973-37978491	-1.99	2424	chr8:41649294-41650373	-1.73
1750	chr3:40919219-40920546	-1.79	2425	chr8:41655054-41656088	-2.18
1751	chr3:41319138-41320069	2.52	2426	chr8:42318589-42318745	1.47
1752	chr3:43458274-43459166	2.33	2427	chr8:47037206-47038014	-1.67
1753	chr3:44753750-44754824	-2.52	2428	chr8:47708990-47709664	1.83
1754	chr3:46399644-46400160	1.56	2429	chr8:48011851-48012601	2.09
1755	chr3:46875149-46875683	-1.98	2430	chr8:48091002-48091947	-2.05
1756	chr3:48632532-48632697	-2.49	2431	chr8:48192098-48193890	-1.88
1757	chr3:48693300-48694160	-3.34	2432	chr8:48436118-48438539	-1.77
1758	chr3:50349111-50350660	-2.60	2433	chr8:49468646-49469448	-2.79
1759	chr3:50377878-50378798	-4.18	2434	chr8:49711739-49712460	2.16
1760	chr3:50567598-50568181	-2.93	2435	chr8:52530226-52531242	-2.17
1761	chr3:51720471-51721975	-1.99	2436	chr8:55038065-55038535	-2.70
1762	chr3:57497895-57498557	-1.93	2437	chr8:55228301-55229126	-2.53
1763	chr3:64962628-64963750	-2.75	2438	chr8:55962514-55963296	2.15

Index	Genomic locus	log2(FC)	Index	Genomic locus	log2(FC)
1764	chr3:65582291-65583997	-2.73	2439	chr8:56831617-56833144	-2.19
1765	chr3:65964084-65965808	-2.31	2440	chr8:59827092-59827833	2.19
1766	chr3:65985334-65986391	-2.32	2441	chr8:60086489-60087208	2.23
1767	chr3:66139235-66140481	-1.98	2442	chr8:60250975-60251279	1.48
1768	chr3:69724544-69725206	-1.99	2443	chr8:60614210-60614507	1.97
1769	chr3:69726443-69727012	-2.35	2444	chr8:61034170-61034982	2.21
1770	chr3:71477774-71478733	-1.74	2445	chr8:61404941-61407754	-1.87
1771	chr3:72149672-72150364	-2.01	2446	chr8:63841112-63841667	1.55
1772	chr3:72396644-72397546	-2.29	2447	chr8:64715244-64715954	3.22
1773	chr3:73273857-73275125	-2.02	2448	chr8:65152280-65153471	2.32
1774	chr3:87137816-87139024	-4.03	2449	chr8:65234942-65235086	1.37
1775	chr3:102229845-102231905	-2.47	2450	chr8:65668614-65670185	-1.94
1776	chr3:105684531-105685601	-2.43	2451	chr8:67143776-67144576	-2.27
1777	chr3:105716181-105717492	-1.86	2452	chr8:67419316-67420355	-2.12
1778	chr3:111904386-111904895	-1.93	2453	chr8:67873359-67875474	-2.63
1779	chr3:113204095-113204524	1.52	2454	chr8:70179960-70180882	-2.21
1780	chr3:113296930-113297395	-2.36	2455	chr8:70983096-70984083	-2.18
1781	chr3:114102315-114103598	-1.87	2456	chr8:71125731-71127971	-2.34
1782	chr3:114119207-114120147	-2.14	2457	chr8:71957372-71958267	-1.79
1783	chr3:114172824-114173288	-1.97	2458	chr8:73256779-73257112	1.55
1784	chr3:114342580-114344010	-2.58	2459	chr8:74376044-74377448	-2.06
1785	chr3:122369871-122371351	2.03	2460	chr8:75186173-75186499	-2.50
1786	chr3:122631665-122632748	-2.30	2461	chr8:75511724-75512792	2.14
1787	chr3:122688014-122689396	-2.04	2462	chr8:77424607-77424754	-2.06
1788	chr3:123518361-123518929	-2.05	2463	chr8:82656695-82658945	-3.56
1789	chr3:126116640-126118982	-1.71	2464	chr8:84932347-84933073	2.10
1790	chr3:126717538-126718424	-1.52	2465	chr8:85337211-85337777	1.94
1791	chr3:127633599-127634584	-3.45	2466	chr8:87922927-87923512	1.53
1792	chr3:128273957-128274799	-2.33	2467	chr8:90710259-90711534	-2.92
1793	chr3:128764493-128766161	-2.61	2468	chr8:90873865-90874745	-2.08
1794	chr3:129344366-129347578	-0.85	2469	chr8:91682685-91683871	-1.56
1795	chr3:129573404-129575763	-2.17	2470	chr8:91996986-91998026	-2.65
1796	chr3:129689948-129690462	2.54	2471	chr8:92805833-92806545	2.19
1797	chr3:129694302-129694954	-2.38	2472	chr8:92903619-92904368	2.36
1798	chr3:130445704-130446487	-2.51	2473	chr8:94843864-94844400	1.58
1799	chr3:131854348-131855330	-2.05	2474	chr8:95168217-95169004	1.39
1800	chr3:132377471-132380368	-0.59	2475	chr8:95458839-95460127	2.32
1801	chr3:133131399-133131812	-1.69	2476	chr8:98708910-98710230	-2.49
1802	chr3:133254808-133255774	-1.81	2477	chr8:99076448-99077488	-2.07
1803	chr3:133464648-133466355	-2.16	2478	chr8:99272019-99273244	2.29
1804	chr3:133667207-133668312	-2.49	2479	chr8:99984425-99985009	-2.43
1805	chr3:134125043-134125996	-2.24	2480	chr8:100040528-100042295	-3.69
1806	chr3:134785667-134787190	-2.36	2481	chr8:100917105-100918134	1.37
1807	chr3:136447311-136448195	-2.03	2482	chr8:102478874-102480058	1.83
1808	chr3:137227970-137229041	1.73	2483	chr8:102526340-102527997	1.39
1809	chr3:138135177-138135755	-1.88	2484	chr8:107092863-107093608	-1.94

Index	Genomic locus	log2(FC)	Index	Genomic locus	log2(FC)
1810	chr3:138152532-138155082	-1.34	2485	chr8:107511620-107513918	-2.94
1811	chr3:138318488-138319853	-2.14	2486	chr8:109942736-109943351	2.34
1812	chr3:138828934-138829771	-1.79	2487	chr8:112428445-112428889	2.09
1813	chr3:141934005-141935696	-2.22	2488	chr8:116004544-116005664	-2.62
1814	chr3:142928693-142929969	-2.07	2489	chr8:116505678-116507332	-2.50
1815	chr3:143200679-143202174	-2.27	2490	chr8:117794130-117794596	-2.04
1816	chr3:146221201-146222897	-2.10	2491	chr8:117913306-117913705	-2.35
1817	chr3:148938671-148940107	-3.26	2492	chr8:118946105-118947133	-2.06
1818	chr3:149050495-149051688	-2.12	2493	chr8:118949390-118950406	-1.98
1819	chr3:149087910-149088411	-1.90	2494	chr8:118958575-118959451	-3.00
1820	chr3:149271368-149273033	-2.87	2495	chr8:120114583-120115137	-1.90
1821	chr3:149292999-149294323	-1.94	2496	chr8:121002933-121003611	-1.93
1822	chr3:149298479-149300517	-1.88	2497	chr8:121031581-121032188	-2.24
1823	chr3:149779108-149781309	-2.82	2498	chr8:121085364-121085907	1.93
1824	chr3:151146853-151147237	-2.12	2499	chr8:121447529-121448043	1.77
1825	chr3:153942152-153942543	1.55	2500	chr8:121653356-121655138	-2.39
1826	chr3:155935496-155936482	1.55	2501	chr8:122360826-122362199	-2.54
1827	chr3:156323512-156324464	-2.71	2502	chr8:123587617-123588609	-1.30
1828	chr3:156443469-156444427	-1.80	2503	chr8:123858477-123858614	1.35
1829	chr3:156816991-156818148	-2.31	2504	chr8:126185905-126187688	-3.05
1830	chr3:159493148-159493504	-1.72	2505	chr8:126231202-126233250	-2.56
1831	chr3:169529523-169532061	-1.90	2506	chr8:127980376-127981584	-2.10
1832	chr3:171578077-171579597	-1.71	2507	chr8:128305905-128308159	-2.56
1833	chr3:179543005-179544406	1.60	2508	chr8:128710993-128713537	-2.76
1834	chr3:181853923-181854426	1.92	2509	chr8:129355931-129356682	1.82
1835	chr3:182082379-182083248	-2.55	2510	chr8:129838819-129839462	-2.48
1836	chr3:182536739-182537184	2.13	2511	chr8:131457097-131457542	-1.88
1837	chr3:183361858-183362272	1.72	2512	chr8:134088335-134088650	1.91
1838	chr3:184732086-184732281	1.38	2513	chr8:134124563-134124774	1.81
1839	chr3:185034341-185036132	-2.00	2514	chr8:134246757-134247463	2.27
1840	chr3:186358190-186359119	-1.71	2515	chr8:134254664-134255849	2.34
1841	chr3:187085765-187087657	-2.57	2516	chr8:134261308-134262580	1.98
1842	chr3:188815831-188818051	4.01	2517	chr8:135469131-135470248	-1.82
1843	chr3:190062972-190064665	-1.82	2518	chr8:135480247-135480504	1.54
1844	chr3:190251055-190252057	-2.75	2519	chr8:135746405-135747336	1.89
1845	chr3:191074356-191075301	-2.05	2520	chr8:136347731-136348386	1.34
1846	chr3:193810853-193811822	-2.23	2521	chr8:141073547-141075197	-2.95
1847	chr3:195566374-195566932	2.65	2522	chr8:141110407-141110994	-2.30
1848	chr3:195949965-195950489	2.06	2523	chr8:142974968-142975476	2.18
1849	chr3:196716619-196717431	2.02	2524	chr8:142986163-142987287	-1.81
1850	chr4:107162-107973	-2.55	2525	chr8:143125534-143125968	2.24
1851	chr4:206362-207877	2.52	2526	chr8:143335160-143335926	1.82
1852	chr4:2341061-2341630	-2.23	2527	chr8:143681062-143682069	-1.74
1853	chr4:2909429-2910224	2.03	2528	chr8:144105437-144105962	-1.91
1854	chr4:3287303-3288372	-2.47	2529	chr8:144107656-144108274	-1.97
1855	chr4:5519906-5520623	2.36	2530	chr8:144441950-144443336	-2.61

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1856	chr4:5595429-5596184	1.74	2531	chr8:144965238-144966443	-2.35
1857	chr4:5709536-5710592	-3.17	2532	chr8:145009903-145011208	-1.73
1858	chr4:5981760-5982114	1.88	2533	chr8:145011772-145014068	-2.25
1859	chr4:7962214-7963376	-1.76	2534	chr8:145100746-145102222	-2.10
1860	chr4:8128048-8130291	-2.53	2535	chr9:534895-535693	-1.91
1861	chr4:8261717-8261939	1.55	2536	chr9:676973-678261	-3.33
1862	chr4:8726223-8727428	-2.16	2537	chr9:692788-695533	-3.15
1863	chr4:13707012-13708350	-2.20	2538	chr9:714467-717075	-2.00
1864	chr4:15199699-15199927	1.51	2539	chr9:1915914-1916893	-2.24
1865	chr4:15779745-15781401	-1.63	2540	chr9:2177921-2179297	-2.40
1866	chr4:17730691-17731137	1.69	2541	chr9:2262467-2263445	-1.86
1867	chr4:18160021-18160467	1.84	2542	chr9:2570565-2571676	-1.83
1868	chr4:26977263-26977975	3.08	2543	chr9:2621069-2623868	-1.02
1869	chr4:37876493-37877183	1.93	2544	chr9:4297277-4300186	-1.36
1870	chr4:37910035-37910918	-2.45	2545	chr9:5683367-5684235	2.25
1871	chr4:38724801-38726108	-2.12	2546	chr9:6314520-6316054	-1.78
1872	chr4:38753738-38755515	-2.40	2547	chr9:6544771-6545850	-1.97
1873	chr4:38821874-38823002	-2.23	2548	chr9:12930824-12931472	-1.89
1874	chr4:38856485-38860175	-2.49	2549	chr9:13513329-13514124	-1.60
1875	chr4:39991690-39993283	-1.94	2550	chr9:13555286-13556232	-2.35
1876	chr4:40909894-40911529	-1.86	2551	chr9:13620695-13621132	-1.84
1877	chr4:41121980-41122795	-2.01	2552	chr9:13716557-13719012	-2.39
1878	chr4:43083927-43084582	1.86	2553	chr9:14178858-14181890	-2.19
1879	chr4:47838137-47839952	-1.11	2554	chr9:14312419-14317792	-0.89
1880	chr4:48484975-48486090	-2.39	2555	chr9:14343979-14351438	-2.33
1881	chr4:52957745-52958585	1.42	2556	chr9:16138776-16139497	-2.26
1882	chr4:53703694-53704504	-1.81	2557	chr9:16442633-16442787	-2.53
1883	chr4:54687404-54688108	-2.09	2558	chr9:16704722-16705637	-3.40
1884	chr4:55096043-55098697	-1.83	2559	chr9:18446777-18448337	-2.48
1885	chr4:55432489-55433248	-2.26	2560	chr9:18711261-18711722	2.13
1886	chr4:56485004-56485854	-2.87	2561	chr9:21267308-21268666	-2.14
1887	chr4:57521511-57522648	-2.95	2562	chr9:21402331-21403187	-2.30
1888	chr4:57750697-57751415	1.88	2563	chr9:21549046-21550117	-2.34
1889	chr4:60072021-60072759	1.71	2564	chr9:21576099-21577244	-3.70
1890	chr4:60463297-60464381	-1.73	2565	chr9:21684631-21685096	-2.07
1891	chr4:67440450-67441392	-1.66	2566	chr9:21770708-21771790	-2.38
1892	chr4:68042800-68043090	1.73	2567	chr9:21986621-21987730	-2.73
1893	chr4:73459470-73460221	2.10	2568	chr9:22005919-22006328	-2.72
1894	chr4:74416403-74417124	2.01	2569	chr9:23524610-23525617	-1.95
1895	chr4:74702007-74702904	-2.01	2570	chr9:23555694-23557066	-1.86
1896	chr4:75340208-75341168	1.91	2571	chr9:23775212-23776215	-2.02
1897	chr4:76975170-76977803	-3.31	2572	chr9:26249799-26250521	1.82
1898	chr4:83808669-83809787	-2.33	2573	chr9:31848669-31849717	-2.69
1899	chr4:84140472-84141316	-2.22	2574	chr9:33150954-33151596	-1.89
1900	chr4:87370032-87370364	2.40	2575	chr9:33750373-33751954	-3.95
1901	chr4:89534662-89535036	-1.95	2576	chr9:35673410-35676463	-2.44

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1902	chr4:93404260-93404471	1.29	2577	chr9:35961997-35963090	-2.23
1903	chr4:99147688-99147934	1.39	2578	chr9:36470684-36471251	-2.00
1904	chr4:99981023-99981924	-1.88	2579	chr9:36560699-36561378	-1.86
1905	chr4:100691967-100692579	2.16	2580	chr9:37226644-37227024	2.48
1906	chr4:109271461-109272141	1.45	2581	chr9:37467713-37467888	-2.10
1907	chr4:113200395-113201314	-1.91	2582	chr9:38026204-38026376	-2.34
1908	chr4:113832152-113832809	-2.56	2583	chr9:40332190-40333070	-2.44
1909	chr4:114823407-114823880	1.77	2584	chr9:44780191-44780773	1.72
1910	chr4:115524725-115525356	-2.23	2585	chr9:72660967-72661912	-1.91
1911	chr4:119340264-119341696	-2.35	2586	chr9:72870876-72871483	-2.28
1912	chr4:119478099-119479014	-1.67	2587	chr9:74061109-74062241	-2.28
1913	chr4:123775548-123776418	-2.35	2588	chr9:75106641-75107639	-2.19
1914	chr4:125038593-125038928	1.51	2589	chr9:75767095-75770104	-2.55
1915	chr4:130263590-130265547	-1.93	2590	chr9:76530940-76531337	1.68
1916	chr4:139176534-139178153	2.03	2591	chr9:80911052-80913512	-0.98
1917	chr4:139603778-139604420	-2.16	2592	chr9:82185193-82188834	-1.05
1918	chr4:140200595-140201563	-2.31	2593	chr9:82589830-82592472	-2.78
1919	chr4:141019791-141020224	-2.17	2594	chr9:86954548-86955726	-1.85
1920	chr4:141188753-141188975	1.69	2595	chr9:89075123-89075772	-2.40
1921	chr4:144833051-144833562	-2.59	2596	chr9:91792403-91793683	-2.16
1922	chr4:152364977-152365264	1.76	2597	chr9:93969241-93970376	-2.30
1923	chr4:153641043-153641940	-2.03	2598	chr9:95945962-95949275	-0.89
1924	chr4:153943045-153943997	-1.92	2599	chr9:95969655-95970695	-2.03
1925	chr4:154087721-154089121	-2.12	2600	chr9:96108447-96109031	-2.18
1926	chr4:154102554-154103074	-2.13	2601	chr9:96622925-96623692	-2.28
1927	chr4:154124943-154128157	-1.74	2602	chr9:96716824-96718589	-2.94
1928	chr4:154133621-154134440	-2.01	2603	chr9:97807049-97808355	-2.10
1929	chr4:154408808-154410803	-1.68	2604	chr9:98111380-98112366	-2.61
1930	chr4:154709753-154710661	-2.44	2605	chr9:98277911-98279488	-1.73
1931	chr4:154904651-154905346	1.86	2606	chr9:98411636-98412898	-2.85
1932	chr4:158595762-158596858	-1.68	2607	chr9:102016046-102016496	-2.05
1933	chr4:164324929-164326652	-2.09	2608	chr9:102021400-102022364	-2.29
1934	chr4:165480158-165480619	1.94	2609	chr9:102130427-102131601	-2.50
1935	chr4:169705648-169706917	-2.39	2610	chr9:106374126-106374718	2.04
1936	chr4:173640776-173641549	-2.62	2611	chr9:110227612-110228692	-2.07
1937	chr4:174317538-174320807	-2.19	2612	chr9:110681011-110681273	1.50
1938	chr4:174450137-174451991	-3.02	2613	chr9:111975691-111976337	1.65
1939	chr4:176049234-176050581	-2.42	2614	chr9:112072819-112074081	-1.97
1940	chr4:183159517-183160335	1.52	2615	chr9:112507072-112508748	-2.28
1941	chr4:183167125-183167999	1.76	2616	chr9:114928263-114929582	-2.17
1942	chr4:183783815-183784495	-2.18	2617	chr9:114951411-114951819	1.46
1943	chr4:183801307-183802278	-2.21	2618	chr9:115526886-115527489	2.41
1944	chr4:184667339-184668434	-2.53	2619	chr9:119244750-119245543	-1.94
1945	chr4:184797359-184798378	-2.02	2620	chr9:126069281-126069497	1.43
1946	chr4:185018075-185018969	-2.37	2621	chr9:126137679-126138594	-1.86
1947	chr4:185469488-185470553	-3.05	2622	chr9:129344339-129345739	1.96

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1948	chr4:186535777-186536188	2.14	2623	chr9:129379042-129379598	2.14
1949	chr4:186559434-186560992	3.03	2624	chr9:129405259-129405802	2.66
1950	chr4:186693280-186697177	-3.17	2625	chr9:129406308-129406518	1.55
1951	chr4:186950874-186952880	-2.71	2626	chr9:129435576-129437113	1.47
1952	chr4:188507629-188508463	-2.59	2627	chr9:130463394-130463537	1.59
1953	chr4:188916559-188917128	-2.22	2628	chr9:130485686-130487672	-2.11
1954	chr5:501525-502426	-1.96	2629	chr9:131955840-131956484	2.44
1955	chr5:504925-505229	-1.76	2630	chr9:132355841-132357881	-2.43
1956	chr5:509587-510635	-2.05	2631	chr9:132476809-132477456	-2.05
1957	chr5:891120-894068	-0.84	2632	chr9:132800162-132800955	-2.63
1958	chr5:979302-980811	-2.19	2633	chr9:133410845-133411833	-2.10
1959	chr5:1073321-1074161	-2.72	2634	chr9:133463892-133464478	1.93
1960	chr5:1161515-1162447	-2.07	2635	chr9:134552646-134554722	-1.67
1961	chr5:1552356-1553259	-3.73	2636	chr9:135089187-135090103	-1.92
1962	chr5:1568249-1569674	-2.91	2637	chr9:135898485-135899431	-2.29
1963	chr5:1764176-1764690	-2.55	2638	chr9:136081580-136085995	-2.42
1964	chr5:1794265-1794810	-2.14	2639	chr9:136127140-136128205	-2.28
1965	chr5:1849766-1850760	-1.93	2640	chr9:136424947-136425846	-2.31
1966	chr5:1930596-1932124	-2.69	2641	chr9:136523568-136524520	1.38
1967	chr5:4615579-4616291	1.74	2642	chr9:137174647-137174974	-1.82
1968	chr5:6349382-6349926	-2.18	2643	chr9:137608978-137609595	-1.89
1969	chr5:6545529-6546605	-1.98	2644	chr9:137834008-137834810	-2.47
1970	chr5:6583053-6583807	-3.11	2645	chr9:138183015-138183360	1.86
1971	chr5:10479554-10479726	-1.90	2646	chr9:139069094-139069489	1.49
1972	chr5:10663410-10664526	-1.76	2647	chrX:3674700-3676140	-2.06
1973	chr5:10724611-10725739	-3.33	2648	chrX:6105033-6105841	1.96
1974	chr5:11062332-11063247	-2.24	2649	chrX:7138369-7138876	1.82
1975	chr5:14039460-14039844	-2.08	2650	chrX:8698355-8700651	1.11
1976	chr5:14440436-14441499	-2.22	2651	chrX:9261021-9261508	1.57
1977	chr5:14577360-14577760	-2.83	2652	chrX:12759266-12759945	1.29
1978	chr5:14869928-14873044	-0.83	2653	chrX:14047138-14048670	0.86
1979	chr5:16595922-16597231	-2.00	2654	chrX:14114002-14114188	1.43
1980	chr5:16666593-16667493	1.61	2655	chrX:15956378-15957019	1.78
1981	chr5:21701140-21702171	-3.56	2656	chrX:20134095-20135251	-2.04
1982	chr5:26388619-26390064	-1.93	2657	chrX:20892049-20892759	2.02
1983	chr5:28397296-28398422	-2.41	2658	chrX:22692923-22693473	1.55
1984	chr5:31274391-31274791	-2.26	2659	chrX:23132136-23132678	1.45
1985	chr5:31618400-31619197	-1.69	2660	chrX:23900622-23902375	-2.12
1986	chr5:32522576-32523540	-2.26	2661	chrX:25046661-25047741	-2.03
1987	chr5:33891292-33892927	-2.76	2662	chrX:25789673-25790469	1.94
1988	chr5:34564057-34564302	-1.85	2663	chrX:26305100-26305295	1.50
1989	chr5:34672531-34674984	-1.87	2664	chrX:26773944-26774294	1.53
1990	chr5:34695941-34696107	-1.80	2665	chrX:34433325-34433990	1.74
1991	chr5:34872917-34873874	1.69	2666	chrX:34972917-34973182	1.62
1992	chr5:35246313-35248394	-1.73	2667	chrX:35239579-35240123	2.78
1993	chr5:35404437-35405572	-3.48	2668	chrX:36253161-36253844	2.14

Index	Genomic locus	log2(FC)	Index	Genomic locus	log2(FC)
1994	chr5:36657653-36658883	-2.09	2669	chrX:36436618-36437039	1.61
1995	chr5:37834664-37835171	-2.25	2670	chrX:37764630-37765848	1.31
1996	chr5:38445639-38446752	-2.84	2671	chrX:38420105-38422438	1.13
1997	chr5:40800483-40801279	-2.56	2672	chrX:39843382-39843702	1.34
1998	chr5:40841148-40842104	-2.44	2673	chrX:40331457-40332043	1.56
1999	chr5:40870933-40872195	-1.94	2674	chrX:41301233-41302428	1.29
2000	chr5:42949095-42952817	-1.66	2675	chrX:46937625-46938247	-2.08
2001	chr5:42991424-42993532	-2.58	2676	chrX:48506900-48507095	1.42
2002	chr5:43032976-43034969	-2.51	2677	chrX:48518331-48519224	-2.05
2003	chr5:43086649-43089651	-3.22	2678	chrX:49139145-49139292	1.42
2004	chr5:54484729-54485424	1.82	2679	chrX:51138777-51139519	-1.89
2005	chr5:54733715-54734940	-1.78	2680	chrX:51298599-51299256	1.66
2006	chr5:55750046-55750333	1.48	2681	chrX:62739042-62739822	2.08
2007	chr5:58187369-58187723	-1.56	2682	chrX:63263640-63264334	2.58
2008	chr5:58218218-58219597	-2.08	2683	chrX:63722326-63722990	2.05
2009	chr5:59994885-59996745	0.51	2684	chrX:65383534-65385311	-2.32
2010	chr5:61040732-61041475	1.74	2685	chrX:65646146-65646860	1.54
2011	chr5:63702767-63703563	1.80	2686	chrX:65858154-65859159	2.18
2012	chr5:65891784-65894638	0.72	2687	chrX:65912167-65912877	1.92
2013	chr5:66037508-66038057	1.60	2688	chrX:66162684-66163385	2.18
2014	chr5:70927017-70928608	1.96	2689	chrX:74836295-74836969	1.66
2015	chr5:71474877-71476229	-1.67	2690	chrX:76199071-76199767	1.47
2016	chr5:77046561-77047803	-2.15	2691	chrX:76266408-76267254	1.76
2017	chr5:80255788-80257050	-2.15	2692	chrX:78622183-78623057	1.94
2018	chr5:81118651-81120023	-2.86	2693	chrX:79181955-79183067	2.26
2019	chr5:81701094-81702715	-1.69	2694	chrX:79412200-79412899	1.91
2020	chr5:89368766-89369787	2.08	2695	chrX:82030345-82032445	-2.25
2021	chr5:92406270-92406896	1.62	2696	chrX:86224661-86225392	1.98
2022	chr5:95826935-95827071	-1.64	2697	chrX:93194771-93195418	1.95
2023	chr5:100113342-100113955	-2.06	2698	chrX:97176100-97176736	2.18
2024	chr5:101490215-101491173	2.73	2699	chrX:100067262-100068150	-1.90
2025	chr5:102087548-102087749	-1.86	2700	chrX:101914620-101915390	2.75
			2701	chrX:109848942-109849715	2.28
			2702	chrX:114827330-114829366	-2.46
			2703	chrX:115592843-115594526	-3.24
			2704	chrX:118868640-118869707	-1.76
			2705	chrX:132399164-132399962	-1.89
			2706	chrX:134566577-134567375	-2.22
			2707	chrX:135614261-135617316	-2.37
			2708	chrX:135718306-135718757	-1.75
			2709	chrX:144841412-144842288	1.69
			2710	chrX:144939714-144940380	2.72
			2711	chrX:146102234-146102720	2.08
			2712	chrX:146228908-146229755	2.45
			2713	chrX:146281873-146282329	1.95
			2714	chrX:152848468-152848667	-2.08

Table 2: Exemplary genomic loci that are differentially H3K27ac modified in ER-positive vs. ER-negative cancer.

Index	Genomic locus	log2(FC)	Index	Genomic locus	log2(FC)
1	chr1:901178-903765	-1.14	701	chr14:60097023-60097669	1.94
2	chr1:1147031-1148958	-1.82	702	chr14:60714953-60716922	0.67
3	chr1:1239611-1241482	-1.18	703	chr14:61201223-61202400	1.01
4	chr1:1356158-1358125	-1.66	704	chr14:61611684-61613230	-1.99
5	chr1:1565980-1567893	-2.26	705	chr14:61613623-61616024	-2.81
6	chr1:2425699-2429218	-1.80	706	chr14:61643599-61645574	-2.28
7	chr1:3229485-3231634	-2.14	707	chr14:62027972-62030192	-1.26
8	chr1:3420428-3421854	-2.33	708	chr14:62228405-62229946	1.05
9	chr1:3455061-3458406	-1.59	709	chr14:64969886-64971948	0.71
10	chr1:3458801-3460755	-2.27	710	chr14:65709750-65711006	1.61
11	chr1:3487387-3489841	-1.75	711	chr14:67946661-67947405	2.71
12	chr1:6473618-6476108	-1.75	712	chr14:67980061-67982407	0.95
13	chr1:6478467-6480679	-1.59	713	chr14:68140646-68142221	0.65
14	chr1:6506455-6509114	-1.91	714	chr14:69012139-69015933	-1.46
15	chr1:7529535-7533704	-1.58	715	chr14:69036312-69037578	1.69
16	chr1:7608948-7612974	-1.53	716	chr14:69065004-69066391	-1.98
17	chr1:7945479-7947071	-1.92	717	chr14:69319686-69321313	1.56
18	chr1:8156433-8157652	-2.04	718	chr14:69726662-69728278	1.42
19	chr1:8263829-8265838	-2.18	719	chr14:70446627-70448223	-2.20
20	chr1:8271345-8272701	-2.72	720	chr14:71184960-71186029	-1.96
21	chr1:8936923-8939550	-1.19	721	chr14:71275074-71277502	0.71
22	chr1:9007239-9009588	-2.25	722	chr14:71786652-71788550	0.59
23	chr1:9045287-9047032	-1.65	723	chr14:73992762-73993853	1.38
24	chr1:9377496-9378477	-1.80	724	chr14:74058291-74059457	1.12
25	chr1:9895281-9897530	-1.95	725	chr14:74078947-74080057	1.18
26	chr1:10474840-10476433	-1.90	726	chr14:75046073-75047395	-1.57
27	chr1:11038865-11040985	-1.86	727	chr14:75084502-75086040	-2.11
28	chr1:12191907-12193851	-2.41	728	chr14:75724888-75727102	0.86
29	chr1:12513304-12514952	-2.23	729	chr14:76032443-76033470	1.35
30	chr1:12654826-12656846	-1.16	730	chr14:76297584-76299458	1.73
31	chr1:12675677-12679955	-1.19	731	chr14:77278440-77279870	0.85
32	chr1:15058686-15060241	-2.58	732	chr14:77294143-77297384	-2.14
33	chr1:15672071-15673492	-1.88	733	chr14:77504417-77504649	-1.68
34	chr1:16082352-16084551	-1.84	734	chr14:77509037-77510606	-2.08
35	chr1:16125496-16127756	-1.24	735	chr14:78447154-78447774	1.42
36	chr1:16465598-16466005	-1.83	736	chr14:81104132-81105011	-1.79
37	chr1:16470086-16473342	-1.91	737	chr14:84105641-84106221	1.72
38	chr1:16480177-16483015	-1.31	738	chr14:85880714-85883389	-2.19
39	chr1:16491012-16492188	-1.94	739	chr14:88593963-88597070	-3.01
40	chr1:17703524-17704311	1.62	740	chr14:91719283-91720469	1.11
41	chr1:17754098-17755072	1.66	741	chr14:91730398-91731250	1.42
42	chr1:17817732-17818699	-1.80	742	chr14:91742514-91742748	1.75
43	chr1:17895473-17896935	-1.57	743	chr14:91744451-91744657	2.48
44	chr1:19252826-19254253	-1.85	744	chr14:93347392-93347616	1.73
45	chr1:19392498-19394586	-1.50	745	chr14:93499732-93500418	1.25

Index	Genomic locus	log2(FC)	Index	Genomic locus	log2(FC)
46	chr1:19600109-19601084	-2.17	746	chr14:94576232-94578236	-1.97
47	chr1:19799095-19799229	1.66	747	chr14:95235881-95237106	1.84
48	chr1:20478441-20481467	-2.14	748	chr14:95522591-95523359	1.47
49	chr1:20820269-20821205	-1.77	749	chr14:96561935-96562788	1.85
50	chr1:21475624-21477387	-1.94	750	chr14:96828606-96830750	0.85
51	chr1:21588139-21589405	-1.93	751	chr14:98242910-98244036	1.57
52	chr1:21842667-21844710	-2.78	752	chr14:99738236-99738546	1.54
53	chr1:21900401-21901661	-2.36	753	chr14:100596843-100598280	1.69
54	chr1:21991902-21992888	-1.54	754	chr14:100653831-100654025	1.80
55	chr1:23158083-23159314	-1.88	755	chr14:101012522-101013653	1.36
56	chr1:24053801-24054602	1.78	756	chr14:101139124-101140008	1.56
57	chr1:24532098-24533359	-1.81	757	chr14:102196974-102198673	-2.35
58	chr1:24604715-24605867	-2.15	758	chr14:102301215-102302148	2.09
59	chr1:24647783-24649803	-1.20	759	chr14:102536954-102538997	-2.37
60	chr1:24691016-24692378	-2.64	760	chr14:102652833-102654998	-1.68
61	chr1:25348328-25350873	-2.23	761	chr14:102785482-102786898	0.77
62	chr1:27174933-27176397	-1.85	762	chr14:103021083-103022140	-2.10
63	chr1:27188747-27192861	-1.08	763	chr14:103057243-103060148	0.59
64	chr1:27383890-27387776	-3.09	764	chr14:103719830-103720771	-1.99
65	chr1:27861305-27863985	-1.56	765	chr14:104006469-104011118	-1.03
66	chr1:28113838-28117321	-2.42	766	chr14:104059782-104061995	-2.13
67	chr1:28189046-28191447	-1.46	767	chr14:105938951-105942821	1.05
68	chr1:28201448-28201799	-1.84	768	chr14:105947433-105950082	0.93
69	chr1:30417372-30417938	2.29	769	chr14:106025882-106026198	2.62
70	chr1:30775398-30776663	2.12	770	chr15:33390442-33391368	-1.90
71	chr1:31400676-31402387	-2.22	771	chr15:33533944-33535525	-1.88
72	chr1:32040746-32042895	-2.04	772	chr15:33571148-33572514	-3.04
73	chr1:36599485-36601637	-1.69	773	chr15:34530984-34532916	-1.88
74	chr1:36626311-36628558	-1.55	774	chr15:36487612-36488020	1.80
75	chr1:36815277-36817521	-2.82	775	chr15:41417604-41419068	-1.80
76	chr1:36986106-36987738	-1.55	776	chr15:45130573-45131946	-2.03
77	chr1:38022296-38023257	1.83	777	chr15:45352730-45354725	-1.86
78	chr1:38331325-38331972	-1.74	778	chr15:45737259-45738451	-1.42
79	chr1:38464797-38465710	-2.14	779	chr15:45746765-45750274	-1.42
80	chr1:39863862-39864892	-1.83	780	chr15:52310871-52312733	1.01
81	chr1:40420257-40422216	-0.88	781	chr15:52970059-52972319	0.95
82	chr1:41574265-41575903	-2.25	782	chr15:53082244-53083036	1.30
83	chr1:41846340-41849084	-1.82	783	chr15:53976398-53976850	1.75
84	chr1:43471284-43472011	1.68	784	chr15:54202667-54203401	1.26
85	chr1:43613138-43613884	1.43	785	chr15:55699205-55701499	0.64
86	chr1:44248710-44251097	-2.34	786	chr15:55920172-55920759	-1.95
87	chr1:44261330-44262890	-2.24	787	chr15:56285245-56286560	0.83
88	chr1:44398852-44400523	-1.52	788	chr15:58551898-58553206	-2.35
89	chr1:45868581-45869197	1.50	789	chr15:58843776-58845585	-2.12
90	chr1:47573111-47574408	-1.92	790	chr15:59085406-59087040	-2.83
91	chr1:47654557-47656724	-2.15	791	chr15:59584848-59588183	-2.23

