A METHOD OF ESTIMATING A CIRCULATING TUMOR DNA BURDEN AND RELATED KITS AND METHODS

TECHNICAL FIELD

The present disclosure relates broadly to a method of estimating a disease burden, such as a circulating tumor DNA (ctDNA) burden, and related kits and methods.

BACKGROUND

Cell-free DNA (cfDNA) is present in the blood circulation of humans. In healthy individuals, the death of normal cells of the hematopoietic lineage is the main contributor of plasma cfDNA. In cancer patients, blood plasma can carry circulating tumor DNA (ctDNA) fragments originating from tumor cells, offering non-invasive access to somatic genetic alterations in tumors. The ctDNA profile of a cancer patient is clinically informative in at least two major ways. Firstly, the profile can provide information about specific actionable mutations that can guide therapy. Secondly, the profile can be used to infer tumor growth dynamics by estimating the amount of ctDNA in the blood. This latter information offers a promising non-invasive approach to track disease progression during clinical trials or therapy, offering a real-time tool to adjust therapy.

Existing next-generation sequencing-based approaches to estimate ctDNA levels in plasma samples are based on somatic single nucleotide variant allele frequencies (SNV VAFs), copy number aberrations (CNAs), or DNA methylation patterns. However, these approaches each have limitations.

Approaches based on somatic variant allele frequencies only work for patients that have known recurring cancer mutations, and reliable estimation requires that multiple mutations are present in the ctDNA. Since cfDNA targeted sequencing typically only covers a few hundred selected cancer genes because of the need for ultra-deep sequencing (~10,000x), most patients will not have a sufficient number of detectable mutations to allow reliable tumor content estimation. ctDNA burden estimation based on SNVs may therefore be challenging when no clonal mutations exist among the targeted genes.

Alternatively, low-pass whole genome sequencing (lp-WGS) yields segmental/arm-level CNAs, or epigenomics-associated fragmentation patterns that allow for inference of ctDNA burden. However, some cancers may not have sufficient levels of aneuploidy and chromosomal instability needed for robust estimation. Therefore, some cancers cannot be accurately monitored with this approach. Furthermore, low-pass whole genome sequencing approaches only work down to ~3% tumor ctDNA fraction and the assay must be performed in addition to the standard targeted panel sequencing, wasting precious blood plasma.

Sequencing of DNA methylation patterns may provide a general approach to quantify the cellular origin of cfDNA. However, this technology is less efficient and more noisy (due to bisulfite conversion step) and is again not directly compatible with standard targeted panel sequencing, thereby wasting precious blood plasma.

Notably, both DNA methylation and lp-WGS profiling require separate assays in addition to standard targeted gene sequencing, highlighting the need for approaches that simultaneously allow for profiling of actionable cancer mutations and quantitative estimation of ctDNA burden.

Thus, there is a need to provide an alternative method of estimating a disease burden, such as a ctDNA burden, and related kits and methods.

SUMMARY

In one aspect, there is provided a method of estimating a circulating tumor DNA (ctDNA) burden in a subject, the method comprising: determining in a blood sample obtained from the subject, a level of cell-free DNA (cfDNA) that maps to one or more nucleosome-depleted region (NDR); and estimating the ctDNA burden based on said level of cfDNA, wherein said NDR (i) comprises the NDR of a gene which transcript is differentially expressed between healthy blood tissue and tumor tissue and/or (ii) is degraded to different extents between healthy blood tissue and blood tissue of a tumor-bearing subject.

In one embodiment, determining in a blood sample obtained from the subject, a level of cfDNA that maps to one or more NDR comprises: sequencing cfDNA fragments in the blood sample to obtain sequencing reads; and determining the number of sequencing reads that align with the one or more NDR to obtain said level of cfDNA that maps to one or more NDR.

In one embodiment, the method further comprises contacting the blood sample with one or more probe capable of binding to the one or more NDR to capture cfDNA fragments comprising the one or more NDR prior to the sequencing step.

In one embodiment, the NDR is selected from the group consisting of: a promoter region, a first exon-intron junction and combinations thereof.

In one embodiment, the estimated ctDNA burden positively correlates with a tumor burden in the subject.

In one embodiment, said transcript that is differentially expressed between healthy blood tissue and tumor tissue comprises a transcript which FPKM (Fragments Per Kilobase of transcript per Million) value differs by at least 10 times between healthy blood tissue and tumor tissue.

In one embodiment, said NDR that is degraded to different extents between healthy blood tissue and blood tissue of a tumor-bearing subject comprises a NDR having different sequencing coverage in healthy blood tissue and in tumor tissue.

In one embodiment, said transcript that is differentially expressed in healthy blood tissue and tumor tissue is selected from the group consisting of: a transcript that is more highly expressed in healthy blood tissue than in tumor tissue, a transcript that is more highly expressed in tumor tissue than in healthy blood tissue and combinations thereof.

In one embodiment, said transcript which is differentially expressed between blood tissue and tumor tissue consists of transcript(s) that is more highly expressed in blood tissue than in tumor tissue.

In one embodiment, the one or more NDR comprises at least two NDRs, optionally six NDRs, further optionally ten NDRs.

In one embodiment, the total length of the one or more NDR is no more than 30 kb.

In one embodiment, the one or more NDR comprises one or more NDR of a gene selected from the group consisting of: SLC11A1, NLRP12, PRTN3, HMBS, LILRB3, ACSL1, GP9, MX2, RASGRP4, ATG16L2 and combinations thereof.

In one embodiment, the method is a method of determining disease progression in a subject and the method further comprises: determining in a subsequent blood sample obtained from the subject, a level of cfDNA that maps to one or more NDR; estimating the ctDNA burden based on said level of cfDNA; comparing the ctDNA burden estimated from said subsequent blood sample with the

ctDNA burden estimated from said blood sample; and identifying the subject as having disease progression if the ctDNA burden estimated from said subsequent blood sample is higher than the ctDNA burden estimated from said blood sample and identifying otherwise if the ctDNA burden estimated from said subsequent blood sample is not higher than the ctDNA burden estimated from said blood sample.

In one embodiment, the method further comprises changing the treatment regimen received by the subject if the subject is identified as having disease progression.

In one embodiment, the tumor comprises colorectal tumor.

In one embodiment, the one or more NDR comprises one or more NDR of a gene selected from the group consisting of: SHKBP1, ACSL1, BCAR1, RAB25, PRTN3, LSR and combinations thereof.

In one aspect, there is provided a kit for estimating a ctDNA burden in a subject, the kit comprising one or more probe that is capable of binding to one or more NDR, wherein said NDR (i) comprises the NDR of a gene which transcript is differentially expressed between healthy blood tissue and tumor tissue and/or (ii) is degraded to different extents between healthy blood tissue and blood tissue of a tumor-bearing subject.

In one embodiment of the kit, said one or more NDR comprises one or more NDR of a gene selected from the group consisting of: SLC11A1, NLRP12, PRTN3, HMBS, LILRB3, ACSL1, GP9, MX2, RASGRP4, ATG16L2 and combinations thereof.

In one embodiment of the kit, said tumor comprises colorectal tumor and said one or more NDR comprises one or more NDR of a gene selected from the group consisting of: SHKBP1, ACSL1, BCAR1, RAB25, PRTN3, LSR and combinations thereof.

In one embodiment of the kit, the one or more probe comprises the sequence of one or more of SEQ ID NO: 1 to SEQ ID NO: 577, or a sequence sharing at least 75% sequence identity thereto.

DEFINITIONS

The term “treatment", "treat" and “therapy”, and synonyms thereof as used herein refer to both therapeutic treatment and prophylactic or preventative measures, wherein the object is to prevent or slow down (lessen) a medical condition, which

includes but is not limited to diseases (such as cancer), symptoms and disorders. A medical condition also includes a body's response to a disease or disorder, e.g. inflammation. Those in need of such treatment include those already with a medical condition as well as those prone to getting the medical condition or those in whom a medical condition is to be prevented.

The term "subject" as used herein includes patients and non-patients. The term "patient" refers to individuals suffering or are likely to suffer from a medical condition such as cancer, while "non-patients" refer to individuals not suffering and are likely to not suffer from the medical condition. "Non-patients" include healthy individuals, non-diseased individuals and/or an individual free from the medical condition. The term "subject" includes humans and animals. Animals include murine and the like. "Murine" refers to any mammal from the family Muridae, such as mouse, rat, and the like.

The term "micro" as used herein is to be interpreted broadly to include dimensions from about 1 micron to about 1000 microns.

The term "nano" as used herein is to be interpreted broadly to include dimensions less than about 1000 nm.

The term "particle" as used herein broadly refers to a discrete entity or a discrete body. The particle described herein can include an organic, an inorganic or a biological particle. The particle used described herein may also be a macro-particle that is formed by an aggregate of a plurality of sub-particles or a fragment of a small object. The particle of the present disclosure may be spherical, substantially spherical, or non-spherical, such as irregularly shaped particles or ellipsoidally shaped particles. The term "size" when used to refer to the particle broadly refers to the largest dimension of the particle. For example, when the particle is substantially spherical, the term "size" can refer to the diameter of the particle; or when the particle is substantially non-spherical, the term "size" can refer to the largest length of the particle.

The terms "coupled" or "connected" as used in this description are intended to cover both directly connected or connected through one or more intermediate means, unless otherwise stated.

The term "associated with", used herein when referring to two elements refers to a broad relationship between the two elements. The relationship includes, but is not limited to a physical, a chemical or a biological relationship. For example, when element A is associated with element B, elements A and B may be directly or indirectly attached to each other or element A may contain element B or vice versa.

The term "adjacent" used herein when referring to two elements refers to one element being in close proximity to another element and may be but is not limited to the elements contacting each other or may further include the elements being separated by one or more further elements disposed therebetween.

The term "and/or", e.g., "X and/or Y" is understood to mean either "X and Y" or "X or Y" and should be taken to provide explicit support for both meanings or for either meaning.

Further, in the description herein, the word "substantially" whenever used is understood to include, but not restricted to, "entirely" or "completely" and the like. In addition, terms such as "comprising", "comprise", and the like whenever used, are intended to be non-restricting descriptive language in that they broadly include elements/components recited after such terms, in addition to other components not explicitly recited. For example, when "comprising" is used, reference to a "one" feature is also intended to be a reference to "at least one" of that feature. Terms such as "consisting", "consist", and the like, may in the appropriate context, be considered as a subset of terms such as "comprising", "comprise", and the like. Therefore, in embodiments disclosed herein using the terms such as "comprising", "comprise", and the like, it will be appreciated that these embodiments provide teaching for corresponding embodiments using terms such as "consisting", "consist", and the like. Further, terms such as "about", "approximately" and the like whenever used, typically means a reasonable variation, for example a variation of +/- 5% of the disclosed value, or a variance of 4% of the disclosed value, or a variance of 3% of the disclosed value, a variance of 2% of the disclosed value or a variance of 1% of the disclosed value.

Furthermore, in the description herein, certain values may be disclosed in a range. The values showing the end points of a range are intended to illustrate a preferred range. Whenever a range has been described, it is intended that the range covers and teaches all possible sub-ranges as well as individual numerical values within that range. That is, the end points of a range should not be interpreted as inflexible limitations. For example, a description of a range of 1% to 5% is intended to have specifically disclosed sub-ranges 1% to 2%, 1% to 3%, 1% to 4%, 2% to 3% etc., as well as individually, values within that range such as 1%, 2%, 3%, 4% and 5%. It is to be appreciated that the individual numerical values within the range also include integers, fractions and decimals. Furthermore, whenever a range has been described, it is also intended that the range covers and teaches values of up to 2 additional

decimal places or significant figures (where appropriate) from the shown numerical end points. For example, a description of a range of 1% to 5% is intended to have specifically disclosed the ranges 1.00% to 5.00% and also 1.0% to 5.0% and all their intermediate values (such as 1.01%, 1.02% ... 4.98%, 4.99%, 5.00% and 1.1%, 1.2% ... 4.8%, 4.9%, 5.0% etc.,) spanning the ranges. The intention of the above specific disclosure is applicable to any depth/breadth of a range.

Additionally, when describing some embodiments, the disclosure may have disclosed a method and/or process as a particular sequence of steps. However, unless otherwise required, it will be appreciated that the method or process should not be limited to the particular sequence of steps disclosed. Other sequences of steps may be possible. The particular order of the steps disclosed herein should not be construed as undue limitations. Unless otherwise required, a method and/or process disclosed herein should not be limited to the steps being carried out in the order written. The sequence of steps may be varied and still remain within the scope of the disclosure.

Furthermore, it will be appreciated that while the present disclosure provides embodiments having one or more of the features/characteristics discussed herein, one or more of these features/characteristics may also be disclaimed in other alternative embodiments and the present disclosure provides support for such disclaimers and these associated alternative embodiments.

DESCRIPTION OF EMBODIMENTS

Exemplary, non-limiting embodiments of a method of estimating a disease burden, such as a ctDNA burden, in a subject and related kits and methods are disclosed hereinafter.

In various embodiments, there is provided a method of estimating, predicting and/or determining one or more of: a disease burden, a cancer burden, a tumor burden, a circulating tumor DNA (ctDNA) burden, a level of ctDNA, an amount of ctDNA, a proportion of ctDNA, a fraction of ctDNA and a ctDNA content in a subject. In various embodiments, the method comprises determining in a sample obtained from the subject, a level, an amount, a proportion, a fraction and/or a content of DNA, optionally cell-free DNA (cfDNA), that aligns with, belongs to, maps to, corresponds to, is similar to and/or identical to at least one genomic region, and estimating,

predicting and/or determining one or more of: the disease burden, the cancer burden, the tumor burden, the ctDNA burden, the level of ctDNA, the amount of ctDNA, the proportion of ctDNA, the fraction of ctDNA and/or the ctDNA content in the subject based on the level, the amount, the proportion, the fraction and/or the content of DNA. In some embodiments, the disease burden, the cancer burden, the tumor burden, the ctDNA burden, the level of ctDNA, the amount of ctDNA, the proportion of ctDNA, the fraction of ctDNA and/or the ctDNA content comprises the absolute disease burden, cancer burden, tumor burden, ctDNA burden, level of ctDNA, amount of ctDNA, proportion of ctDNA, fraction of ctDNA and/or ctDNA content.

The estimation, prediction and/or determination may be quantitative, semi-quantitative or qualitative. In various embodiments, the disease burden, the cancer burden, the tumor burden, the ctDNA burden, the level of ctDNA, the amount of ctDNA, the proportion of ctDNA, the fraction of ctDNA and/or the ctDNA content is associated with or correlates with the level, the amount, the proportion, the fraction and/or the content of DNA, optionally cfDNA, in the subject.

In various embodiments, the at least one genomic region comprises a gene. In various embodiments, the at least one genomic region comprises a coding region. In various embodiments, the at least one genomic region comprises a non-coding region (e.g. a region that is far away from genes, a regulatory region such as enhancer etc.). In various embodiments, the at least one genomic region comprises a nucleosome-depleted region (NDR). In various embodiments, the nucleosome-depleted region comprises a gene. In various embodiments, the nucleosome-depleted region comprises a coding region. In various embodiments, the nucleosome-depleted region comprises a non-coding region.