Index	Genomic locus	log2(FC)	Index	Genomic locus	log2(FC)
92	chr1:48679557-48682538	-2.01	792	chr15:63085966-63087828	-2.22
93	chr1:53611388-53612470	-1.86	793	chr15:63149038-63151025	-2.04
94	chr1:53791181-53794416	-0.78	794	chr15:63568886-63570128	0.88
95	chr1:54006835-54008589	-1.57	795	chr15:64298365-64299690	-1.60
96	chr1:55266047-55267331	-2.09	796	chr15:65424697-65426732	0.73
97	chr1:56590376-56591276	-2.34	797	chr15:67812508-67814345	0.81
98	chr1:59049127-59051195	-1.90	798	chr15:70784496-70787293	-1.67
99	chr1:60138631-60141156	-1.87	799	chr15:71035317-71036759	-1.74
100	chr1:61105712-61106132	2.12	800	chr15:71389119-71389866	1.91
101	chr1:61946348-61947784	-2.61	801	chr15:72528974-72530582	-2.46
102	chr1:64127594-64129236	-3.17	802	chr15:74273900-74277396	-2.30
103	chr1:64412330-64413393	-1.85	803	chr15:74471649-74472918	-1.68
104	chr1:64434349-64435980	-1.87	804	chr15:74509619-74511456	-2.13
105	chr1:64637161-64638557	-1.81	805	chr15:74670681-74671772	-2.06
106	chr1:66747564-66748589	-1.94	806	chr15:74713677-74716028	-2.22
107	chr1:66760621-66761017	-1.61	807	chr15:75850291-75851830	-2.19
108	chr1:66902148-66902910	-1.75	808	chr15:75958813-75960164	-2.04
109	chr1:68213671-68217236	-1.65	809	chr15:79012020-79012744	2.58
110	chr1:68606408-68607977	-2.13	810	chr15:79449418-79452934	-1.71
111	chr1:77461632-77465283	-3.26	811	chr15:82090122-82090722	3.36
112	chr1:82144437-82145318	-1.61	812	chr15:83620844-83621841	0.91
113	chr1:84503266-84504607	-1.76	813	chr15:85455188-85459173	-1.22
114	chr1:85872633-85873893	-1.88	814	chr15:88020677-88021787	1.51
115	chr1:86983034-86983606	-1.93	815	chr15:89089205-89090165	1.19
116	chr1:89239008-89240927	-2.39	816	chr15:89565588-89567379	-2.30
117	chr1:89470349-89472050	-1.97	817	chr15:89740268-89742240	-1.96
118	chr1:89738313-89741794	-2.32	818	chr15:90046476-90047160	-1.34
119	chr1:89828690-89830051	-2.78	819	chr15:90056531-90059078	-1.78
120	chr1:90297926-90299493	-1.81	820	chr15:90754051-90756110	-1.70
121	chr1:90439074-90441086	-2.32	821	chr15:91382546-91383929	-2.32
122	chr1:92196925-92198418	-2.04	822	chr15:91998679-92000375	-1.99
123	chr1:92269267-92271233	-1.77	823	chr15:92104174-92105981	-2.46
124	chr1:92791729-92792605	-1.70	824	chr15:92409510-92411509	-2.42
125	chr1:92948229-92952953	-1.62	825	chr15:92490835-92492510	-2.02
126	chr1:94157905-94159948	-2.54	826	chr15:96417987-96419201	-1.61
127	chr1:94166774-94168563	-1.64	827	chr15:96564739-96566399	-2.03
128	chr1:94453153-94456350	-3.02	828	chr15:96775377-96777782	-1.97
129	chr1:94509577-94511676	-1.53	829	chr15:99104557-99106527	-2.14
130	chr1:94564228-94567475	-1.47	830	chr15:99523019-99524366	-2.14
131	chr1:94764968-94767254	-3.35	831	chr15:99706959-99711345	-2.53
132	chr1:95257574-95259201	-2.15	832	chr15:100154503-100155619	-1.77
133	chr1:95327947-95331053	-1.87	833	chr15:101252397-101255632	-2.07
134	chr1:96207895-96209395	-2.31	834	chr15:101260423-101263449	-1.50
135	chr1:97743710-97744301	-2.32	835	chr15:101400784-101403105	-2.60
136	chr1:98729273-98730137	-1.82	836	chr15:101418428-101422556	-1.18
137	chr1:98788913-98790216	-2.88	837	chr15:101608522-101611741	-2.05

Index	Genomic locus	log2(FC)	Index	Genomic locus	log2(FC)
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139	chr1:109262113-109264201	-1.96	839	chr16:500480-501535	1.66
140	chr1:110229998-110231159	-3.13	840	chr16:1002800-1004059	2.32
141	chr1:110415755-110417196	-2.81	841	chr16:1480279-1481571	1.44
142	chr1:110776533-110779347	-1.65	842	chr16:1844023-1845265	1.41
143	chr1:111644331-111645569	-1.66	843	chr16:1950177-1951123	1.47
144	chr1:112901758-112903795	-1.97	844	chr16:9184058-9186660	0.56
145	chr1:113606041-113607122	-2.11	845	chr16:11391149-11391750	1.58
146	chr1:113733890-113735135	-2.05	846	chr16:11427436-11427755	1.47
147	chr1:115152976-115154434	-2.26	847	chr16:12241263-12242465	-1.84
148	chr1:115604425-115606107	-1.97	848	chr16:12382817-12384075	1.52
149	chr1:115610156-115611862	-2.00	849	chr16:14463978-14465174	1.95
150	chr1:115655699-115658332	-1.51	850	chr16:17398054-17399932	1.44
151	chr1:115726636-115728168	-1.83	851	chr16:19118862-19119826	-1.51
152	chr1:115825954-115826763	-2.45	852	chr16:19342213-19342788	-1.77
153	chr1:115879981-115881170	-2.36	853	chr16:20009191-20009428	2.41
154	chr1:116087712-116089911	-1.96	854	chr16:20019303-20019435	1.88
155	chr1:117236017-117238283	-1.74	855	chr16:23156671-23157125	-2.27
156	chr1:117539057-117540744	-2.06	856	chr16:27337864-27339158	-1.68
157	chr1:145631147-145634597	-1.95	857	chr16:28191404-28193474	-2.25
158	chr1:147228344-147230871	-1.52	858	chr16:29196022-29197348	-2.52
159	chr1:149204472-149206172	1.16	859	chr16:29674234-29676332	-1.90
160	chr1:150033294-150034272	-2.08	860	chr16:48766660-48766995	2.03
161	chr1:151466555-151468718	-1.87	861	chr16:50587686-50588237	-1.91
162	chr1:151690194-151691270	1.49	862	chr16:50733407-50733757	-2.00
163	chr1:153328725-153331030	-1.94	863	chr16:54375920-54377250	-1.71
164	chr1:153462625-153464417	-2.12	864	chr16:54681454-54683653	-2.74
165	chr1:153520892-153522894	-1.47	865	chr16:55697995-55699747	-2.39
166	chr1:153525916-153527981	-1.82	866	chr16:55701633-55703032	-2.40
167	chr1:153536583-153541650	-1.27	867	chr16:55786283-55789314	-2.25
168	chr1:154165968-154167131	1.91	868	chr16:56553407-56554617	0.99
169	chr1:154404862-154406357	-1.46	869	chr16:57534476-57534821	1.60
170	chr1:155829401-155830824	-2.18	870	chr16:57927190-57928481	-2.36
171	chr1:155930686-155931797	-1.79	871	chr16:58065074-58067170	-1.82
172	chr1:156073316-156077226	1.07	872	chr16:66441893-66443209	-2.70
173	chr1:158979169-158981127	-2.36	873	chr16:66555140-66556317	-1.79
174	chr1:159045917-159047644	-2.59	874	chr16:66995700-66997585	-1.70
175	chr1:160377310-160378759	-1.79	875	chr16:68385748-68386383	1.47
176	chr1:162121987-162122459	2.05	876	chr16:68698702-68700575	-2.42
177	chr1:165345064-165346447	-2.10	877	chr16:69110971-69111774	-1.84
178	chr1:165868524-165870450	-1.46	878	chr16:69206646-69207562	-2.15
179	chr1:168172101-168174296	-1.82	879	chr16:69208007-69208669	-2.02
180	chr1:168248645-168248815	1.51	880	chr16:69547290-69549912	-3.55
181	chr1:171187266-171191076	-1.78	881	chr16:69563416-69565124	-2.34
182	chr1:171403464-171404761	-2.11	882	chr16:69646494-69648292	-2.52
183	chr1:175083621-175086338	-2.45	883	chr16:71416136-71418433	-2.26

Index	Genomic locus	log2(FC)	Index	Genomic locus	log2(FC)
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185	chr1:178087970-178089512	-1.99	885	chr16:74774621-74775568	-2.28
186	chr1:178095106-178096970	-2.29	886	chr16:75174453-75175384	-2.00
187	chr1:182838253-182839076	1.51	887	chr16:75226013-75228126	-2.25
188	chr1:183132049-183134979	-2.99	888	chr16:75516647-75518388	-1.99
189	chr1:183203160-183204850	-1.76	889	chr16:78211328-78212546	-1.51
190	chr1:183247629-183249471	-2.06	890	chr16:81440474-81441515	-2.99
191	chr1:183279375-183281113	-1.88	891	chr16:81586254-81587682	-1.88
192	chr1:183970959-183972739	-1.84	892	chr16:81860614-81861573	-2.12
193	chr1:186156098-186157855	-2.51	893	chr16:82172751-82173305	1.95
194	chr1:186587212-186588656	-1.93	894	chr16:84534893-84536417	-2.38
195	chr1:186649000-186650552	-2.21	895	chr16:84636647-84637608	-2.13
196	chr1:193198229-193198907	-1.95	896	chr16:85499727-85500140	1.71
197	chr1:196961023-196961613	1.29	897	chr16:86697649-86699153	-2.28
198	chr1:197589988-197590354	1.87	898	chr16:86749585-86751574	-2.34
199	chr1:197631771-197633050	1.74	899	chr16:86857486-86859834	-2.18
200	chr1:199727932-199728838	-2.48	900	chr16:87551003-87552837	-2.71
201	chr1:199997798-199999341	1.44	901	chr16:87738569-87738944	1.82
202	chr1:200608604-200610965	-2.96	902	chr16:88050593-88050864	1.89
203	chr1:201243496-201247077	-1.33	903	chr16:88363067-88363999	-2.05
204	chr1:202044534-202045550	1.59	904	chr16:88365468-88367740	-1.88
205	chr1:202091786-202092347	1.35	905	chr16:88576644-88577340	1.28
206	chr1:204531061-204531893	1.80	906	chr16:89648483-89652842	-1.68
207	chr1:205144207-205145564	-2.53	907	chr16:89830812-89832196	-2.52
208	chr1:205408835-205411431	-1.84	908	chr17:181158-183495	-2.21
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210	chr1:206686000-206687852	-1.92	910	chr17:1477970-1480881	-2.02
211	chr1:206707598-206709723	-2.08	911	chr17:1971258-1972627	-1.96
212	chr1:207179182-207182144	-2.39	912	chr17:2261379-2263763	-2.31
213	chr1:207192084-207198811	-1.52	913	chr17:2440758-2442236	-2.80
214	chr1:209560405-209561224	-2.49	914	chr17:2466590-2468742	-2.34
215	chr1:209583461-209585769	-2.09	915	chr17:2627205-2628553	-1.88
216	chr1:209940926-209943467	-2.13	916	chr17:3790715-3793928	-1.92
217	chr1:210013195-210013566	-1.94	917	chr17:4299172-4300834	-1.97
218	chr1:211789647-211790595	-1.62	918	chr17:4377630-4381002	-1.55
219	chr1:212380549-212383854	1.32	919	chr17:4850674-4854135	-0.80
220	chr1:214648867-214651277	-2.06	920	chr17:5487194-5488358	-2.12
221	chr1:214665954-214668358	-1.65	921	chr17:6409831-6411538	-2.96
222	chr1:218671440-218673614	-1.74	922	chr17:6658550-6660187	-2.38
223	chr1:218758268-218759797	-2.35	923	chr17:8311262-8312890	-2.80
224	chr1:218878440-218880375	-1.75	924	chr17:9989180-9990570	-2.02
225	chr1:219943407-219945238	-2.19	925	chr17:11181924-11183381	1.89
226	chr1:221198414-221200333	-2.51	926	chr17:14679207-14683351	-2.85
227	chr1:221208106-221210236	-1.71	927	chr17:15301523-15303361	-1.87
228	chr1:221569971-221571495	-1.97	928	chr17:15847900-15852087	-1.84
229	chr1:221611797-221614277	-3.41	929	chr17:15860652-15863458	-2.14

Index	Genomic locus	log2(FC)	Index	Genomic locus	log2(FC)
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231	chr1:223887622-223889303	-2.27	931	chr17:15930491-15931990	-2.58
232	chr1:224098897-224101055	-2.46	932	chr17:16189038-16190796	-2.44
233	chr1:224685326-224687027	-2.25	933	chr17:16917589-16919159	-2.19
234	chr1:224803682-224804443	1.44	934	chr17:16930650-16934632	-2.39
235	chr1:226004373-226006039	-1.42	935	chr17:16974325-16977374	-1.44
236	chr1:227993529-227994227	-2.23	936	chr17:17316183-17317848	-2.86
237	chr1:228122151-228123345	-1.47	937	chr17:17578461-17581047	-2.55
238	chr1:230239872-230241683	-1.46	938	chr17:17588158-17590156	-1.15
239	chr1:230340502-230341763	-2.02	939	chr17:17725768-17728836	-1.01
240	chr1:230442680-230444363	-1.54	940	chr17:17743073-17746083	-0.92
241	chr1:230593783-230596754	-3.33	941	chr17:17893334-17894862	-1.88
242	chr1:230653267-230654843	-2.08	942	chr17:19157544-19158617	1.46
243	chr1:230959455-230962546	-1.96	943	chr17:19967028-19968075	-1.80
244	chr1:230984513-230987520	-1.42	944	chr17:21187576-21191786	-0.82
245	chr1:234630559-234632321	-1.65	945	chr17:25798372-25799789	-1.94
246	chr1:234634641-234637724	-1.55	946	chr17:26550880-26551074	1.70
247	chr1:234666642-234670432	-1.79	947	chr17:27135283-27137216	-2.02
248	chr1:234878845-234880788	-1.78	948	chr17:28112553-28113769	2.40
249	chr1:234944561-234945881	-2.08	949	chr17:29421289-29422888	0.84
250	chr1:234951797-234954720	-2.96	950	chr17:29835508-29837032	1.89
251	chr1:235114620-235117495	-2.23	951	chr17:30877749-30879342	-2.38
252	chr1:235147243-235148807	-2.40	952	chr17:33047459-33050435	-2.83
253	chr1:236029302-236031043	0.78	953	chr17:33640745-33642494	-2.07
254	chr1:236071920-236074836	-1.64	954	chr17:35424793-35425916	2.15
255	chr1:236465024-236465604	1.48	955	chr17:35715049-35716753	1.00
256	chr1:238225078-238226871	-2.06	956	chr17:35848344-35851525	0.82
257	chr1:239055803-239056997	-1.77	957	chr17:36451621-36453895	1.44
258	chr1:239413700-239414113	-1.80	958	chr17:36477750-36478526	1.82
259	chr1:239977753-239978431	-1.37	959	chr17:36728180-36729870	1.90
260	chr1:239979644-239981036	-1.93	960	chr17:36886061-36887837	1.34
261	chr1:244516607-244518018	-1.60	961	chr17:36891582-36892434	2.24
262	chr10:407226-407713	1.89	962	chr17:36898003-36898974	1.71
263	chr10:482022-482669	2.18	963	chr17:36903396-36906455	1.31
264	chr10:988831-991146	-2.14	964	chr17:36955034-36956654	1.20
265	chr10:3137448-3138802	-1.81	965	chr17:37025129-37027459	1.29
266	chr10:3148757-3150227	-2.22	966	chr17:37033365-37034362	2.01
267	chr10:3268725-3271643	-2.29	967	chr17:37054722-37055739	1.57
268	chr10:3664953-3669086	-2.70	968	chr17:37183204-37184026	1.57
269	chr10:3676852-3679409	-4.47	969	chr17:37191948-37192524	1.59
270	chr10:3847656-3849476	-2.16	970	chr17:37493264-37494316	-2.40
271	chr10:3851573-3854636	-2.31	971	chr17:37689756-37692383	-2.96
272	chr10:3992013-3993092	-1.80	972	chr17:37709569-37710584	-2.63
273	chr10:4005129-4006624	-1.90	973	chr17:37752092-37753768	-3.09
274	chr10:4109293-4111822	-2.59	974	chr17:37779047-37784532	-2.30
275	chr10:4385961-4387886	-2.31	975	chr17:37787559-37789964	-2.71

Index	Genomic locus	log2(FC)	Index	Genomic locus	log2(FC)
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278	chr10:4719707-4721673	-2.07	978	chr17:39071100-39072995	-3.02
279	chr10:4727085-4729986	-2.72	979	chr17:39767549-39770196	-1.90
280	chr10:4982200-4984910	-3.00	980	chr17:39778350-39782489	-1.85
281	chr10:5061037-5064229	-3.78	981	chr17:40202002-40203014	1.08
282	chr10:5112084-5114525	-2.52	982	chr17:40560949-40562558	-2.19
283	chr10:5985463-5988323	-1.72	983	chr17:40670216-40672446	-1.28
284	chr10:6000319-6002216	-1.84	984	chr17:40779328-40780176	2.76
285	chr10:6316813-6318025	-2.05	985	chr17:40955375-40958119	2.06
286	chr10:6778338-6782900	-2.78	986	chr17:41977484-41978472	1.32
287	chr10:6820242-6823943	-2.41	987	chr17:42200333-42201750	0.80
288	chr10:8100136-8100974	1.59	988	chr17:42392161-42393215	1.34
289	chr10:8477000-8478090	-2.46	989	chr17:44929770-44930188	1.59
290	chr10:9017491-9018091	1.46	990	chr17:45144364-45144947	1.21
291	chr10:9110953-9111536	1.55	991	chr17:45959228-45963439	-1.23
292	chr10:9230649-9231287	1.60	992	chr17:46005062-46007241	-2.12
293	chr10:11593378-11595185	-2.15	993	chr17:46079417-46081182	-2.15
294	chr10:11923379-11925420	-1.97	994	chr17:46237931-46238454	2.02
295	chr10:12312333-12313722	-1.71	995	chr17:46506810-46508034	2.25
296	chr10:12328809-12330861	-2.42	996	chr17:46604290-46604767	2.07
297	chr10:13923814-13925285	-1.95	997	chr17:46606630-46607829	2.14
298	chr10:15078542-15080343	-2.25	998	chr17:46823246-46825301	2.24
299	chr10:16874111-16875333	-2.42	999	chr17:46833979-46835475	2.43
300	chr10:17007823-17010866	-2.31	1000	chr17:48543474-48544386	2.08
301	chr10:17103879-17106439	-3.13	1001	chr17:48862282-48863331	1.66
302	chr10:17257084-17259465	-3.89	1002	chr17:52977111-52979036	1.33
303	chr10:17270598-17273200	-1.43	1003	chr17:53315379-53316762	1.22
304	chr10:20209227-20211735	-2.61	1004	chr17:54187831-54188739	2.26
305	chr10:20658549-20660030	-2.49	1005	chr17:55975663-55977800	1.32
306	chr10:21001692-21003163	-2.07	1006	chr17:56295909-56297474	1.11
307	chr10:21371820-21373669	-1.70	1007	chr17:56412133-56414259	1.43
308	chr10:21423771-21425413	-1.96	1008	chr17:56468773-56469147	1.76
309	chr10:23112755-23113950	-1.81	1009	chr17:56736101-56737366	2.05
310	chr10:24716793-24717998	-2.20	1010	chr17:57297362-57298774	1.15
311	chr10:25350292-25352067	-2.46	1011	chr17:57407890-57410250	1.18
312	chr10:27069396-27071446	-1.95	1012	chr17:57642379-57643641	1.08
313	chr10:27608062-27609386	-1.97	1013	chr17:57696066-57698495	0.75
314	chr10:29947500-29948632	-1.56	1014	chr17:57969631-57971300	1.46
315	chr10:30046119-30047764	-2.37	1015	chr17:58602391-58604035	1.48
316	chr10:30091700-30095093	-1.75	1016	chr17:58703854-58704049	1.91
317	chr10:30115081-30117918	-2.04	1017	chr17:58754110-58755859	1.73
318	chr10:30246316-30248228	-1.70	1018	chr17:58964112-58965513	3.34
319	chr10:30288991-30290017	-1.68	1019	chr17:59433380-59434582	1.83
320	chr10:30470867-30472783	-2.16	1020	chr17:59476284-59478895	2.23
321	chr10:30508892-30511064	-1.98	1021	chr17:59527891-59528136	2.39

Index	Genomic locus	log2(FC)	Index	Genomic locus	log2(FC)
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324	chr10:33293561-33295221	-1.55	1024	chr17:62501191-62503690	0.96
325	chr10:33422580-33423890	-2.63	1025	chr17:63070825-63071212	1.54
326	chr10:33561361-33563656	-1.77	1026	chr17:64382613-64384066	-2.02
327	chr10:33622878-33626151	-1.95	1027	chr17:67497125-67498951	-2.43
328	chr10:33994921-33995288	-2.51	1028	chr17:69184611-69186154	-2.35
329	chr10:35736645-35738932	-1.36	1029	chr17:69970665-69972702	-2.90
330	chr10:35921943-35923279	-1.80	1030	chr17:70100001-70102180	-3.19
331	chr10:36083300-36085452	-2.36	1031	chr17:70116047-70120536	-1.21
332	chr10:37466912-37467815	2.21	1032	chr17:70406887-70410346	-2.52
333	chr10:44504008-44504567	-2.01	1033	chr17:70415768-70419828	-2.20
334	chr10:45430225-45431502	-1.78	1034	chr17:70598575-70601614	-2.39
335	chr10:45472933-45478109	-1.57	1035	chr17:70609698-70612458	-2.49
336	chr10:46992447-46994262	-1.44	1036	chr17:70626539-70629430	-2.79
337	chr10:47003829-47005485	-1.45	1037	chr17:70656895-70658402	-2.74
338	chr10:47056192-47058465	-1.93	1038	chr17:70711180-70714125	-2.86
339	chr10:48571452-48574909	-1.90	1039	chr17:71285303-71285636	1.55
340	chr10:61438544-61439654	-1.87	1040	chr17:71335832-71336854	-2.26
341	chr10:61750983-61752437	-1.70	1041	chr17:72939327-72940912	-2.23
342	chr10:62205479-62207534	-1.85	1042	chr17:73439666-73442295	-3.03
343	chr10:63580430-63582001	-1.96	1043	chr17:73679784-73681988	-3.03
344	chr10:65311871-65314640	-3.71	1044	chr17:73683938-73686027	-2.62
345	chr10:69853542-69854939	-2.23	1045	chr17:73864768-73866568	-2.08
346	chr10:70981721-70982985	-1.72	1046	chr17:73871723-73875015	-0.84
347	chr10:71701325-71703233	-1.91	1047	chr17:74049870-74050325	-1.89
348	chr10:72091216-72093051	-1.87	1048	chr17:74488536-74490087	-1.89
349	chr10:72689834-72692993	-2.18	1049	chr17:74815017-74817194	1.62
350	chr10:73053307-73054392	-1.57	1050	chr17:75120044-75124459	-2.29
351	chr10:73525586-73528526	-2.22	1051	chr17:75314696-75319897	-1.88
352	chr10:73723596-73726126	-1.50	1052	chr17:75388525-75392344	-2.19
353	chr10:73732574-73736401	-2.05	1053	chr17:76700136-76704186	-3.39
354	chr10:73768151-73770667	-1.91	1054	chr17:76871703-76872036	-1.83
355	chr10:74006972-74008963	-2.08	1055	chr17:76878699-76880900	-2.72
356	chr10:74068174-74071232	-1.52	1056	chr17:77020520-77024507	-2.03
357	chr10:74078665-74083663	-1.72	1057	chr17:77029553-77031516	-2.93
358	chr10:74435986-74437302	-2.09	1058	chr17:77033942-77035723	-3.26
359	chr10:75668819-75669657	-1.68	1059	chr17:77081497-77083783	-2.42
360	chr10:76052819-76054503	-1.90	1060	chr17:78059607-78060688	-2.15
361	chr10:79702456-79704898	-1.56	1061	chr17:78799657-78801988	-2.93
362	chr10:80515925-80518330	-2.00	1062	chr17:78829587-78831287	-2.09
363	chr10:82726460-82727639	2.98	1063	chr17:79030952-79031242	1.35
364	chr10:88545274-88547682	-1.90	1064	chr17:79392984-79395086	-2.22
365	chr10:88842149-88844210	-2.10	1065	chr17:79395124-79397857	-2.52
366	chr10:89394445-89396953	-1.59	1066	chr17:79934538-79936611	0.67
367	chr10:92980058-92981345	1.01	1067	chr17:79961195-79962582	-2.13

Index	Genomic locus	log2(FC)	Index	Genomic locus	log2(FC)
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370	chr10:97153905-97154860	-2.33	1070	chr18:2111254-2112888	-1.95
371	chr10:97168218-97169813	-2.50	1071	chr18:2166852-2170282	-2.49
372	chr10:98828942-98830455	-2.09	1072	chr18:2291983-2294352	-1.77
373	chr10:99628209-99629772	1.17	1073	chr18:2905729-2907302	-1.69
374	chr10:103878858-103881105	0.83	1074	chr18:2978572-2980762	-2.49
375	chr10:104401732-104406173	0.71	1075	chr18:3036704-3038820	-1.42
376	chr10:105504243-105508575	-1.77	1076	chr18:3349283-3351643	-2.32
377	chr10:105629900-105632604	-2.13	1077	chr18:3411544-3413075	-1.61
378	chr10:106087496-106091152	-2.34	1078	chr18:3592346-3596970	-1.03
379	chr10:112095486-112097080	-1.99	1079	chr18:3602305-3605781	-1.73
380	chr10:112582398-112583926	1.99	1080	chr18:3622318-3625654	-2.27
381	chr10:114135166-114136657	-2.00	1081	chr18:3652554-3653544	-3.02
382	chr10:114750746-114753437	-2.07	1082	chr18:5628401-5630657	-1.87
383	chr10:115470578-115471642	-1.80	1083	chr18:6413898-6415391	-3.26
384	chr10:118922402-118923114	1.44	1084	chr18:6728877-6730138	-2.13
385	chr10:121074224-121078193	-1.88	1085	chr18:7038162-7038998	-1.89
386	chr10:122918124-122918567	-1.74	1086	chr18:7921519-7923461	-2.68
387	chr10:124066972-124068757	-2.04	1087	chr18:9016675-9018148	-2.90
388	chr10:126210016-126211645	-1.58	1088	chr18:9657719-9659057	-1.99
389	chr10:126696199-126698400	-2.10	1089	chr18:9672816-9674150	-1.71
390	chr10:126875142-126876498	-1.88	1090	chr18:9741829-9744183	-1.45
391	chr10:126896876-126899013	-2.12	1091	chr18:9823928-9829411	-1.56
392	chr10:126919490-126921302	-2.00	1092	chr18:11856547-11857851	-3.32
393	chr10:126953245-126954420	-1.80	1093	chr18:11859242-11860461	-2.82
394	chr10:127750660-127752347	-1.70	1094	chr18:11946284-11948225	-2.00
395	chr10:128127287-128129723	-3.01	1095	chr18:12005157-12006682	-2.52
396	chr10:128148660-128149395	-1.77	1096	chr18:12015048-12016529	-1.98
397	chr10:130972410-130973805	-2.04	1097	chr18:13387117-13390569	-2.20
398	chr10:134177860-134178347	-2.24	1098	chr18:13487219-13488444	-1.56
399	chr11:318212-321382	-1.56	1099	chr18:14785019-14786968	2.57
400	chr11:459658-461522	-2.51	1100	chr18:14974161-14975805	-1.98
401	chr11:704825-711484	-1.00	1101	chr18:19248897-19250371	-1.85
402	chr11:727186-729466	-1.60	1102	chr18:19971953-19972202	-1.77
403	chr11:2554254-2555993	-2.31	1103	chr18:20130897-20132599	-1.82
404	chr11:2799302-2801674	-1.98	1104	chr18:21441362-21443369	-2.32
405	chr11:3190333-3194017	-2.26	1105	chr18:22343412-22345559	-2.22
406	chr11:3924565-3927510	-2.96	1106	chr18:24059151-24060522	-2.06
407	chr11:6340263-6343136	-4.16	1107	chr18:24061100-24061680	-1.85
408	chr11:8753100-8755602	-1.73	1108	chr18:28620554-28623201	-2.29
409	chr11:8853647-8855364	-1.86	1109	chr18:28810192-28811537	-1.65
410	chr11:8860710-8862626	-2.02	1110	chr18:29089641-29093932	-2.31
411	chr11:9738121-9742245	-2.23	1111	chr18:41921311-41922561	-1.65
412	chr11:10615212-10616610	-1.96	1112	chr18:43900703-43903216	-2.27
413	chr11:12107800-12108762	-1.97	1113	chr18:47606060-47607994	-1.92

Index	Genomic locus	log2(FC)	Index	Genomic locus	log2(FC)
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416	chr11:12244144-12246800	-1.84	1116	chr18:55442952-55443979	-2.02
417	chr11:12308527-12310698	-1.70	1117	chr18:56084066-56085621	-2.13
418	chr11:12451854-12453300	-2.15	1118	chr18:56208424-56209105	-1.82
419	chr11:13237211-13238745	-2.92	1119	chr18:56234363-56235735	-2.08
420	chr11:13281800-13283773	-2.09	1120	chr18:57720465-57721765	-2.06
421	chr11:14865927-14866344	2.06	1121	chr18:60892838-60893668	2.34
422	chr11:15836888-15838988	-2.35	1122	chr18:60925299-60927864	2.92
423	chr11:15997285-15999356	-3.16	1123	chr18:61013080-61014429	-1.92
424	chr11:16902431-16903463	-2.01	1124	chr18:61094381-61094773	-2.85
425	chr11:18267033-18268908	-2.30	1125	chr18:68025085-68025703	-1.48
426	chr11:19049590-19050274	-1.72	1126	chr18:72191276-72192433	-1.81
427	chr11:19100686-19102935	-2.99	1127	chr18:72518131-72519609	-2.22
428	chr11:19401780-19403191	-2.01	1128	chr18:74398605-74400156	2.31
429	chr11:19462925-19464562	-1.89	1129	chr18:74569064-74569646	1.57
430	chr11:20077526-20078172	-1.96	1130	chr18:74789799-74791367	-3.31
431	chr11:20132668-20134739	-1.35	1131	chr18:74812178-74814338	-3.64
432	chr11:33710680-33714793	-2.60	1132	chr18:76822375-76823216	1.50
433	chr11:33716086-33717283	-2.32	1133	chr18:77244742-77246695	-2.16
434	chr11:34255499-34256885	-1.99	1134	chr18:77326219-77328468	-2.61
435	chr11:34793478-34797248	-2.07	1135	chr18:77346946-77350164	-2.39
436	chr11:35030386-35032034	-2.64	1136	chr19:373580-374839	2.09
437	chr11:35109239-35111554	-1.85	1137	chr19:1131121-1133428	-1.66
438	chr11:35165408-35165972	-1.98	1138	chr19:3335418-3335585	1.35
439	chr11:35402255-35402464	2.41	1139	chr19:3336619-3337723	1.10
440	chr11:36476560-36478577	-1.97	1140	chr19:4130703-4132303	-2.23
441	chr11:37927188-37930073	-2.76	1141	chr19:4976076-4976536	1.86
442	chr11:38406089-38407003	-2.00	1142	chr19:8488005-8489543	-1.53
443	chr11:44386158-44388332	-1.99	1143	chr19:11128116-11130762	-1.91
444	chr11:45167652-45169414	1.05	1144	chr19:12977958-12978929	-1.87
445	chr11:57192090-57195727	-1.83	1145	chr19:13119807-13126591	-3.95
446	chr11:58955999-58957597	-1.83	1146	chr19:13134913-13138277	-4.28
447	chr11:60425483-60426368	2.14	1147	chr19:13164315-13166929	-2.97
448	chr11:61588098-61590165	-2.38	1148	chr19:13317804-13319444	-3.78
449	chr11:64774118-64775512	-1.96	1149	chr19:13845841-13846414	-1.92
450	chr11:65558668-65561208	-1.22	1150	chr19:13897935-13899160	-3.32
451	chr11:65666497-65668509	-1.24	1151	chr19:14136351-14137280	-2.25
452	chr11:65682566-65683975	-3.00	1152	chr19:14895581-14897580	-2.30
453	chr11:66153602-66154053	1.55	1153	chr19:15219923-15221344	-2.01
454	chr11:66738168-66739604	-3.19	1154	chr19:15228551-15229696	-2.32
455	chr11:67350305-67352398	-1.47	1155	chr19:15358638-15363001	-1.90
456	chr11:67722486-67723398	1.46	1156	chr19:15939025-15941023	-2.43
457	chr11:67885691-67890563	0.81	1157	chr19:16619777-16621400	-2.27
458	chr11:67979919-67982387	1.31	1158	chr19:16636657-16639331	-2.03
459	chr11:68093668-68096545	-2.45	1159	chr19:16828855-16831248	-1.87

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462	chr11:68713663-68714596	1.85	1162	chr19:23731928-23733537	-2.16
463	chr11:68923526-68925794	-2.12	1163	chr19:28350157-28351888	-2.76
464	chr11:68933580-68936891	-1.80	1164	chr19:31154994-31155169	2.57
465	chr11:68967652-68968372	-2.06	1165	chr19:31704831-31705801	-1.79
466	chr11:70004903-70008019	-1.72	1166	chr19:32063053-32064529	2.25
467	chr11:70650589-70652922	2.44	1167	chr19:35485756-35486255	1.33
468	chr11:71143893-71146498	-1.93	1168	chr19:35581172-35582515	-1.63
469	chr11:71420907-71422526	-2.45	1169	chr19:35644517-35647774	-2.10
470	chr11:71976851-71978419	-2.77	1170	chr19:36094823-36096597	-2.64
471	chr11:72898107-72898391	1.84	1171	chr19:39173362-39177337	-1.10
472	chr11:73239465-73240216	-2.09	1172	chr19:39209212-39213815	-2.03
473	chr11:73362254-73364269	-2.24	1173	chr19:40420840-40422352	-2.23
474	chr11:74316426-74317090	1.93	1174	chr19:40729391-40731429	-2.06
475	chr11:75976270-75978479	-2.07	1175	chr19:41309322-41310140	1.11
476	chr11:76287846-76290117	-2.43	1176	chr19:41426748-41427829	1.43
477	chr11:76557623-76557881	2.02	1177	chr19:44156073-44156577	1.82
478	chr11:77010098-77011472	-2.09	1178	chr19:44178698-44180643	-1.63
479	chr11:77749497-77752383	-1.28	1179	chr19:46225073-46226249	-1.87
480	chr11:82931057-82931812	-1.81	1180	chr19:46245731-46246457	2.09
481	chr11:85826962-85828389	-2.69	1181	chr19:46696176-46696480	-1.57
482	chr11:85861982-85863966	-2.09	1182	chr19:47267653-47269041	-2.38
483	chr11:93275405-93277014	-1.06	1183	chr19:47835041-47835727	2.08
484	chr11:94156342-94157522	-1.88	1184	chr19:49178986-49181288	-2.47
485	chr11:94479571-94482653	-2.78	1185	chr19:49428164-49428704	-1.77
486	chr11:95770037-95772616	-2.79	1186	chr19:49429274-49431285	-2.26
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488	chr11:95830465-95833293	-2.25	1188	chr19:50030654-50032256	-3.20
489	chr11:95867506-95868596	-2.07	1189	chr19:51574893-51575188	1.32
490	chr11:95888029-95889723	-2.88	1190	chr19:55700143-55701356	-1.61
491	chr11:95961040-95962732	-2.44	1191	chr2:628027-629314	-1.87
492	chr11:96039558-96041282	-2.46	1192	chr2:634000-635259	-2.87
493	chr11:96047208-96048997	-2.70	1193	chr2:1711511-1713416	-1.78
494	chr11:96074108-96076365	-1.81	1194	chr2:1719392-1721744	-3.23
495	chr11:96122248-96123944	-1.41	1195	chr2:1724943-1726492	-3.67
496	chr11:100356615-100357973	-1.80	1196	chr2:2664649-2668324	-1.75
497	chr11:100554838-100555948	-1.96	1197	chr2:3226310-3228397	1.86
498	chr11:102176384-102177632	-2.17	1198	chr2:3285921-3288909	-2.06
499	chr11:102358195-102359940	-1.83	1199	chr2:3583148-3584484	-3.15
500	chr11:102422724-102423519	-2.73	1200	chr2:5181638-5184647	-2.39
501	chr11:102434438-102435578	-1.93	1201	chr2:7005127-7006632	-1.63
502	chr11:104321922-104323919	-2.06	1202	chr2:7912124-7915535	-3.63
503	chr11:104915357-104916455	-1.90	1203	chr2:8816279-8820661	-0.91
504	chr11:108486683-108488507	-1.85	1204	chr2:9132864-9134636	-2.44
505	chr11:112270868-112271968	-1.76	1205	chr2:9210971-9212047	-1.73