In various embodiments, the at least one genomic region comprises at least one coding region/gene and at least one non-coding region. In various embodiments, determining in the sample a level (or an amount, a proportion, a fraction and/or a content) of DNA that maps to (or aligns with, corresponds to, belongs to, is similar to and/or is identical to) at least one genomic region comprises determining a level of DNA that maps to each of a plurality of genomic regions, the plurality of genomic regions comprising a greater number/proportion of coding region(s)/gene(s) than non-coding region(s). In other words, in various embodiments, the non-coding regions make up a small/minority set of the plurality of regions that are being mapped to.

A NDR may be a region that has a relatively low nucleosome occupancy level. For example, a promoter region upstream of a transcriptional start site (TSS) often displays low nucleosome occupancy level for a typical gene. For example, regulatory regions tend to be nucleosome depleted. In various embodiments, the at least one NDR comprises a transcription start site, a promoter, an intron-exon junction and/or an exon-intron junction. An intron-exon junction may be a first intron-exon junction, a second intron-exon junction, a third intron-exon junction, a fourth intron-exon junction etc. An exon-intron junction may be a first exon-intron junction, a second exon-intron junction, a third exon-intron junction, a fourth exon-intron junction etc. In various embodiments, the NDR is selected from the group consisting of: a promoter region, a first exon-intron junction and combinations thereof. In various examples, cfDNA coverage/degradation pattern at a first exon-intron junction and/or a promoter region is found to possess the capability or better capability to infer gene expression and/or predict ctDNA burden.

In various embodiments, the NDR comprises the NDR of a gene which is differentially expressed in healthy blood tissue/cell and diseased tissue/cell. In various embodiments, the NDR comprises the NDR of a gene which transcript is differentially expressed in healthy blood tissue/cell and diseased tissue/cell. Because a gene usually comprises multiple alternative transcripts with different genomic positions, determining the gene expression at the transcript level (as compared to at the gene level) may allow for a more precise mapping of the NDR e.g. the promoter and junction locations. A gene which transcript is differentially expressed in healthy blood tissue/cell and diseased tissue/cell may be identified by RNA sequencing or any other suitable methods known in the art. A gene which transcript is differentially expressed in healthy blood tissue/cell and diseased tissue/cell may also be identified by analysing transcript expression data available at public databases e.g. the Genotype-Tissue Expression (GTEx) project, The Cancer Genome Atlas (TCGA) program etc. A transcript which is differentially expressed in healthy blood tissue/cell and diseased tissue/cell may have different FPKM (fragments per kilobase of transcript per million mapped fragments/reads) or RPKM (Reads Per Kilobase of transcript, per Million mapped reads), or TPM (Transcripts Per Million) values in healthy blood tissue/cell and in diseased tissue/cell (e.g. as determined by sequencing).

In various embodiments, the difference in the expression or FPKM/RPKM/TPM value of the transcript in healthy blood tissue/cell and in diseased tissue/cell is at least

about 10%, at least about 20%, at least about 30%, at least about 40%, at least about 50%, at least about 60%, at least about 70%, at least about 80%, at least about 90% or at least about 100%. In various embodiments, the difference in the expression of the transcript FPKM/RPKM/TPM value in healthy blood tissue/cell and in diseased tissue/cell is at least about 0.1 fold, at least about 0.2 fold, at least about 0.3 fold, at least about 0.4 fold, at least about 0.5 fold, at least about 0.6 fold, at least about 0.7 fold, at least about 0.8 fold, at least about 0.9 fold, at least about 1 fold, at least about 2 fold, at least about 3 fold, at least about 4 fold, at least about 5 fold, at least about 6 fold, at least about 7 fold, at least about 8 fold, at least about 9 fold, at least about 10 fold, at least about 11 fold, at least about 12 fold, at least about 13 fold, at least about 14 fold or at least about 15 fold. In various embodiments, the difference in the expression of the transcript FPKM/RPKM/TPM value in healthy blood tissue/cell and in diseased tissue/cell is at least about 0.1 times, at least about 0.2 times, at least about 0.3 times, at least about 0.4 times, at least about 0.5 times, at least about 0.6 times, at least about 0.7 times, at least about 0.8 times, at least about 0.9 times, at least about 1 times, at least about 2 times, at least about 3 times, at least about 4 times, at least about 5 times, at least about 6 times, at least about 7 times, at least about 8 times, at least about 9 times, at least about 10 times, at least about 11 times, at least about 12 times, at least about 13 times, at least about 14 times or at least about 15 times. In various embodiments, the FPKM/RPKM/TPM value comprises a median FPKM/RPKM/TPM value obtained from a plurality of healthy blood tissue/cell samples and/or a plurality of diseased tissue/cell samples.

In various embodiments, the NDR is degraded to different extents in healthy blood tissue/cell and in blood tissue/cell of a diseased subject. In various embodiments, the NDR has different degradation patterns/signals in healthy blood tissue/cell and in blood tissue/cell of a diseased subject. For example, when sequencing cfDNA in a healthy blood tissue/cell sample and in blood tissue/cell sample of a diseased subject, a greater or smaller number/amount (i.e. a substantially different or non-identical number/amount) of fragments/reads may map to the NDR in the healthy blood tissue/cell sample as compared to the blood tissue/cell sample of the diseased subject. For example, when sequencing cfDNA in a healthy blood tissue/cell sample and in a blood tissue/cell sample of a diseased subject, the read depth or coverage of the NDR may be higher or lower in the healthy blood tissue/cell sample as compared to the blood tissue/cell sample of a diseased subject. In various

embodiments therefore, the NDR has different (or non-similar or non-identical) read depth or coverage in healthy blood tissue/cell and in blood tissue/cell of a diseased subject.

The read depth or coverage of a NDR may comprise a relative read depth or relative coverage of the NDR. A relative read depth or relative coverage of a NDR may be obtained, for example, by normalizing/dividing the raw read depth/coverage across the NDR (or optionally a mean raw read depth/coverage across the NDR for multiple samples/runs) by a normalization factor. In one example, the normalization factor comprises the read depth or coverage (or optionally a mean read depth/coverage for multiple samples/runs) of region(s) flanking the NDR e.g. the flanking upstream and/or downstream regions. In one example, the normalization factor is the mean coverage of the upstream and downstream flanks of the NDR. In one example therefore, the relative read depth or relative coverage of a NDR is the mean raw read depth/coverage across the NDR divided by the mean raw read depth/coverage of the upstream and downstream flanks.

In some embodiments, the flanking region(s) is immediately upstream or downstream of the NDR, or contiguous with the NDR. In some embodiments, the flanking region(s) is separated from the NDR by one or more nucleotides/bases. In various embodiments, the flanking region(s) is no more than about 5000 base pairs (bp), no more than about 4500 bp, no more than about 4000 bp, no more than about 3500 bp, no more than about 3000 bp, no more than about 2500 bp or no more than about 2000 bp from the NDR or an end of the NDR. In various embodiments, the flanking region(s) is at least about 50 bp, at least about 100 bp, at least about 150 bp, at least about 200 bp, at least about 250 bp, at least about 300 bp, at least about 350 bp, at least about 400 bp, at least about 450 bp, at least about 500 bp, at least about 550 bp, at least about 600 bp, at least about 650 bp, at least about 700 bp, at least about 750 bp, at least about 800 bp, at least about 850 bp, at least about 900 bp, at least about 950 bp, or least about 1000 bp from the NDR or an end of the NDR.

In various embodiments, the size/length of flanking region(s) is at least about 50 bp, at least about 100 bp, at least about 150 bp, at least about 200 bp, at least about 250 bp, at least about 300 bp, at least about 350 bp, at least about 400 bp, at least about 450 bp, at least about 500 bp, at least about 550 bp, at least about 600 bp, at least about 650 bp, at least about 700 bp, at least about 750 bp, at least about

800 bp, at least about 850 bp, at least about 900 bp, at least about 950 bp, or least about 1000 bp.

In one example, the NDR is about -300 bp to about 300 bp, about -200 bp to about 100 bp or about -150 bp to about 50 bp relative to a transcription start site (TSS) and the normalization factor is the mean coverage of an upstream flank that is about -2000 bp to about -1000 bp relative to the TSS and a downstream flank that is about 1000 bp to about 2000 bp relative to the TSS.

In various embodiments, a NDR that is degraded to different extents in healthy blood tissue/cell and in blood tissue/cell of a diseased subject may be identified by comparing the relative depth/coverage of the NDR in healthy blood tissue/cell and in the blood tissue/cell of a diseased subject. For example, if the relative depth/coverage of the NDR in healthy blood tissue/cell and in the blood tissue/cell of a diseased subject are different, the NDR is considered to a NDR that is degraded to different extents in healthy blood tissue/cell and in blood tissue/cell of a diseased subject. In various embodiments, determining the relative depth/coverage of a NDR in healthy blood tissue/cell and/or in blood tissue/cell of a diseased subject comprises determining the coverage of each position in an about 8k-bp window, about 6k-bp window, about 4k-bp window, about 2k-bp window or about 1k-bp window spanning from about -4000 to +4000 bp, from about -3000 to +3000 bp, from about -2000 to +2000 bp, from about -1000 to +1000 bp or from about -500 to +500 bp with respect the NDR (e.g. end(s) of the NDR); and optionally normalizing the coverage by the mean coverage of the upstream region (e.g. -8000 to -4000 bp, -4000 to -2000 bp, -3000 to -1000 bp, -2000 to -1000 bp or -1000 to -500 bp with respect to the NDR (e.g. end(s) of the NDR)) and/or downstream region (e.g. +4000 bp to +8000 bp, +2000 to +4000 bp, +1000 to +3000 bp +1000 to +2000 bp or +500 to +1000 bp with respect to the NDR (e.g. end(s) of the NDR) to obtain a relative depth/coverage for the NDR. In some examples, the coverage of each position in a region located downstream of a NDR (e.g. a promoter) is determined. In some examples, the coverage of each position in a region located from about -350 bp to about -50 bp or from about -300 to about -100 bp with respect a NDR (e.g. an end of a first exon) is determined.

In various embodiments, the difference in read depth or coverage (or relative read depth or coverage) in healthy blood tissue/cell and in blood tissue/cell of a diseased subject is measured by computing a coverage score (or relative coverage

score). In various embodiments, the coverage score (or relative coverage score) is computed by the following formula:

$$\text{score} = \frac{\text{mean(diseased)} - \text{mean(healthy)}}{\sqrt{\text{s. d. (diseased)}}}$$

where *mean(diseased)* and *mean(healthy)* are the mean of average coverages (or relative coverages) at NDRs across diseased blood tissue/cell (e.g. plasma samples of diseased subjects) and healthy blood tissue/cell (e.g. healthy plasma samples) respectively, and s.d.(diseased) is the standard deviation of average coverages (or relative coverages) at NDRs across diseased blood tissue/cell.

In various embodiments, the coverage values negatively correlate with expression level. In some examples therefore, blood genes/transcripts (e.g. genes/transcripts show a higher FPKM value in normal blood than in tumor) have a higher coverage in diseased samples than in healthy samples. Thus, the blood genes/transcripts have a positive value of relative coverage score, as mean(diseased)> mean(healthy). In some examples, tumor genes/transcripts (e.g. genes/transcripts show a higher FPKM value in tumor than in normal blood) have a lower coverage in disease samples than in healthy samples. Thus, the tumor genes have a negative value of relative coverage score, as mean(diseased) < mean(healthy).

In various embodiments, the NDR has a coverage score or relative coverage score of less than about 0 and/or more than about 0. In various embodiments, the NDR has a coverage score or relative coverage score of less than about -0.1, less than about -0.2, less than about -0.3, less than about -0.4, less than about -0.5, less than about -0.6, less than about -0.7, less than about -0.8, less than about -0.9 or less than about - 1.0. In various embodiments, the NDR has a coverage score or relative coverage score of more than about 0.1, more than about 0.2, more than about 0.3, more than about 0.4, more than about 0.5, more than about 0.6, more than about 0.7, more than about 0.8, more than about 0.9 or more than about 1.0.

As used herein, “blood”, “blood tissue” or “blood sample” refers to whole blood or fractions thereof, such as a plasma fraction or a serum fraction. As used herein “healthy blood”, “healthy blood tissue” or “healthy blood sample” refers to the whole blood or fractions thereof of a healthy subject, or a subject who does not suffer from the disease. Conversely, “diseased blood”, “diseased blood tissue” or “diseased blood sample” as used herein refers to the whole blood or fractions thereof of a diseased

subject, or a subject who suffers from the disease. In various embodiments, "diseased blood", "diseased blood tissue" or "diseased blood sample" does not indicate that a disease necessarily resides in the blood *per se*. For example, "diseased blood", "diseased blood tissue" or "diseased blood sample" may refer to the blood, tissue or sample of a subject suffering from colorectal cancer and having no blood diseases, and "healthy blood", "healthy blood tissue" or "healthy blood sample" may refer to the blood, tissue or sample of a subject who does not suffer from colorectal cancer.

In various embodiments, the sample obtained from the subject comprises a liquid sample. In various embodiments, the sample comprises a biological fluid sample. In various embodiments, the liquid/biological fluid sample comprises one or more of blood, serum, plasma, sputum, lavage fluid, cerebrospinal fluid, interstitial fluid, urine, feces, milk, semen, sweat, tears, saliva, and the like. In various embodiments, the sample comprises a blood sample (e.g. whole blood sample or processed fractions thereof). In various embodiments, the sample comprises a plasma sample. In various embodiments, the sample comprises cfDNA. In various embodiments, the sample comprises cfDNA, for example, cfDNA extracted/isolated/purified from a blood sample obtained from the subject.

In various embodiments, the disease comprises a proliferative disease and the diseased tissue/cell comprises a proliferative tissue/cell. In various embodiments, the disease comprises a malignant disease and the diseased tissue/cell comprises a malignant tissue/cell. In various embodiments, the malignant disease comprises cancer and the diseased tissue/cell comprises a cancer tissue/cell. In various embodiments, the cancer comprises solid tumor cancers.

In various embodiments therefore, there is provided a method of estimating a ctDNA burden in a subject, the method comprising: determining in a blood sample obtained from the subject, a level of cfDNA that maps to one or more nucleosome-depleted region (NDR); and estimating the ctDNA burden based on said level of cfDNA, wherein said NDR (i) comprises the NDR of a gene which transcript is differentially expressed between healthy blood tissue and tumor tissue and/or (ii) is degraded to different extents between healthy blood tissue and blood tissue of a tumor-bearing subject. Advantageously, a level of cfDNA that maps to selected NDR(s) is identified to be a good estimator of or proxy for tumor burden or ctDNA burden.

In various embodiments, the estimated ctDNA burden associates/correlates, optionally positively associates/correlates with a tumor burden in the subject. In various embodiments, the higher the estimated ctDNA burden in the subject, the higher the tumor burden in the subject. In various embodiments, the higher the estimated ctDNA burden in the subject, the higher the estimated amount of cancer/tumor cells in the subject. In various embodiments, the higher the estimated ctDNA burden in the subject, the higher the estimated mass/size/volume of tumor in the subject. In various embodiments, the association/correlation, optionally positive association/correlation, may be linear (i.e. the ratio of change is constant) or non-linear (i.e. the ratio of change is not constant).

In various embodiments, the estimated ctDNA burden is associated/correlated with the level of cfDNA that maps to one or more NDRs. The association/correlation may be positive and/or negative, linear and/or non-linear and monotonic and/or non-monotonic. For example, the estimated ctDNA burden may be positively associated/correlated with the level of cfDNA that maps to a first NDR and negatively associated/correlated with the level of cfDNA burden that maps to a second NDR. For example, the estimated ctDNA burden may be linearly associated/correlated (e.g. positive or negative) with the level of cfDNA that maps to a first NDR and non-linearly associated/correlated with the level of cfDNA burden that maps to a second NDR. For example, the estimated ctDNA burden may be monotonically associated/correlated with the level of cfDNA that maps to a first NDR and non-monotonically associated/correlated with the level of cfDNA that maps to a second NDR.

In one example, the signs of the coefficients for the one or more NDRs in a trained model correspond to the sign of the differential expression of the associated transcripts in tumor tissue relative to healthy blood tissue. In various embodiments, an NDR associated with a cancer-specific gene/transcript or a tumor gene/transcript (e.g. a gene/transcript that shows a higher FPKM value in tumor than in normal blood) has a negative coefficient/correlation with the estimated ctDNA burden. In various embodiments, an NDR associated with a blood gene/transcript (e.g. a gene/transcript that shows a higher FPKM value in normal blood than in tumor) has a positive coefficient/correlation with the estimated ctDNA burden. In various embodiments, the estimated ctDNA burden is negatively associated/correlated with a level of cfDNA that maps to one or more NDR of a gene which transcript is more highly expressed in tumor tissue than in healthy blood tissue and/or the estimated ctDNA burden is positively

associated/correlated with a level of cfDNA that maps to one or more NDR of a gene which transcript is more highly expressed in healthy blood tissue than in tumor tissue. In some embodiments, the estimated ctDNA burden is linearly correlated with the level of cfDNA that maps to one or more NDRs.

In various embodiments, the determining step comprises sequencing the DNA or cfDNA present in the blood sample obtained from the subject. Examples of sequencing techniques include next-generation sequencing, amplicon-based sequencing, paired-end sequencing, Sanger sequencing etc. In some embodiments, sequencing the DNA or cfDNA present in the blood sample comprises subjecting the DNA or cfDNA present in the blood sample to deep sequencing. In one embodiment, sequencing the DNA or cfDNA present in the blood sample comprises subjecting the DNA or cfDNA present in the blood sample to next-generation sequencing. In some examples, deep sequencing is performed such that the depth/coverage at the one or more NDR/ at least one NDR is at least about 10x, at least about 25x, at least about 50x, at least about 100x, at least about 200x, at least about 300x, at least about 400x, at least about 500x, at least about 600x, at least about 700x, at least about 800x, at least about 900x or at least about 1000x, at least about 2000x, at least about 3000x, at least about 4000x, at least about 5000x or at least about 6000x. In various embodiments, the sequencing does not comprise ultra-deep sequencing. In various embodiments, the depth/coverage at the one or more NDR/ at least one NDR is or is kept to less than about 10,000x, less than about 9000x, less than about 8000x, less than about 7000x, less than about 6000x, less than about 5000x, less than about 4000x, less than about 3000x, less than about 2000x or less than about 1000x. In various embodiments, the depth/coverage at the one or more NDR/ at least one NDR is or is kept to no more than about 10,000x, no more than about 9000x, no more than about 8000x, no more than about 7000x, no more than about 6000x, no more than about 5000x, no more than about 4000x, no more than about 3000x, no more than about 2000x or no more than about 1000x.

In various embodiments, determining in a blood sample obtained from the subject, a level of cfDNA that maps to one or more NDR comprises sequencing cfDNA/ cfDNA fragments in the blood sample to obtain sequencing reads; and determining the number of sequencing reads that align with the one or more NDR to obtain said level of cfDNA that maps to one or more NDR. In various embodiments, determining in a blood sample obtained from the subject, a level of cfDNA that maps to one or

more NDR comprises sequencing any cfDNA/ cfDNA fragments present in the blood sample and determining the depth/read depth/coverage/sequencing coverage at the one or more NDR. The depth/read depth/coverage may be a relative depth/read depth/coverage/sequencing coverage. For example, the depth/read depth/coverage/sequencing coverage may be normalized/divided by a normalization factor, for example, a normalization factor as described herein, to obtain the relative depth/read depth/coverage/sequencing coverage. In one example, the relative depth/read depth/coverage/sequencing coverage is obtained by dividing/normalizing the depth/read depth/coverage/sequencing coverage (or mean depth/read depth/coverage/sequencing coverage) across the one or more NDR by the depth/read depth/coverage/sequencing coverage (or mean depth/read depth/coverage/sequencing coverage) of an upstream flank and/or a downstream flank, for example, an upstream flanking region and/or a downstream flanking region as described herein. In some embodiments therefore, the method further comprises determining the number of sequencing reads that align with one or more regions flanking the one of more NDR. In some embodiments, the method further comprises determining the depth/read depth/coverage/sequencing coverage at the one or more region flanking the one of more NDR.

The sequencing may be targeted or untargeted. Where the sequencing comprises targeted sequencing, probe(s) may be used to capture and isolate specific genomic regions for sequencing. In some embodiments therefore, the method further comprises contacting the blood sample with one or more probe capable of binding to the one or more NDR to capture cfDNA/cfDNA fragments comprising the one or more NDR prior to the sequencing step.

In various embodiments, determining in a blood sample obtained from the subject, a level of cfDNA that maps to one or more NDR comprises performing quantitative polymerase chain reaction (qPCR) or real-time polymerase chain reaction (real-time PCR) to determine the amount/proportion of cfDNA that maps to one or more NDR. In various embodiments, the performing step comprises contacting the sample with a primer that is capable of hybridizing/binding (e.g. under stringent conditions) to or a primer that is specific to the one or more NDR.

In various embodiments, the method further comprises amplifying the cfDNA in the blood sample. The amplification step may be carried out before the step of determining a level of cfDNA. The amplification step may also be carried out before

the step of sequencing cfDNA/cfDNA fragments in the blood sample and/or before the step of contacting the blood sample with the one or more probe. Amplification reactions known in the art may be employed. The amplification reactions may include but are not limited to polymerase chain reaction (PCR), ligase chain reaction (LCR), loop mediated isothermal amplification (LAMP), nucleic acid sequence based amplification (NASBA), self-sustained sequence replication (3SR), rolling circle amplification (RCA) or any other process whereby one or more copies of a particular polynucleotide sequence or nucleic acid sequence may be generated from a polynucleotide template sequence or nucleic acid template sequence.

In various embodiments, the method further comprises processing the cfDNA and/or its associated data. In various embodiments, the cfDNA are trimmed at one or both ends to retain only a central region and/or data associated with a central region of the cfDNA. Advantageously, trimming the cfDNA and/or its associated data from one or both ends to retain only a central region and/or data associated with a central region of the cfDNA may amplify a degradation signal and/or increases a coverage signal. In various embodiments, the trimmed cfDNA/central region is no more than about 70 bp, no more than about 60 bp or no more than about 50 bp in length. In various embodiments, the trimmed cfDNA/central region is about 70 bp, about 60 bp or about 50 bp in length. In one embodiment, the central region is about 61 bp. The method may also work with an untrimmed cfDNA (e.g. a cfDNA of about 151 bp), although the signal produced may be weaker.

In various embodiments, the cfDNA and/or its associated data are trimmed *in-silico* e.g. by use of the software BamUtil. In various embodiments, the cfDNA and/or its associated data are trimmed after sequencing.

In various embodiments, said NDR that is degraded to different extents between healthy blood tissue and blood tissue of a tumor-bearing subject comprises a NDR having different depth/read depth/coverage/sequencing coverage in healthy blood tissue and in tumor tissue.

In various embodiments, said transcript that is differentially expressed between healthy blood tissue and tumor tissue comprises a transcript which FPKM value differs by at least about 2 times, at least about 3 times, at least about 4 times, at least about 5 times, at least about 6 times, at least about 7 times, at least about 8 times, at least about 9 times or at least about 10 times between healthy blood tissue and tumor tissue (e.g. as determined by sequencing).

In various embodiments, said transcript that is differentially expressed between healthy blood tissue and tumor tissue comprises a transcript which FPKM value in healthy blood tissue is less than about 30, less than about 20, less than about 10, less than about 5, less than about 3, less than about 1, less than about 0.5, less than about 0.1, less than about 0.05 or less than about 0.01. In one embodiment, the FPKM value of the transcript in healthy blood tissue in less than about 1. In various embodiments, the FPKM value of the transcript in healthy blood tissue is more than about 0.01, more than about 0.05, more than about 0.1, more than about 0.5, more than about 1, more than about 3, more than about 5, more than about 10, more than about 20 or more than about 30. In one embodiment, the FPKM value of the transcript in healthy blood tissue is more than about 10. In various embodiments, the FPKM value of the transcript in healthy blood tissue is between about 0.01 and about 0.1, between about 0.1 and about 1, between about 1 and about 5 or between about 5 and about 30.

In various embodiments, said transcript that is differentially expressed between healthy blood tissue and tumor tissue comprises a transcript which FPKM value in tumor tissue is less than about 30, less than about 20, less than about 10, less than about 5, less than about 3, less than about 1, less than about 0.5, less than about 0.1, less than about 0.05 or less than about 0.01. In one embodiment, the FPKM value of the transcript in tumor tissue in less than about 1. In various embodiments, the FPKM value of the transcript in tumor tissue is more than about 0.01, more than about 0.05, more than about 0.1, more than about 0.5, more than about 1, more than about 3, more than about 5, more than about 10, more than about 20 or more than about 30. In one embodiment, the FPKM value of the transcript in tumor tissue is more than about 10. In various embodiments, the FPKM value of the transcript in tumor tissue is between about 0.01 and about 0.1, between about 0.1 and about 1, between about 1 and about 5 or between about 5 and about 30.

Some transcripts may be more highly expressed in healthy blood tissue than tumor tissue. In various embodiments, a blood transcript comprises a transcript that is more highly expressed in healthy blood tissue than tumor tissue. Some transcripts may be more highly expressed in tumor tissue than blood tissue. In various embodiments, a tumor transcript comprises a transcript that is more highly expressed in tumor tissue than blood tissue. The one or more NDR may comprise at least about 10%, at least about 20%, or at least about 30%, at least about 40%, at least about 50%, at least about 60%, at least about 70%, at least about 80%, at least about 90%

or about 100% NDRs which transcripts more highly expressed in healthy blood tissue than tumor tissue. The one or more NDR may comprise at least about 10%, at least about 20%, or at least about 30%, at least about 40%, at least about 50%, at least about 60%, at least about 70%, at least about 80%, at least about 90% or at about 100% NDRs which transcripts more highly expressed in tumor tissue than in blood tissue. The one or more NDR may comprise at least about one, at least about two or at least about three NDRs which transcripts more highly expressed in healthy blood tissue than tumor tissue and/or at least about one, at least about two or at least about three NDRs which transcripts are more highly expressed in tumor tissue than in blood tissue.

In various embodiments, said transcript which is differentially expressed in healthy blood tissue and tumor tissue is selected from the group consisting of: a transcript that is more highly expressed in healthy blood tissue than tumor tissue, a transcript that is more highly expressed in tumor tissue than healthy blood tissue and combinations thereof. In one embodiment, said transcript which is differentially expressed between blood tissue and tumor tissue consists of transcript(s) that is more highly expressed in tumor tissue than blood tissue. In one embodiment, said transcript which is differentially expressed between blood tissue and tumor tissue consists of transcript(s) that is more highly expressed in blood tissue than tumor tissue. In one embodiment, said transcript does not comprise a transcript which is more highly expressed in tumor tissue than blood tissue. Without being bound by theory, it is believed that tumor-derived DNA component in cancer plasma weakens the blood-specific DNA degradation pattern, and thus the decay of blood-specific signal (alone i.e. without determining the signal of any tumor-associated genes) may be used to robustly estimate a ctDNA content, regardless of cancer types.

In various embodiments therefore, the method is suitable for estimating a disease burden for a specific cancer type, a specific group of cancers, or for all cancers in general (i.e. pan-cancer). In various embodiments, the method comprises a method of estimating a ctDNA burden or tumor burden associated with one or more of the following cancers: bladder cancer, bladder urothelial carcinoma, breast cancer, breast invasive carcinoma, cervical cancer, cervical squamous cell carcinoma, endocervical adenocarcinoma, colorectal cancer, esophageal cancer, esophageal carcinoma, brain cancer, glioblastoma multiforme, head and neck cancer, head and neck squamous cell carcinoma, kidney cancer, renal cell cancer, kidney renal clear cell carcinoma,

kidney renal papillary cell carcinoma, brain lower grade glioma, liver cancer, liver hepatocellular carcinoma, lung cancer, lung adenocarcinoma, lung squamous cell carcinoma, ovarian cancer, ovarian serous cystadenocarcinoma, pancreatic cancer, pancreatic adenocarcinoma, prostate cancer, prostate adenocarcinoma, skin cancer, skin cutaneous melanoma, gastric cancer, stomach cancer, stomach adenocarcinoma, thyroid cancer, thyroid carcinoma, endometrial cancer, uterine cancer, uterine corpus endometrial carcinoma, reproductive cancers, gastrointestinal cancers, respiratory cancers, or subtypes thereof. Thus, in various embodiments, the subject has or suffers from one or more of these cancers. In various embodiments, the tumor-bearing subject bears one or more of these tumors. In various embodiments, the subject or tumor-bearing subject does not have or does not suffer from blood cancer/hematologic cancer/hematologic malignancy.

In one embodiment, the method comprises a method of estimating a tumor burden associated with colorectal cancer. In one embodiment, the subject has or suffers from colorectal cancer. In one embodiment, the tumor-bearing subject bears a colorectal tumor. In one embodiment, the method comprises a method of estimating a ctDNA burden or tumor burden associated with breast cancer. In one embodiment, the subject has or suffers from breast cancer. In one embodiment, the tumor-bearing subject bears a breast tumor.

In one embodiment, where the method comprises a method of estimating a ctDNA burden or tumor burden associated with a specific cancer type or a specific group of cancers, the NDR comprises at least one NDR of a gene which transcript shows a higher FPKM value in tumor belonging to the specific cancer type or the specific group of cancers than in healthy/normal blood. In some examples, the transcript has a $FPKM_{tumor}$> about 5 or > about 10 and a $FPKM_{blood}$ < about 1. In one embodiment, where the method comprises a method of estimating a ctDNA burden or tumor burden associated with any cancer in general (e.g. pan-cancer), the NDR comprises at least one NDR of a gene which transcript shows a higher FPKM value in normal blood than in tumor. In some examples, the transcript has a $FPKM_{blood}$> about 5 or > about 10 and a $FPKM_{tumor}$ < about 1. In various embodiments, where the method comprises a method of estimating a ctDNA burden or tumor burden associated with any cancer in general (e.g. pan-cancer), the NDR consists of NDR(s) of gene(s) which transcript(s) shows a higher FPKM value in normal blood than in tumor.

In various embodiments, the one or more NDR comprises at least about two, at least about three, at least about four, at least about five, at least about six, at least about seven, at least about eight, at least about nine, at least about ten, at least about 11, at least about 12, at least about 13, at least about 14, at least about 15, at least about 16, at least about 17, at least about 18, at least about 19 or at least about 20 NDRs. In various embodiments, the one or more NDR comprises the NDR of at least about two, at least about three, at least about four, at least about five, at least about six, at least about seven, at least about eight, at least about nine, at least about ten genes, at least about 11, at least about 12, at least about 13, at least about 14, at least about 15, at least about 16, at least about 17, at least about 18, at least about 19 or at least about 20 genes or distinct genes.