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508	chr11:113560347-113561992	-1.97	1208	chr2:9389153-9392705	-1.41
509	chr11:118294601-118296143	-2.18	1209	chr2:9455306-9457078	-2.12
510	chr11:119288271-119290212	-2.20	1210	chr2:9526081-9527506	-2.38
511	chr11:119442900-119444616	-2.18	1211	chr2:9815361-9816551	-1.82
512	chr11:120002729-120003709	-1.72	1212	chr2:9878867-9880106	-2.15
513	chr11:120017641-120019138	-2.35	1213	chr2:9892993-9894746	-1.85
514	chr11:121228150-121230742	-2.49	1214	chr2:9940482-9942903	-1.88
515	chr11:122027046-122030199	-2.59	1215	chr2:10037758-10038407	-1.77
516	chr11:122673673-122676072	-2.48	1216	chr2:10152878-10156710	-1.72
517	chr11:125727283-125727741	1.59	1217	chr2:10259960-10263387	-0.74
518	chr11:126000379-126003050	-1.90	1218	chr2:10654275-10655702	-2.02
519	chr11:126455404-126456718	-2.33	1219	chr2:10880676-10882042	-1.69
520	chr11:126461410-126463818	-2.30	1220	chr2:11261998-11262882	1.99
521	chr11:128077296-128079049	-3.13	1221	chr2:11622669-11623984	1.46
522	chr11:128318176-128319717	-2.87	1222	chr2:11638614-11640257	1.81
523	chr11:128336932-128338352	-2.14	1223	chr2:11671066-11671310	2.22
524	chr11:128366081-128368049	-2.82	1224	chr2:11714036-11714939	1.58
525	chr11:128376742-128378305	-2.10	1225	chr2:11836592-11838014	-1.48
526	chr11:128391314-128393517	-2.54	1226	chr2:11872178-11874019	-2.58
527	chr11:129012995-129014588	-2.25	1227	chr2:12727288-12728962	-2.42
528	chr11:129481325-129482864	-2.42	1228	chr2:12994123-12994736	-2.12
529	chr11:130058179-130060765	-1.67	1229	chr2:13024791-13025456	-1.90
530	chr11:130404900-130406435	2.11	1230	chr2:17622337-17623419	-2.47
531	chr11:130450033-130451808	-2.60	1231	chr2:17801388-17802745	-1.85
532	chr11:133903721-133905109	1.44	1232	chr2:17996530-17998340	-2.44
533	chr11:134338078-134338781	1.73	1233	chr2:19330195-19331814	-2.25
534	chr12:1582163-1584271	-2.23	1234	chr2:19556196-19558704	-1.77
535	chr12:2734009-2734626	1.86	1235	chr2:19877693-19878396	-1.70
536	chr12:2903439-2905859	0.97	1236	chr2:20342409-20345915	-1.42
537	chr12:6054011-6054941	1.45	1237	chr2:20383708-20388227	-1.22
538	chr12:9216873-9218241	1.05	1238	chr2:20411850-20413027	-1.26
539	chr12:11948225-11949616	-2.14	1239	chr2:20422303-20425798	-1.02
540	chr12:11964708-11966706	-1.79	1240	chr2:23891611-23893754	-1.57
541	chr12:12111371-12112717	-1.63	1241	chr2:26562022-26562979	-2.11
542	chr12:12161600-12164488	-1.82	1242	chr2:27244015-27245132	-1.94
543	chr12:12955243-12958280	-1.54	1243	chr2:27668107-27670059	-2.35
544	chr12:12987772-12990697	-1.89	1244	chr2:27903901-27906194	-3.13
545	chr12:13250258-13252181	-1.59	1245	chr2:28021611-28023489	-2.98
546	chr12:13317134-13320241	-1.91	1246	chr2:28806622-28807878	-2.05
547	chr12:13324282-13327118	-2.95	1247	chr2:28836065-28837924	-2.17
548	chr12:13331802-13332939	-2.20	1248	chr2:28866331-28867633	-2.13
549	chr12:14719870-14721711	-1.38	1249	chr2:28871806-28873242	-2.39
550	chr12:15815136-15816680	-2.14	1250	chr2:29287580-29290764	-2.23
551	chr12:18958596-18958771	1.74	1251	chr2:29345944-29346666	-2.43

Index	Genomic locus	log2(FC)	Index	Genomic locus	log2(FC)
552	chr12:19318447-19318781	1.75	1252	chr2:30495754-30498168	-2.04
553	chr12:21367562-21368215	2.66	1253	chr2:31606507-31608694	-3.74
554	chr12:21572145-21572590	1.60	1254	chr2:31637048-31639968	-1.92
555	chr12:22464307-22467142	-2.22	1255	chr2:37178895-37181051	-1.83
556	chr12:26451663-26452596	-1.82	1256	chr2:37603107-37604488	-2.02
557	chr12:28210744-28211620	-1.80	1257	chr2:37616692-37618571	-1.65
558	chr12:28763658-28765226	-1.82	1258	chr2:37788657-37789704	-1.93
559	chr12:28913192-28913597	1.72	1259	chr2:37890874-37891591	-1.93
560	chr12:31868133-31868715	1.84	1260	chr2:38002044-38003982	-1.92
561	chr12:34278666-34279780	-1.92	1261	chr2:38029199-38031025	-1.39
562	chr12:40285969-40286253	1.65	1262	chr2:38081941-38083550	-2.14
563	chr12:43024604-43026999	-2.05	1263	chr2:38405488-38406816	-1.98
564	chr12:47301998-47303186	-2.50	1264	chr2:38947702-38949524	-1.51
565	chr12:47664333-47666987	-2.85	1265	chr2:39738098-39739625	-1.50
566	chr12:49297211-49298297	1.77	1266	chr2:39774293-39775809	-2.11
567	chr12:49581086-49583429	1.35	1267	chr2:42086815-42087640	-2.46
568	chr12:49740915-49742290	1.74	1268	chr2:42192314-42195588	-2.43
569	chr12:50478332-50480059	0.98	1269	chr2:42443200-42444667	-1.76
570	chr12:51399325-51400131	1.65	1270	chr2:43181217-43182546	-2.14
571	chr12:52316009-52317412	-1.86	1271	chr2:43258965-43261082	-2.41
572	chr12:52679841-52682742	-1.88	1272	chr2:43265055-43269803	-1.89
573	chr12:52834820-52836998	-2.20	1273	chr2:43283390-43284680	-1.87
574	chr12:52885582-52887605	-3.15	1274	chr2:43300739-43303433	-1.58
575	chr12:52889135-52890845	-2.98	1275	chr2:43313055-43314666	-2.80
576	chr12:57359907-57360226	1.93	1276	chr2:43327695-43328872	-2.58
577	chr12:58148675-58150073	0.95	1277	chr2:43360536-43361856	-1.40
578	chr12:58817828-58820501	-2.01	1278	chr2:43384578-43388038	-2.04
579	chr12:59159553-59160406	2.20	1279	chr2:43411235-43413235	-2.14
580	chr12:62860010-62861375	0.68	1280	chr2:43451494-43455184	-0.92
581	chr12:64173444-64174574	0.82	1281	chr2:43746625-43748936	-2.38
582	chr12:64797463-64800101	0.69	1282	chr2:44496559-44498015	-1.89
583	chr12:64845434-64846994	0.79	1283	chr2:45179089-45180636	-1.78
584	chr12:65152496-65154351	1.10	1284	chr2:45509667-45512071	-2.70
585	chr12:65173973-65175761	1.12	1285	chr2:45685361-45687087	-1.51
586	chr12:65562677-65564631	0.68	1286	chr2:46078043-46079575	-1.51
587	chr12:69002795-69006306	0.84	1287	chr2:46190970-46191482	-1.63
588	chr12:69632903-69634430	0.68	1288	chr2:46390370-46392375	-1.42
589	chr12:70381400-70383348	-2.18	1289	chr2:46523751-46527185	-0.91
590	chr12:70406868-70407497	1.82	1290	chr2:46557268-46559007	-2.12
591	chr12:72240535-72240662	1.97	1291	chr2:47006837-47009795	-2.27
592	chr12:74902763-74903348	1.86	1292	chr2:47073848-47075192	-1.49
593	chr12:76371112-76373189	-1.37	1293	chr2:47076776-47078425	-2.69
594	chr12:76713446-76713925	1.55	1294	chr2:47082061-47084090	-2.52
595	chr12:80871304-80871782	2.73	1295	chr2:47496689-47496968	-1.72
596	chr12:81330360-81331446	1.50	1296	chr2:48338089-48339704	-1.23
597	chr12:83028325-83028996	1.31	1297	chr2:48474822-48477893	-1.96

Index	Genomic locus	log2(FC)	Index	Genomic locus	log2(FC)
598	chr12:83325186-83326255	1.84	1298	chr2:53160084-53162665	-3.18
599	chr12:85711777-85712795	2.30	1299	chr2:54175747-54178524	-2.43
600	chr12:88874343-88875123	1.56	1300	chr2:54270096-54272109	-2.77
601	chr12:90101393-90104041	0.61	1301	chr2:54758264-54761331	-2.02
602	chr12:93322245-93324028	0.67	1302	chr2:54826105-54827733	-2.33
603	chr12:93549428-93550899	1.74	1303	chr2:54900157-54901949	-3.53
604	chr12:93561715-93562730	2.09	1304	chr2:54925483-54926562	-2.53
605	chr12:95049550-95050845	-1.57	1305	chr2:55130650-55132467	-1.83
606	chr12:96182968-96185366	-1.15	1306	chr2:55380703-55382049	-2.00
607	chr12:96199623-96200903	-1.84	1307	chr2:58334742-58335841	-2.71
608	chr12:96709539-96710467	1.62	1308	chr2:60440307-60444060	-1.58
609	chr12:96792892-96795045	0.71	1309	chr2:60512699-60514615	-1.91
610	chr12:106677562-106679108	-1.67	1310	chr2:60533239-60533985	-1.69
611	chr12:109089793-109091114	-2.19	1311	chr2:60704887-60707550	-3.04
612	chr12:109231606-109234075	-2.51	1312	chr2:60776215-60782712	-2.31
613	chr12:113579478-113581014	-1.76	1313	chr2:60829793-60831486	-2.06
614	chr12:113859819-113860904	1.13	1314	chr2:62637950-62639343	-1.53
615	chr12:115812680-115814208	-2.41	1315	chr2:62804515-62807155	-3.43
616	chr12:116737003-116738251	1.60	1316	chr2:62856905-62857893	-2.09
617	chr12:116827221-116828733	1.20	1317	chr2:64097197-64098950	-2.04
618	chr12:116962778-116964458	-1.83	1318	chr2:64437546-64438957	-1.95
619	chr12:118296787-118296968	2.19	1319	chr2:64586759-64587708	-1.52
620	chr12:119613880-119614499	2.04	1320	chr2:64588496-64590547	-1.61
621	chr12:122016931-122019376	0.84	1321	chr2:64630810-64632185	-1.83
622	chr12:122186008-122187084	1.47	1322	chr2:65064396-65066645	-1.87
623	chr12:122237280-122239449	0.77	1323	chr2:65084771-65087771	-1.01
624	chr12:124716396-124717316	1.92	1324	chr2:65258418-65260368	-2.28
625	chr12:125105358-125106947	-1.67	1325	chr2:65526224-65527791	1.47
626	chr12:127609739-127612143	-2.58	1326	chr2:65955142-65957040	-2.70
627	chr12:131912644-131914456	1.83	1327	chr2:66149645-66150533	-1.88
628	chr12:132378855-132381606	0.78	1328	chr2:66801963-66804300	-1.63
629	chr12:132694510-132695289	1.65	1329	chr2:67115759-67116835	-1.99
630	chr13:21606791-21610177	-2.33	1330	chr2:67516531-67518370	-2.21
631	chr13:22572454-22574087	-2.02	1331	chr2:68201306-68202971	-2.21
632	chr13:24612182-24614693	-2.35	1332	chr2:69001583-69003420	-2.27
633	chr13:31384265-31385187	-1.92	1333	chr2:69033631-69035355	-2.30
634	chr13:31406643-31408571	-1.69	1334	chr2:69365408-69366573	-2.05
635	chr13:34184433-34186602	-1.80	1335	chr2:69920397-69922058	-1.71
636	chr13:34371169-34373088	-1.72	1336	chr2:70024825-70026825	-2.00
637	chr13:38230488-38231468	-2.26	1337	chr2:70172129-70174432	-2.07
638	chr13:38882688-38884104	-2.08	1338	chr2:70716124-70716449	1.53
639	chr13:41026403-41028281	-1.93	1339	chr2:70734111-70737572	-2.69
640	chr13:42600420-42602423	-1.97	1340	chr2:71203756-71206258	-1.79
641	chr13:43565821-43567047	-2.28	1341	chr2:71329002-71331478	-1.77
642	chr13:45630013-45631082	-1.72	1342	chr2:72161447-72163626	-2.41
643	chr13:45780646-45782243	-1.93	1343	chr2:75658818-75660708	-2.59

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645	chr13:46963661-46964701	-2.24	1345	chr2:84179431-84181540	-2.10
646	chr13:48409594-48410695	-1.84	1346	chr2:85145718-85147904	-2.12
647	chr13:51251911-51253486	-2.37	1347	chr2:85172657-85174269	-2.02
648	chr13:52569375-52570922	1.45	1348	chr2:85514666-85516183	-2.48
649	chr13:67230358-67232012	-1.78	1349	chr2:88381083-88383790	-2.41
650	chr13:72286971-72287380	1.68	1350	chr2:95905591-95906898	-2.25
651	chr13:73663899-73665470	-2.29	1351	chr2:97151308-97152640	-2.37
652	chr13:73783820-73785115	-1.91	1352	chr2:97641856-97643799	-2.83
653	chr13:73908325-73911943	-2.08	1353	chr2:98380852-98383239	-2.19
654	chr13:77491633-77492626	-1.82	1354	chr2:99377880-99378688	-1.88
655	chr13:80163363-80164633	-2.19	1355	chr2:101396145-101397452	-1.91
656	chr13:80510145-80511995	-2.13	1356	chr2:101677073-101682100	-2.35
657	chr13:102105710-102107455	-1.78	1357	chr2:101740437-101742878	-1.79
658	chr13:103934957-103935867	-2.64	1358	chr2:102246705-102248118	-2.07
659	chr13:104758441-104760158	-2.04	1359	chr2:102608242-102609161	-1.94
660	chr13:106570886-106572760	-2.22	1360	chr2:105488892-105490062	1.47
661	chr13:106752504-106753550	-1.83	1361	chr2:106533861-106536521	-2.03
662	chr13:107123827-107125665	-1.91	1362	chr2:106759562-106760664	-1.50
663	chr13:109806923-109809529	-2.46	1363	chr2:109559681-109561637	-1.97
664	chr13:109916774-109919059	-3.46	1364	chr2:109588236-109589301	-1.71
665	chr13:110657807-110659243	-1.99	1365	chr2:109858084-109860294	-2.01
666	chr13:110778206-110779719	-3.15	1366	chr2:110858152-110861802	-2.60
667	chr13:110998888-111000724	-2.15	1367	chr2:110871500-110874700	-1.53
668	chr13:111039733-111042016	-2.09	1368	chr2:112374285-112376455	-1.59
669	chr13:111560162-111561412	-1.87	1369	chr2:112741040-112742145	-1.70
670	chr13:111606780-111608294	-2.23	1370	chr2:113384784-113385143	-1.56
671	chr13:111616610-111618561	-2.56	1371	chr2:113997688-113999923	-1.96
672	chr13:112101945-112103942	-2.34	1372	chr2:114040480-114042499	-1.81
673	chr13:113375010-113377150	-1.88	1373	chr2:114734796-114736981	-1.82
674	chr13:113840687-113841767	-2.00	1374	chr2:118980949-118983167	-3.63
675	chr13:114523703-114525358	-1.91	1375	chr2:119067017-119068931	-2.80
676	chr13:114599903-114601337	-1.78	1376	chr2:119563657-119566263	-2.38
677	chr14:21183011-21184639	-2.90	1377	chr2:119581248-119583091	-2.16
678	chr14:22025011-22026661	1.45	1378	chr2:119590105-119594088	-2.45
679	chr14:23082388-23084177	-1.79	1379	chr2:119597898-119601083	-3.02
680	chr14:24100861-24101153	-1.76	1380	chr2:119602237-119606322	-2.00
681	chr14:25064126-25065502	-1.77	1381	chr2:119728496-119730088	-2.16
682	chr14:27148043-27148781	1.86	1382	chr2:119738824-119740412	-2.72
683	chr14:31159526-31160509	2.19	1383	chr2:119745158-119748701	-1.96
684	chr14:31712791-31714247	-1.80	1384	chr2:120301775-120302668	1.11
685	chr14:31961483-31962800	-1.32	1385	chr2:121932297-121933802	-2.41
686	chr14:36789082-36790359	1.09	1386	chr2:121953180-121955608	-2.19
687	chr14:45366402-45367345	0.88	1387	chr2:122456527-122458420	-1.64
688	chr14:50159543-50160617	1.14	1388	chr2:127821506-127823661	-1.50
689	chr14:50697670-50699004	0.95	1389	chr2:127974739-127978008	-2.31

Index	Genomic locus	log2(FC)	Index	Genomic locus	log2(FC)
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691	chr14:50862273-50864502	-0.97	1391	chr2:128394603-128398286	-1.45
692	chr14:51133792-51135474	0.78	1392	chr2:129103790-129106164	-1.94
693	chr14:51848563-51850031	-1.71	1393	chr2:129152549-129154496	-3.28
694	chr14:53018486-53020962	0.82	1394	chr2:129163590-129163851	-1.67
695	chr14:53196504-53197977	1.18	1395	chr2:129182549-129184066	-2.48
696	chr14:55543590-55545761	-2.32	1396	chr2:129577565-129579890	-2.14
697	chr14:58666208-58667599	0.77	1397	chr2:130058758-130060227	-1.96
698	chr14:58763879-58766632	0.79	1398	chr2:130737162-130737738	1.86
699	chr14:59112982-59113786	2.10	1399	chr2:131085269-131086473	-2.14
700	chr14:60043022-60043525	1.62	1400	chr2:131564898-131566769	-2.54

Index	Genomic locus	log2(FC)	Index	Genomic locus	log2(FC)
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1402	chr2:131584751-131587223	-1.88	2102	chr5:142024230-142025350	-1.88
1403	chr2:131639233-131640153	-1.61	2103	chr5:142224696-142226293	-2.31
1404	chr2:133195069-133197737	-1.74	2104	chr5:142250367-142250972	-1.74
1405	chr2:134976095-134979604	-2.13	2105	chr5:142622600-142625447	-2.46
1406	chr2:136823143-136825921	-1.97	2106	chr5:143301978-143303811	-2.20
1407	chr2:137084727-137085297	1.55	2107	chr5:146783434-146784464	-1.76
1408	chr2:142943015-142944077	-2.28	2108	chr5:148169813-148171675	-2.38
1409	chr2:143569662-143569821	1.74	2109	chr5:148329517-148330275	-1.87
1410	chr2:145114922-145116865	-2.15	2110	chr5:148441425-148444208	-2.13
1411	chr2:145417096-145418821	-1.79	2111	chr5:148452762-148455296	-2.26
1412	chr2:145708009-145709689	-2.07	2112	chr5:148532919-148534045	1.62
1413	chr2:148122066-148123345	-1.66	2113	chr5:149851959-149854006	-1.66
1414	chr2:148127202-148127454	1.62	2114	chr5:150420826-150422706	-1.68
1415	chr2:149371260-149373290	-2.44	2115	chr5:150462711-150466692	-1.95
1416	chr2:151335290-151336518	-1.69	2116	chr5:150473272-150474027	-1.89
1417	chr2:152560977-152561375	1.79	2117	chr5:150969173-150971309	-1.83
1418	chr2:153191194-153193379	-0.96	2118	chr5:154070663-154072171	-1.68
1419	chr2:153277423-153278929	-2.20	2119	chr5:159252634-159254552	-1.65
1420	chr2:158113917-158115304	-2.23	2120	chr5:159868541-159871088	-1.91
1421	chr2:158687330-158688350	-1.63	2121	chr5:167379472-167381007	1.75
1422	chr2:161063618-161065350	-1.18	2122	chr5:169382094-169384895	-2.44
1423	chr2:161503535-161505807	-1.58	2123	chr5:169577820-169580408	-1.74
1424	chr2:161522395-161523741	-2.93	2124	chr5:170171350-170174121	-1.11
1425	chr2:163100965-163103040	-2.09	2125	chr5:170177512-170179914	-1.66
1426	chr2:165117985-165118301	1.39	2126	chr5:170877448-170878924	-2.42
1427	chr2:165753412-165754128	-1.60	2127	chr5:171597654-171598995	-2.26
1428	chr2:172947343-172948202	-2.02	2128	chr5:171788153-171789880	-2.33
1429	chr2:172949055-172952113	-1.30	2129	chr5:172158214-172161280	-1.74
1430	chr2:172959099-172962128	-1.65	2130	chr5:172167580-172168854	-2.70
1431	chr2:173095391-173100387	-1.87	2131	chr5:172246565-172247948	-1.53
1432	chr2:173116925-173118968	-1.70	2132	chr5:180212353-180214136	-1.73
1433	chr2:173306380-173307515	-1.68	2133	chr6:224293-225845	-1.87
1434	chr2:173700791-173702164	-1.81	2134	chr6:1286638-1288124	-2.66
1435	chr2:174855348-174857408	-1.57	2135	chr6:1324196-1326549	-2.11
1436	chr2:177354506-177355939	-1.92	2136	chr6:1525507-1527886	-1.94
1437	chr2:178106276-178110973	-1.39	2137	chr6:1574237-1577765	-2.28
1438	chr2:178115473-178118226	-1.90	2138	chr6:1593609-1595030	-2.06
1439	chr2:178256916-178258129	-1.47	2139	chr6:1604400-1606051	-1.76
1440	chr2:178261691-178262854	-1.77	2140	chr6:1609404-1612196	-1.78
1441	chr2:182257966-182259071	-2.05	2141	chr6:1613971-1615764	-3.06
1442	chr2:183237012-183238109	-2.06	2142	chr6:1619801-1620827	-2.40
1443	chr2:186447357-186448480	-1.84	2143	chr6:1624274-1625835	-2.63
1444	chr2:191044857-191045864	-1.52	2144	chr6:1670771-1671807	-1.70
1445	chr2:191501586-191503037	-1.81	2145	chr6:1685872-1686466	-2.67

Index	Genomic locus	log2(FC)	Index	Genomic locus	log2(FC)
1446	chr2:192502051-192503535	-1.59	2146	chr6:1702314-1704615	-2.16
1447	chr2:192606356-192607610	-2.66	2147	chr6:1724143-1725905	-1.92
1448	chr2:192711194-192712231	-1.87	2148	chr6:1952750-1953813	-2.69
1449	chr2:201170673-201172495	-1.29	2149	chr6:2432740-2435190	-2.95
1450	chr2:201269824-201272286	-1.96	2150	chr6:2578038-2580291	-2.55
1451	chr2:202860056-202862687	-2.18	2151	chr6:2588879-2591355	-2.33
1452	chr2:203113569-203115015	-2.00	2152	chr6:2631588-2635263	-1.82
1453	chr2:206549199-206551663	-1.71	2153	chr6:2817828-2819377	-2.36
1454	chr2:206567464-206569365	-1.93	2154	chr6:3205717-3206838	-1.84
1455	chr2:208199007-208200417	-3.62	2155	chr6:3389705-3391012	-2.35
1456	chr2:208258925-208260447	-2.48	2156	chr6:3750415-3752937	-1.31
1457	chr2:214859764-214861418	-1.81	2157	chr6:3795731-3798762	-2.16
1458	chr2:216846708-216846993	1.66	2158	chr6:3803595-3805212	-1.87
1459	chr2:217497969-217499180	1.30	2159	chr6:3808899-3809595	-1.68
1460	chr2:218474723-218476289	1.48	2160	chr6:3825026-3827036	-1.53
1461	chr2:218521023-218521181	1.81	2161	chr6:4351702-4352866	-2.26
1462	chr2:219581605-219582723	-1.88	2162	chr6:6694546-6695866	-2.06
1463	chr2:219609112-219611341	-3.27	2163	chr6:6758797-6760185	1.93
1464	chr2:220109757-220110862	0.82	2164	chr6:6803247-6804895	-2.24
1465	chr2:220315933-220319116	-2.67	2165	chr6:6810613-6812400	-2.36
1466	chr2:221524808-221526004	-2.18	2166	chr6:6820570-6821877	-2.08
1467	chr2:221988940-221989998	-1.74	2167	chr6:7691405-7692907	-2.45
1468	chr2:225084862-225086969	-1.74	2168	chr6:10403528-10405810	-0.77
1469	chr2:227049669-227050675	-2.46	2169	chr6:10441148-10442811	-2.26
1470	chr2:228271164-228272390	-1.74	2170	chr6:10450697-10453140	-2.52
1471	chr2:228277744-228282147	-1.69	2171	chr6:10522167-10525109	-2.37
1472	chr2:228735634-228736733	-2.55	2172	chr6:10733949-10735052	-1.74
1473	chr2:230309310-230311175	-2.72	2173	chr6:11206713-11208219	-1.78
1474	chr2:230492365-230493068	-1.69	2174	chr6:11609418-11610319	-1.93
1475	chr2:231206573-231207203	3.50	2175	chr6:11632062-11634672	-2.34
1476	chr2:232259848-232262584	-1.54	2176	chr6:11770224-11772478	-3.09
1477	chr2:233165331-233166504	1.65	2177	chr6:13397175-13399222	-2.89
1478	chr2:233179831-233181337	-1.91	2178	chr6:13406103-13408660	-2.52
1479	chr2:233435699-233436779	-2.45	2179	chr6:13511176-13512811	-2.07
1480	chr2:233852196-233854066	-1.80	2180	chr6:13678021-13679083	2.32
1481	chr2:234322176-234324581	-1.72	2181	chr6:13724199-13726641	-1.51
1482	chr2:234607439-234609052	-2.21	2182	chr6:17101722-17103136	1.55
1483	chr2:234881030-234884205	-2.92	2183	chr6:17389442-17390581	1.47
1484	chr2:235872318-235873649	-1.39	2184	chr6:17740981-17742528	-1.73
1485	chr2:236662801-236663963	1.63	2185	chr6:17864137-17866736	-2.45
1486	chr2:236986546-236987869	-1.40	2186	chr6:17907353-17908827	-2.27
1487	chr2:237721638-237722832	1.83	2187	chr6:17993162-17994485	-2.56
1488	chr2:238263162-238264741	-2.21	2188	chr6:18346742-18348724	-1.88
1489	chr2:238421746-238421977	1.44	2189	chr6:19756947-19759635	-1.91
1490	chr2:239896003-239897068	-2.11	2190	chr6:20689017-20689519	-1.68
1491	chr20:1396488-1397293	-1.64	2191	chr6:21033602-21034581	-2.21

Index	Genomic locus	log2(FC)	Index	Genomic locus	log2(FC)
1492	chr20:1458523-1460014	-3.47	2192	chr6:21219788-21221181	-2.01
1493	chr20:1480145-1482005	-2.31	2193	chr6:21507847-21509713	-2.39
1494	chr20:2245234-2245779	1.90	2194	chr6:22892405-22893103	-1.84
1495	chr20:2310506-2311506	1.79	2195	chr6:24357660-24358732	1.59
1496	chr20:4017818-4019155	-1.68	2196	chr6:24743251-24744345	-2.50
1497	chr20:4021871-4022945	-2.03	2197	chr6:26016317-26018346	-3.05
1498	chr20:4593027-4596578	-2.77	2198	chr6:27099067-27102758	-1.04
1499	chr20:4899912-4900467	-1.80	2199	chr6:29730773-29731885	-1.86
1500	chr20:5045997-5047311	-2.44	2200	chr6:30495389-30496332	-2.26
1501	chr20:5295809-5298077	-2.17	2201	chr6:30731524-30732165	-1.84
1502	chr20:5335001-5336656	-2.24	2202	chr6:30802973-30804528	-1.81
1503	chr20:5344217-5345491	-2.54	2203	chr6:31153179-31155438	-2.95
1504	chr20:5627396-5628684	-3.04	2204	chr6:31275552-31276724	2.12
1505	chr20:6688329-6689922	-2.22	2205	chr6:31441476-31443116	-2.45
1506	chr20:7783972-7784789	-2.16	2206	chr6:31912715-31914353	-1.74
1507	chr20:10308779-10310060	-1.90	2207	chr6:32787065-32788441	-1.74
1508	chr20:10647270-10648255	-1.91	2208	chr6:33557619-33559435	-1.39
1509	chr20:11432431-11433097	-1.93	2209	chr6:33636077-33637829	-1.92
1510	chr20:11771960-11773594	-2.01	2210	chr6:34211626-34212896	-1.14
1511	chr20:13227706-13228506	-1.77	2211	chr6:36965089-36967337	-2.37
1512	chr20:16542976-16543276	1.79	2212	chr6:36991787-36993891	-2.22
1513	chr20:17702511-17702824	1.48	2213	chr6:37136866-37139518	-1.00
1514	chr20:17829822-17831140	-2.17	2214	chr6:37207576-37208258	-1.65
1515	chr20:17836265-17838223	-2.09	2215	chr6:37209885-37211274	-2.10
1516	chr20:18232503-18234210	-3.44	2216	chr6:37284968-37289629	-3.21
1517	chr20:19255850-19257353	1.79	2217	chr6:37597889-37599050	-2.32
1518	chr20:24898921-24899093	1.53	2218	chr6:39383742-39385393	-2.01
1519	chr20:24985979-24987293	2.28	2219	chr6:41397608-41398799	-2.26
1520	chr20:30147079-30150367	-1.60	2220	chr6:41604306-41605722	-1.77
1521	chr20:30190552-30194911	-1.28	2221	chr6:41679278-41682567	-1.63
1522	chr20:32375736-32379087	-1.03	2222	chr6:41690951-41692112	-1.85
1523	chr20:32902138-32903797	-1.84	2223	chr6:43088134-43090847	-2.07
1524	chr20:33539397-33540432	-1.91	2224	chr6:43878704-43880867	1.25
1525	chr20:33780043-33780681	2.09	2225	chr6:44008983-44011400	-1.29
1526	chr20:33893111-33894389	-1.71	2226	chr6:45557491-45559289	-2.31
1527	chr20:36771473-36773619	-2.38	2227	chr6:47073944-47075219	-1.96
1528	chr20:37054560-37054722	1.59	2228	chr6:47709432-47710271	-1.82
1529	chr20:37062399-37063985	-0.85	2229	chr6:48118410-48119675	-1.64
1530	chr20:37416550-37419199	-2.23	2230	chr6:48792931-48795647	-2.92
1531	chr20:37560561-37562123	-3.11	2231	chr6:52202272-52203513	-2.16
1532	chr20:39636850-39637343	-1.90	2232	chr6:53480022-53482154	-2.27
1533	chr20:39994918-39995685	-1.89	2233	chr6:53492318-53494326	-2.46
1534	chr20:42295262-42296774	-1.00	2234	chr6:53599529-53600311	-1.97
1535	chr20:42780048-42780772	-2.12	2235	chr6:53617242-53618749	-2.30
1536	chr20:42930785-42931221	2.01	2236	chr6:54355428-54357355	-2.47
1537	chr20:43123553-43125704	-2.49	2237	chr6:55732060-55734974	-2.11

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1538	chr20:43229436-43231342	-1.75	2238	chr6:74159715-74162285	-2.12
1539	chr20:44406740-44409474	-1.54	2239	chr6:74289076-74290989	-1.15
1540	chr20:44411773-44413653	-1.99	2240	chr6:82603266-82606085	-2.15
1541	chr20:44539367-44541179	-1.99	2241	chr6:82647245-82649886	-2.31
1542	chr20:45592055-45594777	-1.83	2242	chr6:82853678-82855175	-2.08
1543	chr20:45760867-45763138	-2.10	2243	chr6:85472089-85474780	-2.28
1544	chr20:45949966-45950817	1.52	2244	chr6:85481677-85484806	-2.93
1545	chr20:46060252-46061954	-2.20	2245	chr6:85901731-85903308	-2.52
1546	chr20:46092970-46094338	2.07	2246	chr6:86071513-86071689	-1.99
1547	chr20:47481295-47481719	2.42	2247	chr6:86170419-86172241	-2.46
1548	chr20:47961485-47962944	-2.57	2248	chr6:89744537-89746438	-2.33
1549	chr20:48183993-48185540	-1.92	2249	chr6:90006267-90009154	-2.69
1550	chr20:48236658-48238194	-2.07	2250	chr6:91594606-91595949	-1.74
1551	chr20:48247241-48248599	-1.66	2251	chr6:100911726-100913687	-2.60
1552	chr20:48313658-48313990	-1.86	2252	chr6:104609558-104611186	-2.02
1553	chr20:48341164-48342259	-2.28	2253	chr6:105875572-105877184	-2.19
1554	chr20:48363636-48365176	-1.90	2254	chr6:106048702-106050107	-3.12
1555	chr20:48719881-48721133	-1.96	2255	chr6:106227791-106229983	-3.31
1556	chr20:48780093-48780941	-1.64	2256	chr6:106442006-106443138	-1.78
1557	chr20:48859089-48861287	-1.54	2257	chr6:106607193-106608966	-2.38
1558	chr20:48882508-48885078	-2.34	2258	chr6:106993354-106995578	-1.64
1559	chr20:48924985-48926723	-1.22	2259	chr6:107187063-107189281	-2.32
1560	chr20:48936602-48938924	-1.67	2260	chr6:107305949-107309304	-1.70
1561	chr20:48954519-48956806	-1.87	2261	chr6:112619333-112621134	-2.54
1562	chr20:48961759-48964178	-1.75	2262	chr6:113951162-113953700	-2.71
1563	chr20:49055691-49058284	-2.36	2263	chr6:116203296-116204999	-2.32
1564	chr20:49464963-49466132	-2.01	2264	chr6:116362724-116363938	-1.66
1565	chr20:50005292-50007891	-2.61	2265	chr6:117488625-117489846	-2.68
1566	chr20:50039614-50042506	-2.67	2266	chr6:125444665-125446088	-1.69
1567	chr20:50067651-50067806	1.44	2267	chr6:125746195-125747846	-2.63
1568	chr20:50103602-50105085	-1.98	2268	chr6:126091194-126092472	-1.56
1569	chr20:50450102-50450414	1.76	2269	chr6:126239538-126242767	-2.37
1570	chr20:50601724-50602580	-1.89	2270	chr6:127686973-127688410	-2.25
1571	chr20:52402885-52404271	1.68	2271	chr6:128829714-128831403	-1.67
1572	chr20:52486064-52487075	1.61	2272	chr6:128899964-128902012	-3.29
1573	chr20:52748220-52751346	-2.05	2273	chr6:129811278-129813583	-3.26
1574	chr20:52824307-52825409	1.21	2274	chr6:129822242-129823225	-1.72
1575	chr20:55310137-55310728	1.77	2275	chr6:130837680-130839985	-3.47
1576	chr20:56592245-56593924	-2.28	2276	chr6:131374640-131376407	-1.92
1577	chr20:56628927-56630446	1.49	2277	chr6:134354800-134358989	-2.74
1578	chr20:57088659-57090318	-1.96	2278	chr6:134438699-134438930	1.97
1579	chr20:57997252-57999463	-2.15	2279	chr6:134756958-134758760	-2.46
1580	chr20:60640531-60642283	1.34	2280	chr6:135229423-135231032	-2.37
1581	chr20:60871865-60873249	-2.06	2281	chr6:137554287-137555770	-3.10
1582	chr20:61296798-61299090	-1.87	2282	chr6:138187381-138189362	-1.14
1583	chr20:61402579-61405512	-2.27	2283	chr6:138427029-138430585	-0.96