In some embodiments, the one or more NDR comprises at least about two NDRs, optionally about six NDRs, further optionally about ten NDRs. In some embodiments, the one or more NDR comprises the NDR of at least about two genes (or distinct genes), optionally about six genes (or distinct genes), further optionally about ten genes (or distinct genes). In some embodiments, the one or more NDR comprises at least about four NDRs or the NDRs of at least about four genes or distinct genes. In some embodiments, the one or more NDR comprises no more than about nine NDRs or NDRs of no more than about nine genes or distinct genes. In some embodiments, the one or more NDR comprises about four to about nine NDRs or NDRs of about four to about nine genes or distinct genes. In some embodiments, the one or more NDR comprises about six NDRs or NDRs of about six genes or distinct genes. In some embodiments, the one or more NDR comprises no more than about 13 NDRs or NDRs of no more than about 13 genes or distinct genes. In some embodiments, the one or more NDR comprises about nine, about 10, about 11, about 12 or about 13 NDRs or NDRs of about nine, about 10, about 11, about 12 or about 13 genes or distinct genes. The suitable number of NDRs, genes or features may be further varied, and is within the purview of a person skilled in the art. The number or the reasonable range of numbers of NDRs, genes or features may be determined, for example, by checking an error evolution with the number of top predictive genes or features (e.g. genes or features that are selected most frequently as being predictive by a machine learning model in multiple iterations).

In various embodiments, the NDRs/genes comprises one or more NDRs/genes listed in one or more of Table 1, Table 2, Table S3, Table S10, Table S14, Table S15, Table S16, Table S17, Table S18, Table S19, Table S20 and Table S21.

In various embodiments, the NDRs/genes comprises one or more, or at least about one, at least about two, at least about three, at least about four, at least about five, at least about six, at least about seven, at least about eight, at least about nine, or at least about ten of the following genes/associated NDRs (e.g. a transcription start site, a promoter, an intron-exon junction and/or an exon-intron junction): ABHD5, ABTB1, ACAP1, ACO1, ACRBP, ACSL1, ADAM8, ADIRF, AGR2, AGR3, AHSP, AK2, AKNA, ALAS2, ALDH18A1, ALOX5, ANKS4B, ANPEP, AOAH, APOBEC3A, ARAP1, ARHGAP25, ARHGAP26, ARHGAP30, ARHGAP9, ARHGEF16, ARHGEF35, ARID5A, ARRB2, ARSE, ATG16L2, ATP2A2, ATP2C2, ATP5G1, ATP5G3, ATP6V1B2, AXIN2, AZGP1, AZU1, B3GNT3, BATF2, BCAR1, BCL2L15, BCL2L2, BCL6, BDH1, BDH2, BEST1, BGN, BIN2, BIRC5, BMP4, BMX, BOK, BPI, BSPRY, BTK, BTNL8, C10orf54, C11orf21, C16orf54, C19orf33, C19orf35, C1orf162, C1orf210, C1orf228, C1QTNF5, C3, C5AR2, C6orf203, C6orf25, C8orf59, CA1, CA4, CALD1, CAMP, CAPN5, CARS2, CCDC88B, CCL20, CCM2, CCND3, CCR7, CD177, CD244, CD276, CD300E, CD300LB, CD300LF, CD37, CD44, CD53, CD55, CDC42SE1, CDCP1, CDH1, CDH17, CDHR5, CDK4, CDK5RAP2, CDX1, CEACAM1, CEACAM3, CEACAM4, CEACAM5, CELF2, CENPF, CFD, CFP, CFTR, CHCHD6, CHID1, CKB, CKMT1B, CLC, CLDN7, CLEC12A, CLEC4D, CLEC4E, CMTM2, CNN2, CORO1A, CORO7, COTL1, COX6C, CR1, CRB3, CSF3R, CTGF, CTNND1, CXCR1, CXCR2, CYBA, CYTH4, DDC, DDR1, DDX10, DEF8, DEFA1, DEFA1B, DEFA3, DEFA4, DENND1C, DENND3, DHRS13, DHX34, DMTN, DNAH17, DOCK2, DOK3, DPEP2, DYSF, ECE1, ECT2, EEF1E1, EFNA3, EGLN2, EI24, ELANE, ELF3, EMP1, ENTPD2, ENTPD6, EPB42, EPCAM, EPHA2, EPS8L3, ERBB2, ERBB3, EVI2B, F3, FAM101A, FAM109A, FAM212B, FAM213B, FAM49B, FAM60A, FAM65B, FAM83E, FAM84A, FBL, FBXL5, FCAR, FCGR2A, FCGR3B, FCN1, FERMT1, FERMT3, FES, FFAR2, FGD3, FGFR4, FGFRL1, FGR, FKBP8, FLOT2, FMNL1, FN1, FOLR3, FOXA2, FPR1, FPR2, FUT2, FUT6, FUT7, GATA1, GBP3, GCA, GGT6, GJB2, GLRX3, GLT1D1, GMFG, GMNN, GNG2, GNLY, GOLT1A, GP9, GPC4, GPR35, GPRC5A, GPSM3, GPX2, GRAMD1A, GRAP2, GRTP1, GZMH, H2AFY2, HBA1, HBA2, HBB, HBD, HBG1, HBG2, HBM, HBQ1, HCK, HCLS1, HID1, HK3, HKDC1, HMBS, HMGB3, HMGCS2, HN1L, HNF4A, HTRA1,

ICAM3, IFI30, IFITM1, IFITM2, IFT172, IKZF1, IL16, IL18RAP, IL1R2, IL1RN, IL2RG, IL32, ILVBL, IMPDH1, INPP5D, IPO5, ITGA2B, ITGAL, ITGAM, ITGAX, ITGB2, ITGB4, JAK3, JUND, JUP, KCNAB2, KCNE1, KIAA1191, KIFC1, KLF1, LAD1, LAMB2, LAMC2, LAPTM5, LCP2, LDHA, LGALS3BP, LGALS4, LGMN, LILRA1, LILRA5, LILRB2, LILRB3, LIMD2, LIPH, LMNB1, LMO7, LPAR2, LRCH4, LRRC25, LSP1, LSR, LST1, LTB, LYL1, MACROD1, MAGED1, MAN2A2, MAP1LC3A, MEFV, MEP1A, MFAP4, MIS18A, MISP, MKNK1, MLKL, MMAB, MME, MMP11, MMP25, MMP7, MMP8, MORN2, MPO, MPP1, MPZL2, MRPL17, MSL3, MSRB1, MTIF2, MUC13, MX2, MXD3, MYL4, MYO1A, MYO1F, MYO1G, MZT2A, NABP1, NADK, NAIP, NAMPT, NARF, NBEAL2, NCF1, NCF2, NCF4, NDEL1, NDUFAF4, NDUFB5, NEK2, NFAM1, NFE2, NKG7, NLRC4, NLRC5, NLRP12, NNMT, NOX1, NQO1, NTMT1, NTPCR, NUPR1, OAZ1, ORM1, OSCAR, P2RX1, PADI2, PADI4, PALLD, PARVG, PDHA1, PDHX, PGD, PGLYRP1, PHC2, PHF21A, PHGR1, PHOSPHO1, PIK3R5, PIN4, PLB1, PLBD1, PLCB2, PLCD3, PLCG2, PLEKHA1, PLS3, POF1B, POLR2H, POSTN, PPBP, PPIL1, PPM1M, PPP1R16A, PPP1R1B, PRAM1, PRAP1, PREX1, PRKCB, PROCR, PROK2, PRR15, PRR15L, PRRC1, PRSS22, PRSS8, PRTN3, PSTPIP1, PTK2B, PTPN6, PYCR1, PYGL, R3HDM4, RAB24, RAB25, RAC2, RARRES2, RASAL3, RASGRP2, RASGRP4, RASSF2, REG4, RELT, REM2, RETN, RFC3, RGL4, RGS19, RHOD, RHPN2, RIN3, RNASE4, RND3, RNF166, RNF167, RPL41, RPS6KA1, RPS9, S100A12, S100A14, S100A8, S1PR4, SAP25, SASH3, SCNN1A, SCOC, SDCBP2, SEC11C, SECTM1, SELL, SEMA4D, SEPP1, SEPTIN10, SFN, SHKBP1, SIGLEC5, SIPA1, SIRPB1, SLC11A1, SLC12A9, SLC16A3, SLC25A37, SLC2A3, SLC2A8, SLC38A5, SLC39A5, SLC43A2, SLCO3A1, SMAP2, SMIM22, SNCA, SORD, SORL1, SPATS2L, SPI1, SRC, ST20, STAP2, STARD10, STAT5B, STEAP1, STK10, STX11, STXBP2, SULT2B1, SYTL3, TACC3, TAGAP, TALDO1, TBC1D10C, TBX21, TBXAS1, TCEAL4, TFF3, THBS2, THEMIS2, TIMM8B, TINAGL1, TJP3, TLR6, TM4SF5, TMBIM6, TMC4, TMCC2, TMEM106C, TMEM126B, TMEM14A, TMEM14C, TMEM71, TMEM91, TMEM97, TMPRSS2, TMPRSS4, TNFRSF10C, TNS3, TOP2A, TPM1, TRAF3IP3, TREM1, TREML2, TRIM22, TRIM25, TSKU, TSPAN15, TSPAN8, TUBA4A, TUBB1, TYMS, TYROBP, UBE2C, UBE2D3, UBE2T, UGT8, UNC13D, UQCC2, URI1, USB1, USH1C, VARS, VASP, VAV1, VMP1, VNN2, VNN3, VPS51, VSTM1, VWA1, WAS, WDR12, WFS1, XPO6, ZAP70, ZDHHC18, ZDHHC19, ZDHHC9, ZNF467, ZWINT and parts thereof.

In some embodiments, the one or more NDR comprises one or more NDR of a gene selected from the group consisting of: SHKBP1, ACSL1, BCAR1, RAB25, PRTN3, LSR, SLC11A1, NLRP12, HMBS, LILRB3, GP9, MX2, RASGRP4, ATG16L2 and combinations thereof. In some embodiments, the one or more NDR comprises one or more NDR of a gene selected from the group consisting of: SLC11A1, NLRP12, PRTN3, HMBS, LILRB3, ACSL1, GP9, MX2, RASGRP4, ATG16L2 and combinations thereof. In some embodiments, the one or more NDR comprises one or more NDR of a gene selected from the group consisting of: SHKBP1, ACSL1, BCAR1, RAB25, PRTN3, LSR and combinations thereof.

In various embodiments, where the method comprises a method of estimating a ctDNA burden or tumor burden associated with a specific cancer type or a specific group of cancers, the NDR comprises one or more, or at least about one, at least about two, at least about three, at least about four, at least about five, at least about six, at least about seven, at least about eight, at least about nine, or at least about ten of the following genes/associated NDRs (e.g. a transcription start site, a promoter, an intron-exon junction and/or an exon-intron junction): ABTB1, ACAP1, ACO1, ACSL1, ADIRF, AGR2, AGR3, AK2, AKNA, ALDH18A1, ANKS4B, ARAP1, ARHGAP25, ARHGAP30, ARHGAP9, ARHGEF16, ARHGEF35, ARID5A, ARRB2, ARSE, ATG16L2, ATP2A2, ATP2C2, ATP5G1, ATP5G3, AXIN2, AZGP1, B3GNT3, BATF2, BCAR1, BCL2L15, BCL2L2, BCL6, BDH1, BDH2, BEST1, BGN, BIN2, BIRC5, BMP4, BOK, BSPRY, C10orf54, C11orf21, C16orf54, C19orf33, C1orf162, C1orf210, C1QTNF5, C3, C5AR2, C6orf203, C8orf59, CA1, CALD1, CAMP, CAPN5, CCL20, CCM2, CCR7, CD177, CD276, CD300LF, CD37, CD44, CD55, CDC42SE1, CDCP1, CDH1, CDH17, CDHR5, CDK4, CDK5RAP2, CDX1, CEACAM1, CEACAM4, CEACAM5, CENPF, CFD, CFTR, CHCHD6, CHID1, CKB, CKMT1B, CLDN7, CLEC4E, CORO1A, COTL1, COX6C, CR1, CRB3, CSF3R, CTGF, CTNND1, CXCR1, CXCR2, DDC, DDR1, DDX10, DENND1C, DMTN, DOK3, DPEP2, ECT2, EEF1E1, EFNA3, EI24, ELF3, EMP1, ENTPD2, ENTPD6, EPCAM, EPHA2, EPS8L3, ERBB2, ERBB3, EVI2B, F3, FAM101A, FAM109A, FAM212B, FAM213B, FAM60A, FAM65B, FAM83E, FAM84A, FBL, FBXL5, FCAR, FCGR2A, FCN1, FERMT1, FFAR2, FGD3, FGFR4, FGFRL1, FGR, FMNL1, FN1, FOLR3, FOXA2, FPR1, FUT2, FUT6, GATA1, GBP3, GGT6, GJB2, GLRX3, GLT1D1, GMFG, GMNN, GNLY, GOLT1A, GPC4, GPR35, GPRC5A, GPX2, GRTP1, GZMH, H2AFY2, HBB, HBD, HBG2, HBM, HBQ1, HCK, HID1, HK3, HKDC1, HMGB3, HMGCS2, HN1L, HNF4A, HTRA1, ICAM3,

IFITM1, IFITM2, IFT172, IKZF1, IL1R2, IL1RN, IL32, ILVBL, IPO5, ITGA2B, ITGAM, ITGB4, JUND, JUP, KIAA1191, KIFC1, LAD1, LAMB2, LAMC2, LDHA, LGALS3BP, LGALS4, LGMN, LILRB2, LILRB3, LIMD2, LIPH, LMNB1, LMO7, LRRC25, LSR, LST1, MACROD1, MAGED1, MAP1LC3A, MEP1A, MFAP4, MIS18A, MISP, MKNK1, MMAB, MME, MMP11, MMP25, MMP7, MMP8, MORN2, MPP1, MPZL2, MRPL17, MSRB1, MTIF2, MUC13, MXD3, MYL4, MYO1A, MYO1F, MZT2A, NAMPT, NCF1, NCF2, NCF4, NDUFAF4, NDUFB5, NEK2, NFAM1, NFE2, NKG7, NNMT, NOX1, NQO1, NTMT1, NTPCR, NUPR1, OAZ1, ORM1, OSCAR, P2RX1, PADI4, PALLD, PDHA1, PDHX, PGLYRP1, PHC2, PHGR1, PHOSPHO1, PIK3R5, PIN4, PLCD3, PLEKHA1, PLS3, POF1B, POLR2H, POSTN, PPIL1, PPM1M, PPP1R16A, PPP1R1B, PRAM1, PRAP1, PRKCB, PROCR, PRR15, PRR15L, PRRC1, PRSS22, PRSS8, PRTN3, PSTPIP1, PTPN6, PYCR1, RAB25, RARRES2, RASGRP2, RASGRP4, RASSF2, REG4, RETN, RFC3, RHOD, RHPN2, RIN3, RNASE4, RND3, RPL41, RPS6KA1, RPS9, S100A12, S100A14, S100A8, S1PR4, SCNN1A, SCOC, SDCBP2, SEC11C, SEPP1, SEPTIN10, SFN, SHKBP1, SIGLEC5, SIRPB1, SLC11A1, SLC25A37, SLC2A8, SLC39A5, SMIM22, SNCA, SORD, SPATS2L, SPI1, SRC, STAP2, STARD10, STEAP1, STX11, SULT2B1, SYTL3, TBC1D10C, TCEAL4, TFF3, THBS2, THEMIS2, TIMM8B, TINAGL1, TJP3, TM4SF5, TMBIM6, TMC4, TMEM106C, TMEM126B, TMEM14A, TMEM14C, TMEM71, TMEM91, TMEM97, TMPRSS2, TMPRSS4, TNFRSF10C, TNS3, TOP2A, TPM1, TRAF3IP3, TREM1, TRIM22, TSKU, TSPAN15, TSPAN8, TYMS, TYROBP, UBE2C, UBE2T, UGT8, UQCC2, URI1, USH1C, VARS, VAV1, VMP1, VNN2, VPS51, VSTM1, VWA1, WAS, WDR12, WFS1, XPO6, ZAP70, ZDHHC19, ZDHHC9, ZNF467 and ZWINT.

In some embodiments, where the method comprises a method of estimating a ctDNA burden or tumor burden associated with a specific cancer type or a specific group of cancers, the NDR comprises one or more, or at least about one, at least about two, at least about three, at least about four, at least about five, at least about six, at least about seven, at least about eight, at least about nine, or at least about ten of the following genes/associated NDRs (e.g. a transcription start site, a promoter, an intron-exon junction and/or an exon-intron junction): ACAP1, ACSL1, ADIRF, ANKS4B, ARHGAP30, ARSE, ATP5G3, BCAR1, BCL6, BGN, BIN2, BMP4, C19orf33, C1orf162, C5AR2, CCR7, CD276, CD37, CD44, CDC42SE1, CDH17, CDK5RAP2, CHCHD6, CKB, CLDN7, CLEC4E, CTGF, DDX10, ELF3, ERBB3, F3, FAM101A, FAM65B, FAM84A, FBXL5, FCAR, FCN1, FERMT1, FFAR2, FOLR3, FOXA2, FUT2,

GMFG, GPRC5A, GPX2, HBB, HBD, HID1, LAMC2, LDHA, LGALS4, LGMN, LIMD2, LRRC25, LSR, MAGED1, MPZL2, MRPL17, MXD3, MYO1A, NCF1, NCF2, NFE2, OAZ1, PHOSPHO1, PLCD3, POF1B, POSTN, PPP1R16A, PRAP1, PRR15L, PRSS8, PRTN3, RAB25, RASGRP4, RFC3, S100A12, SCOC, SDCBP2, SEPP1, SHKBP1, SLC11A1, SORD, SRC, STAP2, STARD10, STX11, SYTL3, TCEAL4, TFF3, TM4SF5, TMC4, TMEM126B, TMPRSS2, TNFRSF10C, TRAF3IP3, TREM1, TRIM22, TYMS, TYROBP, UBE2C, UGT8, UQCC2, VAV1, VNN2, WAS and ZDHHC9.

In some embodiments, where the method comprises a method of estimating a ctDNA burden or tumor burden associated with a specific cancer type or a specific group of cancers, the NDR comprises one or more, or at least about one, at least about two, at least about three, at least about four, at least about five, at least about six, at least about seven, at least about eight, at least about nine, or at least about ten of the following genes/associated NDRs (e.g. a transcription start site, a promoter, an intron-exon junction and/or an exon-intron junction): ACSL1, ANKS4B, ARHGAP30, ATP5G3, B3GNT3, BCL6, BIN2, BMP4, C19orf33, C1orf162, CD37, CLEC4E, ERBB3, FBXL5, FCAR, FCN1, FERMT1, FFAR2, FOXA2, GMFG, HBB, HID1, ICAM3, LGALS4, LGMN, LSR, MXD3, MYO1A, NCF1, NCF2, NFE2, OAZ1, PHOSPHO1, PLCD3, PRAP1, PRSS8, PRTN3, RAB25, RASGRP4, SCOC, SDCBP2, SEPP1, SHKBP1, SYTL3, TFF3, TM4SF5, TMC4, TMPRSS2, TRAF3IP3, TRIM22, TYROBP, UGT8, VAV1 and WAS.

In some embodiments, where the method comprises a method of estimating a ctDNA burden or tumor burden associated with a specific cancer type or a specific group of cancers, the NDR comprises the following: first exon-intron junction of SHKBP1, first exon-intron junction of ACSL1, first exon-intron junction of BCAR1, promoter of RAB25, promoter of PRTN3 and/or promoter of LSR.

In some embodiments, the method further comprises assigning the most weight to the level of cfDNA that maps to the first exon-intron junction of SHKBP1 and less weight to the level of cfDNA that maps to the other NDR(s) when estimating the ctDNA burden. In some embodiments, the method comprises assigning more weight to the level of cfDNA that maps to the first exon-intron junction of SHKBP1 and relatively less weight to the level of cfDNA that maps to one or more of the following NDRs: the first exon-intron junction of ACSL1, the first exon-intron junction of BCAR1, the promoter of RAB25, the promoter of LSR and the promoter of PRTN3. In some embodiments,

the method comprises assigning more weight to the level of cfDNA that maps to the first exon-intron junction of ACSL1 and relatively less weight to the level of cfDNA that maps to one or more of the following NDRs: the first exon-intron junction of BCAR1, the promoter of RAB25, the promoter of LSR and the promoter of PRTN3. In some embodiments, the method comprises assigning more weight to the level of cfDNA that maps to the first exon-intron junction of BCAR1 and relatively less weight to the level of cfDNA that maps to one or more of the following NDRs: the promoter of RAB25, the promoter of LSR and the promoter of PRTN3. In some embodiments, the method comprises assigning more weight to the level of cfDNA that maps to the promoter of RAB25 and relatively less weight to the level of cfDNA that maps to one or more of the following NDRs: the promoter of LSR and the promoter of PRTN3. In various embodiments, the method comprises assigning more weight to the level of cfDNA that maps to the promoter of LSR and relatively less weight to the level of cfDNA that maps to the promoter of PRTN3. In some embodiments, the method comprises assigning more weight to the level of cfDNA that maps to a first exon-intron junction and relatively less weight to the level of cfDNA that maps to a promoter.

In various embodiments, the specific cancer type or specific group of cancers comprises colorectal cancer.

In various embodiments, where the method comprises a method of estimating a ctDNA burden or tumor burden associated with any cancer or cancer in general (pan cancer), the NDR comprises one or more, or at least about one, at least about two, at least about three, at least about four, at least about five, at least about six, at least about seven, at least about eight, at least about nine, or at least about ten of the following genes/associated NDRs (e.g. a transcription start site, a promoter, an intron-exon junction and/or an exon-intron junction): ABHD5, ABTB1, ACAP1, ACRBP, ACSL1, ADAM8, AHSP, AKNA, ALAS2, ALOX5, ANPEP, AOAH, APOBEC3A, ARAP1, ARHGAP26, ARHGAP9, ARID5A, ARRB2, ATG16L2, ATP6V1B2, AZU1, BIN2, BMX, BPI, BTK, BTNL8, C11orf21, C19orf35, C1orf162, C1orf228, C6orf25, CA1, CA4, CAMP, CARS2, CCDC88B, CCND3, CD177, CD244, CD300E, CD300LB, CD37, CD44, CD53, CDK5RAP2, CEACAM3, CEACAM4, CELF2, CFP, CLC, CLEC12A, CLEC4D, CLEC4E, CMTM2, CNN2, CORO1A, CORO7, CR1, CSF3R, CXCR1, CXCR2, CYBA, CYTH4, DEF8, DEFA1, DEFA1B, DEFA3, DEFA4, DENND1C, DENND3, DHRS13, DHX34, DMTN, DNAH17, DOCK2, DOK3, DYSF, ECE1, EGLN2, ELANE, EPB42, FAM49B, FAM65B, FBXL5, FCAR, FCGR2A,

FCGR3B, FCN1, FERMT3, FES, FFAR2, FGD3, FGR, FKBP8, FLOT2, FMNL1, FOLR3, FPR2, FUT7, GATA1, GCA, GNG2, GNLY, GP9, GPSM3, GRAMD1A, GRAP2, HBA1, HBA2, HBB, HBD, HBG1, HBG2, HBM, HBQ1, HCK, HCLS1, HK3, HMBS, ICAM3, IFI30, IFITM1, IFITM2, IL16, IL18RAP, IL1R2, IL2RG, IMPDH1, INPP5D, ITGA2B, ITGAL, ITGAM, ITGAX, ITGB2, JAK3, KCNAB2, KCNE1, KLF1, LAPTM5, LCP2, LILRA1, LILRA5, LILRB2, LILRB3, LPAR2, LRCH4, LSP1, LST1, LTB, LYL1, MAN2A2, MEFV, MKNK1, MLKL, MMP25, MMP8, MPO, MPP1, MSL3, MSRB1, MX2, MXD3, MYL4, MYO1F, MYO1G, NABP1, NADK, NAIP, NAMPT, NARF, NBEAL2, NCF1, NCF2, NDEL1, NFE2, NLRC4, NLRC5, NLRP12, P2RX1, PADI2, PADI4, PARVG, PGD, PGLYRP1, PHF21A, PHOSPHO1, PIK3R5, PLB1, PLBD1, PLCB2, PLCG2, PPBP, PRAM1, PREX1, PROK2, PRTN3, PSTPIP1, PTK2B, PTPN6, PYGL, R3HDM4, RAB24, RAC2, RASAL3, RASGRP2, RASGRP4, RELT, REM2, RGL4, RGS19, RIN3, RNF166, RNF167, SAP25, SASH3, SECTM1, SELL, SEMA4D, SHKBP1, SIGLEC5, SIPA1, SIRPB1, SLC11A1, SLC12A9, SLC16A3, SLC2A3, SLC38A5, SLC43A2, SLCO3A1, SMAP2, SORL1, SPI1, ST20, STAT5B, STK10, STXBP2, TACC3, TAGAP, TALDO1, TBC1D10C, TBX21, TBXAS1, THEMIS2, TLR6, TMCC2, TMEM71, TNFRSF10C, TRAF3IP3, TREML2, TRIM25, TUBA4A, TUBB1, UBE2D3, UNC13D, USB1, VASP, VAV1, VMP1, VNN3, VSTM1, WAS, XPO6, ZAP70, ZDHHC18 and ZDHHC19.

In some embodiments, where the method comprises a method of estimating a ctDNA burden or tumor burden associated with any cancer or cancer in general (pan cancer), the NDR comprises one or more, or at least about one, at least about two, at least about three, at least about four, at least about five, at least about six, at least about seven, at least about eight, at least about nine, or at least about ten of the following genes/associated NDRs (e.g. a transcription start site, a promoter, an intron-exon junction and/or an exon-intron junction): ABTB1, ACAP1, ACSL1, ARHGAP9, ATG16L2, ATP6V1B2, BIN2, BTK, BTNL8, C19orf35, CA4, CD37, CDK5RAP2, CEACAM4, CFP, CLEC12A, CLEC4D, CLEC4E, CSF3R, CXCR2, CYTH4, DEF8, DENND1C, DENND3, DHRS13, DOK3, FAM49B, FBXL5, FCGR2A, FCN1, FES, FFAR2, FKBP8, FMNL1, FOLR3, FUT7, GNG2, GP9, GPSM3, HBD, HK3, HMBS, IFI30, IL16, IL1R2, ITGA2B, JAK3, KCNE1, LCP2, LILRB2, LILRB3, LYL1, MAN2A2, MKNK1, MLKL, MPO, MX2, MYO1F, NCF1, NFE2, NLRP12, PADI2, PADI4, PARVG, PGLYRP1, PHOSPHO1, PREX1, PRTN3, PSTPIP1, RAC2, RASAL3, RASGRP4,

RELT, RNF166, RNF167, SHKBP1, SLC11A1, SLC12A9, SLC16A3, SLCO3A1, SORL1, SPI1, TBC1D10C, TBXAS1, USB1, VAV1, VSTM1, XPO6 and ZDHHC18.

In some embodiments, where the method comprises a method of estimating a ctDNA burden or tumor burden associated with any cancer or cancer in general (pan cancer), the NDR comprises one or more, or at least about one, at least about two, at least about three, at least about four, at least about five, at least about six, at least about seven, at least about eight, at least about nine, or at least about ten of the following genes/associated NDRs (e.g. a transcription start site, a promoter, an intron-exon junction and/or an exon-intron junction): ABTB1, ACAP1, ACSL1, ATG16L2, ATP6V1B2, BTK, BTNL8, C19orf35, CEACAM4, CLEC4E, CSF3R, DENND1C, DENND3, DHRS13, FBXL5, FCAR, FCN1, FFAR2, FKBP8, FMNL1, GNG2, GP9, GPSM3, HBD, HMBS, IFI30, IL18RAP, ITGA2B, LCP2, LILRB3, LYL1, MAN2A2, MKNK1, MPO, MX2, MXD3, MYO1F, NFE2, NLRP12, PADI4, PHOSPHO1, PREX1, RASGRP2, RASGRP4, RGL4, RNF166, RNF167, SHKBP1, SLC11A1, SLC12A9, TBC1D10C, TBXAS1, USB1 and VSTM1.

In some embodiments, where the method comprises a method of estimating a ctDNA burden or tumor burden with any cancer or cancer in general (pan cancer), the NDR comprises the following: promoter of SLC11A1, promoter of NLRP12, promoter of PRTN3, promoter of HMBS, promoter of LILRB3, first exon-intron junction of ACSL1, first exon-intron junction of GP9, promoter of MX2, promoter of RASGRP4 and/or promoter of ATG16L2.

In some embodiments, the method further comprises assigning the most weight to the level of cfDNA that maps to the promoter of HMBS and/or the first exon-intron junction of GP9 and relatively less weight to the level of cfDNA that maps to the other NDR(s) when estimating the ctDNA burden. In some embodiments, the method comprises assigning more weight to the level of cfDNA that maps to the promoter of HMBS and/or the first exon-intron junction of GP9 and relatively less weight to the level of cfDNA that maps to one or more of the following NDRs: the promoter of RASGRP4, the promoter of NLRP12, the promoter of ATG16L2, the promoter of SLC11A1, the promoter of LILRB3, the promoter of PRTN3, the promoter of MX2 and the first exon-intron junction of ACSL1. In some embodiments, the method comprises assigning more weight to the level of cfDNA that maps to the promoter of RASGRP4 and relatively less weight to the level of cfDNA that maps to one or more of the following NDRs: the promoter of NLRP12, the promoter of ATG16L2, the promoter of

SLC11A1, the promoter of LILRB3, the promoter of PRTN3, the promoter of MX2 and the first exon-intron junction of ACSL1. In some embodiments, the method comprises assigning more weight to the level of cfDNA that maps to the promoter of NLRP12 and relatively less weight to the level of cfDNA that maps to one or more of the following NDRs: the promoter of ATG16L2, the promoter of SLC11A1, the promoter of LILRB3, the promoter of PRTN3, the promoter of MX2 and the first exon-intron junction of ACSL1. In some embodiments, the method comprises assigning more weight to the level of cfDNA that maps to the promoter of ATG16L2 and relatively less weight to the level of cfDNA that maps to one or more of the following NDRs: the promoter of SLC11A1, the promoter of LILRB3, the promoter of PRTN3, the promoter of MX2 and the first exon-intron junction of ACSL1. In some embodiments, the method comprises assigning more weight to the level of cfDNA that maps to the promoter of SLC11A1 and relatively less weight to the level of cfDNA that maps to one or more of the following NDRs: the promoter of LILRB3, the promoter of PRTN3, the promoter of MX2 and the first exon-intron junction of ACSL1. In some embodiments, the method comprises assigning more weight to the level of cfDNA that maps to the promoter of LILRB3 and relatively less weight to the level of cfDNA that maps to one or more of the following NDRs: the promoter of PRTN3, the promoter of MX2 and the first exon-intron junction of ACSL1. In some embodiments, the method comprises assigning more weight to the level of cfDNA that maps to the promoter of PRTN3 and relatively less weight to the level of cfDNA that maps to one or more of the following NDRs: the promoter of MX2 and the first exon-intron junction of ACSL1. In some embodiments, the method comprises assigning similar weights to the level of cfDNA that maps to the promoter of HMBS and the level of cfDNA that maps to the first exon-intron junction of GP9. In some embodiments, the method comprises assigning similar weights to the level of cfDNA that maps to the promoter of MX2 and the level of cfDNA that maps to the first exon-intron junction of ACSL1.