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1586	chr20:62688095-62689264	-1.81	2286	chr6:145243487-145245599	-2.07
1587	chr20:62762218-62764789	1.82	2287	chr6:147234977-147236953	-2.69
1588	chr21:17497194-17498715	-2.24	2288	chr6:150175247-150176979	-1.52
1589	chr21:17959122-17961164	-1.67	2289	chr6:150461913-150465398	-1.64
1590	chr21:18882619-18886134	-1.32	2290	chr6:150576702-150578959	-2.59
1591	chr21:18983282-18985695	-1.65	2291	chr6:150617400-150619403	-2.24
1592	chr21:19060781-19064206	-1.98	2292	chr6:150697677-150698940	-2.14
1593	chr21:19113506-19115233	-2.81	2293	chr6:150811256-150812593	-2.10
1594	chr21:19272393-19275092	-2.37	2294	chr6:150813715-150815170	-2.46
1595	chr21:19301938-19303490	-1.98	2295	chr6:151177955-151179832	-2.50
1596	chr21:22397528-22397747	2.21	2296	chr6:151814719-151816209	1.82
1597	chr21:22429807-22430275	2.03	2297	chr6:151954896-151955153	1.97
1598	chr21:32726196-32727541	-2.17	2298	chr6:151989554-151990813	1.79
1599	chr21:32738584-32739693	-1.59	2299	chr6:152011215-152012918	2.32
1600	chr21:32873838-32875103	-1.60	2300	chr6:152433945-152435454	-1.76
1601	chr21:33736583-33737466	-1.95	2301	chr6:154704462-154706672	-2.05
1602	chr21:33783755-33786211	-0.95	2302	chr6:157273613-157275279	-1.87
1603	chr21:33822732-33824814	-2.87	2303	chr6:157469742-157470114	-1.86
1604	chr21:33944779-33945936	-1.81	2304	chr6:157625668-157626879	-2.28
1605	chr21:34751865-34753982	-1.34	2305	chr6:157637098-157639465	-2.00
1606	chr21:34755052-34756078	-1.74	2306	chr6:158437931-158441357	-1.98
1607	chr21:35347965-35349566	-2.95	2307	chr6:158447101-158448485	-1.97
1608	chr21:35947607-35949399	-2.57	2308	chr6:159458929-159461110	-2.34
1609	chr21:36179564-36181281	-2.07	2309	chr6:159998139-160000541	-3.40
1610	chr21:36258287-36263670	-0.71	2310	chr6:160015142-160017164	-3.02
1611	chr21:36457705-36459708	-1.94	2311	chr6:160209469-160212432	-0.71
1612	chr21:37109911-37111472	-2.52	2312	chr6:161694314-161695819	-2.11
1613	chr21:37749068-37750505	-1.83	2313	chr6:161789717-161791158	-1.76
1614	chr21:38090626-38092069	-2.41	2314	chr6:161854798-161857435	-2.18
1615	chr21:38571197-38573411	-1.89	2315	chr6:163647476-163648787	-1.66
1616	chr21:38578984-38581822	-1.84	2316	chr6:166352710-166355235	-2.64
1617	chr21:39037174-39038945	-2.49	2317	chr6:166670566-166672768	-2.09
1618	chr21:40138395-40141787	-3.38	2318	chr6:167031860-167034634	-1.92
1619	chr21:40165623-40168071	-2.43	2319	chr6:168082901-168084497	-2.18
1620	chr21:40377534-40379177	-1.74	2320	chr6:168435765-168439594	-1.61
1621	chr21:40823571-40825147	1.85	2321	chr6:168789250-168790195	2.15
1622	chr21:42518858-42520538	-1.94	2322	chr6:168791376-168792078	1.84
1623	chr21:42542747-42543275	-2.38	2323	chr6:169531008-169532960	-2.41
1624	chr21:43032454-43036951	-3.18	2324	chr6:169639131-169642284	-2.22
1625	chr21:43054296-43055753	-2.04	2325	chr7:88602-89836	-1.67
1626	chr21:43145906-43148385	-1.46	2326	chr7:293488-294371	1.86
1627	chr21:43183937-43184602	-1.90	2327	chr7:643574-645062	-2.07
1628	chr21:43513359-43515380	-2.42	2328	chr7:680680-680898	1.69
1629	chr21:43653404-43655570	1.16	2329	chr7:689859-691248	-1.69

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1630	chr21:43735305-43735925	1.69	2330	chr7:869827-872413	-2.01
1631	chr21:44580673-44583620	-2.46	2331	chr7:2057517-2060349	-1.81
1632	chr21:44726323-44727874	-2.19	2332	chr7:2145014-2147396	-1.95
1633	chr21:44833669-44835301	-1.63	2333	chr7:2263690-2266116	-2.97
1634	chr21:44860340-44861752	-3.02	2334	chr7:2288668-2289456	-1.87
1635	chr21:44865443-44867858	-2.83	2335	chr7:2656116-2657597	-2.29
1636	chr21:44896359-44898944	-1.46	2336	chr7:2679461-2681833	-1.81
1637	chr21:44913250-44915271	-1.82	2337	chr7:2701302-2703825	-1.88
1638	chr21:44998647-44998823	1.62	2338	chr7:2796113-2798568	-1.95
1639	chr21:45176240-45179549	-3.41	2339	chr7:2860217-2862081	-2.07
1640	chr21:45202887-45203211	-1.59	2340	chr7:3220764-3222354	-2.25
1641	chr21:45604546-45605718	-1.74	2341	chr7:4652665-4653822	-1.93
1642	chr21:46336470-46338793	-2.93	2342	chr7:4707059-4708608	-2.21
1643	chr21:46783237-46785745	-1.94	2343	chr7:5567476-5573041	-1.01
1644	chr21:47187495-47190773	-1.71	2344	chr7:5631837-5636269	-1.14
1645	chr21:47300138-47300911	-1.76	2345	chr7:5646029-5648625	-1.90
1646	chr21:47413932-47417290	-1.57	2346	chr7:6116535-6117381	-2.30
1647	chr22:17491477-17494600	-3.12	2347	chr7:6322110-6324979	-2.08
1648	chr22:18055901-18057430	-1.90	2348	chr7:6483120-6484050	-2.14
1649	chr22:18262556-18265128	-1.92	2349	chr7:6669769-6670332	1.56
1650	chr22:18514018-18516298	-2.56	2350	chr7:12105404-12107245	-2.60
1651	chr22:19738609-19739171	1.37	2351	chr7:12341856-12343210	-1.90
1652	chr22:20777215-20779305	-1.78	2352	chr7:16523840-16525592	-2.08
1653	chr22:22191026-22192651	-1.99	2353	chr7:16829281-16830120	2.21
1654	chr22:22296202-22297377	-2.08	2354	chr7:17273383-17274930	-2.22
1655	chr22:22315564-22316726	-1.71	2355	chr7:17409918-17412140	-3.14
1656	chr22:23533996-23535560	1.61	2356	chr7:17447869-17448543	-1.58
1657	chr22:23623413-23625329	-1.78	2357	chr7:17563391-17564851	-2.41
1658	chr22:24677798-24679168	-2.01	2358	chr7:17701617-17702895	-1.79
1659	chr22:25338408-25339803	-2.38	2359	chr7:18547749-18549862	-4.27
1660	chr22:25371896-25374262	-1.74	2360	chr7:18885394-18886750	1.81
1661	chr22:25763629-25764349	-2.00	2361	chr7:19997524-19998937	-1.97
1662	chr22:26865981-26869046	-2.57	2362	chr7:20146815-20147900	-2.05
1663	chr22:28113800-28115714	-1.81	2363	chr7:20244895-20246310	-1.82
1664	chr22:28216658-28218099	-3.46	2364	chr7:20380819-20381939	-2.84
1665	chr22:28408356-28410503	-1.89	2365	chr7:20391076-20393240	-2.62
1666	chr22:28837998-28839495	-2.32	2366	chr7:22611594-22613175	-1.82
1667	chr22:30591387-30593697	-2.00	2367	chr7:23282649-23283534	-1.71
1668	chr22:30605725-30606942	-1.84	2368	chr7:24113619-24115247	-2.19
1669	chr22:32076330-32077085	-1.85	2369	chr7:24860628-24861940	-1.87
1670	chr22:35918983-35919785	1.59	2370	chr7:26137036-26137886	-2.12
1671	chr22:36006853-36009325	-2.27	2371	chr7:27152778-27154015	-1.88
1672	chr22:36726754-36729772	-1.43	2372	chr7:27716886-27719106	-2.65
1673	chr22:37701981-37704528	-2.84	2373	chr7:27737512-27738198	-1.72
1674	chr22:37921191-37922763	-2.89	2374	chr7:29246845-29248865	-1.93
1675	chr22:37940355-37943242	-1.40	2375	chr7:30209151-30209465	-1.58

Index	Genomic locus	log2(FC)	Index	Genomic locus	log2(FC)
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1677	chr22:38294079-38295543	-2.05	2377	chr7:30898721-30900811	-1.74
1678	chr22:38392307-38395751	-1.84	2378	chr7:30954592-30955223	-1.97
1679	chr22:38429416-38431295	-1.89	2379	chr7:31013618-31014993	-1.85
1680	chr22:38434236-38436616	-3.38	2380	chr7:32132023-32134084	-2.24
1681	chr22:38484418-38485614	-1.83	2381	chr7:32708416-32710502	-1.55
1682	chr22:38694342-38697331	-2.86	2382	chr7:33025996-33029241	-1.77
1683	chr22:39070386-39071479	-1.97	2383	chr7:34075460-34077279	1.61
1684	chr22:39381364-39381844	-1.75	2384	chr7:36158118-36160386	-1.77
1685	chr22:39388865-39389629	-2.10	2385	chr7:40961145-40963660	-1.76
1686	chr22:39409819-39411044	-2.33	2386	chr7:43607562-43609561	-2.70
1687	chr22:39442835-39443632	-1.95	2387	chr7:43687007-43691590	-2.34
1688	chr22:39649459-39651793	-1.22	2388	chr7:43911922-43913059	-3.19
1689	chr22:39823898-39826974	-2.58	2389	chr7:44677266-44681136	-1.36
1690	chr22:40342303-40344909	-2.88	2390	chr7:44749664-44751700	-1.80
1691	chr22:41047396-41049514	-1.09	2391	chr7:44932960-44934692	-1.72
1692	chr22:41577339-41579237	-1.88	2392	chr7:44999507-45002984	-1.44
1693	chr22:42417857-42419466	-2.08	2393	chr7:46017006-46020075	-1.27
1694	chr22:42712681-42715290	-2.78	2394	chr7:46255006-46256695	-2.74
1695	chr22:42751552-42754408	-1.87	2395	chr7:46258857-46260652	-2.95
1696	chr22:42835954-42837490	-2.05	2396	chr7:46329988-46331766	-2.38
1697	chr22:43003225-43006162	-3.91	2397	chr7:46690808-46692324	-3.32
1698	chr22:43072498-43073364	-1.94	2398	chr7:47823218-47823682	-1.76
1699	chr22:43083808-43085531	-1.59	2399	chr7:47825830-47827522	-1.56
1700	chr22:43522397-43525082	-2.01	2400	chr7:50580671-50582100	-2.06
1701	chr22:43547264-43549047	-0.75	2401	chr7:51711524-51712061	-1.73
1702	chr22:44433673-44434074	-1.77	2402	chr7:53670436-53672364	-2.41
1703	chr22:44704273-44705486	-2.64	2403	chr7:54881168-54881818	-2.13
1704	chr22:44758840-44760017	-2.24	2404	chr7:54891023-54893390	-2.12
1705	chr22:44946225-44947909	-2.43	2405	chr7:54898396-54899673	-2.07
1706	chr22:44982250-44983489	-2.16	2406	chr7:55013739-55015363	-3.00
1707	chr22:44994842-44995780	-1.63	2407	chr7:55034148-55036037	-2.42
1708	chr22:45593957-45594416	1.73	2408	chr7:55053242-55054148	-2.22
1709	chr22:45993233-45994004	2.28	2409	chr7:55086121-55089053	-2.08
1710	chr22:46402455-46404522	-2.63	2410	chr7:55120321-55122514	-3.30
1711	chr22:46457123-46458104	-3.09	2411	chr7:55132997-55134712	-2.38
1712	chr22:46480714-46482203	-1.73	2412	chr7:55140902-55142147	-2.21
1713	chr22:46566703-46568695	-3.02	2413	chr7:55153644-55154656	-2.76
1714	chr22:47187015-47190050	-2.49	2414	chr7:55195550-55195984	-2.16
1715	chr22:49097989-49100751	-2.22	2415	chr7:55200168-55202233	-3.84
1716	chr22:50976705-50978644	-2.28	2416	chr7:55766395-55769016	-2.29
1717	chr22:51143612-51144458	-1.94	2417	chr7:67161416-67162714	-1.97
1718	chr3:4515800-4517103	-1.71	2418	chr7:69642948-69644945	-2.11
1719	chr3:4777951-4778651	-1.94	2419	chr7:70064251-70065427	-2.74
1720	chr3:5036234-5037814	-1.59	2420	chr7:70193418-70195385	-1.66
1721	chr3:9245901-9246228	1.77	2421	chr7:72837644-72839099	-2.11

Index	Genomic locus	log2(FC)	Index	Genomic locus	log2(FC)
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1723	chr3:10230963-10231285	-1.72	2423	chr7:73506986-73509338	-1.92
1724	chr3:11177756-11179527	-2.70	2424	chr7:73512463-73513184	-1.96
1725	chr3:11195926-11196448	-1.87	2425	chr7:73517571-73519648	-2.28
1726	chr3:11266590-11268450	-2.57	2426	chr7:73726634-73728378	-1.34
1727	chr3:11330249-11331161	-2.85	2427	chr7:75935821-75937097	1.24
1728	chr3:11609387-11610953	-2.05	2428	chr7:75939605-75940300	1.01
1729	chr3:11679686-11681426	-2.19	2429	chr7:76052409-76053732	-1.98
1730	chr3:13605354-13608063	-1.95	2430	chr7:80351541-80353474	-2.58
1731	chr3:14058052-14061543	-2.30	2431	chr7:80789432-80791436	-2.41
1732	chr3:16105465-16107121	-1.79	2432	chr7:84041506-84042143	-1.99
1733	chr3:16142602-16144032	-2.81	2433	chr7:87920563-87921739	-1.77
1734	chr3:17780900-17781870	-2.37	2434	chr7:89808021-89808225	-1.97
1735	chr3:17902406-17902857	2.73	2435	chr7:92346356-92348434	-1.55
1736	chr3:23709838-23710201	-1.90	2436	chr7:92438566-92439781	-1.42
1737	chr3:25468955-25473076	-2.06	2437	chr7:92462046-92466458	-1.37
1738	chr3:27574683-27576998	-1.76	2438	chr7:94330035-94332810	-1.85
1739	chr3:30730196-30731182	-2.40	2439	chr7:95763799-95767231	-2.00
1740	chr3:31315960-31317619	-1.75	2440	chr7:97760987-97761482	-1.62
1741	chr3:36738298-36740645	-1.75	2441	chr7:97792367-97794132	-2.64
1742	chr3:37238606-37240330	-1.64	2442	chr7:97914473-97915689	-1.48
1743	chr3:37532702-37535455	-2.18	2443	chr7:98759725-98761317	-2.09
1744	chr3:37636605-37637627	1.60	2444	chr7:98797729-98799912	-3.05
1745	chr3:37694105-37696032	-2.36	2445	chr7:98864717-98866820	-2.32
1746	chr3:38070749-38073680	-1.64	2446	chr7:99050277-99051049	-1.50
1747	chr3:38192628-38196723	-1.86	2447	chr7:99540626-99543806	-3.44
1748	chr3:38337355-38339230	-1.90	2448	chr7:99570156-99574782	-1.71
1749	chr3:40841019-40842368	-2.54	2449	chr7:101241138-101242836	-1.84
1750	chr3:41158001-41160087	-1.82	2450	chr7:102515814-102516895	-1.69
1751	chr3:43256374-43256714	1.57	2451	chr7:106065473-106066293	-1.97
1752	chr3:43458549-43458986	1.81	2452	chr7:106377139-106377811	-1.60
1753	chr3:44924849-44928784	-1.68	2453	chr7:106463663-106465534	-2.14
1754	chr3:52079061-52081716	-2.02	2454	chr7:114870883-114871982	-1.82
1755	chr3:52096361-52097686	-1.93	2455	chr7:115994336-115997653	-1.70
1756	chr3:52229584-52230617	-1.75	2456	chr7:116164697-116166993	-1.52
1757	chr3:52704064-52705556	-2.50	2457	chr7:116292632-116293840	-1.81
1758	chr3:53143010-53144640	-1.88	2458	chr7:117287587-117289052	-1.74
1759	chr3:58983815-58985375	-2.02	2459	chr7:120383208-120383925	-1.79
1760	chr3:63121988-63122313	1.80	2460	chr7:123262908-123263885	1.81
1761	chr3:64962524-64963868	-2.77	2461	chr7:129471594-129472192	-2.10
1762	chr3:65131177-65132929	-2.28	2462	chr7:129933067-129933760	-1.81
1763	chr3:65929957-65932240	-1.82	2463	chr7:129939179-129940474	-1.79
1764	chr3:72201876-72202437	1.46	2464	chr7:130002842-130004155	-1.84
1765	chr3:73560281-73561986	-2.35	2465	chr7:130594511-130598949	-2.57
1766	chr3:77886837-77887106	1.39	2466	chr7:130605680-130607614	-2.52
1767	chr3:78991014-78991636	-1.96	2467	chr7:130643441-130646694	-2.98

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1769	chr3:89678168-89679005	1.48	2469	chr7:131222784-131227017	-1.82
1770	chr3:97589802-97591979	-2.32	2470	chr7:134211824-134213686	-1.64
1771	chr3:98450942-98452688	-1.84	2471	chr7:134233698-134234522	-2.76
1772	chr3:99396559-99397450	-2.03	2472	chr7:134860967-134863549	-2.13
1773	chr3:100754453-100756107	-1.73	2473	chr7:134937959-134939778	-1.58
1774	chr3:105120179-105122131	-2.28	2474	chr7:138435407-138438553	-2.36
1775	chr3:105684330-105686098	-2.03	2475	chr7:138549658-138550759	-2.07
1776	chr3:105716023-105717712	-1.61	2476	chr7:139615757-139616707	-2.29
1777	chr3:106935679-106936149	-2.66	2477	chr7:141373125-141375258	-2.99
1778	chr3:107590419-107590953	-1.78	2478	chr7:141491604-141493006	-2.48
1779	chr3:107849930-107852621	-1.88	2479	chr7:148929863-148931681	-2.19
1780	chr3:111215088-111217093	-2.15	2480	chr7:149670079-149670941	1.61
1781	chr3:111621471-111624472	-2.35	2481	chr7:150600389-150601717	-1.72
1782	chr3:111760340-111762621	-2.02	2482	chr7:151124048-151126174	-1.56
1783	chr3:112388965-112391661	-2.47	2483	chr7:155108046-155109502	2.76
1784	chr3:112518438-112519197	-2.00	2484	chr7:155743731-155745331	-3.00
1785	chr3:114118554-114120232	-3.69	2485	chr7:156944587-156945261	1.79
1786	chr3:114342450-114344244	-2.28	2486	chr7:157101828-157104375	-2.98
1787	chr3:121713897-121715081	-2.25	2487	chr7:157139584-157139993	-1.91
1788	chr3:122687838-122689855	-2.35	2488	chr7:157351396-157353167	-2.28
1789	chr3:122992159-122992840	-1.74	2489	chr8:6691956-6693356	-2.05
1790	chr3:126116484-126119042	-2.55	2490	chr8:6720647-6723237	-2.92
1791	chr3:126499928-126502131	-2.84	2491	chr8:6758233-6759317	-2.45
1792	chr3:126629936-126631570	-2.78	2492	chr8:9045246-9047397	-2.39
1793	chr3:126992799-126995156	-2.70	2493	chr8:10487869-10489681	-1.79
1794	chr3:127629563-127630719	-1.88	2494	chr8:10529310-10530750	-1.86
1795	chr3:128134719-128136463	-1.91	2495	chr8:10547908-10549875	-1.81
1796	chr3:128266854-128268834	-2.13	2496	chr8:11057543-11059437	-2.49
1797	chr3:128273827-128274639	-1.99	2497	chr8:18998278-18999296	-2.08
1798	chr3:129180042-129181005	-1.92	2498	chr8:19265527-19267291	-1.92
1799	chr3:129573005-129576287	-2.13	2499	chr8:19796522-19798499	-2.31
1800	chr3:131853175-131856254	-3.53	2500	chr8:23020659-23022234	-1.94
1801	chr3:133259644-133261402	-1.65	2501	chr8:23076134-23077271	-1.77
1802	chr3:133667015-133669042	-1.65	2502	chr8:23202762-23204777	-2.04
1803	chr3:134044488-134047478	-1.64	2503	chr8:23398231-23399623	-1.72
1804	chr3:134052411-134056246	-1.85	2504	chr8:25237210-25238692	-2.17
1805	chr3:134785411-134787073	-2.59	2505	chr8:26466514-26469480	-2.49
1806	chr3:136712495-136715408	-1.63	2506	chr8:29827011-29828185	-1.96
1807	chr3:138075182-138076990	-1.92	2507	chr8:37000208-37001204	1.75
1808	chr3:138108109-138109618	-1.88	2508	chr8:37001705-37003837	3.14
1809	chr3:138580422-138583493	-2.61	2509	chr8:37159359-37160796	1.60
1810	chr3:139018054-139019224	-2.26	2510	chr8:37402887-37403632	1.42
1811	chr3:139634888-139636643	1.76	2511	chr8:37455425-37456969	2.37
1812	chr3:140185418-140186888	-2.02	2512	chr8:37460775-37461070	1.90
1813	chr3:141110924-141113235	-1.42	2513	chr8:37468293-37469316	1.50

Index	Genomic locus	log2(FC)	Index	Genomic locus	log2(FC)
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1815	chr3:146220410-146222893	-2.69	2515	chr8:37593523-37595679	1.32
1816	chr3:146225103-146225484	-2.18	2516	chr8:37643539-37644406	1.61
1817	chr3:148360626-148362089	-2.35	2517	chr8:37706709-37708569	1.63
1818	chr3:148938774-148940142	-2.13	2518	chr8:37713809-37714952	2.86
1819	chr3:149083454-149085449	-1.87	2519	chr8:37748499-37750387	1.74
1820	chr3:149092985-149098634	-1.37	2520	chr8:37755119-37757364	1.89
1821	chr3:149271369-149274255	-2.20	2521	chr8:37760333-37762697	1.84
1822	chr3:149293314-149294413	-2.47	2522	chr8:37782189-37783147	2.47
1823	chr3:149298987-149300409	-2.03	2523	chr8:38367800-38368360	1.76
1824	chr3:150515858-150516485	1.57	2524	chr8:39797189-39797989	-2.04
1825	chr3:152760330-152761846	-1.86	2525	chr8:39799774-39801460	-3.31
1826	chr3:153002996-153005867	-1.87	2526	chr8:41649088-41650314	-1.71
1827	chr3:155421087-155424863	-2.45	2527	chr8:41655049-41656235	-2.19
1828	chr3:155935465-155936291	1.81	2528	chr8:48012215-48012532	2.10
1829	chr3:156343083-156344529	-1.67	2529	chr8:48435641-48440050	-2.33
1830	chr3:156845824-156849472	-1.70	2530	chr8:49700424-49702354	-1.57
1831	chr3:158489355-158491987	-2.55	2531	chr8:49730102-49732328	-1.65
1832	chr3:159479660-159483660	-1.45	2532	chr8:49774783-49778291	-2.42
1833	chr3:159646157-159647980	-1.75	2533	chr8:54792397-54795076	-1.46
1834	chr3:160393703-160397036	-1.84	2534	chr8:54857277-54858958	-1.91
1835	chr3:161571725-161573107	-2.35	2535	chr8:56791563-56793418	-1.60
1836	chr3:165360547-165361825	-2.35	2536	chr8:56818122-56820419	-2.96
1837	chr3:167097544-167098301	1.28	2537	chr8:56858060-56859615	-2.04
1838	chr3:169487172-169487550	1.15	2538	chr8:56890781-56895832	-1.89
1839	chr3:170061475-170062744	-1.78	2539	chr8:62633823-62635656	-2.38
1840	chr3:170444132-170445656	-1.77	2540	chr8:62672068-62674255	-2.08
1841	chr3:171506189-171510279	-2.56	2541	chr8:63624416-63625795	-1.94
1842	chr3:171526575-171529951	-1.32	2542	chr8:65646929-65648457	-2.80
1843	chr3:171653004-171655688	-3.20	2543	chr8:65668810-65670804	-3.04
1844	chr3:171678248-171679466	-1.66	2544	chr8:66841841-66843588	-2.46
1845	chr3:171926598-171928067	-1.79	2545	chr8:67042358-67043210	-1.55
1846	chr3:172035766-172036787	-1.45	2546	chr8:67419316-67420908	-2.03
1847	chr3:172324856-172326947	-2.26	2547	chr8:67421718-67423973	-2.02
1848	chr3:172402876-172404382	-2.24	2548	chr8:67437590-67437778	1.15
1849	chr3:175244275-175245190	-2.04	2549	chr8:67866843-67867377	1.95
1850	chr3:177062251-177064192	-1.52	2550	chr8:71125620-71128244	-2.55
1851	chr3:177216073-177216659	-1.67	2551	chr8:71157631-71160014	-2.86
1852	chr3:178389023-178390429	-2.83	2552	chr8:74002105-74003069	-1.72
1853	chr3:182927940-182929436	-1.77	2553	chr8:74004145-74005966	-1.85
1854	chr3:182970947-182972650	-2.04	2554	chr8:74245722-74248299	-1.97
1855	chr3:183002275-183005234	-2.63	2555	chr8:74326137-74328028	-2.75
1856	chr3:184143856-184147433	-2.13	2556	chr8:74846054-74846908	-1.82
1857	chr3:185033984-185037307	-3.20	2557	chr8:75058187-75059634	-1.98
1858	chr3:185406060-185407404	-2.01	2558	chr8:75088820-75090482	-1.92
1859	chr3:185512871-185515966	-2.29	2559	chr8:75733637-75735560	-2.11

Index	Genomic locus	log2(FC)	Index	Genomic locus	log2(FC)
1860	chr3:185540964-185544392	-1.61	2560	chr8:80597254-80598547	-1.84
1861	chr3:185676488-185679011	-2.98	2561	chr8:80788587-80790745	-2.60
1862	chr3:187085255-187086964	-2.36	2562	chr8:81112654-81114599	-2.36
1863	chr3:187326342-187327606	-1.86	2563	chr8:81810618-81813256	-1.88
1864	chr3:187672035-187673830	-2.63	2564	chr8:81937903-81939089	-2.17
1865	chr3:188012181-188013791	-1.92	2565	chr8:81940232-81942131	-2.27
1866	chr3:188617359-188619487	-2.01	2566	chr8:82451896-82452196	-1.79
1867	chr3:188664883-188667135	-1.22	2567	chr8:82656669-82658978	-3.66
1868	chr3:188696120-188699110	2.13	2568	chr8:84932619-84932841	1.59
1869	chr3:188815847-188817817	4.94	2569	chr8:90741079-90743027	-2.00
1870	chr3:189230600-189231860	-2.23	2570	chr8:90826824-90829716	-2.08
1871	chr3:189305739-189307123	-2.29	2571	chr8:94885664-94887733	-2.45
1872	chr3:189645413-189646780	-2.81	2572	chr8:94916052-94917654	-2.80
1873	chr3:189947764-189950608	-1.99	2573	chr8:94947078-94949094	-2.41
1874	chr3:190006193-190007130	-1.80	2574	chr8:95322476-95324026	-2.12
1875	chr3:190062518-190064730	-2.16	2575	chr8:95626521-95626650	1.67
1876	chr3:190103823-190104327	-2.34	2576	chr8:96755995-96758249	-1.64
1877	chr3:190249082-190252410	-2.33	2577	chr8:98709021-98710396	-1.89
1878	chr3:191376666-191377820	1.81	2578	chr8:102099112-102100041	-1.91
1879	chr3:193116453-193119564	-2.21	2579	chr8:102478549-102479230	1.97
1880	chr3:193135404-193138035	-2.10	2580	chr8:102526325-102527995	1.54
1881	chr3:193805955-193809525	-1.64	2581	chr8:103523472-103524436	1.49
1882	chr3:193851697-193853138	0.84	2582	chr8:103612325-103614622	1.63
1883	chr3:194039496-194041922	-1.83	2583	chr8:103698211-103698365	1.56
1884	chr3:194435150-194437566	-2.10	2584	chr8:103800645-103804556	-1.25
1885	chr3:195573828-195576787	-1.84	2585	chr8:104383267-104384719	-1.55
1886	chr3:196043865-196045634	0.66	2586	chr8:105290130-105292019	-2.06
1887	chr3:196064159-196067047	-2.54	2587	chr8:105564961-105566401	-2.34
1888	chr3:196438513-196440078	0.66	2588	chr8:107094170-107096029	-3.32
1889	chr3:196513817-196514748	1.68	2589	chr8:107281752-107284312	-1.72
1890	chr3:197439004-197440847	-2.25	2590	chr8:107383661-107384655	-2.08
1891	chr3:197615463-197617635	-2.65	2591	chr8:107510885-107513957	-3.71
1892	chr4:990913-991728	1.60	2592	chr8:107515627-107516405	-2.64
1893	chr4:1015194-1017373	-1.94	2593	chr8:108388815-108389983	-2.04
1894	chr4:1728572-1730834	-1.68	2594	chr8:109588480-109589429	-2.06
1895	chr4:2419710-2421418	1.12	2595	chr8:115588781-115588965	1.53
1896	chr4:3287244-3288640	-2.34	2596	chr8:116004667-116005621	-2.37
1897	chr4:3767202-3768616	1.58	2597	chr8:116878953-116881118	2.20
1898	chr4:3829056-3830034	1.55	2598	chr8:117058997-117060942	-2.35
1899	chr4:5519950-5520299	2.48	2599	chr8:117435690-117437175	-2.39
1900	chr4:6472201-6473366	1.45	2600	chr8:117942999-117945046	-3.66
1901	chr4:6632762-6635398	1.50	2601	chr8:118690428-118691154	-1.78
1902	chr4:6783845-6785323	0.88	2602	chr8:118946102-118946976	-1.59
1903	chr4:7036192-7037059	1.93	2603	chr8:118957901-118960034	-2.39
1904	chr4:7844573-7846041	-2.49	2604	chr8:119029676-119031956	-3.20
1905	chr4:7961730-7964575	-3.41	2605	chr8:121710891-121714855	-3.00

Index	Genomic locus	log2(FC)	Index	Genomic locus	log2(FC)
1906	chr4:7971940-7975169	-1.24	2606	chr8:122557525-122559066	-2.04
1907	chr4:8189631-8191536	-1.77	2607	chr8:122823210-122824766	-2.28
1908	chr4:8261710-8261925	2.03	2608	chr8:122954045-122955873	-1.93
1909	chr4:8721271-8721550	1.82	2609	chr8:123475896-123476704	-2.24
1910	chr4:10033872-10035602	-1.62	2610	chr8:123579604-123581722	-2.07
1911	chr4:35759805-35760508	-1.86	2611	chr8:124069191-124071333	-1.87
1912	chr4:38212653-38213660	-1.80	2612	chr8:124682619-124684437	-2.06
1913	chr4:39991344-39993274	-1.66	2613	chr8:124692317-124693626	-2.70
1914	chr4:40457379-40457656	1.42	2614	chr8:125282751-125284434	-2.01
1915	chr4:40674429-40675859	-1.76	2615	chr8:125859808-125861564	-2.73
1916	chr4:40909708-40912059	-1.56	2616	chr8:126107926-126109160	-1.97
1917	chr4:42908750-42909790	-1.90	2617	chr8:126153626-126156415	-2.09
1918	chr4:53703705-53705369	-1.74	2618	chr8:126185218-126189265	-3.32
1919	chr4:54373943-54374620	-2.08	2619	chr8:126270569-126273166	-3.07
1920	chr4:54751324-54753110	-3.10	2620	chr8:126422671-126426009	-1.67
1921	chr4:57750719-57751247	1.99	2621	chr8:126708607-126710417	-2.13
1922	chr4:57975713-57977425	-1.74	2622	chr8:127437976-127438404	1.77
1923	chr4:58367452-58369523	-2.29	2623	chr8:127517983-127519372	-2.24
1924	chr4:62512570-62513143	1.69	2624	chr8:127548516-127549580	-2.17
1925	chr4:67693194-67694695	-1.90	2625	chr8:128053521-128054631	-2.34
1926	chr4:74542642-74542838	-1.61	2626	chr8:128234559-128237917	-3.13
1927	chr4:74569208-74570874	-1.91	2627	chr8:128305348-128309211	-4.47
1928	chr4:74980212-74980678	-2.49	2628	chr8:128382465-128384457	-2.25
1929	chr4:75545496-75545940	1.81	2629	chr8:128521185-128522886	-2.11
1930	chr4:76971713-76974115	-2.19	2630	chr8:128560143-128561057	-2.06
1931	chr4:77172237-77173559	1.12	2631	chr8:128672903-128676254	-2.62
1932	chr4:77506600-77507832	1.39	2632	chr8:128678857-128683620	-1.51
1933	chr4:77723148-77726143	-1.80	2633	chr8:128747120-128754679	-1.36
1934	chr4:77995745-77997933	0.68	2634	chr8:129102793-129104827	1.57
1935	chr4:79454692-79457111	-2.35	2635	chr8:129154040-129155078	1.96
1936	chr4:82413398-82415463	-2.43	2636	chr8:129165005-129166797	1.82
1937	chr4:82552782-82554096	-1.72	2637	chr8:130898912-130900750	-1.76
1938	chr4:84490553-84491922	-2.34	2638	chr8:131203717-131205533	-2.22
1939	chr4:86954165-86954613	-2.52	2639	chr8:133905671-133906343	1.64
1940	chr4:88631566-88631936	2.11	2640	chr8:133910215-133911739	1.89
1941	chr4:89256357-89256897	2.00	2641	chr8:134115063-134115753	1.85
1942	chr4:90043651-90045925	-1.66	2642	chr8:134332060-134334261	-1.97
1943	chr4:90674171-90674895	-1.91	2643	chr8:134352419-134354488	-1.88
1944	chr4:90721077-90722388	-1.99	2644	chr8:134632313-134632830	1.50
1945	chr4:100379509-100381113	-3.03	2645	chr8:135746738-135747337	1.46
1946	chr4:111208022-111209432	-1.52	2646	chr8:139842788-139844479	-2.26
1947	chr4:114388955-114390155	-1.82	2647	chr8:141713932-141715579	-2.19
1948	chr4:114936755-114937439	-1.66	2648	chr8:141901603-141902272	-1.83
1949	chr4:125098679-125100084	-2.49	2649	chr8:142974839-142975187	1.98
1950	chr4:128777679-128778780	-2.17	2650	chr8:143780718-143782652	-2.23
1951	chr4:130263157-130264580	-1.93	2651	chr8:144105412-144106245	-1.97

Index	Genomic locus	log2(FC)	Index	Genomic locus	log2(FC)
1952	chr4:140357209-140357729	-2.15	2652	chr8:144107545-144108374	-1.55
1953	chr4:141348066-141349340	1.10	2653	chr8:145007987-145008780	-1.42
1954	chr4:146694005-146696259	-2.06	2654	chr8:145009504-145011467	-1.74
1955	chr4:148463305-148464444	-2.10	2655	chr8:145012479-145018561	-1.35
1956	chr4:149874698-149875862	-1.94	2656	chr8:145870152-145873704	-1.55
1957	chr4:154036256-154037362	-2.09	2657	chr8:145992408-145994182	-1.27
1958	chr4:154101486-154103053	-1.96	2658	chr9:691675-695869	-3.08
1959	chr4:154125552-154127950	-1.40	2659	chr9:737393-739111	-2.73
1960	chr4:155449853-155451695	-1.99	2660	chr9:750493-753032	-2.41
1961	chr4:156313909-156314357	-1.76	2661	chr9:2228157-2230367	-2.39
1962	chr4:156587768-156589510	-1.45	2662	chr9:2316392-2318050	-2.05
1963	chr4:159926810-159928065	-1.96	2663	chr9:2621024-2623784	-1.18
1964	chr4:169598311-169598505	1.48	2664	chr9:6314456-6316054	-2.19
1965	chr4:185469036-185470568	-2.11	2665	chr9:7121171-7122503	-2.06
1966	chr4:185765948-185768375	-1.91	2666	chr9:7210648-7212559	-1.91
1967	chr4:186300475-186302008	-2.19	2667	chr9:12859298-12861131	-2.94
1968	chr4:186693231-186697117	-2.76	2668	chr9:13513261-13514448	-2.08
1969	chr4:186741578-186744314	-2.12	2669	chr9:13687928-13689200	-1.65
1970	chr4:187686250-187688077	-2.79	2670	chr9:13899041-13901217	-2.48
1971	chr4:188942919-188945814	-2.14	2671	chr9:14346396-14350799	-2.81
1972	chr5:154006-154962	-1.93	2672	chr9:14560742-14563749	-3.23
1973	chr5:217734-219872	-0.76	2673	chr9:16336055-16337976	-2.08
1974	chr5:251397-254113	-2.48	2674	chr9:16442646-16442793	-1.83
1975	chr5:398477-401759	-2.97	2675	chr9:16704748-16705545	-2.32
1976	chr5:415059-416630	-2.18	2676	chr9:18610432-18612375	-2.10
1977	chr5:458061-459208	-2.04	2677	chr9:19161237-19162455	-2.25
1978	chr5:500884-502596	-2.34	2678	chr9:21558707-21560952	-2.51
1979	chr5:509578-510820	-2.30	2679	chr9:21575504-21577359	-3.27
1980	chr5:663695-665791	-1.74	2680	chr9:21687443-21688780	-2.07
1981	chr5:828340-828608	-2.59	2681	chr9:21836323-21837051	-1.74
1982	chr5:861677-864340	-1.74	2682	chr9:22208790-22209358	-1.65
1983	chr5:891500-894013	-1.16	2683	chr9:33099676-33104411	-2.82
1984	chr5:910765-913485	-3.94	2684	chr9:33390323-33392292	-2.31
1985	chr5:945731-947630	-1.90	2685	chr9:34185262-34186860	-1.52
1986	chr5:956621-961269	-2.89	2686	chr9:34484598-34485547	1.42
1987	chr5:978939-980932	-2.68	2687	chr9:35923614-35925478	-2.84
1988	chr5:981726-982872	-2.36	2688	chr9:35961982-35963128	-2.11
1989	chr5:1160411-1162687	-2.32	2689	chr9:36125743-36127481	-1.95
1990	chr5:1522345-1524731	-1.33	2690	chr9:36306714-36307142	-1.76
1991	chr5:1567923-1569475	-2.53	2691	chr9:36319044-36320695	-1.81
1992	chr5:1793548-1795020	-2.71	2692	chr9:36566275-36567746	-1.84
1993	chr5:1827650-1828162	-1.75	2693	chr9:37410538-37413439	-1.27
1994	chr5:1889517-1889972	-2.04	2694	chr9:37984326-37985917	-1.89
1995	chr5:1930613-1932060	-2.21	2695	chr9:71120723-71120927	1.64
1996	chr5:2333414-2337029	-2.79	2696	chr9:72289401-72290708	-1.59
1997	chr5:3276221-3276545	-2.05	2697	chr9:72660724-72661766	-1.63

Index	Genomic locus	log2(FC)	Index	Genomic locus	log2(FC)
1998	chr5:3310167-3312625	-3.00	2698	chr9:73168588-73170222	-2.56
1999	chr5:3740260-3742255	-2.69	2699	chr9:75140466-75143227	-1.57
2000	chr5:5351394-5352370	-2.02	2700	chr9:80911044-80913129	-1.66
2001	chr5:6544774-6546700	-2.06	2701	chr9:82185406-82188800	-1.73
2002	chr5:6632457-6634312	-0.77	2702	chr9:84174600-84175339	-1.99
2003	chr5:7066596-7069060	-2.10	2703	chr9:85103470-85105620	-1.77
2004	chr5:9924262-9925317	-2.03	2704	chr9:85833592-85835205	1.46
2005	chr5:10551021-10553056	-2.14	2705	chr9:86152620-86153882	0.93
2006	chr5:10595073-10596574	-1.50	2706	chr9:89335917-89337692	-2.35
2007	chr5:10703345-10705811	-2.26	2707	chr9:91652656-91654185	-1.81
2008	chr5:10724638-10727447	-2.83	2708	chr9:92449275-92449951	1.68
2009	chr5:14035021-14039791	-3.02	2709	chr9:93720469-93721098	1.46
2010	chr5:14184975-14186382	-2.58	2710	chr9:93939720-93941069	-1.73
2011	chr5:14455399-14456411	-2.33	2711	chr9:93961611-93963154	-2.16
2012	chr5:14675672-14676868	-1.62	2712	chr9:93969246-93971648	-2.48
2013	chr5:14742247-14745284	-2.45	2713	chr9:94063848-94066225	-2.09
2014	chr5:14809843-14811540	-2.20	2714	chr9:96002894-96004585	-2.06
2015	chr5:17160268-17161350	-1.91	2715	chr9:96006477-96008106	-2.24
2016	chr5:17185492-17186861	-1.90	2716	chr9:97410739-97412162	-2.29
2017	chr5:19530711-19532369	-1.64	2717	chr9:98412058-98413033	-1.96
2018	chr5:19555331-19555868	-1.76	2718	chr9:100272976-100274638	-1.71
2019	chr5:20275965-20277625	-2.04	2719	chr9:100465628-100467488	-1.90
2020	chr5:20601438-20602171	-1.81	2720	chr9:101010622-101011729	-2.30
2021	chr5:21807859-21808658	-1.60	2721	chr9:101543854-101544685	-1.71
2022	chr5:23466533-23467852	-1.77	2722	chr9:108147785-108148023	1.62
2023	chr5:23631437-23632105	-2.28	2723	chr9:109181974-109183178	-1.76
2024	chr5:23687932-23688969	-2.13	2724	chr9:110033628-110034896	1.88
2025	chr5:24804000-24804977	-2.05	2725	chr9:110473324-110474660	-2.09
2026	chr5:26388445-26390621	-2.45	2726	chr9:111206447-111209035	-1.38
2027	chr5:32038877-32039940	-1.94	2727	chr9:111313302-111315425	-1.70
2028	chr5:32042736-32043539	-1.81	2728	chr9:112889495-112891463	-1.76
2029	chr5:32217381-32219315	-1.91	2729	chr9:112903451-112905526	-2.39
2030	chr5:32507697-32508810	-2.08	2730	chr9:113506334-113508654	-2.87
2031	chr5:32522312-32523788	-2.82	2731	chr9:114605148-114606877	-1.85
2032	chr5:32531017-32532859	-2.47	2732	chr9:114928454-114929694	-2.38
2033	chr5:33147404-33148979	-3.06	2733	chr9:118434339-118436030	-3.26
2034	chr5:33641779-33642927	1.85	2734	chr9:123693746-123694171	-2.23
2035	chr5:34529130-34530867	-2.00	2735	chr9:126029787-126031806	0.82
2036	chr5:34608494-34610444	-2.08	2736	chr9:127057638-127060169	-1.81
2037	chr5:34672608-34675321	-2.98	2737	chr9:127072098-127072659	-2.14
2038	chr5:34805344-34805537	-1.97	2738	chr9:127572739-127574760	-1.86
2039	chr5:36456860-36457521	-1.88	2739	chr9:130462447-130462868	1.97
2040	chr5:36574770-36576510	-2.40	2740	chr9:130906898-130908997	-1.83
2041	chr5:36657865-36659455	-2.26	2741	chr9:130910809-130912500	-1.96
2042	chr5:38445492-38446710	-2.13	2742	chr9:131533165-131535053	0.76
2043	chr5:38830114-38832321	-1.87	2743	chr9:131652290-131653057	-1.66

Index	Genomic locus	log2(FC)	Index	Genomic locus	log2(FC)
2044	chr5:38853746-38855326	-2.21	2744	chr9:131664024-131665677	-2.11
2045	chr5:39194786-39197924	-2.60	2745	chr9:131955821-131956610	2.48
2046	chr5:40796763-40799126	-0.85	2746	chr9:132262463-132262988	-1.62
2047	chr5:40833909-40836526	-0.84	2747	chr9:132650537-132651550	-1.90
2048	chr5:40841095-40842548	-2.22	2748	chr9:132800186-132800925	-2.31
2049	chr5:40871331-40872719	-2.30	2749	chr9:133226844-133228770	-2.52
2050	chr5:42810774-42812219	1.56	2750	chr9:133837218-133839317	-2.36
2051	chr5:42990887-42994046	-2.89	2751	chr9:135514332-135515962	-2.77
2052	chr5:43510495-43511744	-2.10	2752	chr9:136022699-136025449	0.89
2053	chr5:43771377-43773772	-2.03	2753	chr9:137699296-137699974	2.13
2054	chr5:55971122-55972752	-1.76	2754	chr9:139119865-139120794	-1.58
2055	chr5:56013198-56013633	1.65	2755	chr9:139445013-139447323	-1.27
2056	chr5:65105821-65108086	-2.33	2756	chr9:139775991-139777569	-1.49
2057	chr5:65158164-65158722	-2.61	2757	chr9:140444327-140444799	1.20
2058	chr5:66311046-66311720	-2.27	2758	chrX:3614255-3616879	-2.63
2059	chr5:66511190-66512452	1.77	2759	chrX:9753875-9755160	1.31
2060	chr5:66530344-66531059	1.73	2760	chrX:13046711-13048749	1.02
2061	chr5:67069198-67070103	-2.32	2761	chrX:16887598-16889942	0.88
2062	chr5:72111775-72113253	0.93	2762	chrX:16964131-16965699	1.01
2063	chr5:72606337-72608725	-2.06	2763	chrX:23900952-23902383	-2.24
2064	chr5:73233749-73235549	-2.40	2764	chrX:25031111-25032141	1.55
2065	chr5:73312528-73314163	-1.76	2765	chrX:25046336-25047841	-2.12
2066	chr5:74632000-74633802	0.83	2766	chrX:39618738-39619691	1.51
2067	chr5:74861560-74863680	-1.52	2767	chrX:39842886-39844066	1.82
2068	chr5:78488977-78490212	1.49	2768	chrX:39964042-39966296	1.03
2069	chr5:78531345-78533628	0.84	2769	chrX:39967939-39969251	1.75
2070	chr5:78580795-78582937	-2.15	2770	chrX:40367056-40367876	1.91
2071	chr5:81118661-81120042	-1.81	2771	chrX:41134913-41136469	0.91
2072	chr5:81701082-81702740	-2.15	2772	chrX:41781917-41783689	1.18
2073	chr5:86370504-86371977	-2.18	2773	chrX:47862797-47863914	1.39
2074	chr5:86410189-86411742	-1.94	2774	chrX:48506906-48507090	2.36
2075	chr5:86593166-86594937	-2.00	2775	chrX:48567929-48568328	1.68
2076	chr5:87974156-87974522	2.35	2776	chrX:48619774-48620811	1.60
2077	chr5:92498024-92499009	-1.81	2777	chrX:48693483-48693974	1.67
2078	chr5:95360772-95362847	-2.87	2778	chrX:48774778-48776927	1.13
2079	chr5:96270008-96272659	0.53	2779	chrX:51188827-51190459	1.48
2080	chr5:98355113-98356690	-1.99	2780	chrX:55034501-55036274	-1.78
2081	chr5:99982986-99983824	1.52	2781	chrX:64862299-64865143	-2.12
2082	chr5:103224553-103224771	2.36	2782	chrX:64896892-64898644	-1.90
2083	chr5:105732395-105734089	-1.73	2783	chrX:64925573-64927622	-1.99
2084	chr5:106015849-106017236	-2.02	2784	chrX:65091643-65092555	-2.03
2085	chr5:106115215-106116658	1.45	2785	chrX:82000344-82002604	-2.26
2086	chr5:113183131-113183655	1.79	2786	chrX:82790378-82791185	-1.85
2087	chr5:121498791-121500337	-2.81	2787	chrX:91417858-91418757	-1.93
2088	chr5:131713983-131715068	1.98	2788	chrX:100067005-100068036	-1.96
2089	chr5:132842191-132842922	1.80	2789	chrX:112209953-112212100	-2.20

Index	Genomic locus	log2(FC)	Index	Genomic locus	log2(FC)
2090	chr5:133388486-133391015	-2.40	2790	chrX:118108583-118110805	-1.30
2091	chr5:133394083-133396022	-2.55	2791	chrX:118634698-118638031	-1.35
2092	chr5:133435025-133436930	-2.13	2792	chrX:118868467-118870100	-1.74
2093	chr5:133457922-133460289	-1.85	2793	chrX:119683299-119684383	-1.96
2094	chr5:133615183-133616189	1.54	2794	chrX:121227581-121229211	-1.96
2095	chr5:135355849-135356598	-1.80	2795	chrX:127517406-127518745	-1.75
2096	chr5:136957418-136959068	-1.55	2796	chrX:130880379-130881267	1.79
2097	chr5:139035460-139035744	1.30	2797	chrX:132656000-132658528	-2.25
2098	chr5:139247753-139251115	-2.20	2798	chrX:132677183-132679620	-2.25
2099	chr5:139329626-139332153	-2.15	2799	chrX:135435587-135436950	-1.90
2100	chr5:140105403-140105818	1.65	2800	chrX:135646057-135646931	-1.85
			2801	chrX:140227217-140228619	-1.86
			2802	chrX:151150433-151151718	-1.94
			2803	chrX:152051446-152051759	1.54
			2804	chrX:152997530-152999309	-2.10
			2805	chrX:153828344-153829697	-2.14

Index	Genomic locus	log2(FC)	Index	Genomic locus	log2(FC)
1	chr1:1141525-1142216	-4.76	489	chr14:70512579-70513161	-3.19
2	chr1:1244990-1245258	-4.50	490	chr14:71282898-71284387	-1.88
3	chr1:1494523-1494804	-2.89	491	chr14:71967468-71967872	-1.45
4	chr1:1552123-1553151	-2.94	492	chr14:74009791-74009946	-2.53
5	chr1:1610439-1610744	-3.98	493	chr14:74683258-74683735	1.49
6	chr1:1611801-1612234	-2.74	494	chr14:75421869-75423394	1.26
7	chr1:1786781-1787209	-2.16	495	chr14:78446502-78447872	-3.22
8	chr1:1981380-1982458	-3.40	496	chr14:80351456-80351716	-3.58
9	chr1:2781110-2781875	2.43	497	chr14:90139278-90139719	-3.68
10	chr1:3400054-3401054	-3.65	498	chr14:91799219-91799420	-2.64
11	chr1:3691761-3692702	-3.73	499	chr14:93478119-93478715	-4.25
12	chr1:6094537-6096215	-3.22	500	chr14:94426117-94426475	1.83
13	chr1:6555154-6556756	-3.55	501	chr14:94791495-94791910	1.33
14	chr1:6672237-6672513	-3.20	502	chr14:95678664-95679424	-2.36
15	chr1:6841315-6841789	-2.13	503	chr14:96230784-96232039	2.17
16	chr1:8173822-8174244	-1.99	504	chr14:96505185-96506515	-3.71
17	chr1:8204377-8205382	-2.14	505	chr14:96670483-96670834	-3.53
18	chr1:8243026-8243374	-2.24	506	chr14:96689233-96689667	1.13
19	chr1:8257835-8259668	-1.34	507	chr14:97097855-97098418	1.84
20	chr1:8364340-8364747	-2.21	508	chr14:97105661-97106126	1.50
21	chr1:8823588-8823984	-2.00	509	chr14:97158976-97159393	1.88
22	chr1:8889096-8889489	-4.07	510	chr14:97536558-97536881	1.63
23	chr1:9170296-9172465	-0.97	511	chr14:99752465-99752749	2.60
24	chr1:9476592-9477991	-2.27	512	chr14:100055418-100055860	-3.71
25	chr1:9853265-9853589	-1.75	513	chr14:100624276-100626506	-5.37
26	chr1:9894883-9895213	-2.11	514	chr14:100736356-100739473	-3.71
27	chr1:9923029-9923263	-3.08	515	chr14:100773419-100774018	-4.52
28	chr1:10574233-10574520	-2.32	516	chr14:101046156-101046827	1.51
29	chr1:10615846-10616732	-3.70	517	chr14:101276639-101277607	2.40
30	chr1:10781696-10783296	-2.05	518	chr14:102779155-102781298	-2.80
31	chr1:10810536-10811880	-2.13	519	chr14:102807680-102810225	-2.94
32	chr1:10833257-10835324	-2.08	520	chr14:102817384-102818497	-2.50
33	chr1:10839363-10839732	-3.30	521	chr14:103028501-103029372	-2.20
34	chr1:11140983-11141378	-2.60	522	chr14:103047654-103049514	-3.08
35	chr1:12546533-12547653	-2.14	523	chr14:104072714-104074498	-5.07
36	chr1:12587425-12588903	-1.60	524	chr14:105260461-105260817	-3.14
37	chr1:12637708-12639382	-1.21	525	chr14:105388306-105389972	-2.92
38	chr1:12678034-12679589	2.95	526	chr14:105511965-105512374	-5.34
39	chr1:15942470-15942907	-3.54	527	chr14:106021397-106021673	2.03
40	chr1:16213758-16214533	-2.59	528	chr14:106243079-106243915	2.59
41	chr1:16434491-16434939	-1.88	529	chr15:29362712-29363311	-3.13
42	chr1:16493923-16494647	-3.89	530	chr15:32291098-32291620	-2.47
43	chr1:19579048-19579658	-3.04	531	chr15:33628923-33632155	-2.74
44	chr1:20810224-20811323	-4.58	532	chr15:33690802-33691943	-3.25
45	chr1:20812996-20813726	-4.12	533	chr15:33717861-33718165	-2.75

Index	Genomic locus	log2(FC)	Index	Genomic locus	log2(FC)
46	chr1:21644300-21646907	-1.81	534	chr15:33803935-33804459	-3.12
47	chr1:22912952-22913250	1.30	535	chr15:33806903-33807225	-2.44
48	chr1:25070844-25071192	-3.53	536	chr15:33846481-33846888	-4.01
49	chr1:27143661-27145687	-0.65	537	chr15:37398726-37399581	-3.00
50	chr1:27517677-27519202	-2.53	538	chr15:42221522-42221707	-2.75
51	chr1:27694731-27696008	-1.65	539	chr15:42447066-42448469	-2.25
52	chr1:27854154-27855266	-4.46	540	chr15:43415169-43416900	-2.63
53	chr1:27894730-27895566	-3.92	541	chr15:43621478-43622879	-3.47
54	chr1:31320169-31320751	1.91	542	chr15:44091837-44092509	-3.40
55	chr1:32149520-32150116	-2.15	543	chr15:45722223-45723017	-5.81
56	chr1:33210418-33211892	-1.80	544	chr15:60862120-60862402	-2.49
57	chr1:33592630-33593449	-2.80	545	chr15:62637126-62637376	-4.04
58	chr1:35450578-35451112	-3.57	546	chr15:63673207-63674783	-4.16
59	chr1:35664464-35664801	-2.50	547	chr15:63795140-63797781	-3.15
60	chr1:36771633-36773057	-4.67	548	chr15:66208996-66209471	-2.15
61	chr1:36880933-36881617	-3.14	549	chr15:67371277-67371727	-1.08
62	chr1:36947709-36948618	-3.00	550	chr15:68503012-68503438	-1.72
63	chr1:38021406-38022904	-1.01	551	chr15:70387677-70388100	-3.57
64	chr1:39416963-39417269	-2.86	552	chr15:71407099-71407593	-2.54
65	chr1:41431095-41431554	-2.27	553	chr15:71408731-71409119	-3.40
66	chr1:41796862-41797187	-2.06	554	chr15:71769416-71769819	1.10
67	chr1:41827899-41828465	-3.13	555	chr15:72667378-72668680	1.83
68	chr1:41888367-41890034	-3.54	556	chr15:75081324-75081854	-2.98
69	chr1:46055898-46056220	-2.72	557	chr15:78295863-78296081	-2.58
70	chr1:46705741-46708036	-0.82	558	chr15:79012334-79012766	-3.39
71	chr1:48246739-48247243	-2.67	559	chr15:83875427-83877361	-3.81
72	chr1:51477899-51478395	-0.99	560	chr15:87459920-87460191	1.88
73	chr1:55326296-55326661	-2.05	561	chr15:89179395-89179705	-3.12
74	chr1:59041734-59043180	-4.62	562	chr15:90455256-90456401	3.46
75	chr1:59279994-59280627	-3.45	563	chr15:96752670-96752866	-2.62
76	chr1:61649831-61650163	-4.40	564	chr15:98139706-98140020	-2.41
77	chr1:64605781-64605971	-1.99	565	chr15:98503407-98504789	-4.34
78	chr1:72748417-72750419	-4.07	566	chr15:99411097-99411398	-1.98
79	chr1:78510029-78510262	-1.42	567	chr15:101435376-101436149	-1.37
80	chr1:80549163-80549595	-2.13	568	chr16:159900-162910	-3.09
81	chr1:82265922-82269104	-3.57	569	chr16:376998-377507	-3.33
82	chr1:86296112-86296645	-2.90	570	chr16:381741-383409	-4.25
83	chr1:86936594-86936941	-2.31	571	chr16:474709-475213	4.96
84	chr1:86988782-86990117	-1.13	572	chr16:496686-499923	-3.10
85	chr1:87095566-87096112	-1.62	573	chr16:729329-729844	-3.68
86	chr1:88928242-88928762	-3.24	574	chr16:776588-776755	-3.90
87	chr1:89129920-89130333	-0.77	575	chr16:1234919-1237303	0.87
88	chr1:89132021-89132556	-0.73	576	chr16:1255986-1256241	2.23
89	chr1:89241441-89241981	-0.84	577	chr16:1279222-1280803	2.23
90	chr1:89974050-89974607	-1.01	578	chr16:1297104-1297745	2.97
91	chr1:90086689-90088343	-0.98	579	chr16:1680794-1681427	-5.70

Index	Genomic locus	log2(FC)	Index	Genomic locus	log2(FC)
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93	chr1:90187350-90187919	-0.85	581	chr16:1862796-1862973	-3.37
94	chr1:90449439-90450787	-0.95	582	chr16:2061039-2063957	-3.22
95	chr1:92243191-92243492	-2.47	583	chr16:4007568-4008232	-4.01
96	chr1:92285810-92286318	-1.10	584	chr16:4094745-4095020	-2.81
97	chr1:93251340-93251646	2.05	585	chr16:4302406-4303253	-2.61
98	chr1:94047785-94048554	-2.01	586	chr16:4460623-4462801	-3.45
99	chr1:94073945-94074178	-2.00	587	chr16:8806429-8807736	1.98
100	chr1:94911206-94911477	-3.95	588	chr16:9861877-9863076	-2.42
101	chr1:100232751-100233247	-1.56	589	chr16:14401742-14402138	-3.02
102	chr1:100432076-100432395	-2.44	590	chr16:14464164-14464401	-2.22
103	chr1:107599937-107600596	-3.56	591	chr16:16592994-16593493	1.85
104	chr1:109372984-109373584	-2.71	592	chr16:20006025-20007093	2.01
105	chr1:110707637-110708000	-2.41	593	chr16:20013500-20013846	2.12
106	chr1:112457947-112458444	1.62	594	chr16:20041855-20043804	2.17
107	chr1:113004625-113005083	-3.95	595	chr16:20069944-20070459	2.32
108	chr1:113256730-113257324	-3.18	596	chr16:20134675-20135036	2.64
109	chr1:117112551-117112744	-2.80	597	chr16:20242116-20242712	1.88
110	chr1:118149480-118150007	-3.34	598	chr16:23435947-23436327	-2.81
111	chr1:145476962-145477524	2.53	599	chr16:25636276-25636701	-3.65
112	chr1:150977636-150977867	-1.99	600	chr16:27246819-27247592	-1.87
113	chr1:151169362-151170218	-3.71	601	chr16:27348166-27349580	-2.15
114	chr1:154300966-154301638	-3.55	602	chr16:27862197-27862655	1.63
115	chr1:155015744-155016059	-3.38	603	chr16:27903472-27904468	2.17
116	chr1:155660623-155661062	-3.38	604	chr16:28385546-28385931	-3.38
117	chr1:156432059-156432754	-2.96	605	chr16:29823663-29824056	-3.67
118	chr1:157791882-157792399	-2.23	606	chr16:32880806-32881391	2.92
119	chr1:158973307-158973816	-1.88	607	chr16:46918686-46919583	2.27
120	chr1:158982892-158983311	-2.16	608	chr16:46934597-46934965	-2.55
121	chr1:159034259-159035150	-2.38	609	chr16:48733413-48733843	2.12
122	chr1:161067968-161068990	-3.42	610	chr16:48807946-48808642	1.51
123	chr1:163038943-163039381	-3.64	611	chr16:48816815-48817296	2.19
124	chr1:164569526-164570506	-1.76	612	chr16:48839280-48839602	2.85
125	chr1:168356187-168356828	-3.64	613	chr16:54966008-54967723	-7.54
126	chr1:168538899-168539281	-3.82	614	chr16:56224398-56226339	-3.66
127	chr1:179835623-179835909	-2.91	615	chr16:60222576-60222958	2.17
128	chr1:190421642-190422705	-2.73	616	chr16:60527993-60528458	2.29
129	chr1:198668602-198668943	-5.36	617	chr16:60701059-60701522	2.00
130	chr1:201475752-201476651	-3.49	618	chr16:60730752-60731239	2.06
131	chr1:201950321-201951283	-1.83	619	chr16:67562193-67562533	-2.53
132	chr1:204182861-204183647	-3.71	620	chr16:67933255-67933527	-1.96
133	chr1:204346535-204346990	-3.35	621	chr16:71677432-71677708	-2.14
134	chr1:206948406-206948710	1.55	622	chr16:71705490-71705974	-1.48
135	chr1:207073561-207073838	-2.29	623	chr16:71841002-71841334	-2.96
136	chr1:207223914-207224617	4.11	624	chr16:73948507-73948841	-2.82
137	chr1:208011615-208012201	-2.12	625	chr16:75034105-75034752	-2.85

Index	Genomic locus	log2(FC)	Index	Genomic locus	log2(FC)
138	chr1:208040648-208041092	-2.54	626	chr16:75525286-75525583	-2.00
139	chr1:211306132-211307782	-2.77	627	chr16:79674056-79675194	-2.72
140	chr1:212321315-212321666	-2.72	628	chr16:80649321-80650030	-2.58
141	chr1:212780092-212781039	-6.24	629	chr16:81087440-81087602	-2.20
142	chr1:213370163-213370480	-3.23	630	chr16:81323309-81323822	-2.01
143	chr1:220921140-220922315	-3.57	631	chr16:82172713-82173496	-3.36
144	chr1:221752844-221753297	-2.30	632	chr16:82791197-82791667	-3.63
145	chr1:223297039-223297376	-3.21	633	chr16:82877926-82878453	-3.01
146	chr1:223936167-223937122	-1.04	634	chr16:82889632-82889996	-3.79
147	chr1:225906198-225907143	-1.42	635	chr16:82945536-82946608	-2.97
148	chr1:226162176-226163750	-2.21	636	chr16:82999598-83000104	-2.84
149	chr1:228289653-228290157	-3.33	637	chr16:83033890-83034585	-3.58
150	chr1:228871703-228872486	-3.33	638	chr16:83144596-83144867	-3.72
151	chr1:233116434-233116637	-3.17	639	chr16:83154411-83154745	-2.93
152	chr1:233160763-233161187	-2.23	640	chr16:83169799-83172191	-3.11
153	chr1:234722985-234723342	-2.06	641	chr16:83386166-83386542	-2.63
154	chr1:235009723-235012046	-1.75	642	chr16:83460484-83460827	-3.34
155	chr1:235093568-235097049	-3.60	643	chr16:84128804-84129480	-3.31
156	chr1:235098986-235099239	-3.46	644	chr16:84860090-84861827	-2.86
157	chr1:235793619-235794077	-2.69	645	chr16:85180782-85181341	-3.31
158	chr1:236686428-236687711	-4.95	646	chr16:85455680-85456367	-4.85
159	chr1:238090009-238090924	-2.61	647	chr16:85604968-85605306	-3.23
160	chr1:238972689-238973170	-2.36	648	chr16:85721164-85722069	-3.56
161	chr1:239401294-239401657	-1.58	649	chr16:85741335-85741724	-4.66
162	chr1:240053321-240053676	-1.81	650	chr16:85783155-85784109	-3.64
163	chr1:240097889-240098244	-2.30	651	chr16:85849818-85850160	1.68
164	chr1:241360501-241360978	-3.30	652	chr16:85886530-85886906	2.23
165	chr1:242182873-242183091	-3.05	653	chr16:86135012-86135502	2.77
166	chr1:243094388-243095952	-2.51	654	chr16:86139242-86139401	2.04
167	chr1:243596521-243596791	-2.80	655	chr16:86225258-86225662	2.80
168	chr1:244444571-244445080	-2.12	656	chr16:86232290-86234095	3.55
169	chr1:244624034-244625455	-3.28	657	chr16:86793702-86795575	-4.60
170	chr10:2585584-2585853	1.88	658	chr16:87766923-87767131	-2.37
171	chr10:3948671-3949041	-2.07	659	chr16:89128809-89129513	2.37
172	chr10:4001135-4001420	-1.72	660	chr16:89449881-89450232	-3.97
173	chr10:4193588-4194696	-1.25	661	chr16:89567026-89569330	-2.82
174	chr10:4551591-4551840	-2.05	662	chr16:89902762-89904317	-2.79
175	chr10:5874934-5875733	-2.31	663	chr16:89991908-89993222	-7.07
176	chr10:6317002-6317582	2.03	664	chr16:90014184-90014664	-3.79
177	chr10:6546833-6547285	-2.81	665	chr17:201958-202369	-3.01
178	chr10:7984851-7985343	-2.31	666	chr17:1734071-1735524	-1.94
179	chr10:8105635-8106245	-2.05	667	chr17:1871166-1871798	-2.48
180	chr10:11872311-11872589	-1.87	668	chr17:1890061-1890390	-1.68
181	chr10:12762952-12763318	-3.59	669	chr17:1926574-1928607	-4.33
182	chr10:13845966-13846252	-2.36	670	chr17:2516678-2517285	-1.71
183	chr10:14646847-14647175	-3.77	671	chr17:3800748-3801511	-1.19

Index	Genomic locus	log2(FC)	Index	Genomic locus	log2(FC)
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186	chr10:15408848-15409241	-2.42	674	chr17:8092223-8092668	-3.10
187	chr10:16931560-16932569	-3.05	675	chr17:8279859-8280180	-4.53
188	chr10:16990376-16990677	-2.27	676	chr17:15952432-15952738	-2.20
189	chr10:17070396-17070716	-2.38	677	chr17:16419914-16420381	-4.07
190	chr10:17495327-17496877	-4.79	678	chr17:16471746-16473141	-3.46
191	chr10:18916270-18916957	-4.16	679	chr17:16492272-16492595	-3.09
192	chr10:21815970-21816577	-4.74	680	chr17:17014901-17016323	-1.63
193	chr10:22517933-22518587	-3.39	681	chr17:17672648-17674243	-1.06
194	chr10:22614226-22614963	-4.24	682	chr17:19881450-19881789	-2.86
195	chr10:27794407-27794847	-3.54	683	chr17:21432756-21433260	-2.91
196	chr10:29414055-29414524	-3.81	684	chr17:26879097-26879887	-5.99
197	chr10:29480187-29480910	-2.83	685	chr17:28087765-28089243	-2.55
198	chr10:29910738-29911364	-1.51	686	chr17:29886482-29887559	-3.60
199	chr10:30274928-30275069	-1.27	687	chr17:33640439-33641518	-2.90
200	chr10:30842847-30843159	-3.15	688	chr17:36774777-36775261	2.21
201	chr10:32226285-32227118	-1.83	689	chr17:36791786-36792078	2.05
202	chr10:32649599-32649817	-1.77	690	chr17:36798791-36799241	2.24
203	chr10:33637320-33637614	-1.98	691	chr17:36808480-36808978	2.47
204	chr10:34234540-34235014	-2.50	692	chr17:36837705-36838211	1.85
205	chr10:36794908-36795206	-1.85	693	chr17:36841763-36842107	1.92
206	chr10:38624895-38625221	-2.65	694	chr17:36851839-36852237	1.88
207	chr10:43891158-43893019	-3.68	695	chr17:36901248-36901645	2.03
208	chr10:48573114-48573725	2.94	696	chr17:36936263-36937048	1.93
209	chr10:52833378-52834990	-4.89	697	chr17:36946521-36949769	2.10
210	chr10:63557579-63557861	-1.14	698	chr17:36960857-36961248	1.91
211	chr10:71094275-71095631	-2.07	699	chr17:36988525-36991723	1.66
212	chr10:71211095-71212188	-5.09	700	chr17:37017022-37020208	1.69
213	chr10:73855289-73855774	-1.76	701	chr17:37022766-37025463	2.63
214	chr10:73869501-73871771	-1.78	702	chr17:37093928-37094262	2.72
215	chr10:75579160-75579787	-5.58	703	chr17:37121846-37124175	2.19
216	chr10:76992326-76992768	-1.92	704	chr17:37188318-37188850	2.20
217	chr10:79631919-79632602	-2.40	705	chr17:37254174-37255383	3.49
218	chr10:80853752-80854244	-3.52	706	chr17:37622312-37626188	-3.11
219	chr10:80999519-81000118	-6.40	707	chr17:37641032-37641544	-2.14
220	chr10:81020705-81021241	-2.76	708	chr17:37647455-37649091	-2.71
221	chr10:89060694-89061530	-2.46	709	chr17:37649987-37652095	-2.72
222	chr10:89419193-89420110	4.40	710	chr17:37658238-37658771	-2.66
223	chr10:92053050-92053461	-2.32	711	chr17:37666039-37667342	-3.71
224	chr10:94831554-94832342	-4.32	712	chr17:37696908-37698565	-2.94
225	chr10:95504555-95504982	-1.76	713	chr17:37700709-37702841	-2.64
226	chr10:95753254-95754351	4.64	714	chr17:37776529-37776900	-3.08
227	chr10:100696844-100697373	1.65	715	chr17:37793149-37794990	-3.76
228	chr10:100744435-100744696	1.58	716	chr17:37887196-37887435	-3.16
229	chr10:100800529-100800863	1.48	717	chr17:38182423-38183838	-2.83

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232	chr10:102791620-102792338	-3.90	720	chr17:38462171-38463541	-4.44
233	chr10:103070046-103070671	-6.08	721	chr17:38465183-38465662	-2.94
234	chr10:104813758-104814004	-2.80	722	chr17:38477198-38477816	-3.73
235	chr10:106014187-106015137	-3.52	723	chr17:38598113-38600377	-3.17
236	chr10:115859792-115862187	-2.05	724	chr17:39060171-39060657	-3.39
237	chr10:120381641-120381926	1.25	725	chr17:39682229-39682959	-3.82
238	chr10:125033696-125035057	-3.28	726	chr17:41363488-41364493	-4.26
239	chr10:126381700-126382277	-2.20	727	chr17:42060958-42061896	-3.47
240	chr10:126983623-126983913	-3.68	728	chr17:42090303-42093208	1.68
241	chr10:127747072-127747386	-4.13	729	chr17:42633654-42634004	3.04
242	chr10:128193073-128193647	-3.32	730	chr17:46287273-46287725	2.28
243	chr10:132858463-132859880	2.06	731	chr17:46390427-46390629	2.84
244	chr11:564674-565659	-1.58	732	chr17:46402222-46402736	2.86
245	chr11:1454670-1457578	-3.62	733	chr17:46408706-46409114	3.00
246	chr11:12070340-12071544	-1.18	734	chr17:46420044-46420383	2.47
247	chr11:14379767-14380902	3.05	735	chr17:46457027-46457418	3.13
248	chr11:17034574-17035448	-3.77	736	chr17:46475987-46476311	3.14
249	chr11:29259096-29259479	-2.22	737	chr17:46482907-46484217	3.17
250	chr11:30534332-30534581	1.62	738	chr17:46521397-46522938	2.43
251	chr11:33035795-33038040	2.46	739	chr17:46557725-46558309	2.13
252	chr11:34378102-34378629	2.87	740	chr17:46573718-46574136	2.05
253	chr11:40314635-40316384	-3.57	741	chr17:46651109-46651883	2.44
254	chr11:44642673-44643201	-2.17	742	chr17:46713805-46714259	-3.11
255	chr11:45182738-45183294	-4.08	743	chr17:46755283-46756198	-4.59
256	chr11:47736554-47737214	-3.97	744	chr17:48134135-48134745	-3.23
257	chr11:57243546-57244624	-6.98	745	chr17:49021531-49022574	-6.72
258	chr11:61198525-61200770	-3.13	746	chr17:55255196-55256116	1.55
259	chr11:62314656-62315213	-4.63	747	chr17:55363891-55364121	-2.58
260	chr11:62316332-62316497	-2.88	748	chr17:55434700-55435072	-2.93
261	chr11:62473971-62474338	-3.54	749	chr17:56667299-56667749	1.46
262	chr11:63325744-63326080	-3.03	750	chr17:56703519-56703865	1.90
263	chr11:63728488-63729476	-4.50	751	chr17:56768462-56769980	1.34
264	chr11:64003804-64005293	-6.19	752	chr17:56816600-56818165	1.38
265	chr11:64878780-64881157	-2.94	753	chr17:56848172-56848796	1.91
266	chr11:64990861-64991855	-2.91	754	chr17:56906371-56908014	1.98
267	chr11:65066313-65068424	-3.01	755	chr17:56966658-56967038	1.98
268	chr11:65072960-65074870	-2.90	756	chr17:57006032-57006455	2.67
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270	chr11:65139036-65140503	-3.40	758	chr17:57072052-57072474	1.89
271	chr11:65222183-65223414	-3.18	759	chr17:57096782-57097180	1.76
272	chr11:65280357-65281794	-2.51	760	chr17:57141981-57142494	1.69
273	chr11:65419660-65420654	-5.81	761	chr17:57176129-57176714	1.58
274	chr11:65842360-65844343	-2.19	762	chr17:57363316-57363725	1.44
275	chr11:65866752-65868438	-2.80	763	chr17:57410009-57410260	2.65