In various embodiments, the total length/size of the one or more NDR is no more than about 100 kilobase pairs (kb), no more than about 90kb, no more than about 80kb, no more than about 70 kb, no more than about 60 kb, no more than about 50 kb, no more than about 30 kb, no more than about 20 kb or more than about 10 kb. In some embodiments, the total length/size of the one or more NDR is no more than about 30 kb. In some embodiments, the total length/size of the one or more NDR is no

more than about 25 kb. In some embodiments, the total length/size of the one or more NDR is about 24 kb.

In various embodiments, the method does not comprise sequencing one or more regions that collectively spans more than about 100 kb, more than about 95 kb, more than about 90 kb, more than about 85 kb, more than about 80 kb, more than about 75 kb, more than about 70 kb, more than about 65 kb, more than about 60 kb, more than about 55 kb, more than about 50 kb, more than about 45 kb, more than about 40 kb, more than about 35 kb, more than about 30 kb, more than about 25 kb, more than about 20 kb, more than about 15 kb, more than about 10 kb or more than about 5 kb in length. In various embodiments, the method does not comprise sequencing a continuous/contiguous region that spans more than about 4 kb, more than about 5 kb, more than about 6 kb, more than about 7 kb, more than about 8 kb, more than about 9 kb or more than about 10 kb in length. In various embodiments, the method does not comprise whole genome sequencing of the cfDNA. Advantageously, embodiments of the method are efficient in terms of time and resources, and provide a fast turnaround time.

As may be appreciated, by following the teachings herein/ carrying out the steps of this disclosure, a person skilled in the art will also be able to identify further genomic regions (including non-coding regions), other than the ones highlighted in this disclosure, that are also predictive of the disease burden, the cancer burden, the tumor burden, the ctDNA burden, the level of ctDNA, an amount of ctDNA, the proportion of ctDNA, the fraction of ctDNA and the ctDNA content. Hence, the genes/regions highlighted in this disclosure are non-exhaustive. Indeed, a person skilled in the art would understand that the genomic regions that may be used to predict the disease burden, the cancer burden, the tumor burden, the ctDNA burden, the level of ctDNA, an amount of ctDNA, the proportion of ctDNA, the fraction of ctDNA and/or the ctDNA content are not limited to the particular gene-encoding regions described herein, and may also include non-coding regions (including regions that are far away from genes e.g. regulatory regions such as enhancers).

In various embodiments, the method further comprises removing particulate blood components from the sample (e.g. a blood sample) to leave behind blood plasma for use in the determining step. In various embodiments, plasma is separated from blood shortly after (e.g. within about 2 hours of) venipuncture. In various embodiments, plasma is separated from blood by centrifugation e.g. at 10 min x 300g

and 10 min x 9370 g). In various embodiments, the plasma is stored at low temperature e.g. at -80°C after separation. In various embodiments, the particulate blood components are selected from the group consisting red blood cells, white blood cells, platelets and combinations thereof. In various embodiments, the method further comprising extracting/isolating/purifying the cfDNA from the sample/blood plasma.

In various embodiments, the method requires no more than about 20 milliliters, no more than about 19.5 milliliters, no more than about 19 milliliters, no more than about 18.5 milliliters, no more than about 18 milliliters, no more than about 17.5 milliliters, no more than about 17 milliliters, no more than about 16.5 milliliters, no more than about 16 milliliters, no more than about 15.5 milliliters, no more than about 15 milliliters, no more than about 14.5 milliliters, no more than about 14 milliliters, no more than about 13.5 milliliters, no more than about 13 milliliters, no more than about 12.5 milliliters, no more than about 12 milliliters, no more than about 11.5 milliliters, no more than about 11 milliliters, no more than about 10.5 milliliters, no more than about 10 milliliters, no more than about 9.5 milliliters, no more than about 9 milliliters, no more than about 8.5 milliliters, no more than about 8 milliliters, no more than about 7.5 milliliters, no more than about 7 milliliters, no more than about 6.5 milliliters, no more than about 6 milliliters, no more than about 5.5 milliliters, no more than about 5 milliliters, no more than about 4.5 milliliters, no more than about 4 milliliters, no more than about 3.5 milliliters, no more than about 3 milliliters, no more than about 2.5 milliliters, no more than about 2 milliliters, no more than about 1.5 milliliters, no more than about 1 milliliters, no more than about 0.9 milliliters, no more than about 0.8 milliliters, no more than about 0.7 milliliters, no more than about 0.6 milliliters, no more than about 500 microliters, no more than about 450 microliters, no more than about 400 microliters, no more than about 350 microliters or no more than about 300 microliters of sample.

In various embodiments, the method further comprises obtaining the sample from the subject prior to the determining step. In various embodiments, the step of obtaining the sample from the subject is a non-surgical step, a non-invasive step or a minimally invasive step. In various embodiments, the step of obtaining the sample from the subject comprises withdrawing a blood sample from the subject.

In various embodiments, the method is capable of precisely estimating one or more of: a disease burden, a cancer burden, a tumor burden, a ctDNA burden, a level of ctDNA, an amount of ctDNA, a proportion of ctDNA, a fraction of ctDNA and a ctDNA

content such that the estimated disease burden, cancer burden, tumor burden, ctDNA burden, level of ctDNA, amount of ctDNA, proportion of ctDNA, fraction of ctDNA and/or ctDNA content has an absolute deviation/absolute error/mean absolute deviation/mean absolute error of no more than about 5.0%, no more than about 4.9%, no more than about 4.8%, no more than about 4.7%, no more than about 4.6%, no more than about 4.5%, no more than about 4.4%, no more than about 4.3%, no more than about 4.2%, no more than about 4.1%, no more than about 4.0%, no more than about 3.9%, no more than about 3.8%, no more than about 3.7%, no more than about 3.6%, no more than about 3.5%, no more than about 3.4%, no more than about 3.3%, no more than about 3.2%, no more than about 3.1%, no more than about 3%, no more than about 2.9%, no more than about 2.8%, no more than about 2.7%, no more than about 2.6%, no more than about 2.5%, no more than about 2.4%, no more than about 2.3%, no more than about 2.2%, no more than about 2.1%, no more than about 2%, no more than about 1.9%, no more than about 1.8%,no more than about 1.7%, no more than about 1.6%, or no more than about 1.5% from a true/expected/measured disease burden, cancer burden, tumor burden, ctDNA burden, level of ctDNA, amount of ctDNA, proportion of ctDNA, fraction of ctDNA and/or ctDNA content.

In various embodiments, the method has a predictive accuracy of at least about 90%, at least about 91%, at least about 92%, at least about 93%, at least about 94%, at least about 95%, at least about 96%, at least about 97%, at least about 98%, at least about 99%, at least about 99.1%, at least about 99.2%, at least about 99.3%, at least about 99.4%, at least about 99.5%, at least about 99.6%, at least about 99.7%, at least about 99.8%, at least about 99.9% or at least about 100%.

In various embodiments, the method comprises a machine learning-based method.

In various embodiments, the method further comprises training a machine learning model with a first training data set defining a level (or an amount, a proportion, a fraction and/or a content) of DNA, optionally cfDNA, that maps to (or aligns with, corresponds to, belongs to, is similar to and/or is identical to) the one or more NDR (e.g. in the form of a read depth coverage) as features and a measured disease burden/ tumor burden/ ctDNA burden/ ctDNA level/ ctDNA amount/ ctDNA proportion/ ctDNA fraction/ ctDNA content; and selecting a first set of one or more features that is predictive of the disease burden/ tumor burden/ ctDNA burden/ ctDNA level/ ctDNA amount/ ctDNA proportion/ ctDNA fraction/ ctDNA content.

In various embodiments, a subset of samples may be randomly selected from a training data set to train the machine learning model to identify the most predictive features. In various embodiments, the foregoing may be repeated independently multiple times, e.g. 1000 times, and the time(s) each feature is chosen as a predictive feature is counted. In various embodiments, the feature(s) that is/are selected most frequently is/are extracted to train a final model comprising all samples in the training data set (e.g. the first training data set) to identify one or more features (e.g. the first set of one or more features) that is predictive of the disease burden/ tumor burden/ ctDNA burden/ ctDNA level/ ctDNA amount/ ctDNA proportion/ ctDNA fraction/ ctDNA content. In various embodiments, cross validation (e.g. five-fold cross validation, eight-fold cross validation, ten-fold cross validation) is carried out during the machine learning process for identifying the most predictive features.

In various embodiments, the selecting step further comprises employing a linear model/regression, optionally a sparse linear model/regression, further optionally a Lasso (least square absolute shrinkage and selection operator) model to identify the first set of one or more features that is predictive of the disease burden/ tumor burden/ ctDNA burden/ ctDNA level/ ctDNA amount/ ctDNA proportion/ ctDNA fraction/ ctDNA content.

In various embodiments, the method further comprises providing a test data set to the trained machine learning model, the test data set defining at least the first set of one or more selected features; and estimating the disease burden/ tumor burden/ ctDNA burden/ ctDNA level/ ctDNA amount/ ctDNA proportion/ ctDNA fraction/ ctDNA content based on at least the first set of one or more selected features.

In various embodiments, the method further comprises comparing the estimated disease burden/ tumor burden/ ctDNA burden/ ctDNA level/ ctDNA amount/ ctDNA proportion/ ctDNA fraction/ ctDNA content with a true/expected/measured disease burden/ tumor burden/ ctDNA burden/ ctDNA level/ ctDNA amount/ ctDNA proportion/ ctDNA fraction/ ctDNA content of the test data set; and calculating an absolute deviation/ absolute error/ mean absolute deviation/ mean absolute error between the estimated and the true/expected/measured disease burden/ tumor burden/ ctDNA burden/ ctDNA level/ ctDNA amount/ ctDNA proportion/ ctDNA fraction/ ctDNA content to evaluate a performance/ prediction accuracy of the model.

In various embodiments, the method further comprises obtaining/collecting blood samples comprising cfDNA from cancer patients and healthy individuals;

measuring a level (or an amount, a proportion, a fraction and/or a content) of DNA that maps to (or aligns with, corresponds to, belongs to, is similar to and/or is identical to) the one or more NDR (e.g. in the form of a read depth coverage) to obtain the features of the first training data set; and measuring a disease burden/ tumor burden/ ctDNA burden/ ctDNA level/ ctDNA amount/ ctDNA proportion/ ctDNA fraction/ ctDNA content (e.g. by whole genome sequencing, deep whole genome sequencing etc.) to obtain the disease burden/ tumor burden/ ctDNA burden/ ctDNA level/ ctDNA amount/ ctDNA proportion/ ctDNA fraction/ ctDNA content of the first training data set. In various embodiments, the method further comprises determining/measuring an expression of the plurality of genes associated with the NDR in the blood samples.

In various embodiments, the method further comprises obtaining/collecting tumor/tumor biopsy samples from cancer patients; extracting/isolating/purifying nucleic acids from the tumor/tumor biopsy samples; measuring from the nucleic acids a level (or an amount, a proportion, a fraction and/or a content) of DNA that maps to (or aligns with, corresponds to, belongs to, is similar to and/or is identical to) the one or more NDR (e.g. in the form of a read depth coverage); and measuring from the nucleic acids an expression of the genes associated with the one or more NDR in the tumor/tumor biopsy samples.

In various embodiments, the method further comprises comparing said level (or an amount, a proportion, a fraction and/or a content) of DNA (e.g. in the form of a read depth coverage) and/or the expression of the genes between the blood samples and the tumor/tumor biopsy samples; identifying genes that show substantially different level (or an amount, a proportion, a fraction and/or a content) of DNA (e.g. substantially different read depth coverages) and/or substantially different expressions between the blood samples and the tumor/tumor biopsy samples; and selecting the level (or an amount, a proportion, a fraction and/or a content) of DNA (e.g. in the form of a read depth coverage) of these identified genes in the blood sample as features to be input in the first training data set.

The method may further comprise removing the first set of one or more features from the first training data set to form a second training data set; and training the machine learning model with the second training data set to select a second set of one or more features that is predictive of the disease burden, the cancer burden, the tumor burden, the ctDNA burden, the level of ctDNA, an amount of ctDNA, the proportion of ctDNA, the fraction of ctDNA and/or the ctDNA content. These steps may be repeated

one or more times to obtain a third, fourth, fifth etc. set of one or more features that is predictive of the disease burden, the cancer burden, the tumor burden, the ctDNA burden, the level of ctDNA, an amount of ctDNA, the proportion of ctDNA, the fraction of ctDNA and/or the ctDNA content by removing the second, third, fourth etc. set of one or more features from the second, third, fourth etc. training data set to form a third, fourth, fifth etc. training data set respectively.

In various embodiments, the method further comprises screening for/detecting a tumor-specific mutation in the cfDNA/ctDNA present in the blood sample. Advantageously, embodiments of the method simultaneously allow for profiling of actionable cancer mutations and quantitative estimation of the disease burden, the cancer burden, the tumor burden, the ctDNA burden, the level of ctDNA, an amount of ctDNA, the proportion of ctDNA, the fraction of ctDNA and/or the ctDNA content. The method may be performed in combination with or complimentary to existing sequencing-based methods in cancer detection/monitoring.

In various embodiments, the method is an *in vitro* or *ex vivo* method.

In various embodiments, the method is a liquid biopsy method.

In various embodiments, the method is a method of determining disease progression in a subject and the method further comprises: determining in a subsequent blood sample obtained from the subject, a level of cfDNA that maps to one or more NDR; estimating the ctDNA burden or tumor burden based on said level of cfDNA; comparing the ctDNA burden or tumor burden estimated from said subsequent blood sample with the ctDNA burden or tumor burden estimated from said blood sample; and optionally identifying the subject as having disease progression if the ctDNA burden or tumor burden estimated from said subsequent blood sample is higher than the ctDNA burden or tumor burden estimated from said blood sample or identifying otherwise if the ctDNA burden or tumor burden estimated from said subsequent blood sample is not higher than the ctDNA burden or tumor burden estimated from said blood sample. In various embodiments, where the ctDNA burden or tumor burden estimated from said subsequent blood sample is lower than the ctDNA burden or tumor burden estimated from said blood sample, the disease identified to be improving/abating in the subject. In various embodiments, where the ctDNA burden or tumor burden estimated from said subsequent blood sample is substantially the same as the ctDNA burden or tumor burden estimated from said blood sample, the disease is identified to be stable in the subject.