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278	chr11:66789422-66791581	-5.10	766	chr17:58094673-58096693	1.54
279	chr11:66892352-66893730	-2.05	767	chr17:58344255-58345020	1.75
280	chr11:66908779-66911524	-3.09	768	chr17:58440515-58440869	1.89
281	chr11:67182711-67183602	-4.44	769	chr17:58882728-58883593	1.74
282	chr11:67359740-67361027	-3.66	770	chr17:59052206-59052750	1.30
283	chr11:67563260-67565555	-4.07	771	chr17:60748965-60749258	-3.36
284	chr11:67806209-67806857	3.67	772	chr17:60878485-60878849	-1.62
285	chr11:68147555-68149115	-3.36	773	chr17:60885012-60886760	-2.70
286	chr11:68639691-68639966	-4.26	774	chr17:64298068-64300272	3.44
287	chr11:68673520-68674413	-2.74	775	chr17:64960270-64962451	-4.68
288	chr11:69311053-69312479	2.61	776	chr17:66643102-66643531	-3.47
289	chr11:69458389-69458907	-3.57	777	chr17:66770462-66770831	-2.34
290	chr11:70823961-70824434	-2.28	778	chr17:66802203-66802566	-2.89
291	chr11:71016399-71018253	-3.08	779	chr17:66913021-66913533	-2.57
292	chr11:71506887-71508173	-1.26	780	chr17:66980939-66982400	-2.70
293	chr11:72928603-72930121	-3.85	781	chr17:67577666-67578148	-2.24
294	chr11:75054766-75055117	-2.54	782	chr17:67858289-67858686	-3.13
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296	chr11:75133528-75133836	-3.01	784	chr17:67908219-67908492	-1.86
297	chr11:77773292-77773702	-2.05	785	chr17:67926617-67927011	-2.84
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299	chr11:86716038-86716364	-3.46	787	chr17:68031461-68032049	-2.02
300	chr11:92245845-92246442	-4.19	788	chr17:68037590-68037794	-2.21
301	chr11:92974510-92974797	-2.17	789	chr17:68039713-68040065	-2.16
302	chr11:94376894-94377514	-0.86	790	chr17:68053996-68054950	-2.72
303	chr11:94532553-94533540	-1.09	791	chr17:68171081-68172175	-2.68
304	chr11:94602314-94602814	-1.09	792	chr17:68373277-68373850	-2.34
305	chr11:95671781-95672179	-1.11	793	chr17:68449199-68449550	-2.24
306	chr11:96128614-96128961	-2.05	794	chr17:70026353-70026918	-3.25
307	chr11:98050096-98050538	-1.35	795	chr17:70049554-70050090	-2.77
308	chr11:98551483-98551993	-1.69	796	chr17:70206978-70207324	-2.19
309	chr11:98891198-98892068	-4.32	797	chr17:70514767-70515815	-3.76
310	chr11:105892384-105893367	-5.23	798	chr17:70547187-70547592	-2.93
311	chr11:106888254-106890129	-4.15	799	chr17:70552437-70553202	-3.13
312	chr11:109557074-109557449	-2.41	800	chr17:71160387-71162465	-4.01
313	chr11:109821415-109821801	-1.98	801	chr17:71286804-71287012	-2.77
314	chr11:111789815-111790923	-2.59	802	chr17:71621987-71622454	2.12
315	chr11:113344856-113346545	-3.08	803	chr17:73976518-73978129	-3.62
316	chr11:117443759-117444046	1.67	804	chr17:75102329-75104397	-3.62
317	chr11:120505365-120505670	1.44	805	chr17:75260738-75263395	-2.49
318	chr11:121348917-121350033	-5.15	806	chr17:75271190-75274238	-3.00
319	chr11:121563436-121563839	-2.93	807	chr17:75281763-75282597	-5.75
320	chr11:121636867-121637337	-3.48	808	chr17:75308188-75309414	-2.99
321	chr11:121665386-121666041	-2.99	809	chr17:75310541-75311918	-3.54

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324	chr11:121725561-121726837	-4.14	812	chr17:76213532-76214808	-3.35
325	chr11:121728763-121729149	-2.74	813	chr17:76253906-76254978	-3.00
326	chr11:121739348-121739690	-2.71	814	chr17:76380198-76381699	-3.39
327	chr11:121759278-121759482	-2.98	815	chr17:76417775-76418130	-4.53
328	chr11:121826760-121827192	-2.93	816	chr17:77477916-77478340	3.18
329	chr11:121830654-121831032	-2.83	817	chr17:77728375-77729890	-3.99
330	chr11:121918638-121920307	-3.81	818	chr17:78021020-78022033	-3.88
331	chr11:121942366-121942718	-3.42	819	chr17:78042624-78042906	-3.12
332	chr11:121970666-121971795	-3.44	820	chr17:78138196-78140273	-3.57
333	chr11:121998021-121998467	-4.52	821	chr17:78194725-78197486	-3.81
334	chr11:122215726-122216107	-3.10	822	chr17:78225759-78228142	-4.48
335	chr11:122234443-122234856	-2.68	823	chr17:78639343-78639796	-2.07
336	chr11:122277561-122278115	-2.63	824	chr17:79808826-79811940	-3.14
337	chr11:122372528-122372899	-3.74	825	chr17:80060521-80062800	-4.63
338	chr11:122380493-122381108	-2.84	826	chr17:80110649-80110959	-3.01
339	chr11:124733074-124733545	-4.32	827	chr17:80731398-80733276	-3.65
340	chr11:126685385-126685878	-3.63	828	chr17:80797677-80798751	-5.22
341	chr11:127166331-127166862	-2.92	829	chr18:3900843-3901236	-2.77
342	chr11:127517537-127518057	-2.11	830	chr18:5488793-5489364	-3.92
343	chr11:127691279-127691664	-2.81	831	chr18:5704217-5704562	-2.52
344	chr11:127767747-127769042	-2.72	832	chr18:5949500-5949902	-1.89
345	chr11:127796488-127798102	-2.38	833	chr18:5965248-5965636	-2.43
346	chr11:127810974-127811913	-3.38	834	chr18:5969283-5969775	-2.88
347	chr11:127868748-127869324	-2.20	835	chr18:5995053-5995409	-2.32
348	chr11:127907628-127908649	-2.64	836	chr18:6032116-6032330	-2.47
349	chr11:128006366-128006759	-2.06	837	chr18:6038230-6038631	-3.31
350	chr11:128008178-128008606	-3.17	838	chr18:6051083-6051863	-2.94
351	chr11:128009908-128010309	-2.28	839	chr18:6095306-6095910	-3.32
352	chr11:128040292-128041370	-2.62	840	chr18:6193539-6194473	-2.94
353	chr11:128042769-128043396	-2.10	841	chr18:6206410-6206629	-2.21
354	chr11:128085046-128085845	-2.27	842	chr18:6238183-6239409	-2.62
355	chr11:128106729-128107474	-2.28	843	chr18:6257645-6257980	-2.31
356	chr11:128111661-128112042	-3.13	844	chr18:6269171-6269477	-2.70
357	chr11:128217021-128217462	-3.77	845	chr18:6271327-6272132	-2.83
358	chr11:128294823-128295174	-3.06	846	chr18:6303746-6304076	-2.57
359	chr11:128305567-128305904	-3.23	847	chr18:6307174-6307487	-3.28
360	chr11:128321088-128322096	-2.71	848	chr18:6328971-6329520	-2.99
361	chr11:128332104-128332509	-3.80	849	chr18:6466131-6466695	-2.18
362	chr11:128345394-128345799	-3.33	850	chr18:6575895-6576308	-3.45
363	chr11:128369487-128369819	-3.66	851	chr18:6599943-6600304	-2.98
364	chr11:128375586-128376776	-3.55	852	chr18:6659548-6659837	-2.70
365	chr11:128391553-128392744	4.43	853	chr18:6682752-6683831	-3.65
366	chr11:128436332-128436715	-3.10	854	chr18:6758224-6758670	-2.42
367	chr11:128440958-128441558	-2.14	855	chr18:6772693-6772937	-2.81

Index	Genomic locus	log2(FC)	Index	Genomic locus	log2(FC)
368	chr11:128470660-128471133	-2.50	856	chr18:6797635-6798494	-2.73
369	chr11:128484913-128485356	-2.68	857	chr18:6803747-6804109	-3.41
370	chr11:128526874-128527527	-2.56	858	chr18:6839183-6839647	-3.39
371	chr11:128601523-128601973	-2.57	859	chr18:6855621-6856189	-3.15
372	chr11:128615337-128615845	-1.98	860	chr18:6870788-6871164	-2.77
373	chr11:128637844-128638389	-2.45	861	chr18:6877186-6877798	-3.74
374	chr11:128646430-128647327	-2.96	862	chr18:6893858-6894156	-2.47
375	chr11:128680161-128680735	-2.22	863	chr18:6903526-6904353	-2.51
376	chr11:130915674-130916959	-3.89	864	chr18:6959170-6959528	-2.29
377	chr11:130922902-130923336	-2.52	865	chr18:7129188-7129615	-3.00
378	chr11:131226809-131227134	-3.32	866	chr18:9757858-9759182	-2.07
379	chr11:131231036-131231373	-3.06	867	chr18:10131762-10132312	-5.88
380	chr11:132790657-132790959	-2.85	868	chr18:14429779-14432296	-4.06
381	chr11:133781657-133781973	2.28	869	chr18:20184521-20184797	-3.18
382	chr11:133894130-133894795	2.66	870	chr18:20681552-20681873	-3.51
383	chr11:134561449-134561718	-2.98	871	chr18:20716561-20717306	-3.15
384	chr12:287199-287515	-4.11	872	chr18:20836520-20838781	-2.84
385	chr12:7070459-7071180	-3.83	873	chr18:33767686-33768243	2.87
386	chr12:7526978-7527421	-2.57	874	chr18:34973861-34974571	-4.15
387	chr12:12867169-12867931	-3.94	875	chr18:40176423-40176855	-2.23
388	chr12:13035942-13036172	-3.26	876	chr18:43651765-43652789	-1.99
389	chr12:15373882-15374593	-3.55	877	chr18:44700772-44701130	-2.02
390	chr12:24564950-24566051	1.59	878	chr18:46141821-46142772	-4.74
391	chr12:31744621-31744878	-3.20	879	chr18:60985005-60986015	-4.53
392	chr12:40618243-40619091	-4.00	880	chr18:65183207-65184402	-3.87
393	chr12:45268865-45270927	-3.27	881	chr18:71909790-71910195	-2.83
394	chr12:47473646-47474927	-4.44	882	chr18:71958129-71959864	-4.30
395	chr12:49672267-49672802	-3.31	883	chr18:74060570-74060855	-3.24
396	chr12:51399845-51400179	-3.59	884	chr18:74203608-74204555	-3.74
397	chr12:51785085-51786683	-4.38	885	chr18:74206723-74208710	-3.17
398	chr12:52206616-52209059	1.56	886	chr18:74532379-74532777	-3.61
399	chr12:52511566-52512000	-2.28	887	chr18:76546803-76547676	-3.21
400	chr12:52557080-52558776	-1.45	888	chr18:76801935-76802414	1.77
401	chr12:53216639-53217096	-2.17	889	chr19:999734-1001105	-4.21
402	chr12:57479848-57481001	-3.39	890	chr19:1165064-1165274	-3.51
403	chr12:59271086-59271494	-2.68	891	chr19:1166243-1169139	-4.16
404	chr12:59312960-59313674	2.86	892	chr19:1531744-1539313	3.81
405	chr12:64540896-64541507	0.71	893	chr19:1565257-1566877	-3.80
406	chr12:64713554-64714169	0.76	894	chr19:1748137-1750264	-4.06
407	chr12:64848378-64848867	0.57	895	chr19:1784514-1785802	2.32
408	chr12:64946462-64946944	0.99	896	chr19:1831267-1834616	-2.93
409	chr12:64993293-64993840	-2.61	897	chr19:1846741-1847240	-3.02
410	chr12:65075913-65076458	0.70	898	chr19:1871188-1874053	-4.77
411	chr12:65103937-65104437	0.71	899	chr19:2030269-2031712	-3.17
412	chr12:69867636-69868083	-1.94	900	chr19:2413531-2418119	-3.17
413	chr12:70083057-70083211	2.23	901	chr19:3375236-3376390	-2.89

Index	Genomic locus	log2(FC)	Index	Genomic locus	log2(FC)
414	chr12:77272243-77273650	1.93	902	chr19:3390209-3390502	-2.93
415	chr12:79764159-79764700	0.73	903	chr19:3514060-3516827	-5.15
416	chr12:79926403-79926875	-2.98	904	chr19:4389619-4391096	-3.77
417	chr12:81101528-81102947	0.91	905	chr19:4427722-4430150	-3.05
418	chr12:81330268-81331930	-4.56	906	chr19:4554983-4558614	2.99
419	chr12:84484431-84484858	2.37	907	chr19:4603863-4607954	2.92
420	chr12:89744376-89746056	3.97	908	chr19:4660472-4660973	-3.23
421	chr12:89858255-89858580	-2.90	909	chr19:4715719-4716688	-4.87
422	chr12:93708310-93709278	-5.79	910	chr19:4908739-4909482	-3.45
423	chr12:96588927-96589266	2.76	911	chr19:4970737-4972239	-5.61
424	chr12:97492288-97493136	1.93	912	chr19:4975977-4979061	-5.15
425	chr12:98019367-98019837	1.49	913	chr19:4980896-4981307	-2.71
426	chr12:98080869-98081422	1.82	914	chr19:4983321-4988544	-4.19
427	chr12:98159481-98159885	1.44	915	chr19:5582279-5582586	-2.70
428	chr12:98256115-98256609	1.57	916	chr19:5822204-5822700	-4.31
429	chr12:98366650-98367042	1.30	917	chr19:6020414-6020817	-5.32
430	chr12:99037490-99037869	2.41	918	chr19:6236478-6237239	-3.69
431	chr12:103482468-103482984	1.65	919	chr19:6350462-6352094	-2.66
432	chr12:103728242-103728741	1.99	920	chr19:6392868-6396692	-2.78
433	chr12:103775297-103775683	1.83	921	chr19:7162588-7163639	-2.73
434	chr12:105956106-105956742	2.87	922	chr19:7476938-7480448	-3.57
435	chr12:112432101-112432287	-2.59	923	chr19:7565186-7565907	-2.91
436	chr12:113942858-113943346	2.02	924	chr19:8512627-8516092	-4.82
437	chr12:124701949-124702540	-3.06	925	chr19:8660962-8662205	-4.09
438	chr12:124802893-124803572	-5.11	926	chr19:8761459-8761984	-3.87
439	chr12:124844551-124845427	-4.63	927	chr19:9042966-9043361	-2.47
440	chr12:132159811-132160196	2.43	928	chr19:9227669-9228063	-2.91
441	chr12:132176890-132177459	2.51	929	chr19:10597308-10597614	-2.99
442	chr12:133032192-133034816	1.16	930	chr19:10694941-10695250	-1.38
443	chr12:133656743-133657906	2.86	931	chr19:10855703-10856071	-2.52
444	chr12:133757876-133758391	3.32	932	chr19:11457969-11459286	-3.30
445	chr13:22104769-22105161	-2.46	933	chr19:11806200-11807566	-2.70
446	chr13:22211460-22211954	3.04	934	chr19:15319078-15319767	-2.65
447	chr13:28531637-28531906	-3.36	935	chr19:16192223-16193010	-2.33
448	chr13:30002374-30003076	-3.02	936	chr19:16551580-16554902	-4.69
449	chr13:31490267-31490780	-4.32	937	chr19:16556860-16557200	-2.29
450	chr13:32502370-32502796	-3.33	938	chr19:16571551-16572396	-0.92
451	chr13:33213029-33213190	-2.10	939	chr19:16575588-16575869	-2.32
452	chr13:33923767-33924980	-3.72	940	chr19:17006578-17008954	-1.31
453	chr13:35516211-35517669	-5.66	941	chr19:18530923-18531656	-3.01
454	chr13:47234159-47234516	-1.80	942	chr19:20011638-20012284	-3.47
455	chr13:47689420-47689807	-2.82	943	chr19:22034195-22035068	-3.31
456	chr13:52493746-52494037	-2.98	944	chr19:30151859-30152178	-2.06
457	chr13:52668562-52668965	0.93	945	chr19:31061008-31061532	2.16
458	chr13:67804378-67805572	-4.83	946	chr19:31172562-31173407	2.53
459	chr13:72438594-72441191	-3.95	947	chr19:32004722-32005212	2.69

Index	Genomic locus	log2(FC)	Index	Genomic locus	log2(FC)
460	chr13:76210963-76211380	4.21	948	chr19:34217713-34218896	2.20
461	chr13:86083136-86083433	-2.44	949	chr19:34554392-34554553	1.45
462	chr13:96742362-96744198	-5.23	950	chr19:36294299-36294606	1.81
463	chr13:100751609-100751858	-2.99	951	chr19:36394287-36394948	-3.62
464	chr13:107185472-107187210	-3.70	952	chr19:37406334-37407555	-4.95
465	chr13:108866900-108868091	-5.00	953	chr19:37663387-37663954	-3.27
466	chr13:110778865-110779196	1.88	954	chr19:37997096-37998205	-3.93
467	chr13:112075752-112078928	-2.43	955	chr19:38545101-38547874	-2.81
468	chr13:113255704-113255940	-2.44	956	chr19:38553781-38554131	-3.43
469	chr13:113790996-113791368	-2.76	957	chr19:39328833-39329262	-4.82
470	chr13:114074301-114075115	-2.19	958	chr19:40784552-40786286	-2.14
471	chr14:21788407-21788874	-2.99	959	chr19:40940232-40940792	-2.05
472	chr14:22104869-22105385	1.67	960	chr19:41102066-41103371	-3.18
473	chr14:23623352-23624096	-3.40	961	chr19:41633736-41634229	-5.04
474	chr14:27065832-27068435	-3.55	962	chr19:42408204-42408635	-5.94
475	chr14:45722559-45723588	4.03	963	chr19:42497704-42498104	2.25
476	chr14:50118726-50119047	-3.22	964	chr19:45005081-45005627	2.22
477	chr14:50320286-50320847	3.30	965	chr19:45146914-45147653	4.02
478	chr14:50777626-50778010	2.81	966	chr19:45221657-45222020	-2.79
479	chr14:52117023-52117783	2.40	967	chr19:45279521-45280363	-3.16
480	chr14:53198124-53199748	0.76	968	chr19:45299905-45300394	-3.32
481	chr14:53367679-53368118	-2.79	969	chr19:45618775-45621227	-1.64
482	chr14:54412738-54413996	-2.63	970	chr19:47636472-47637374	-2.53
483	chr14:59157583-59157861	-2.44	971	chr19:48150949-48151649	-4.85
484	chr14:62035207-62035750	-4.87	972	chr19:48564842-48565460	-5.97
485	chr14:62217605-62218221	-3.12	973	chr19:48833366-48834641	-3.98
486	chr14:65173265-65173582	-2.24	974	chr19:48993674-48995888	-4.85
487	chr14:67988596-67989166	1.00	975	chr19:49064764-49065045	-2.03
488	chr14:69322013-69322671	-1.14	976	chr19:50977544-50980289	1.28

Table 3: Exemplary genomic loci that are differentially DNA methylated in ER-positive vs. ER-negative cancer.

Index	Genomic locus	log2(FC)	Index	Genomic locus	log2(FC)
977	chr19:51061684-51062328	1.80	1465	chr6:3455585-3456349	-3.89
978	chr19:51226228-51227428	2.72	1466	chr6:3665095-3665348	-3.56
979	chr19:51512236-51512766	-2.82	1467	chr6:4135130-4135926	-3.60
980	chr19:51871045-51871830	-3.12	1468	chr6:4806104-4807350	-2.26
981	chr19:52531234-52531853	-4.11	1469	chr6:6748953-6749224	-3.30
982	chr19:53072921-53074126	-4.21	1470	chr6:6759632-6760149	-3.65
983	chr19:54642426-54642889	-2.46	1471	chr6:10771610-10771991	-1.59
984	chr19:56153825-56154503	-4.65	1472	chr6:12757906-12758332	1.89
985	chr19:56291087-56291415	-2.40	1473	chr6:12864572-12864912	1.72
986	chr19:58144227-58145024	-3.73	1474	chr6:13797543-13798265	-3.31
987	chr19:58608214-58610051	-4.02	1475	chr6:15254928-15255231	-2.88
988	chr19:58661622-58662347	-3.57	1476	chr6:18136590-18137069	-2.45
989	chr19:58665988-58666746	-4.03	1477	chr6:19869781-19870579	-1.93
990	chr19:59025242-59025840	-6.05	1478	chr6:21587083-21587761	-4.21
991	chr2:45242-46552	-4.41	1479	chr6:25165191-25165619	-2.88
992	chr2:263297-264211	-4.67	1480	chr6:27473454-27473807	-2.61
993	chr2:8703300-8704871	-1.39	1481	chr6:27834705-27835484	-3.33
994	chr2:10161994-10162608	-1.98	1482	chr6:28303295-28304290	-3.48
995	chr2:10425874-10427195	-4.23	1483	chr6:28351026-28351538	-3.61
996	chr2:10598659-10599329	-1.83	1484	chr6:28761865-28763881	-3.10
997	chr2:10600510-10600929	-3.01	1485	chr6:29716068-29717243	2.88
998	chr2:10925014-10925156	-2.60	1486	chr6:30746668-30747045	-2.06
999	chr2:11681472-11681727	-2.40	1487	chr6:31465377-31467032	-4.68
1000	chr2:11724769-11725152	1.83	1488	chr6:33395964-33396472	-4.17
1001	chr2:11924776-11925611	-1.84	1489	chr6:34518470-34520280	-3.74
1002	chr2:20647173-20648641	-3.49	1490	chr6:34522795-34522964	-2.72
1003	chr2:20666574-20667134	-3.46	1491	chr6:35265275-35266067	-3.57
1004	chr2:21499029-21499450	2.11	1492	chr6:35453492-35454636	-5.42
1005	chr2:23683497-23683824	-2.39	1493	chr6:38669725-38670120	-1.98
1006	chr2:25583930-25585993	-2.49	1494	chr6:41620727-41621445	-6.01
1007	chr2:27958086-27958823	-3.14	1495	chr6:42097662-42098075	-4.26
1008	chr2:28612843-28613473	-3.13	1496	chr6:42105281-42105861	-2.75
1009	chr2:28907033-28907473	-2.00	1497	chr6:42183932-42184737	-2.24
1010	chr2:36668324-36668727	-2.57	1498	chr6:42397108-42397508	-2.49
1011	chr2:37551014-37552562	3.03	1499	chr6:42858312-42859502	-3.46
1012	chr2:38365134-38365840	-1.39	1500	chr6:43044581-43045163	4.23
1013	chr2:43201921-43202791	-2.69	1501	chr6:47276380-47276933	3.78
1014	chr2:44111243-44111573	-1.93	1502	chr6:49518058-49519375	-3.14
1015	chr2:44513430-44514144	-2.14	1503	chr6:52858715-52860641	1.93
1016	chr2:46512749-46513305	-0.90	1504	chr6:65185012-65185602	-1.94
1017	chr2:46635024-46635540	-2.27	1505	chr6:70310977-70311462	-4.24
1018	chr2:48013565-48013818	-1.65	1506	chr6:84729048-84729553	-1.87
1019	chr2:55364484-55365167	-1.11	1507	chr6:85421401-85421992	-2.96
1020	chr2:55908833-55909406	-1.34	1508	chr6:85532357-85532801	-2.31
1021	chr2:56410934-56412166	-3.27	1509	chr6:110650702-110651500	-2.56

Index	Genomic locus	log2(FC)	Index	Genomic locus	log2(FC)
1022	chr2:60645074-60645513	-2.04	1510	chr6:114178103-114179089	3.35
1023	chr2:60783755-60784927	-4.05	1511	chr6:117197467-117199211	-3.47
1024	chr2:61134824-61135191	-3.27	1512	chr6:117761229-117761631	-1.43
1025	chr2:64955289-64956460	-1.02	1513	chr6:125525551-125526000	-1.92
1026	chr2:65527409-65527877	-5.35	1514	chr6:125854939-125855522	-3.52
1027	chr2:65615069-65615583	-2.09	1515	chr6:138185055-138185593	-1.22
1028	chr2:67089322-67089658	-1.76	1516	chr6:138745030-138745960	-0.78
1029	chr2:67111990-67112457	-2.02	1517	chr6:138751443-138753567	-0.86
1030	chr2:67114751-67115056	-2.55	1518	chr6:138785143-138785684	-0.67
1031	chr2:67701024-67701553	-0.92	1519	chr6:138893005-138893908	-4.44
1032	chr2:70313114-70313578	2.98	1520	chr6:138978567-138978995	-0.98
1033	chr2:74667466-74669448	-4.57	1521	chr6:138991329-138992586	-0.85
1034	chr2:74670843-74671228	-2.22	1522	chr6:139163501-139163938	-0.97
1035	chr2:75720205-75720799	-7.07	1523	chr6:141496009-141497708	-0.96
1036	chr2:76975666-76976047	-3.18	1524	chr6:141776191-141776572	-1.00
1037	chr2:84743299-84743901	-3.20	1525	chr6:143998883-143999876	3.26
1038	chr2:86783637-86784146	-2.90	1526	chr6:144604623-144604808	-2.51
1039	chr2:88354085-88354562	-3.06	1527	chr6:145140999-145141607	-1.78
1040	chr2:88848521-88849825	-3.33	1528	chr6:145454896-145455230	-1.71
1041	chr2:96348227-96348905	-4.43	1529	chr6:146136214-146136952	3.26
1042	chr2:97535906-97536414	-3.63	1530	chr6:146919829-146920371	-3.43
1043	chr2:97617788-97618278	-4.73	1531	chr6:147319342-147319809	-1.17
1044	chr2:98308051-98308440	-1.90	1532	chr6:148578746-148579126	-2.08
1045	chr2:100252914-100253488	-2.79	1533	chr6:148599035-148599483	-1.84
1046	chr2:100484297-100484550	1.65	1534	chr6:148602640-148603078	-1.51
1047	chr2:100684445-100684738	-4.31	1535	chr6:148611378-148611945	-0.94
1048	chr2:100937387-100939198	-4.35	1536	chr6:148638550-148641026	-0.93
1049	chr2:101412378-101412832	-1.23	1537	chr6:148658200-148658800	-0.96
1050	chr2:105911922-105912321	-1.54	1538	chr6:148665896-148666191	-2.21
1051	chr2:105986265-105986849	-3.70	1539	chr6:149381405-149381888	-2.74
1052	chr2:107921355-107921717	-2.87	1540	chr6:150462886-150465537	3.62
1053	chr2:109329103-109330105	-1.16	1541	chr6:150920871-150922162	3.87
1054	chr2:109635480-109635696	-2.78	1542	chr6:151186842-151189744	1.53
1055	chr2:110969719-110970330	-5.86	1543	chr6:151655746-151656059	-2.63
1056	chr2:113969820-113970552	-2.05	1544	chr6:151776752-151777167	-2.06
1057	chr2:118627423-118628812	-1.31	1545	chr6:151814868-151816117	-6.02
1058	chr2:119887511-119887900	-2.65	1546	chr6:152128372-152130498	-3.75
1059	chr2:121793385-121793753	-3.16	1547	chr6:154679937-154680218	-1.48
1060	chr2:129063647-129064206	-4.43	1548	chr6:154936748-154937210	-4.14
1061	chr2:129143584-129144086	-2.47	1549	chr6:155478581-155478950	-1.11
1062	chr2:130737118-130737812	-5.60	1550	chr6:156121821-156122153	-1.39
1063	chr2:132121204-132121871	-3.85	1551	chr6:157313623-157314028	-1.81
1064	chr2:134325754-134326217	-6.38	1552	chr6:158093516-158095345	-0.72
1065	chr2:136875673-136877207	-4.16	1553	chr6:158320545-158321701	-3.70
1066	chr2:145271137-145271488	-2.91	1554	chr6:161351800-161352591	-3.43
1067	chr2:151349937-151350278	-1.14	1555	chr6:161559817-161561750	-0.95

Index	Genomic locus	log2(FC)	Index	Genomic locus	log2(FC)
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1069	chr2:153192407-153193219	3.42	1557	chr6:161685330-161685849	-2.29
1070	chr2:159823985-159824732	-3.99	1558	chr6:162210220-162210578	-2.58
1071	chr2:164592333-164593831	-3.19	1559	chr6:163387505-163390084	-2.84
1072	chr2:165477557-165478548	-3.69	1560	chr6:163624059-163624708	-2.46
1073	chr2:167232321-167233120	-2.91	1561	chr6:166705951-166706370	-3.39
1074	chr2:170551811-170552257	-4.16	1562	chr6:166876013-166877422	-1.26
1075	chr2:171784849-171785229	2.79	1563	chr6:166915971-166916129	-2.94
1076	chr2:173330110-173330546	-4.43	1564	chr6:166976336-166979237	-1.34
1077	chr2:180886410-180887000	-1.92	1565	chr6:167027037-167027893	-1.25
1078	chr2:181846434-181846766	2.93	1566	chr6:167089876-167090025	-3.01
1079	chr2:190421073-190421425	-2.17	1567	chr6:168238906-168239058	-2.13
1080	chr2:190445026-190446403	-2.98	1568	chr7:66363-67543	-3.79
1081	chr2:196427711-196428039	-4.77	1569	chr7:102759-104250	-4.72
1082	chr2:201346136-201346597	-3.50	1570	chr7:138216-139803	-3.46
1083	chr2:202813918-202814476	-4.42	1571	chr7:311961-314118	-3.02
1084	chr2:216808210-216808857	-1.14	1572	chr7:349229-351458	-3.34
1085	chr2:216843841-216844195	-2.73	1573	chr7:676775-678532	-4.68
1086	chr2:225196722-225197021	-2.00	1574	chr7:722239-724048	-4.31
1087	chr2:227655846-227656636	-3.95	1575	chr7:764520-764907	-2.61
1088	chr2:230931373-230933626	-3.62	1576	chr7:849608-851404	-4.66
1089	chr2:231604208-231604522	-2.58	1577	chr7:1172491-1175387	-5.15
1090	chr2:233497814-233499899	-3.68	1578	chr7:1500474-1501529	-3.05
1091	chr2:233520461-233520830	-2.57	1579	chr7:1568232-1569322	-3.06
1092	chr2:235372611-235373042	-4.83	1580	chr7:1596883-1599404	-2.60
1093	chr2:235404165-235407020	1.06	1581	chr7:1620233-1622463	-4.33
1094	chr2:235935995-235936747	-3.40	1582	chr7:1714656-1716731	-3.29
1095	chr2:236516348-236516895	-2.05	1583	chr7:1739749-1740772	-4.03
1096	chr2:236526050-236526786	-2.65	1584	chr7:2222143-2224631	-3.84
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1098	chr2:238258582-238258965	-2.56	1586	chr7:2267510-2268052	-3.23
1099	chr2:238411871-238412328	-2.46	1587	chr7:2359160-2361674	-3.51
1100	chr2:238467465-238468675	-4.17	1588	chr7:2365886-2369628	-4.39
1101	chr2:238642307-238642612	-4.57	1589	chr7:2390550-2393027	-4.34
1102	chr2:239956648-239957513	2.51	1590	chr7:2461689-2463229	-3.21
1103	chr2:240188910-240189548	-3.72	1591	chr7:2505690-2506544	-2.63
1104	chr2:241042967-241043479	1.71	1592	chr7:2550376-2551824	-3.53
1105	chr2:241050406-241050842	3.19	1593	chr7:2595739-2598009	-4.22
1106	chr2:242832905-242833859	-4.63	1594	chr7:2723260-2733350	-5.38
1107	chr20:327303-327995	-3.37	1595	chr7:2810728-2811027	-3.13
1108	chr20:1448343-1448754	-2.44	1596	chr7:2842354-2843084	-4.62
1109	chr20:2186488-2187988	-3.16	1597	chr7:2878670-2881024	-4.25
1110	chr20:2245274-2245645	-3.93	1598	chr7:2908456-2910935	-3.79
1111	chr20:3387134-3387641	-3.23	1599	chr7:3140337-3142568	-3.54
1112	chr20:4850357-4851203	-2.69	1600	chr7:3340098-3341788	-5.02
1113	chr20:6103242-6104131	5.01	1601	chr7:4016181-4017429	-3.34

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1116	chr20:6982091-6982693	-3.24	1604	chr7:4689401-4690644	-2.21
1117	chr20:7028030-7028569	-3.93	1605	chr7:4692865-4694832	-3.85
1118	chr20:7146388-7146756	-2.63	1606	chr7:4713036-4714473	-3.15
1119	chr20:7192686-7193115	-2.20	1607	chr7:4726527-4728206	-3.56
1120	chr20:7199044-7199455	-2.34	1608	chr7:4729417-4730876	-3.22
1121	chr20:7332902-7333256	-2.44	1609	chr7:4813326-4814638	-3.15
1122	chr20:7820304-7820639	-2.41	1610	chr7:5059509-5060758	-3.53
1123	chr20:17548196-17548618	-1.73	1611	chr7:5061899-5063609	-4.35
1124	chr20:23617172-23618802	-4.11	1612	chr7:5071890-5075315	-4.45
1125	chr20:23667553-23668046	1.38	1613	chr7:5079354-5080680	-3.05
1126	chr20:31097629-31099004	-2.23	1614	chr7:5204640-5205432	2.22
1127	chr20:32320854-32321472	-3.52	1615	chr7:5466918-5469666	-4.92
1128	chr20:32450026-32450893	-2.11	1616	chr7:5574239-5575941	-3.54
1129	chr20:32898492-32900528	-5.07	1617	chr7:5601649-5602802	-3.61
1130	chr20:33621617-33622109	3.13	1618	chr7:5603769-5605693	-4.03
1131	chr20:35087986-35089338	-1.82	1619	chr7:5636903-5638672	-3.57
1132	chr20:35202829-35203755	-3.96	1620	chr7:5679296-5679838	-3.08
1133	chr20:35463985-35464415	-3.41	1621	chr7:5687953-5689134	-3.07
1134	chr20:35492652-35493579	-3.56	1622	chr7:5691082-5691538	-3.06
1135	chr20:42810201-42810659	-2.87	1623	chr7:5694730-5696331	-3.38
1136	chr20:43374293-43374993	-7.00	1624	chr7:5712674-5713917	-3.65
1137	chr20:44047833-44049371	-2.27	1625	chr7:5718795-5720404	-3.74
1138	chr20:45338024-45340033	-3.34	1626	chr7:5741538-5742673	-3.18
1139	chr20:45342878-45343475	-2.59	1627	chr7:5809691-5811823	-3.64
1140	chr20:45963374-45963732	2.04	1628	chr7:6046952-6048216	-2.98
1141	chr20:46292028-46292504	1.65	1629	chr7:6152427-6154623	-3.13
1142	chr20:46293615-46295682	1.43	1630	chr7:6182380-6182868	-2.62
1143	chr20:46300832-46301322	1.98	1631	chr7:6240673-6243651	-4.24
1144	chr20:46302843-46303772	1.87	1632	chr7:6307115-6308218	-2.61
1145	chr20:46329590-46331622	1.93	1633	chr7:6404488-6407416	-2.59
1146	chr20:46339186-46340020	2.23	1634	chr7:6412942-6413745	-3.36
1147	chr20:47090316-47090671	2.15	1635	chr7:6417882-6419341	-3.20
1148	chr20:48703278-48703809	-3.73	1636	chr7:6516727-6516939	-2.46
1149	chr20:48758968-48760221	-3.51	1637	chr7:6724612-6727415	-3.11
1150	chr20:48845609-48845949	-3.04	1638	chr7:6785783-6789207	-2.84
1151	chr20:50158783-50160826	-3.59	1639	chr7:6825894-6826848	-2.76
1152	chr20:51962171-51963284	-3.89	1640	chr7:6839680-6841877	-3.52
1153	chr20:52257047-52259140	2.00	1641	chr7:6901971-6904785	-2.87
1154	chr20:52362996-52364059	1.83	1642	chr7:23386175-23386536	-2.74
1155	chr20:52373980-52374497	1.55	1643	chr7:23423325-23423708	-1.83
1156	chr20:52429459-52431259	1.61	1644	chr7:23469694-23470171	-3.39
1157	chr20:52440258-52440829	1.98	1645	chr7:25017097-25021622	1.43
1158	chr20:52491963-52493682	1.60	1646	chr7:25529112-25529537	-2.32
1159	chr20:52510403-52510855	1.90	1647	chr7:26903792-26904930	4.05

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1162	chr20:53188713-53189055	-2.83	1650	chr7:36319624-36320892	1.92
1163	chr20:53233290-53233797	-2.94	1651	chr7:38670272-38671279	-4.03
1164	chr20:53238081-53239433	-2.64	1652	chr7:42532914-42533541	-3.84
1165	chr20:53604651-53605181	-1.88	1653	chr7:43803696-43803938	-3.80
1166	chr20:54126470-54127054	-3.07	1654	chr7:50560224-50561024	-3.37
1167	chr20:54332595-54332867	-2.64	1655	chr7:55038218-55038508	-2.18
1168	chr20:54345261-54345730	-2.58	1656	chr7:55248715-55249281	-3.96
1169	chr20:55588748-55589329	-3.39	1657	chr7:55617887-55618523	-2.18
1170	chr20:55678731-55680053	2.28	1658	chr7:69062028-69065374	-4.64
1171	chr20:55711210-55711682	2.06	1659	chr7:70995581-70995949	-2.83
1172	chr20:55717609-55718086	2.48	1660	chr7:71152203-71152579	-3.00
1173	chr20:56053298-56054136	-3.34	1661	chr7:71154912-71155366	-3.10
1174	chr20:56057286-56060074	1.99	1662	chr7:73867489-73868182	-3.37
1175	chr20:56785722-56786158	2.17	1663	chr7:73880522-73881774	-3.13
1176	chr20:56854837-56855350	1.50	1664	chr7:80572334-80572513	-3.98
1177	chr20:57618239-57618744	2.79	1665	chr7:87094235-87094655	-2.20
1178	chr20:57846136-57846699	-2.96	1666	chr7:89783512-89784196	2.45
1179	chr20:58247614-58249215	3.51	1667	chr7:92237847-92238397	-6.06
1180	chr20:58293720-58294180	2.49	1668	chr7:92554104-92554918	-1.83
1181	chr20:58316252-58319333	3.42	1669	chr7:96746519-96747346	4.38
1182	chr20:58328192-58328484	3.57	1670	chr7:99516549-99517430	4.11
1183	chr20:58330257-58331790	3.25	1671	chr7:99768729-99770192	-2.71
1184	chr20:59756086-59756490	-3.44	1672	chr7:100451056-100451329	-2.58
1185	chr20:59933769-59934665	-3.55	1673	chr7:100875502-100876188	-3.97
1186	chr20:60119185-60120885	-4.39	1674	chr7:101499898-101501061	-3.52
1187	chr20:60131639-60133049	-3.85	1675	chr7:101957600-101958067	-1.63
1188	chr20:60169649-60170931	-4.28	1676	chr7:107060868-107061317	-2.62
1189	chr20:60453848-60458282	-3.87	1677	chr7:108095218-108097979	-3.63
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1192	chr20:62153028-62153424	-3.87	1680	chr7:129945432-129948565	-1.29
1193	chr20:62283213-62285416	-4.23	1681	chr7:130674508-130675265	-3.00
1194	chr21:15646061-15646686	-4.25	1682	chr7:130819817-130820283	-3.03
1195	chr21:16580337-16580767	-3.45	1683	chr7:135205047-135205362	-2.12
1196	chr21:18040051-18040612	-1.39	1684	chr7:138742225-138742650	-2.36
1197	chr21:18835039-18835451	-1.38	1685	chr7:139717221-139717804	-3.91
1198	chr21:18956633-18958176	-2.29	1686	chr7:150946377-150946522	2.14
1199	chr21:19138401-19138748	-1.87	1687	chr7:152408041-152409342	-2.84
1200	chr21:30391223-30392391	-2.86	1688	chr7:154218917-154219933	-3.07
1201	chr21:30720954-30721520	-1.72	1689	chr7:155005610-155006821	-4.52
1202	chr21:30755607-30755996	-1.94	1690	chr7:155087826-155089062	-3.40
1203	chr21:33251763-33252029	2.18	1691	chr7:156308699-156309497	-2.61
1204	chr21:35986364-35987025	3.72	1692	chr7:156672008-156672374	-2.27
1205	chr21:37105136-37105811	-2.36	1693	chr7:157122174-157122639	-2.72

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1207	chr21:38026478-38027040	-1.40	1695	chr8:2976417-2976725	-2.77
1208	chr21:38937770-38938003	-3.18	1696	chr8:3027595-3028103	-2.58
1209	chr21:39018828-39019367	-3.12	1697	chr8:3982530-3983071	-2.14
1210	chr21:39082675-39083787	-2.39	1698	chr8:6009975-6011552	-3.89
1211	chr21:40337826-40338441	-3.36	1699	chr8:6762255-6762953	-2.24
1212	chr21:40759484-40760879	-3.74	1700	chr8:8092645-8095084	-1.33
1213	chr21:40951814-40952232	-2.60	1701	chr8:8820690-8821307	-2.96
1214	chr21:41654138-41654514	2.53	1702	chr8:10336745-10337164	-2.57
1215	chr21:42213367-42214305	-6.40	1703	chr8:10928796-10929364	-3.16
1216	chr21:43199468-43199769	-2.88	1704	chr8:10992507-10994058	-2.32
1217	chr21:43372707-43374609	3.66	1705	chr8:11053115-11053484	-2.39
1218	chr21:43382903-43385060	-3.41	1706	chr8:11080808-11081334	-2.74
1219	chr21:43389665-43389953	-2.07	1707	chr8:11719274-11719747	-2.35
1220	chr21:43480216-43483965	-3.37	1708	chr8:11843626-11844462	-2.60
1221	chr21:44421763-44424346	-3.65	1709	chr8:15351703-15352155	-2.47
1222	chr21:44426653-44426982	-3.59	1710	chr8:20126320-20126786	2.64
1223	chr21:44707034-44708227	-2.92	1711	chr8:22624942-22626538	-2.22
1224	chr21:44748982-44753926	-3.40	1712	chr8:22925572-22925851	2.79
1225	chr21:45131323-45131645	-3.13	1713	chr8:24086306-24086453	-2.40
1226	chr21:45592637-45593090	-3.81	1714	chr8:26061665-26062050	-3.39
1227	chr21:46193288-46193838	-3.72	1715	chr8:28269041-28270021	-3.53
1228	chr21:46354891-46356122	-2.51	1716	chr8:30294441-30294766	-2.72
1229	chr21:46934642-46937317	-1.48	1717	chr8:36979209-36979681	1.94
1230	chr21:47704129-47704446	-4.25	1718	chr8:37004957-37005896	3.51
1231	chr22:19738106-19738457	-2.35	1719	chr8:37029144-37029859	1.94
1232	chr22:19767263-19768606	-2.94	1720	chr8:37082089-37082759	1.93
1233	chr22:21275949-21276348	-4.17	1721	chr8:37164397-37165034	2.38
1234	chr22:22590986-22591621	-2.92	1722	chr8:37183294-37183863	2.17
1235	chr22:24237833-24238233	-2.68	1723	chr8:37188135-37189557	1.99
1236	chr22:24593198-24593615	-1.96	1724	chr8:37206262-37206892	1.61
1237	chr22:24941588-24942337	-2.16	1725	chr8:37214476-37215066	2.10
1238	chr22:25297725-25298041	-1.95	1726	chr8:37261381-37261761	2.25
1239	chr22:27152612-27153259	-3.98	1727	chr8:37317718-37319166	1.90
1240	chr22:27160044-27160347	-2.80	1728	chr8:37350440-37351795	2.18
1241	chr22:29188977-29189919	-2.13	1729	chr8:37369195-37370805	2.29
1242	chr22:29280482-29281290	-2.69	1730	chr8:37374908-37375469	2.22
1243	chr22:29319717-29320269	-5.33	1731	chr8:37378110-37379159	2.30
1244	chr22:29731186-29731926	-2.66	1732	chr8:37386511-37388100	1.89
1245	chr22:29866070-29866933	-3.79	1733	chr8:37415072-37415550	2.45
1246	chr22:31740398-31741667	-6.72	1734	chr8:37417721-37419206	2.48
1247	chr22:31975324-31975736	-2.60	1735	chr8:37422234-37422818	2.46
1248	chr22:34248551-34249030	-2.02	1736	chr8:37429854-37430821	2.33
1249	chr22:34485351-34485663	1.82	1737	chr8:37438171-37440524	2.23
1250	chr22:35919050-35919472	-2.18	1738	chr8:37493868-37494365	1.89
1251	chr22:36744270-36745185	-1.28	1739	chr8:37499340-37500381	2.24

Index	Genomic locus	log2(FC)	Index	Genomic locus	log2(FC)
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1253	chr22:36756307-36756775	-1.47	1741	chr8:37530608-37533185	2.24
1254	chr22:38051012-38051684	-0.86	1742	chr8:37561277-37561453	2.22
1255	chr22:38092523-38094186	-3.74	1743	chr8:37578024-37578657	2.28
1256	chr22:38577649-38579282	-3.40	1744	chr8:37592884-37593949	1.98
1257	chr22:38613116-38615885	-1.18	1745	chr8:37605144-37605809	1.96
1258	chr22:38805755-38806621	-0.69	1746	chr8:37617737-37619476	2.03
1259	chr22:39571236-39573071	-2.08	1747	chr8:37621081-37621776	2.32
1260	chr22:39637891-39638441	-3.28	1748	chr8:37625278-37626341	1.89
1261	chr22:39647906-39648280	-2.29	1749	chr8:37630704-37631254	1.89
1262	chr22:39758208-39758484	-1.40	1750	chr8:37633444-37634042	1.75
1263	chr22:40334469-40335053	-2.78	1751	chr8:37635234-37635836	2.13
1264	chr22:40785156-40785849	-0.73	1752	chr8:37645119-37646257	1.69
1265	chr22:41003095-41004373	-2.01	1753	chr8:37653798-37657003	2.31
1266	chr22:41013350-41014237	-0.97	1754	chr8:37671852-37673557	1.78
1267	chr22:41124745-41125042	-2.48	1755	chr8:37684982-37686157	1.94
1268	chr22:41126893-41127676	-1.28	1756	chr8:37690460-37693496	1.79
1269	chr22:41297542-41298587	-1.13	1757	chr8:37702138-37702760	2.48
1270	chr22:41413778-41415720	-0.89	1758	chr8:37704381-37705806	2.21
1271	chr22:41583396-41584184	-1.39	1759	chr8:37707951-37708320	3.71
1272	chr22:41890417-41891962	-0.88	1760	chr8:37729452-37731067	2.11
1273	chr22:42260342-42260764	-2.35	1761	chr8:37734539-37734993	2.53
1274	chr22:42287517-42288807	-0.79	1762	chr8:37746295-37746809	2.32
1275	chr22:43066746-43067878	-2.40	1763	chr8:37784498-37785849	1.84
1276	chr22:43510558-43510875	-3.66	1764	chr8:37815529-37815992	1.66
1277	chr22:43792774-43793421	-5.31	1765	chr8:37818114-37818420	1.86
1278	chr22:44759074-44759835	2.65	1766	chr8:37822305-37825209	2.05
1279	chr22:44851581-44851891	-2.89	1767	chr8:37844020-37844472	1.73
1280	chr22:44928491-44928822	-2.95	1768	chr8:37846237-37846837	1.96
1281	chr22:45064022-45065180	-3.69	1769	chr8:37869781-37870294	1.63
1282	chr22:45106846-45108457	-1.24	1770	chr8:37959908-37961909	1.58
1283	chr22:45377608-45378333	1.78	1771	chr8:38857494-38857920	2.29
1284	chr22:45592168-45593902	-0.82	1772	chr8:42749660-42750064	-4.90
1285	chr22:45647137-45648747	-2.30	1773	chr8:42751084-42751472	2.59
1286	chr22:45659663-45659968	-3.10	1774	chr8:54987888-54988138	-2.50
1287	chr22:45931142-45931343	-3.09	1775	chr8:59077512-59079040	-2.38
1288	chr22:45987867-45988599	-1.50	1776	chr8:59571505-59572594	2.80
1289	chr22:46255072-46257364	-2.33	1777	chr8:59904289-59904739	-3.62
1290	chr22:46326225-46327515	-0.88	1778	chr8:61193208-61194310	-3.65
1291	chr22:46557557-46559753	-1.37	1779	chr8:62722720-62723043	-3.33
1292	chr22:46861415-46862205	-4.37	1780	chr8:65541435-65541727	-2.06
1293	chr22:46873930-46875430	-1.54	1781	chr8:65746979-65747491	-2.64
1294	chr22:46942277-46946509	-3.08	1782	chr8:67454270-67455220	-7.62
1295	chr22:46993397-46993686	-2.40	1783	chr8:67782774-67783589	2.88
1296	chr22:47211073-47212193	-4.02	1784	chr8:70404651-70405456	-4.19
1297	chr22:47572997-47573360	-1.53	1785	chr8:74332328-74333821	-3.52

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1299	chr22:50360632-50363195	-2.94	1787	chr8:91094711-91096634	-4.29
1300	chr22:50481693-50481964	-3.80	1788	chr8:94967649-94968361	-4.31
1301	chr3:9811310-9811900	-4.15	1789	chr8:95021362-95021970	-3.48
1302	chr3:9941414-9941900	-3.35	1790	chr8:95960678-95961001	-3.30
1303	chr3:9993619-9994726	-5.47	1791	chr8:96068671-96069385	-2.51
1304	chr3:11581237-11582689	-1.46	1792	chr8:102450661-102452576	-2.57
1305	chr3:11684045-11685495	2.70	1793	chr8:102486063-102486366	-3.55
1306	chr3:12851420-12852119	-5.14	1794	chr8:102524627-102525195	-2.76
1307	chr3:13515314-13515989	-3.84	1795	chr8:102606352-102606496	-1.90
1308	chr3:23784750-23785283	-3.09	1796	chr8:103611800-103613555	-3.80
1309	chr3:29542919-29543137	-1.91	1797	chr8:105885853-105886203	-3.55
1310	chr3:29688619-29688823	-2.63	1798	chr8:117000666-117001006	-3.29
1311	chr3:31933590-31934044	-2.10	1799	chr8:118532064-118532427	-4.40
1312	chr3:43020590-43021464	-5.61	1800	chr8:125462935-125463890	-3.72
1313	chr3:44155596-44156020	-2.37	1801	chr8:128192641-128192946	-1.56
1314	chr3:45186979-45188107	-3.81	1802	chr8:128872170-128872662	-3.72
1315	chr3:46607276-46608161	-5.64	1803	chr8:128923488-128924015	-2.63
1316	chr3:48310395-48310839	-2.38	1804	chr8:129037275-129037589	-3.69
1317	chr3:48316529-48316749	-2.36	1805	chr8:129165316-129165881	-5.40
1318	chr3:49026996-49028521	-5.29	1806	chr8:136527272-136527682	-2.55
1319	chr3:49208565-49209366	-3.73	1807	chr8:139171111-139171685	-2.20
1320	chr3:50382799-50383476	-3.39	1808	chr8:141343437-141344749	-3.04
1321	chr3:52505615-52506229	-4.62	1809	chr8:142745174-142746823	3.77
1322	chr3:53879521-53881062	-4.82	1810	chr8:143125208-143125906	-3.29
1323	chr3:57967305-57968401	-0.92	1811	chr8:143265152-143265370	2.69
1324	chr3:58476948-58477244	-2.85	1812	chr8:143767606-143767993	-3.32
1325	chr3:59649705-59650150	-3.13	1813	chr8:143819285-143819863	-3.04
1326	chr3:64142796-64143158	-3.69	1814	chr8:143850963-143851456	-3.31
1327	chr3:72704187-72704823	-4.21	1815	chr8:144098206-144099725	-4.52
1328	chr3:72787904-72788665	-5.34	1816	chr8:144120040-144124982	-3.53
1329	chr3:89156413-89157221	-4.07	1817	chr8:144130237-144130675	-3.60
1330	chr3:89163499-89164197	-3.29	1818	chr8:144451741-144452604	-3.53
1331	chr3:107718541-107718940	-1.76	1819	chr8:144953976-144955521	-2.55
1332	chr3:107810023-107810915	-2.97	1820	chr8:145027516-145029297	-2.99
1333	chr3:113213057-113213548	-1.64	1821	chr8:145979426-145979860	-3.10
1334	chr3:113251327-113252692	-3.02	1822	chr8:146283913-146284215	-1.89
1335	chr3:117715526-117716712	-4.19	1823	chr9:2211149-2211726	-1.32
1336	chr3:120438020-120439464	-1.74	1824	chr9:4066792-4066974	-2.03
1337	chr3:125305373-125305722	-2.44	1825	chr9:4864356-4864963	-2.75
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1339	chr3:132378454-132379701	5.17	1827	chr9:5721426-5722203	-2.39
1340	chr3:137228085-137228936	-2.84	1828	chr9:7147679-7149606	-1.56
1341	chr3:139653169-139655123	-3.59	1829	chr9:12779239-12779705	-2.17
1342	chr3:141174146-141175401	-4.30	1830	chr9:13277403-13279841	-2.27
1343	chr3:143315910-143316376	-2.29	1831	chr9:16133788-16135501	-2.18

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1346	chr3:174987131-174987459	-3.12	1834	chr9:16523048-16523757	-2.14
1347	chr3:180396998-180397955	-4.18	1835	chr9:16663106-16663356	-2.26
1348	chr3:184053476-184054384	-4.81	1836	chr9:17215485-17216067	-2.87
1349	chr3:185827657-185828450	-2.83	1837	chr9:17268312-17269185	-3.13
1350	chr3:188816784-188817126	-2.61	1838	chr9:20144236-20144565	-2.87
1351	chr3:190039641-190040509	3.56	1839	chr9:21029698-21029946	-2.68
1352	chr3:190965610-190965912	-1.52	1840	chr9:21395819-21396510	-6.50
1353	chr3:192444711-192445703	-3.85	1841	chr9:22160696-22160994	-1.87
1354	chr3:193554022-193555054	-2.58	1842	chr9:27177347-27177708	-1.96
1355	chr3:193857170-193857726	-2.96	1843	chr9:30060504-30060958	-2.90
1356	chr3:196227514-196227992	3.26	1844	chr9:34593046-34593323	-3.48
1357	chr4:330015-332827	-6.31	1845	chr9:35810843-35812453	-4.34
1358	chr4:686770-687371	-3.91	1846	chr9:35986551-35987641	-2.57
1359	chr4:689001-690233	-2.25	1847	chr9:36448858-36449883	-1.69
1360	chr4:776563-776725	-4.11	1848	chr9:37797929-37798533	-1.71
1361	chr4:787377-787887	-3.73	1849	chr9:38022309-38022789	-2.51
1362	chr4:990872-991585	-4.14	1850	chr9:38766689-38767157	-2.57
1363	chr4:1404007-1404524	-3.53	1851	chr9:38863030-38864447	-2.59
1364	chr4:2794238-2795591	-3.37	1852	chr9:40305776-40306191	-2.64
1365	chr4:2819296-2820587	-6.08	1853	chr9:40333731-40334580	-1.79
1366	chr4:3216942-3217283	-3.34	1854	chr9:40336221-40336552	-2.43
1367	chr4:3464713-3466114	-3.89	1855	chr9:40378258-40378623	-2.12
1368	chr4:3726081-3726984	3.06	1856	chr9:40734083-40734390	-1.90
1369	chr4:6273138-6273853	-3.53	1857	chr9:40741727-40742025	-2.33
1370	chr4:6282487-6282744	-2.20	1858	chr9:40748219-40748715	-1.87
1371	chr4:6445010-6445399	1.80	1859	chr9:40762864-40763076	-2.47
1372	chr4:6472163-6474629	-3.84	1860	chr9:44542505-44542845	-2.01
1373	chr4:6689888-6691583	-3.15	1861	chr9:73984384-73984647	-2.64
1374	chr4:6697316-6697732	-3.97	1862	chr9:81468434-81468780	-1.39
1375	chr4:6765186-6765653	-3.10	1863	chr9:82184165-82188586	2.23
1376	chr4:6909398-6909937	-3.12	1864	chr9:83935396-83935773	-3.10
1377	chr4:7047697-7047979	-2.67	1865	chr9:84138414-84138793	-2.19
1378	chr4:8429046-8429354	-2.63	1866	chr9:91148961-91151290	-3.25
1379	chr4:8440375-8440824	-3.02	1867	chr9:93279785-93280251	-2.94
1380	chr4:9153823-9155600	3.20	1868	chr9:95363133-95363927	-2.08
1381	chr4:9533698-9534729	-3.18	1869	chr9:95709487-95710762	-3.17
1382	chr4:10625800-10626359	-2.48	1870	chr9:95766149-95766610	-3.34
1383	chr4:10656395-10657658	-1.77	1871	chr9:95824227-95824635	-2.37
1384	chr4:24975476-24975986	-4.23	1872	chr9:96671203-96671573	-5.27
1385	chr4:40449707-40450208	-2.05	1873	chr9:97401065-97402684	-3.52
1386	chr4:40478914-40480334	-1.92	1874	chr9:98268462-98269206	3.46
1387	chr4:74903700-74904437	4.09	1875	chr9:98277745-98280200	1.29
1388	chr4:74964251-74965351	2.47	1876	chr9:98931671-98932158	-4.62
1389	chr4:77173180-77173511	-2.39	1877	chr9:99380027-99382307	1.44

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1392	chr4:104854488-104854878	-4.21	1880	chr9:112027391-112027740	-2.58
1393	chr4:109434200-109434664	-2.95	1881	chr9:115478332-115479327	-2.80
1394	chr4:118006399-118006894	-3.98	1882	chr9:115518719-115519156	-3.18
1395	chr4:120376993-120377389	3.31	1883	chr9:116327078-116328143	3.46
1396	chr4:120691084-120691512	-2.30	1884	chr9:120053440-120053928	1.92
1397	chr4:130168311-130168691	-2.66	1885	chr9:130306850-130308403	-3.27
1398	chr4:156712291-156712873	-1.19	1886	chr9:130325202-130326131	-2.91
1399	chr4:164252193-164253579	-5.17	1887	chr9:130375197-130375877	-3.15
1400	chr4:169598768-169599379	-2.06	1888	chr9:130608449-130609938	-2.28
1401	chr4:175749826-175750840	-3.30	1889	chr9:130732265-130733258	-2.91
1402	chr4:184357414-184357609	-1.67	1890	chr9:130832236-130833216	-2.91
1403	chr4:186435306-186435986	-2.78	1891	chr9:130954682-130955945	-3.34
1404	chr4:186535927-186536392	-2.60	1892	chr9:132081261-132083751	-3.11
1405	chr4:188851178-188851603	-1.89	1893	chr9:132168559-132169079	-3.24
1406	chr4:190291338-190291825	-2.64	1894	chr9:132220697-132222417	-5.26
1407	chr5:317375-317769	-2.36	1895	chr9:132381827-132383117	-5.49
1408	chr5:2000760-2002132	-3.50	1896	chr9:132646728-132648537	-4.53
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1410	chr5:5242163-5242535	-2.48	1898	chr9:133319746-133321080	3.01
1411	chr5:5271343-5272873	-3.01	1899	chr9:133966921-133967442	-2.25
1412	chr5:5287748-5288539	-3.08	1900	chr9:134420134-134423510	-4.96
1413	chr5:5317937-5319341	-3.08	1901	chr9:136019213-136020222	-2.36
1414	chr5:5333423-5334920	-2.28	1902	chr9:136343963-136345026	3.09
1415	chr5:5349771-5350128	-3.09	1903	chr9:136930584-136930844	-2.78
1416	chr5:10301573-10302031	-3.35	1904	chr9:137220535-137221280	-5.27
1417	chr5:10453366-10453813	-2.31	1905	chr9:137249741-137250132	-4.77
1418	chr5:11903025-11904853	-3.23	1906	chr9:137251115-137255767	-1.22
1419	chr5:11961803-11962187	-3.54	1907	chr9:137258987-137259979	-3.83
1420	chr5:12691589-12691739	-2.60	1908	chr9:137267360-137270221	-1.81
1421	chr5:14364734-14365124	-1.98	1909	chr9:137816243-137816655	2.21
1422	chr5:14725515-14726008	-2.19	1910	chr9:137970173-137970401	1.99
1423	chr5:23530142-23530410	-3.11	1911	chr9:138009131-138009482	3.14
1424	chr5:28862617-28862942	-2.58	1912	chr9:138108856-138112077	2.81
1425	chr5:32616457-32616662	-1.89	1913	chr9:138259629-138260198	2.37
1426	chr5:35617589-35618648	-4.58	1914	chr9:138277294-138277693	2.89
1427	chr5:40838463-40838756	-1.82	1915	chr9:138301239-138301621	2.62
1428	chr5:42423593-42425189	-3.04	1916	chr9:139573915-139574155	-3.00
1429	chr5:54529953-54530350	2.62	1917	chr9:140093451-140094406	-4.47
1430	chr5:55393339-55393928	-2.94	1918	chrX:9432672-9436112	-3.70
1431	chr5:55775506-55777690	-2.46	1919	chrX:9844911-9845554	0.86
1432	chr5:56013540-56013777	-2.08	1920	chrX:9866185-9866497	1.37
1433	chr5:66029257-66029534	1.17	1921	chrX:9872413-9873782	0.93
1434	chr5:70927198-70927800	-2.72	1922	chrX:9907159-9910060	0.87
1435	chr5:71044049-71044469	-3.46	1923	chrX:13752387-13753346	-3.53

Index	Genomic locus	log2(FC)	Index	Genomic locus	log2(FC)
1436	chr5:72236478-72237635	-1.68	1924	chrX:14047640-14048386	-4.98
1437	chr5:78985354-78986393	-6.13	1925	chrX:16157306-16157615	1.09
1438	chr5:79783240-79783446	-2.86	1926	chrX:16437899-16438265	1.26
1439	chr5:87438206-87438519	-3.26	1927	chrX:16440563-16441326	1.44
1440	chr5:88179796-88180309	3.35	1928	chrX:16515400-16515938	1.21
1441	chr5:94981766-94982242	-2.05	1929	chrX:16552376-16553150	0.88
1442	chr5:107004663-107006209	3.16	1930	chrX:37764877-37765503	-3.40
1443	chr5:116171530-116172126	1.20	1931	chrX:41301325-41302095	-4.60
1444	chr5:118787956-118788965	-3.74	1932	chrX:44562938-44563309	1.25
1445	chr5:121412514-121414200	2.35	1933	chrX:46306137-46307137	-3.33
1446	chr5:127091521-127092006	-2.92	1934	chrX:66763711-66766589	-3.46
1447	chr5:131706616-131707018	-3.84	1935	chrX:70315413-70316741	-2.91
1448	chr5:132386950-132387513	4.22	1936	chrX:73398289-73398755	-2.73
1449	chr5:134368552-134368900	3.23	1937	chrX:80063939-80065734	-2.87
1450	chr5:139016850-139018132	-7.42	1938	chrX:84258090-84259247	-4.25
1451	chr5:139029674-139030523	-4.20	1939	chrX:101854185-101854687	-3.52
1452	chr5:139035209-139035685	-2.97	1940	chrX:105412060-105412543	-3.01
1453	chr5:139531767-139532280	-3.27	1941	chrX:106869698-106869852	-2.93
1454	chr5:141736776-141737193	2.64	1942	chrX:113903981-113904232	-1.62
1455	chr5:142589681-142589987	-3.00	1943	chrX:117982348-117982671	-1.75
1456	chr5:143308598-143309070	-3.40	1944	chrX:118140270-118140887	-1.52
1457	chr5:172753598-172757326	-3.52	1945	chrX:119619579-119620219	-3.23
1458	chr5:172924550-172925067	-3.12	1946	chrX:122782287-122782532	-2.16
1459	chr5:173193641-173194063	-3.16	1947	chrX:130902210-130903160	-1.77
1460	chr5:174151309-174153007	-4.37	1948	chrX:130945874-130946355	-1.53
1461	chr5:174178048-174179092	-3.68	1949	chrX:132755309-132755479	-2.41
1462	chr5:176740317-176742406	-2.77	1950	chrX:135291372-135291973	-3.01
1463	chr5:179640017-179640180	2.25	1951	chrX:139569524-139569859	1.80
1464	chr6:1070083-1070602	-4.48	1952	chrX:154444317-154445301	-3.51

OTHER EMBODIMENTS

[0344] It will be appreciated that the scope of the present disclosure is to be defined by that which may be understood from the disclosure and claims rather than by the specific embodiments that have been presented by way of example. Elements described with respect to one aspect or embodiment of the present disclosure are also contemplated with respect to other aspects or embodiments of the present disclosure. For example, elements of claims that depend directly or indirectly from a certain independent claim presented herein serve as support for those elements being presented in additional dependent claims of one or more other independent claims. Throughout the description, where compositions or methods are described as having, including, or comprising specific elements, it is to be understood that compositions or methods that consist essentially of, consist of, or do not comprise the recited elements are likewise hereby disclosed. All references cited herein are hereby incorporated by reference.

CLAIMS

What is claimed is:

1. A method of determining the ER status of a cancer in a subject, the method comprising:
quantifying, at one or more genomic loci in cell-free DNA (cfDNA) from a liquid biopsy sample obtained or derived from the subject, one or more epigenetic biomarkers, wherein the one or more epigenetic biomarkers comprise:
 - (i) one or more histone modifications,
 - (ii) chromatin accessibility,
 - (iii) binding of one or more transcription factors, and/or
 - (iv) DNA methylation; anddetermining the ER status of the cancer in the subject by comparing the level of the one or more epigenetic biomarkers at the one or more genomic loci to a reference;
wherein the one or more genomic loci comprise (i) one or more genomic loci with an increased level of the one or more epigenetic biomarkers in subjects with an ER-positive cancer as compared to subjects with an ER-negative cancer, and/or (ii) one or more genomic loci with an increased level of the one or more epigenetic biomarkers in subjects with ER-negative cancer as compared to subjects with an ER positive cancer.
2. The method of claim 1, wherein:
 - (a) the liquid biopsy sample is a plasma sample, serum sample, or urine sample;
 - (b) the method comprises isolating cfDNA from about 1 mL of the liquid biopsy sample (e.g., plasma sample); and/or
 - (c) the sample comprises a detectable amount of ctDNA (e.g., wherein estimated tumor fraction is >3% for the cfDNA, e.g., as determined by iChorCNA).
3. The method of claim 1 or 2, wherein the one or more histone modifications are quantified using a histone modification assay that measures one or more of H3K9ac, H3K14ac, H3K18ac, H3K23ac, H3K27ac, H3K4me1, H3K4me2, H3K4me3, and pan-acetylation.
4. The method of any one of claims 1-3, wherein:

(a) the one or more histone modifications are quantified using an assay selected from ChIP-seq (Chromatin ImmunoPrecipitation sequencing), CUT&RUN (Cleavage Under Targets and Release Using Nuclease) sequencing, and CUT&Tag (Cleavage Under Targets and Tagmentation) sequencing;

(b) the chromatin accessibility is quantified using a chromatin accessibility assay selected from ATAC-seq (Assay of Transpose Accessible Chromatin sequencing), NOMe-seq (Nucleosome Occupancy and Methylome sequencing), FAIRE-seq (Formaldehyde-Assisted Isolation of Regulatory Elements sequencing), MNase-seq (Micrococcal Nuclease digestion with sequencing), and a DNase hypersensitivity assay;

(c) the binding of one or more transcription factors is quantified using a transcription factor binding assay that detects binding of one or more of p300, mediator complex, cohesin complex, RNA pol II, FOXA1, ESR1, PR, MYC, EN1, FOXM1, KLF4, AP-2, RARa, or RUNX1, optionally wherein the transcription factor binding assay is selected from ChIP-seq (Chromatin ImmunoPrecipitation sequencing), CUT&RUN (Cleavage Under Targets and Release Using Nuclease) sequencing, and CUT&Tag (Cleavage Under Targets and Tagmentation) sequencing; and/or

(d) DNA methylation is quantified using Bisulfite sequencing (BS-Seq), Whole Genome Bisulfite Sequencing (WGBS), Methylated DNA ImmunoPrecipitation sequencing (MeDIP-seq), or Methyl-CpG-Binding Domain sequencing (MBD-seq).

5. The method of any one of claims 1-4, wherein the method comprises:

(a) quantifying H3K4me3 modifications at one or more genomic loci using an assay that comprises enriching for cfDNA comprising one or more H3K4me3 modifications (e.g., using a method that comprises incubating with an agent that binds H3K4me3 modifications) and sequencing the cfDNA enriched for H3K4me3 modifications to determine a count of sequences with one or more H3K4me3 modifications;

(b) quantifying H3K27ac modifications at one or more genomic loci using an assay that comprises enriching for cfDNA comprising one or more H3K27ac modifications (e.g., using a method that comprises incubating with an agent that binds H3K27ac modifications) and sequencing the cfDNA enriched for H3K27ac modifications to determine a count of sequences with one or more H3K27ac modifications; and/or

(c) quantifying methylated DNA at one or more genomic loci using an assay that comprises enriching for methylated cfDNA (e.g., using a method that comprises incubating with an agent that binds methylated DNA) and sequencing the enriched cfDNA to determine a count of sequences with one or more methylated nucleotides; and

optionally:

(d) if the method comprises use of an agent that binds H3K4me3 modifications, an agent that binds H3K27ac modifications, and/or an agent that binds methylated DNA, the agent(s) are attached (e.g., via a covalent or noncovalent bond) to a physical support (e.g., a bead, a magnetic bead, an agarose bead, or a magnetic epoxy bead) prior to incubating with the sample; and/or

(e) if the method comprises incubating with two or more of an agent that binds H3K4 modifications, an agent that binds H3K27ac modifications, and an agent that binds methylated DNA, the sample is incubated with the two or more agents (i) in sequence or (ii) in parallel (e.g., wherein the sample is divided into fractions and each fraction is incubated with a different agent).

6. The method of any one of claims 1-5, comprising mapping sequence reads to a reference genome, optionally wherein non-uniquely mapped and redundant sequence reads are discarded and/or peaks in high noise regions are removed.

7. The method of claim 6, wherein the one or more genomic loci correspond to sequence read peaks, wherein a sequence read peak corresponds to a region of the genome that has a higher number of sequence reads than the local background.

8. The method of any one of claims 5-7, wherein quantifying H3K4me3 modifications, H3K27ac modifications, and/or DNA methylation comprises summing the number of sequence reads having at least one nucleotide overlap with the one or more genomic loci,

optionally wherein:

sequence reads are adjusted on the basis of sequencing depth (e.g., quantile normalizing sequence reads to a common reference distribution) and/or ChIP quality prior to summing;

sequence counts are normalized to aggregate counts in a given sample across a set of regions (e.g., 10,000 regions) previously determined to have DNase hypersensitivity in most cell types; and/or

an estimate of local background signal is subtracted from the sequence reads at each genomic loci prior to summing.

9. The method of any one of claims 1-8, wherein the reference is a predetermined threshold, a measurement from a liquid biopsy sample, a measurement from liquid biopsy samples obtained from a cohort of subjects, and/or a normalized value, wherein:

the predetermined threshold and the normalized value were previously shown to distinguish ER-positive and ER-negative subjects (e.g., distinguish with an AUROC of greater than 0.5);

the reference is a measurement from a liquid biopsy sample obtained from a cohort of subjects who have previously been determined to have an ER-positive or ER-negative cancer.

10. The method of any one of claims 5-9, comprising calculating sequence read density at the one or more genomic loci, optionally wherein sequence read density is calculated by:

(a) summing background adjusted sequence counts at each of the one or more genomic loci and dividing by the sum of the kilobases of the one or more genomic loci; or

(b) for each genomic loci, dividing background adjusted fragment count by the number of kilobases of the genomic loci, and then summing for each loci.

11. The method of claim 10, comprising calculating an ER-positive/ER-negative ratio score by a method comprising:

(a) calculating an ER-positive sequence read density by a method comprising summing background adjusted sequence counts at each of the one or more genomic loci with an increased level of the one or more epigenetic biomarkers in sample(s) obtained from subjects with an ER-positive cancer as compared to samples obtained from subjects with ER-negative cancer;

(b) calculating an ER-negative sequence read density by a method comprising summing background adjusted sequence counts at each of the one or more genomic loci with an

increased level of the one or more epigenetic biomarkers in sample(s) obtained from subjects with an ER-negative cancer as compared to samples obtained from subjects with an ER-positive cancer; and

(c) dividing the ER-positive sequence read density by the ER-negative sequence read density.

12. The method of claim 11, comprising:

- (a) determining an ER-positive/ER-negative ratio score for H3K4me3 modifications;
- (b) determining an ER-positive/ER-negative ratio score for H3K27ac modifications;

and/or

- (c) determining an ER-positive/ER-negative ratio score for methylated DNA; and

if each of (a)-(c) is performed, optionally combining each of the ratio scores (e.g., using fitted values determined using a logistic regression).

13. The method of any one of claims 1-12, wherein the method comprises quantifying the one or more of the epigenetic biomarkers at one or more genomic loci in Tables 1-3;

optionally, wherein the method comprises quantifying:

(a) H3K4me3 modifications for at least 5, 10, 20, 30, 40, or 50 genomic loci listed in Table 1;

(b) H3K27ac modifications for at least 5, 10, 20, 30, 40, or 50 genomic loci listed in Table 2; and/or

(c) DNA methylation for at least 5, 10, 20, 30, 40, or 50 genomic loci listed in Table 3.

14. The method of any one of claims 1-13, wherein the method provides an area under the receiver operating characteristic (AUROC) for determining if a subject has an ER-positive cancer vs. an ER-negative cancer of greater than 0.5 (*e.g.*, greater than 0.55, greater than 0.6, greater than 0.65, greater than 0.7, greater than 0.75, greater than 0.8, greater than 0.85, greater than 0.9, or greater than 0.95).