Disease progression in a subject may be indicative of resistance to the current treatment regimen received by the subject. Thus, the method may also be useful for identifying resistance to treatment in a subject. In various embodiments therefore, the method further comprises changing the treatment regimen received by the subject if the subject is identified as having disease progression. Changing the treatment regimen may involve subjecting/exposing the subject to a second therapy that is different from the current or the first therapy. Changing the treatment regimen may involve replacing the current treatment regimen received by the subject with another treatment regimen, or it may involve administering to the subject additional therapies in addition to the current treatment regimen. In some embodiments, where a subject is already receiving combination therapy, changing the treatment regimen may also involve removing one or more therapies from the combination therapy. Examples of treatment regimens/therapies include, but are not limited to, chemotherapy, radiotherapy, gene therapy, hormonal therapy, immunotherapy, surgical therapy, combination therapy, alternative therapy/complementary therapy and combinations thereof. In various embodiments, changing the treatment regimen does not necessarily entail switching from one class of therapy (e.g. one of chemotherapy, radiotherapy, gene therapy, hormonal therapy, immunotherapy, surgical therapy, combination therapy, alternative therapy/complementary therapy and combinations thereof) to another class of therapy, although it may involve such a switch. Changing the treatment regimen may involve changing from one specific therapy to another specific therapy within the same therapy class. For example, changing the treatment regimen may involve changing the particular chemotherapy drug received by the subject.

In various embodiments, there is provided a method of monitoring disease progression in a subject, the method comprising: determining in a first sample comprising cfDNA obtained from the subject at a first time point, a first level (or an amount, a proportion, a fraction and/or a content) of cfDNA that maps to one or more NDR; estimating a first ctDNA burden or tumor burden (or a disease burden, a cancer burden, a level of ctDNA, an amount of ctDNA, a proportion of ctDNA, a fraction of ctDNA and a ctDNA content) in the subject based on the first level of cfDNA, determining in a second sample comprising cfDNA obtained from the subject at a second time point, a second level of DNA that maps to the one or more NDR, estimating a second ctDNA burden or tumor burden based on the second level of

cfDNA; and comparing the first and the second estimated ctDNA burden or tumor burden to determine whether the disease has progressed, wherein the second time point is later than the first time point. In various embodiments, where the second estimated ctDNA burden or tumor burden is higher than the first estimated ctDNA burden or tumor burden, the disease is considered to have progressed/worsened. In various embodiments, where the second estimated ctDNA burden or tumor burden is lower than or is substantially the same as the first estimated ctDNA burden or tumor burden, the disease is considered to have abated or stabilized.

In various embodiments, there is provided a method of evaluating treatment efficacy/response in a subject, the method comprising: determining in a first sample comprising cfDNA obtained from the subject before/during a treatment/treatment stage, a first level (or an amount, a proportion, a fraction and/or a content) of cfDNA that maps to one or more NDR; estimating a first ctDNA burden or tumor burden (or a disease burden, a cancer burden, a level of ctDNA, an amount of ctDNA, a proportion of ctDNA, a fraction of ctDNA and a ctDNA content) in the subject based on the first level of cfDNA, determining in a second sample comprising cfDNA obtained from the subject after the treatment/treatment stage, a second level of DNA that maps to the one or more NDR, estimating a second ctDNA burden or tumor burden based on the second level of cfDNA; and comparing the first and the second estimated ctDNA burden or tumor burden to determine whether the treatment is effective/the subject is responding to the treatment. In various embodiments, where the second estimated ctDNA burden or tumor burden is higher than the first estimated ctDNA burden or tumor burden, the treatment is considered to be not effective or the subject is considered to be not responding to the treatment. In various embodiments, where the treatment is considered to be not effective or the subject is considered to be not responding to the treatment, the method further comprises adjusting/altering/stopping/halting/discontinuing the treatment regimen. In various embodiments, where the second estimated ctDNA burden or tumor burden is lower than or substantially the same as the first estimated ctDNA burden or tumor burden, the treatment is considered to be effective or the subject is considered to be responding to the treatment. In various embodiments, where the treatment is considered to be effective or the subject is considered to be responding to the treatment, the method further comprises continuing the treatment regimen.

In various embodiments, there is provided a method of determining a risk of cancer (e.g. a risk of development, predisposition, progression, relapse, recurrence, metastasis, abatement of cancer) in a subject, the method comprising: determining in a blood sample obtained from the subject, a level (or an amount, a proportion, a fraction and/or a content) of cfDNA that maps to one or more NDR, optionally estimating a disease burden (or a cancer burden, a tumor burden, a ctDNA burden, a level of ctDNA, an amount of ctDNA, a proportion of ctDNA, a fraction of ctDNA or a ctDNA content) based on said level of cfDNA, and determining the risk of cancer based on the level of cfDNA that maps to the one or more NDR, or the estimated disease burden. In various embodiments, where the level of cfDNA/the estimated disease burden exceeds a predetermined threshold level, the subject is concluded to have an elevated risk of cancer. In various embodiments, where the level of cfDNA/the estimated disease burden does not exceed the predetermined threshold level, the subject is concluded to have a reduced/low/minimal/no risk of cancer. It will be appreciated that it is within the purview of a person skilled in the art to determine the suitable threshold level. For example, the suitable threshold level may be determined by determining the mean level of cfDNA/the mean estimated disease burden of a healthy population e.g. a population that does not suffer from cancer.

In various embodiments, there is provided a method of treating cancer in a subject, the method comprising: determining in a blood sample obtained from the subject, a level of cfDNA that maps to one or more NDR and estimating a ctDNA burden or tumor burden based on said level of cfDNA. In various embodiments, where the level of cfDNA/the estimated ctDNA burden or tumor burden exceeds a predetermined threshold level, the subject is subjected to treatment selected from the group consisting of chemotherapy, radiotherapy, gene therapy, hormonal therapy, immunotherapy, surgical therapy, combination therapy, alternative therapy/complementary therapy and combinations thereof. It will be appreciated that it is within the purview of a person skilled in the art to determine the suitable threshold level. For example, the suitable threshold level may be determined by determining the mean level of cfDNA/the mean estimated ctDNA burden or tumor burden of a healthy population e.g. a population that does not suffer from cancer.

In various embodiments, there is provided a method of profiling a subject, the method comprising: determining in a blood sample obtained from the subject, a level

of cfDNA that maps to one or more NDR and estimating a ctDNA burden or tumor burden based on said level of cfDNA.

In various embodiments, there is provided a kit/panel/probe set/primer set, optionally a kit/panel/probe set/primer set for estimating a tumor burden or ctDNA burden in a subject, the kit/panel/probe set/primer set comprising one or more probe/primer that is capable of hybridizing/binding to one or more NDR, where said NDR (i) comprises the NDR of a gene which transcript is differentially expressed between healthy blood tissue and tumor tissue and/or (ii) is degraded to different extents between healthy blood tissue and blood tissue of a tumor-bearing subject. In various embodiments, the one or more probe/primer is capable of hybridizing/binding to a central genomic region related to the one or more NDR. The size of the central genomic region may be about 1 kb, about 2 kb, about 3 kb, about 4 kb, about 5 kb, about 6 kb, about 7 kb, about 8 kb, about 9 kb or about 10 kb. In one example, a plurality of probes/primers hybridize/bind to an approximately 4 kb region centred at an NDR. The binding sites of a plurality of probes/primers to a central genomic region may be continuous or discontinuous within the central genomic region. In various embodiments, the one or more probe/primer has a sequence that is complementary to a sequence of the one or more NDR or parts thereof. In various embodiments, the one or more probe/primer has a sequence that is complementary to a sequence sharing at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 91%, at least about 92%, at least about 93%, at least about 94%, at least about 95%, at least about 96%, at least about 97%, at least about 98% or at least about 99% sequence identity with the one or more NDR or parts thereof. In various embodiments, the one or more probe/primer has a sequence that is complementary to a sequence that differs from the one or more NDR or parts thereof by about one, about two, about three, about four or about five nucleotides/bases. In various embodiments, the one or more probe/primer has a sequence that is complementary to a central genomic region or parts thereof related to the one or more NDR. In various embodiments, the one or more probe/primer has a sequence that is complementary to a sequence sharing at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 91%, at least about 92%, at least about 93%, at least about 94%, at least about 95%, at least about 96%, at least about 97%, at least about 98% or at least about 99% sequence identity with the central genomic region or parts thereof. In various embodiments, the one or more probe/primer has a

sequence that is complementary to a sequence that differs from the central genomic region or parts thereof or parts thereof by about one, about two, about three, about four or about five nucleotides/bases. In one example, the one or more probe/primer has a sequence that is complementary to an approximately 4 kb region centred at an NDR. A skilled person would be able to determine the suitable conditions that would allow the probe/primer to hybridize to the one or more NDR.

In various embodiments, the one or more NDR comprises one or more NDR of a gene listed in one or more of Table 1, Table 2, Table S3, Table S10, Table S14, Table S15, Table S16, Table S17, Table S18, Table S19, Table S20 and Table S21. In various embodiments, the one or more NDR comprises one or more NDR of a gene selected from the group consisting of: SLC11A1, NLRP12, PRTN3, HMBS, LILRB3, ACSL1, GP9, MX2, RASGRP4, ATG16L2 and combinations thereof. In various embodiments, the one or more NDR comprises one or more NDR of a gene selected from the group consisting of: SHKBP1, ACSL1, BCAR1, RAB25, PRTN3, LSR and combinations thereof.

In various embodiments, the kit/panel or the probe set/ primer set further comprises a probe/primer for detecting a tumor-specific mutation.

In various embodiments, the one or more probe/primer comprises from about 50 to about 200 nucleotides/bases, from about 90 to about 150 nucleotides/bases or from about 110 to about 130 nucleotides/bases. In various embodiments, the one or more probe/primer comprises no more than about 200, no more than about 190, no more than about 180, no more than about 170, no more than about 160, no more than about 150, no more than about 140, no more than about 130 or no more than about 120 nucleotides/bases. In various embodiments, the one or more probe/primer comprises at least about 50, at least about 60, at least about 70, at least about 80, at least about 90, at least about 100, at least about 110 or at least about 120 nucleotides/bases. In various embodiments, the one or more probe/primer comprises about 120 nucleotides/bases.

In various embodiments, the one or more probe/primer comprises the sequence of one or more of SEQ ID NO: 1 to SEQ ID NO: 577 (i.e. SEQ ID NO; 1, SEQ ID NO:2, SEQ ID NO: 3, and so forth till SEQ ID NO: 577, see Supplementary Data 3) or a sequence sharing at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 91%, at least about 92%, at least about 93%, at least about 94%, at least about 95%, at least about 96%, at least about 97%, at least about 98%,

at least about 99% sequence identity thereto. In various embodiments, the sequence sharing at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 99% sequence identity with any one of SEQ ID NO: 1 to SEQ ID NO: 577 is capable of hybridizing/binding to the one or more NDR.

In various embodiments, the kit/panel or the probe set/ primer set comprises a plurality of probes/primers.

In various embodiments, the kit/panel/primer set/probe set is for estimating a tumor burden or ctDNA burden associated with cancer, optionally colorectal cancer. In various embodiments, the one or more probe/primer is capable of hybridizing/binding to a genomic region of one or more of the following genes: ARID1A, CCNE1, CDH1, CDK6, CTNNB1, EGFR, ERBB2, KRAS, MUC6, MYC, RHOA, RNF43, SMAD4, TP53 or parts thereof. In various embodiments, the one or more probe/primer has a sequence that is complementary to a genomic region of one or more of ARID1A, CCNE1, CDH1, CDK6, CTNNB1, EGFR, ERBB2, KRAS, MUC6, MYC, RHOA, RNF43, SMAD4, TP53 or parts thereof. In various embodiments, the one or more probe/primer has a sequence that is complementary to a sequence sharing at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 91%, at least about 92%, at least about 93%, at least about 94%, at least about 95%, at least about 96%, at least about 97%, at least about 98% or at least about 99% sequence identity with the genomic region of one or more of ARID1A, CCNE1, CDH1, CDK6, CTNNB1, EGFR, ERBB2, KRAS, MUC6, MYC, RHOA, RNF43, SMAD4, TP53 or parts thereof. In various embodiments, the one or more probe/primer has a sequence that is complementary to a sequence that differs from the genomic region of one or more of ARID1A, CCNE1, CDH1, CDK6, CTNNB1, EGFR, ERBB2, KRAS, MUC6, MYC, RHOA, RNF43, SMAD4, TP53 or parts thereof by about one, about two, about three, about four or about five nucleotides.

In various embodiments, the one or more probes/primers cover at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 96%, at least about 97%, at least about 98%, at least about 99% or about 100% of the target NDR(s)/genomic region(s). In some embodiments, the one or more probes/primers do not overlap each other i.e. the probes/primer are aligned side-by-side when hybridized/bound to the target NDR(s)/genomic region(s). In some embodiments, there is some degree of overlap among adjacent probes/primers (e.g. an overlap of 10 bp, 30 bp, 50 bp, 70 bp, 90 bp etc.).

The number of probes/primers may vary depending on the number of target NDRs/genomic regions, the length/size of the target NDRs/genomic regions and/or the length/size of the probes/primers etc. Higher probe numbers/density may lead to better sampling, although it can also increase the cost of the method. In various embodiments, the number of probes/primers is in the range of from about 25 to about 50, from about 60 to about 80, from about 90 to about 110, from about 125 to about 150, from about 160 to about 180, from about 190 to about 210, from about 225 to about 250, from about 260 to about 280, from about 290 to about 310, from about 325 to about 350, from about 365 to about 390, from about 405 to about 430, from about 445 to about 470, from about 485 to about 510, from about 525 to about 550, or from about 565 to about 590. In various embodiments, the number of probes/primers is at least about 10, at least about 20, at least about 30, at least about 40, at least about 50, at least about 75, at least about 100, at least about 125, at least about 150, at least about 175, at least about 200, at least about 225, at least about 250, at least about 275 or at least about 300. In various embodiments, the number of probes/primers is no more than about 400, no more than about 375, no more than about 350, no more than about 325, no more than about 300, no more than about 275, no more than about 250, no more than about 225 or no more than about 200.

In various embodiments, there is provided a method or a product as described herein.

BRIEF DESCRIPTION OF FIGURES

FIG. 1 Overview of approach. Deep cfDNA WGS profiles of plasma samples from healthy individuals and cancer patients were compared to identify nucleosome depleted regions (NDRs) with tumor/blood tissue-specific expression and differential cfDNA coverage. A model was trained to predict ctDNA levels from NDR cfDNA coverage. A compact assay targeting predictive NDRs was used to perform longitudinal profiling of ctDNA levels and dynamics.

FIG. 2 Characteristics of cfDNA degradation patterns at promoters and exon-intron junctions. (**a**) Systematic analysis of gene regulatory regions for association of gene expression and cfDNA relative coverage. Relative coverage refers to cfDNA coverage across the given region when normalized to +/-1 kb flanking regions. The

nucleosome depleted regions of promoter (NDR, -150 to 50 bp relative to TSS) and first exon-intron junction (NDR, -300 to -100 bp relative to first exon end) are highlighted. (**b**) Relative cfDNA coverage of promoter and junction NDRs for expressed (fpkm≥30 in whole blood) and unexpressed genes. (**c**) Distribution of promoter and junction NDR relative coverage for expressed and unexpressed genes.

FIG. 3 Quantitative estimation of colorectal cancer ctDNA burden. (**a**) cfDNA relative coverage for the promoter region of *PPP1R16A* (ENST00000528430) overexpressed in CRC tumors relative to whole blood, and cfDNA relative coverage for the junction region of *GMFG* (ENST00000602185) overexpressed in whole blood relative to CRC tumors. The grey curve shows the mean coverage across CRC samples. (**b**) Relative coverage score (see Methods) of NDRs in transcripts differentially expressed between CRC tumors and whole blood. (**c**) Schematic showing how the predictive model of ctDNA fractions was developed: Differentially expressed genes in CRC and blood were identified, NDR relative coverage features were obtained from *in silico* generated cfDNA samples, predictive features were selected, and a quantitative model was fitted. (**d, e**) Comparison of expected (*in silico* simulation) and observed ctDNA fractions across the CRC cfDNA samples in the **d**) training and **e**) test set, respectively. The mean absolute error (MAE) is listed for each sample. (**f**) Comparison between observed and expected ctDNA fractions in the test set.