15. The method of any one of claims 1-14, wherein the subject has previously been determined to have cancer, the subject has an increased susceptibility to cancer, and/or wherein the method further comprises determining whether the subject has cancer.
16. The method of any one of claims 1-15, wherein the ER-positive cancer is an ER-positive cancer based on IHC testing and the ER-negative cancer is an ER-negative cancer based on IHC testing.
17. The method of any one of claims 1-16, wherein the cancer is breast cancer (e.g., metastatic breast cancer), ovarian cancer, or endometrial cancer.
18. A method of treating a subject having a cancer, the method comprising:
administering a cancer therapy to the subject based on the ER status of the cancer, wherein the ER status of the cancer has been determined using the method of any one of claims 1-17, and wherein:
- (a) if the cancer has been determined to be ER-positive, the cancer therapy administered comprises an ER-targeted agent; and
 - (b) if the cancer has been determined to be ER-negative, not administering an ER-targeted agent, optionally wherein the therapy administered is one that is suitable for an ER-negative cancer (e.g., a therapy that (i) does not comprise administering an ER-targeted agent, (ii) comprises surgery, and/or (iii) comprises radiation therapy).
19. A method of monitoring the ER status of a cancer in a subject, and optionally treating the cancer, the method comprising determining the ER status of the cancer using the method of any one of claims 1-17 at first and second time points, optionally wherein the subject has been administered an ER-targeted agent at or prior to the first time point, or after the first time point and before the second time point.
20. The method of claim 18 or 19, further comprising administering a cancer therapy, optionally an ER-targeted agent, to the subject based on the ER status of the cancer at the second

time point, optionally wherein the type, dose and/or frequency of administration of the cancer therapy is adjusted based on the ER status of the cancer at the second time point.

21. A method of treating a subject having a cancer, the method comprising:

administering an ER-targeted agent to the subject if the subject has been determined to have a validated epigenetic profile indicative of an ER-positive cancer based on analysis of a biological sample, optionally of cell-free DNA (cfDNA) from a liquid biopsy sample, obtained or derived from the subject, and not administering the ER-targeted agent if the subject has not been determined to have a validated epigenetic profile indicative of an ER-positive cancer,

wherein the presence of the validated epigenetic profile has been determined using a validated classifier,

wherein the validated classifier has been obtained by:

(a) determining a genomic profile of one or more histone modifications, chromatin accessibility, binding of one or more transcription factors, and/or DNA methylation in (i) one or more ER-positive cell lines or (ii) biological samples obtained from a first cohort of subjects who have previously been determined to have an ER-positive cancer;

(b) determining a genomic profile of one or more histone modifications, chromatin accessibility, binding of one or more transcription factors, and/or DNA methylation in (i) one or more ER-negative cell lines or (ii) biological samples obtained from a second cohort of healthy subjects or subjects who have previously been determined to have an ER-negative cancer;

(c) comparing the genomic profile determined in step (a) and the genomic profile determined in step (b), to identify genomic loci that have statistically different histone modification, chromatin accessibility, binding of transcription factor, and/or DNA methylation levels ("differential loci");

(d) training a classifier on histone modification, chromatin accessibility, binding of transcription factor, and/or DNA methylation levels in the differential loci to distinguish between (i) samples from one or more ER-positive cell lines or biological samples obtained from the first cohort, and (ii) samples from one or more ER-negative cell lines or biological samples obtained from the second cohort, to identify samples

having a profile of histone modification, chromatin accessibility, binding of transcription factor, and/or DNA methylation levels (“epigenetic profile”) that indicates that the samples are likely obtained from an ER-positive cell line or from the first cohort; and

(e) obtaining the validated classifier by validating the classifier from step (d) on a third cohort comprising an independent and group of subjects with ER-positive and ER-negative cancers and selecting a threshold such that the validated classifier predicts ER-positive cancers, with an area under the receiver operating characteristic (AUROC) greater than 0.5 (*e.g.*, greater than 0.55, greater than 0.6, greater than 0.65, greater than 0.7, greater than 0.75, greater than 0.8, greater than 0.85, greater than 0.9, or greater than 0.95), wherein subjects falling within the group of predicted ER-positive cancers display the validated epigenetic profile and subjects that do not fall within the group of ER-positive cancers lack the validated epigenetic profile.

22. The method of claim 21, wherein:

(a) the differential loci in step (c) were identified by comparing the genomic profile of one or more histone modifications and/or DNA methylation in (i) one or more ER-positive cell lines and (ii) one or more ER-negative cell lines;

(b) the classifier in step (d) was trained on histone modification, chromatin accessibility, binding of transcription factor, and/or DNA methylation levels in the differential loci that were obtained by *in silico* mixing sequence data from one or more ER-positive cell lines and sequence data obtained from liquid biopsy samples of healthy subjects;

(c) the validated classifier in step (e) was validated using liquid biopsy samples from the third cohort;

(d) the classifier in step (d) was trained on one or more (*e.g.*, two or more) histone modification levels and/or DNA methylation levels in the differential loci, optionally wherein the one or more histone modification levels comprise H3K4me3 and H3K27ac modification levels; and/or

(e) the classifier in step (d) was trained using ridge regression, elastic-net regression, or lasso regression.

23. A kit comprising reagents for quantifying one or more histone modifications, chromatin accessibility, binding of one or more transcription factors, and/or DNA methylation at one or more genomic loci, wherein the one or more genomic loci are selected from Tables 1-3; optionally, wherein the kit comprises reagents for quantifying:
- (a) H3K4me3 modifications for at least 5, 10, 20, 30, 40, or 50 genomic loci in Table 1;
 - (b) H3K27ac modifications for at least 5, 10, 20, 30, 40, or 50 genomic loci in Table 2;
 - (c) DNA methylation for at least 5, 10, 20, 30, 40, or 50 genomic loci in Table 3; or
 - (d) any combination of (a)-(c).
24. The kit of claim 23, wherein the kit comprises:
- (a) one or more antibodies for use in ChIP-seq, optionally wherein the one or more antibodies specifically bind H3K4me3- or H3K27ac-modified histones;
 - (b) one or more methyl-binding domains for use in MBD-seq or one or more antibodies that bind methylated DNA for use in MeDIP;
 - (c) reagents for isolation of cell-free DNA (cfDNA) from a liquid biopsy sample;
 - (d) reagents for library preparation for sequencing;
 - (e) reagents for sequencing;
 - (f) instructions for determining if a subject has an ER-positive cancer; or
 - (g) any combination of (a)-(f).
25. A non-transitory computer readable storage medium encoded with a computer program, wherein the program comprises instructions that when executed by one or more processors cause the one or more processors to perform operations to perform the method of any one of claims 1-22.
26. A computer system comprising a memory and one or more processors coupled to the memory, wherein the one or more processors are configured to perform operations to perform the method of any one of claims 1-22.

27. A system for determining the ER status of a cancer in a subject, the system comprising a sequencer configured to generate a sequencing dataset from a sample; and a non-transitory computer readable storage medium of claim 25 and/or a computer system of claim 26,

optionally wherein the sequencer is configured to generate a Whole Genome Sequencing (WGS) dataset from the sample.

28. The system of claim 26 or 27 further comprising:

a sample preparation device configured to prepare the sample for sequencing from a biological sample (e.g., a liquid biopsy sample);

optionally wherein the sample preparation device comprises reagents for quantifying one or more histone modifications, chromatin accessibility, binding of one or more transcription factors, and/or DNA methylation at one or more genomic loci in cell-free DNA (cfDNA) from the biological sample, optionally the liquid biopsy sample.

29. The system of any one of claims 26-28, wherein the one or more genomic loci are selected from Tables 1-3;

optionally, wherein:

(a) the device comprises reagents for quantifying H3K4me3, *e.g.*, for at least 5, 10, 20, 30, 40, or 50 genomic loci in Table 1;

(b) the device comprises reagents for quantifying H3K27ac, *e.g.*, for at least 5, 10, 20, 30, 40, or 50 genomic loci in Table 2.

(c) the device comprises reagents for quantifying DNA methylation, *e.g.*, for at least 5, 10, 20, 30, 40, or 50 genomic loci in Table 3; or

(d) a combination of (a)-(c).

30. The system of claim 29, wherein:

(a) the reagents comprise one or more antibodies for use in ChIP-seq, optionally wherein the one or more antibodies specifically bind H3K4me3- or H3K27ac-modified histones;

(b) the reagents comprise one or more methyl-binding domains for use in MBD-seq;

(c) the device comprises reagents for isolation of cell-free DNA (cfDNA) from the biological sample, optionally the liquid biopsy sample;

- (d) the device comprises reagents for library preparation for sequencing; and/or
- (e) the sequencer comprises reagents for sequencing.

31. A method of determining the ER status of a cancer in a subject (e.g., patient), the method comprising:

receiving (e.g., by a processor of a computing device) one or more genomic profiles of one or more histone modifications, chromatin accessibility, binding of one or more transcription factors, and/or DNA methylation for the subject; and

determining whether the subject has an epigenetic profile indicative of an ER-positive cancer by classifying (e.g., by the processor) the genomic profile using the ER classifier.

32. The method of claim 31, wherein the ER classifier has been trained using one or more genomic profiles of one or more histone modifications, chromatin accessibility, binding of one or more transcription factors, and/or DNA methylation for (i) one or more ER-positive cell lines and one or more ER-negative cell lines and/or (ii) one or more biological samples obtained from one or more cohorts of subjects who have previously been determined to have an ER-positive cancer and one or more biological samples obtained from one or more cohorts of subjects who have previously been determined to have an ER-negative cancer,

optionally wherein the one or more genomic profiles used to train the ER classifier comprise one or more genomic profiles generated by *in silico* diluting sequence data from ER-positive or ER-negative cell lines with sequence data obtained from healthy donor plasma samples so as to achieve a simulated ctDNA percentage ranging from 0.5% to 50%.

33. The method of claim 32, wherein the one or more genomic profiles used to train the ER classifier are for differential loci having statistically significant differences in levels of one or more histone modifications, chromatin accessibility, binding of one or more transcription factors, and/or DNA methylation levels in (a) one or more ER-positive cell lines as compared to one or more ER-negative cell lines and/or (b) one or more biological samples obtained from one or more cohorts of subjects who have previously been determined to have an ER-positive cancer and one or more biological samples obtained from one or more cohorts of subjects who have previously been determined to have an ER-negative cancer,

optionally wherein the differential loci were identified by comparing genomic profiles of one or more histone modifications and/or DNA methylation in (i) one or more ER-positive cell lines and (ii) one or more ER-negative cell lines.

34. The method of any one of claims 31-33, wherein the ER classifier has been trained using:

- (a) genomic profiles of two or more histone modification levels in the differential loci or,
- (b) genomic profiles of one or more histone modification levels and DNA methylation levels in the differential loci.

35. The method of any one of claims 31-34, comprising receiving:

- (a) one or more genomic profiles of two or more histone modification levels, optionally wherein the two or more histone modifications comprise H3K4me3 and H3K27ac modifications;
- (b) one or more genomic profiles of one or more histone modifications and DNA methylation, optionally wherein the one or more histone modifications comprise H3K4me3 and/or H3K27ac modifications.

36. The method of any one of claims 31-35, wherein the ER classifier is a validated classifier, wherein the ER classifier has been validated by selecting a threshold such that the validated classifier predicts ER-positive cancers with an area under the receiver operating characteristic (AUROC) greater than 0.5 (*e.g.*, greater than 0.55, greater than 0.6, greater than 0.65, greater than 0.7, greater than 0.75, greater than 0.8, greater than 0.85, greater than 0.9, or greater than 0.95), and

optionally wherein:

- (a) the ER classifier has been validated on a a group of subjects with ER-positive or ER-negative cancers, wherein subjects falling within a group of predicted ER-positive cancers display a validated epigenetic profile and subjects that do not fall within a group of ER-positive cancers lack the validated epigenetic profile; and/or
- (b) the ER classifier has been validated using liquid biopsy sample data.

37. A non-transitory computer readable storage medium encoded with a computer program, wherein the program comprises instructions that when executed by one or more processors cause the one or more processors to perform operations to perform the method of any one of claims 31-36.

38. A computer system comprising a memory and one or more processors coupled to the memory, wherein the one or more processors are configured to perform operations to perform the method of any one of claims 31-37.

39. A method of treating a subject having a cancer, the method comprising:
administering an ER-targeted agent to the subject, wherein the subject has been determined to have a validated epigenetic profile indicative of an ER-positive cancer based on analysis of a biological sample, optionally of cell-free DNA (cfDNA) from a liquid biopsy sample, obtained or derived from the subject,

wherein the presence of the validated epigenetic profile has been determined using a classifier (e.g., a validated classifier) according to a method of any one of claims 31-37.

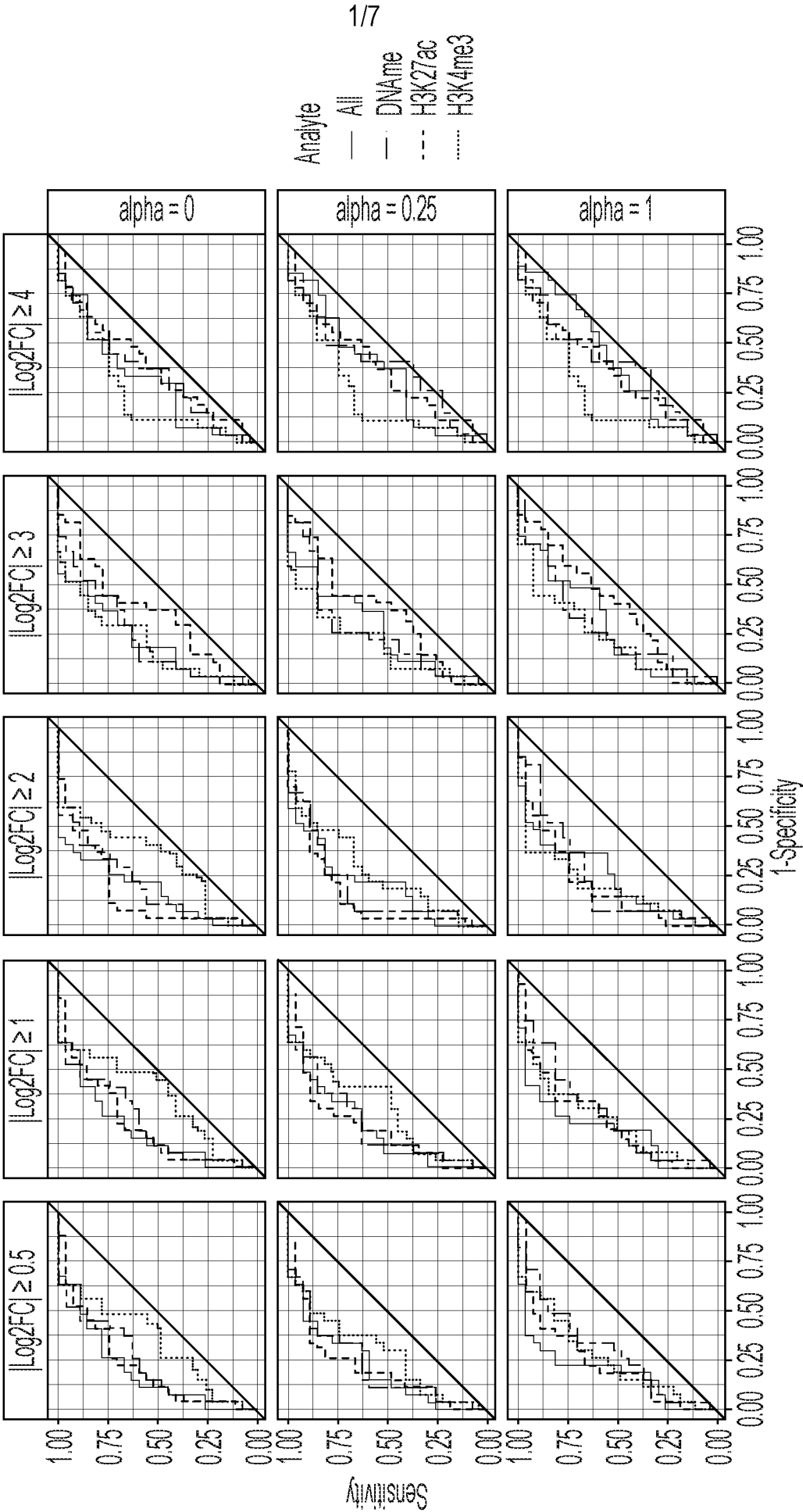


FIG. 1

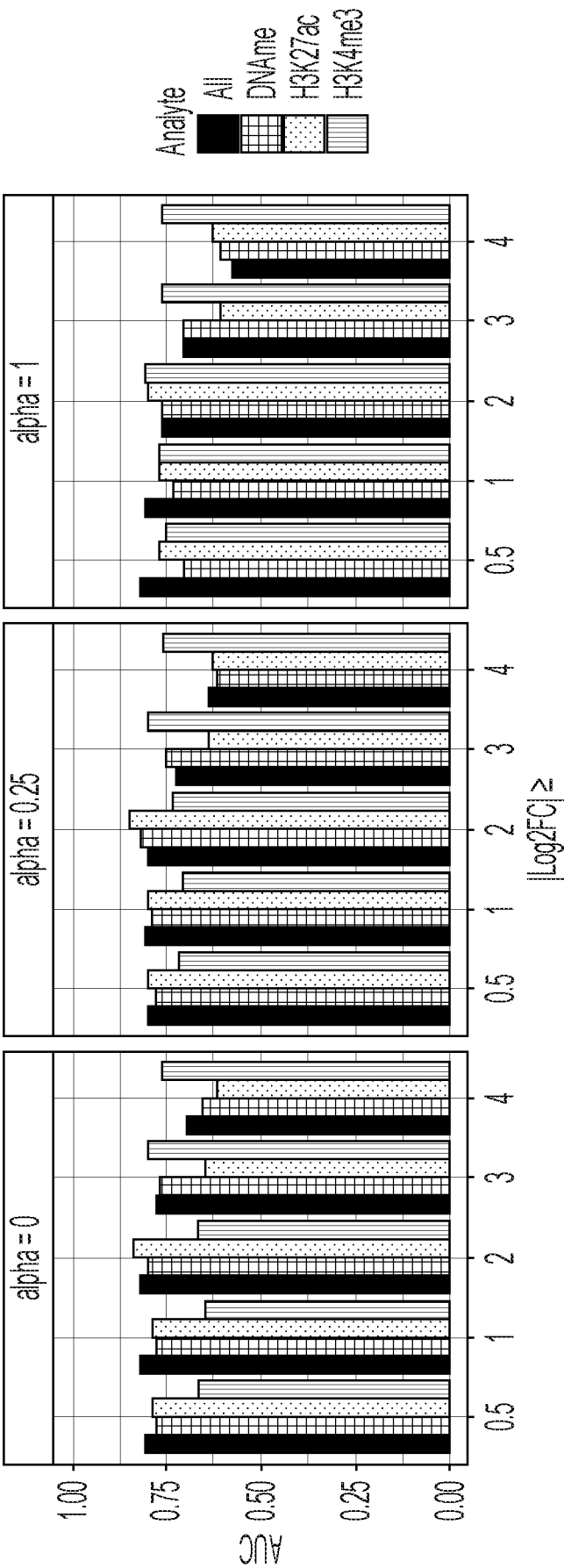


FIG. 2

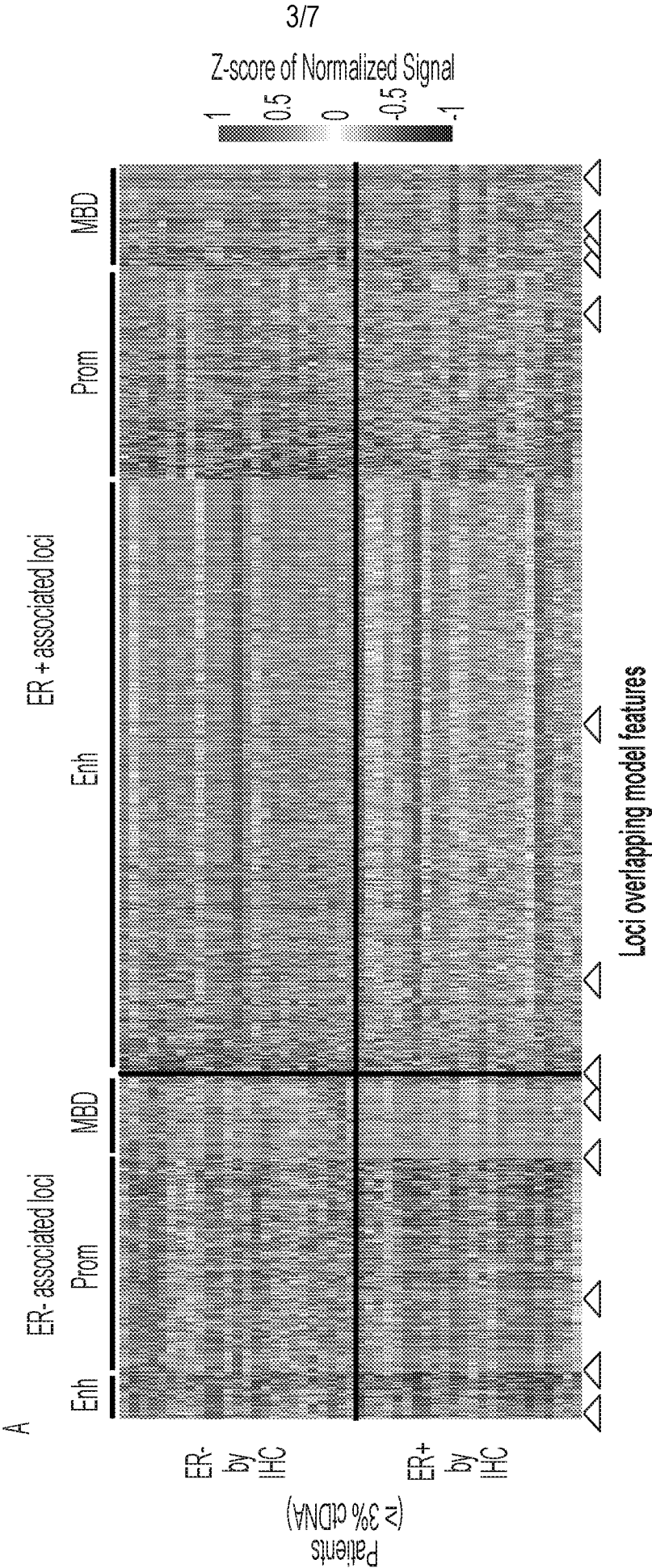


FIG. 3

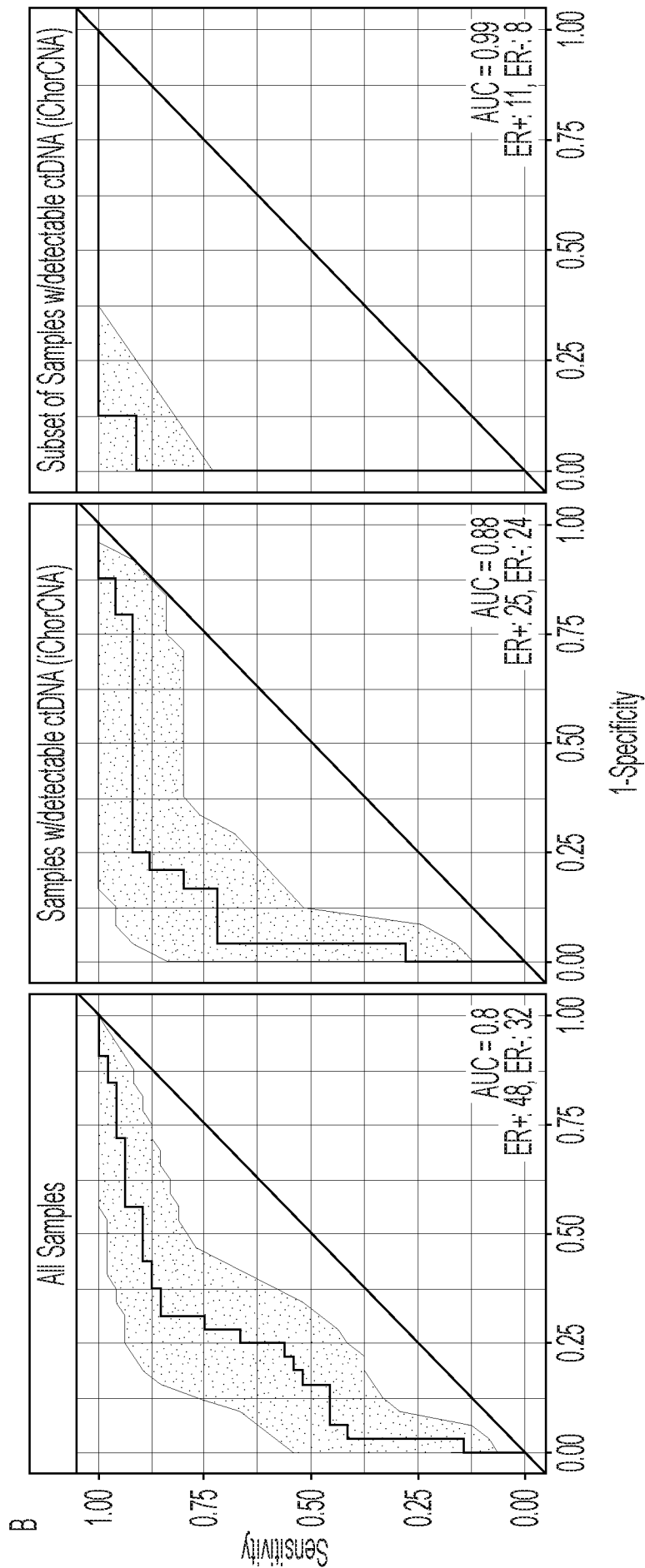


FIG. 3
CONTINUED

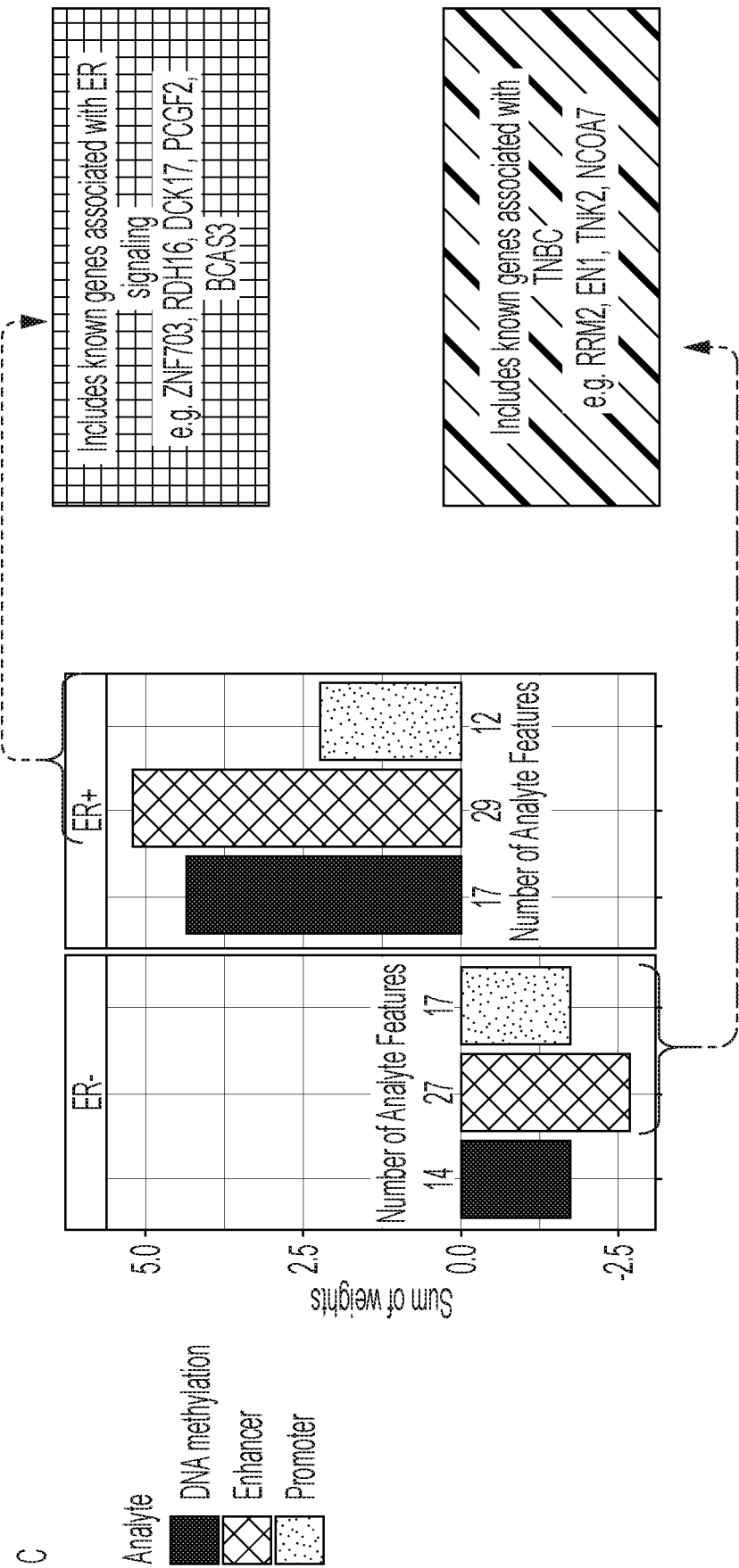


FIG. 3
CONTINUED

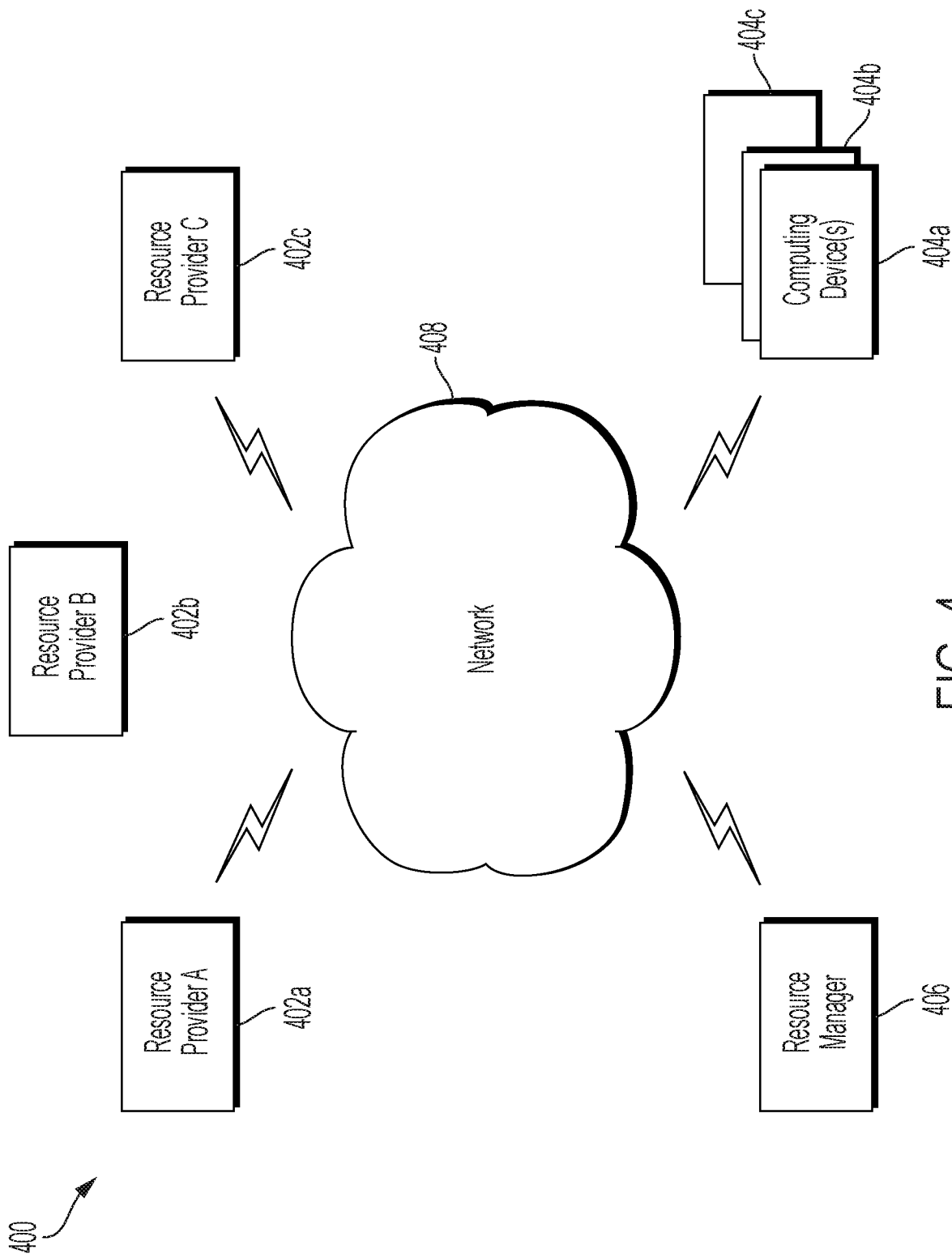


FIG. 4

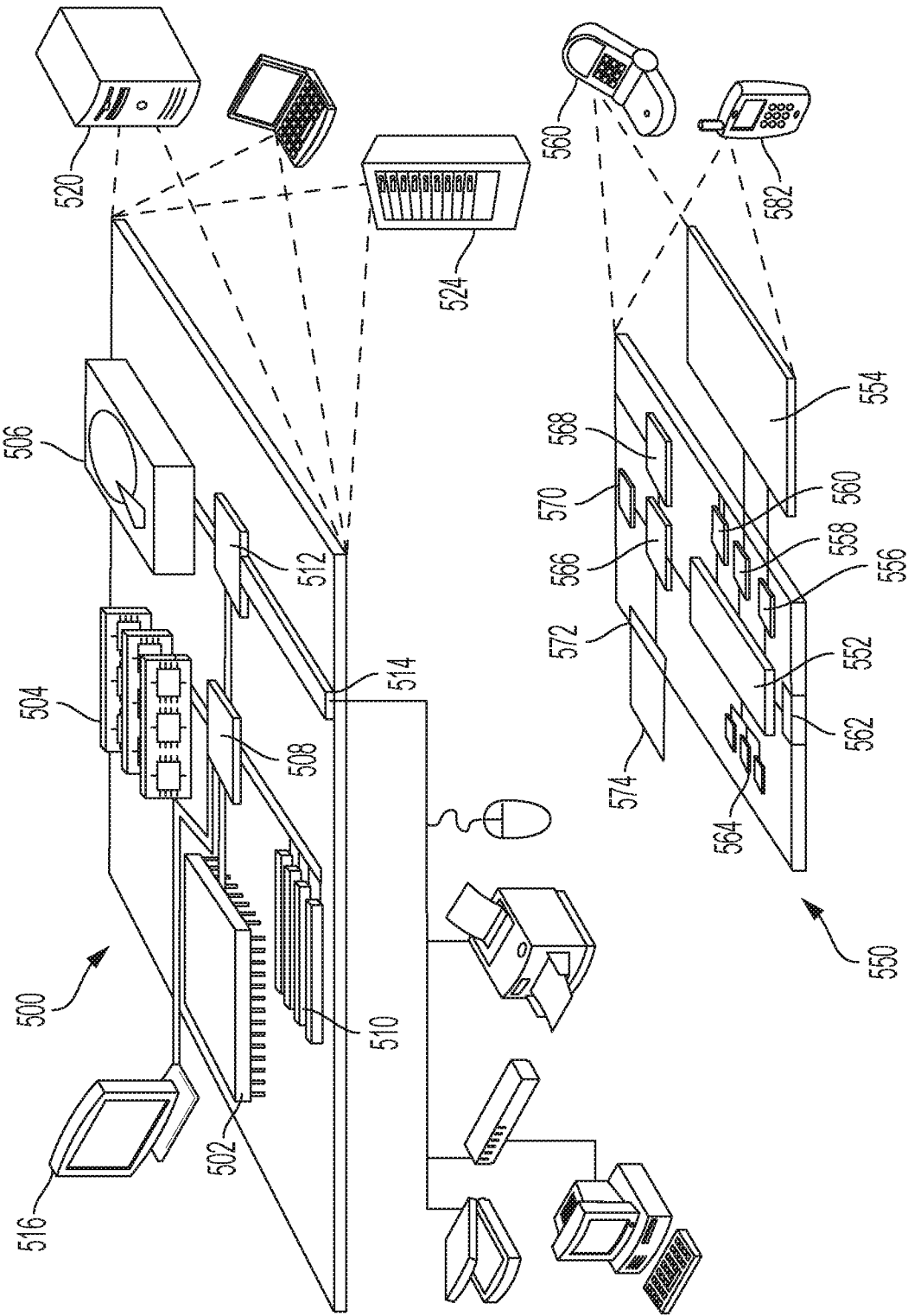


FIG. 5