FIG. 4 Targeted NDR assay to quantify ctDNA burden and monitor cancer progression. (**a**) Schematic showing how targeted NDR sequencing, low-pass WGS, and targeted gene sequencing was performed on a cohort of 53 CRC plasma samples. (**b**) Comparison of ctDNA fractions inferred by targeted NDR-sequencing and low-pass WGS (ichorCNA). (**c**) Comparison of ctDNA fractions inferred by targeted NDR-sequencing and maximum VAFs (maximum VAF of all SNVs identified in a given plasma sample). (**d**) NDR-quantified ctDNA burden across serial plasma samples and its association with events of cancer progression treatment response. Somatic SNV VAFs are highlighted for each timepoint; SNVs detected in at least two timepoints are shown. SNVs undetected with standard filtering criteria at given timepoints are indicated with a dashed line. Treatment types and intervals are highlighted. Events of disease progression as inferred by computerized tomography (CT) scans are shown.

FIG. 5 Estimation of ctDNA burden across two distinct cancer types. (**a**) cfDNA relative coverage across the promoter region of the blood-specific gene, *RASGRP4* (ENST00000615340). Dark grey and light grey curves show the mean of the coverages from plasma samples from CRC and BRCA patients respectively, respectively. (**b**) Schematic showing how the ctDNA content prediction model across CRC and BRCA samples was developed. (**c, d**) Comparison of expected (*in silico* simulation) and observed ctDNA fractions across CRC and BRCA cfDNA samples in the **c**) training and **d**) test set, respectively. The mean absolute error is listed for each sample.

FIG. 6 A systematic analysis of gene regions for association of gene expression and cfDNA relative coverage. Relative cfDNA coverage (normalized to +/-1-2kb regions) for sets of genes grouped by expression level in whole blood cells across **a**) first, **b**) second, **c**) third exon-intron junctions, **d**) first, **e**) second, **f**) third intron-exon junctions, as well as **g**) promoter, and **h**) transcript end region.

FIG. 7 Correlation between relative coverage of NDRs and epigenetic features. For each candidate covariate/predictor, a linear regression is fitted with relative coverage as the response. The Pearson correlation coefficient (y axis, signed square root of R-squared from regression) is shown for each candidate variable. Whole blood gene expression (fpkm) is binned into 6 bins [unexpressed, $0.01 < \text{fpkm} \leqslant 0.1$, $0.1 < \text{fpkm} \leqslant 1$, $1 < \text{fpkm} \leqslant 5$, $5 < \text{fpkm} \leqslant 30$, $\text{fpkm} > 30$] and fitted as a categorical covariate with the unexpressed group as the reference group. Peak files of epigenetic features [DNase, H3K4me3, H3K36me3, H3K27ac, H3K4me1, H3K9me3 and H3K27me3] from primary T-cells (E034) were obtained from the Roadmap Epigenomics Project. Epigenetic features are fitted as binary covariates with no signal as the reference group. Barplots of the correlation (r, square root of R2 multiplied by the coefficient sign) between each feature and relative coverage for (**a**) Promoter NDRs and (**b**) Junction NDRs are shown.

FIG. 8 Transcripts differentially expressed between CRC tumors and whole-blood. CRC ($\text{fpkm}_{\text{CRC}} > 20$, $\text{fpkm}_{\text{blood}} < 0.1$, dark grey) and whole-blood ($\text{fpkm}_{\text{CRC}} < 0.1$, $\text{fpkm}_{\text{blood}} > 10$, light grey) specific transcripts are identified from expression data from TCGA and GTEx.

FIG. 9 The evolution of predictive error with model complexity. Mean absolute error between expected and predicted ctDNA fractions of CRC samples is estimated as a function of model complexity (number of predictive features). The error bar size is the standard deviation of MAE values from 231 CRC training samples (light grey).

FIG. 10 Model performance on 10 test sets generated using different (withheld) healthy samples from the training sets. Individual normal samples (n=29) in the healthy cohort were evenly split into 2 sets, used to dilute the plasma samples from CRC patients in training (CRC-1 to 8 in Table S1) and test (CRC-9 to 12) sets separately. (**a**) The correlation (Pearson and Spearman) between the expected and observed ctDNA fractions across the 10 test sets. (**b**) The mean absolute error (MAE) between the expected and observed ctDNA fractions for the 10 test sets.

FIG. 11 Comparison of expected and ichorCNA-predicted ctDNA fractions across the CRC cfDNA samples. (**a**) ctDNA fractions across the CRC cfDNA samples. (**b**) Comparison of expected and ichorCNA-predicted ctDNA fractions.

FIG. 12 Performance of ichorCNA when applied to the samples with low ctDNA burden. 31 out of 120 low-ctDNA samples of CRC were predicted as non-cancerous by ichorCNA, highlighted in black. Grey dashed line indicates ctDNA fraction of 0.

FIG. 13 Predictive error as a function of model complexity for two distinct cancer types. The error bar size is the standard deviation of MAE values from 446 training samples (light grey).

FIG. 14 Comparison of expected and observed ctDNA fractions in test set across two distinct cancer types.

FIG. 15 A BRCA model using BRCA tumor-specific NDRs. (**a**) The list of top BRCA tumor-specific NDRs that were used for ctDNA content prediction. (**b, c**) Comparison of expected and observed ctDNA fractions across the BRCA cfDNA samples in the test set.

FIG. 16 Comparison of the ctDNA fractions determined by the CRC model and the "CRC+BRCA" model for the CRC samples in the test set.

FIG. 17 Comparison of the observed ctDNA fractions in the 53 original cfDNA samples with capture-based NDR sequencing (mean coverage ~300x) and their downsampled counterparts (100x, 50x, 25x, and 10x, respectively).

FIG. 18 Genomic regions over promoters (top) and first exon-intron junction (bottom) used to calculate relative coverage. The mean coverage of the up and downstream 2kbp flanks (grey) is used as a "normalization factor" for the region of interest (black).

FIG. 19 Overview of machine learning feature selection, model fitting, and train/test set performance for colorectal cancer.

FIG. 20 Extensive identification of all predictive CRC features/regions.

FIG. 21 Pan-cancer model training: Overview of Machine Learning feature selection, model fitting, and train/test set performance for pan-cancer features.

FIG. 22 Pan-cancer feature combinations: Extensive identification of all predictive pan-cancer features/regions

FIG. 23 Additional CRC and pan-cancer feature combinations: Extensive identification of all predictive feature combinations using in silico samples generated with random subsets of healthy samples

FIG. 24 The flow chart of establishing a machine learning model based on expression-specific DNA degradation patterns to predict ctDNA fractions for potentially clinical use

FIG. 25 The evolution of the error between observed and calculated ctDNA fractions with the number of top features for CRC prediction model

FIG. 26 The evolution of the error between observed and calculated ctDNA fractions with the number of top features for pan-cancer prediction model

EXAMPLES

Example embodiments of the disclosure will be better understood and readily apparent to one of ordinary skill in the art from the following discussions and if

applicable, in conjunction with the figures. It will be appreciated that the example embodiments are illustrative, and that various modifications may be made without deviating from the scope of the invention. Example embodiments are not necessarily mutually exclusive as some may be combined with one or more embodiments to form new exemplary embodiments.

It is shown that the size distribution of cfDNA fragments has a mode of ~166 bp, suggesting that nucleosome-bound DNA fragments are protected/preserved during cell death and shed into the circulation. Nucleosome depleted regions (NDRs) are therefore more frequently degraded, yielding a nucleosome-dependent degradation footprint in cfDNA profiles, which can be used to infer tissue of origin. The read depth coverage from sequencing plasma cfDNA is shown to be able to identify nucleosome depletion at a gene's promoter and thus infer gene expression. The coverage of the nucleosome-depleted region at a gene's promoter is negatively correlated with the gene's expression level: a highly expressed gene will tend to have less nucleosome binding across its promoter and therefore lower level of protection and higher levels of DNA degradation. Moreover, plasma cfDNA degradation patterns in cancer patients can be used to infer tumor gene expression.

Here, it is hypothesized that a limited set of tumor or blood-specific NDRs could be used to infer the ctDNA burden (fraction) in the blood circulation of cancer patients. ctDNA burden refers to the relative amount of ctDNA out of all cfDNA molecules in a plasma sample. Using deep cfDNA WGS data from cancer patients and healthy individuals, a quantitative model that infers the ctDNA burden using cfDNA sequencing data from a limited set of NDRs is trained and test. This model is shown to be accurate for plasma samples from both colorectal cancer (CRC) and breast cancer (BRCA) patients (mean absolute error ≤ 4.3%), and deployment is explored using a compact targeted sequencing assay for low-cost and quantitative tracking of patient ctDNA dynamics.

The examples demonstrate two components. The first component is a method for estimating ctDNA burden specifically in liquid biopsies from colorectal cancer (CRC) patients. The second component is a method for estimating ctDNA burden in liquid biopsies from any solid tumor (pan-cancer). Both colorectal cancer and pan-cancer models have high prediction accuracy, but the pan-cancer model has the added advantage that it can be applied to any solid tumors.

In one example, the colorectal cancer ctDNA burden estimation model is built as follow. Machine learning was used to develop a predictive model that uses cfDNA coverage patterns at the promoter and junction regions of selected genes to infer ctDNA burden in the blood samples of colorectal cancer patients. The model was trained using data from an in silico "dilution" of 8 samples from 5 cancer patients and healthy individuals, resulting in a training set of 231 "virtual" samples of various ctDNA content (see Table S2). The candidate tumor/blood transcripts that showed both differential expression signal and differential DNA degradation signal at NDRs between CRC tumor and blood were shortlisted. The tumor and blood transcripts were pooled together and their promoter and junction NDR coverage scores were defined as (totally 908) input "features" (see Table S3). The coverage value of each position was normalized by the mean coverage of the upstream (-2000 to -1000 bp) and downstream (+1000 to +2000 bp) regions with respect to transcription start site (for promoter) and exon boundary (for junction) respectively. A Lasso (least absolute shrinkage and selection operator) model was employed to identify features predictive of ctDNA proportions. Half of the training data was extracted randomly to run Lasso (using 1000 repetitions), consequently discovering 6 stable features (probability≥0.99) from this stability-based exploration (FIG. 19). To develop an accurate ctDNA burden estimation model with a minimal sequencing cost, using the 4 to 10 robust features is an optimal solution, because increasing the number of features to over 10 fails in improving the prediction accuracy of test set and thus over-interprets the training set data (see FIG. 25) in one example. Here, the top 6 features were employed as an example to train and test the machine learning model.

The model may also be applicable to other cancer types, subtypes, or specific therapeutic settings, considering tissue-of-origin of cfDNA molecules can be principally informed from tissue-specific DNA degradation pattern. Compared with plasma from healthy people, tumor-derived DNA component in cancer plasma samples weakens the blood-specific DNA degradation pattern, which suggests the decay of blood-specific signal might be informative of robustly estimating the ctDNA content regardless of cancer types. Therefore, the ctDNA content estimation method is also extended to the pan-cancer level.

In one example, a pan-cancer ctDNA burden estimation model is built as follows. This pan-cancer model relates to a quantitative method that only uses blood-based features/regions (and no use of tumor type specific regions). First, blood

transcripts that are highly expressed in blood and lowly expressed in tumors of all 20 cancer types (BLCA, BRCA, CESC, CRC, ESCA, GBM, HNSC, KIRC, KIRP, LGG, LIHC, LUAD, LUSC, OV, PAAD, PRAD, SKCM, STAD, THCA, and UCEC) where shortlisted. These yielded 792 promoter and junction NDR candidate coverage features (Table S10). 215 in-silico samples diluted from the plasma samples of 7 breast cancer (BRCA) patients were added into the existing training set of colorectal cancer samples, as well as 93 in-silico samples diluted from the plasma samples of 3 BRCA patients into the existing test set (see Table S2). The same protocol of feature selection and model training that were used for colorectal cancer ctDNA burden estimation above was performed. It was found that using around 10 blood features is able to predict the ctDNA content in plasma samples (see FIG. 26). An example of employing 10 stable features (probability≥0.99) (Table 2) that are predictive of ctDNA burden in the training set is shown, with a mean absolute error of ~2.2% between the calculated and observed ctDNA proportions (FIG. 21). The trained model with those 10 features is able to accurately predict the ctDNA content in the test set (MAE of ~4.3%). The prediction on breast cancer cases show a promising prediction power of the pan-cancer model.

Based on the guidance provided by this disclosure, users can follow the methodology details to reproduce the work or apply the method to their own data with a full flexibility of tuning the number of features for their model, as long as the selection can achieve high prediction accuracy and prevent data over-interpretation. As described in the examples herein, users can check the error evolution with the number of top features to determine a reasonable range of numbers of features.

Embodiments of a machine learning model based on expression-specific DNA degradation patterns to predict ctDNA fractions for potentially clinical use are described herein (FIG. 24). Embodiments of the method enable detection of tumor DNA burden (even of very low frequency) in the blood by only sequencing these selected nucleosome-depleted regions in cfDNA assays. These regions comprise < 50kb (4kb × 6 features or 4kb × 10 features) DNA sequence in total, and may therefore allow for an extremely cost-effective approach to ctDNA content estimation (order of magnitude less DNA sequencing needed compared to standard targeted sequencing assays, usually >1000kb). Furthermore, embodiments of the assay can be implemented as an extension/add-on to a standard targeted panel assay, allowing for an extremely cost-effective approach to generic ctDNA profiling. The colorectal and

pan-cancer models have some key differences. Both colorectal cancer and pan-cancer models have high prediction accuracy, but the pan-cancer model can generalize to most/all solid tumor types (pending validation data in other cancer types).

Results

Overview of approach

Blood samples (n=29) were collected from healthy individuals and plasma cfDNA was extracted for paired-end WGS (merged ~150x coverage) (FIG. 1). Targeted sequencing (see Methods) of plasma samples (CRC n=65, BRCA n=36) from cancer patients was performed and samples (CRC n=12, BRCA n=10) with high SNV VAFs (indicating high ctDNA burden) were selected for deep ~90x cfDNA WGS (Table S1). In these high ctDNA burden WGS samples, ctDNA burden estimates could be obtained using existing methods (see Methods, Oesper L, Satas G, Raphael BJ. Quantifying tumor heterogeneity in whole-genome and whole-exome sequencing data. *Bioinformatics* **30**, 3532-3540 (2014), Ha G, *et al.* TITAN: inference of copy number architectures in clonal cell populations from tumor whole-genome sequence data. *Genome research* **24**, 1881-1893 (2014), Bao L, Pu M, Messer K. AbsCN-seq: a statistical method to estimate tumor purity, ploidy and absolute copy numbers from next-generation sequencing data. *Bioinformatics* **30**, 1056-1063 (2014) and Larson NB, Fridley BL. PurBayes: estimating tumor cellularity and subclonality in next-generation sequencing data. *Bioinformatics* **29**, 1888-1889 (2013)) that infer tumor purity using matched tumor and germline high-depth WGS data. To identify candidate NDR features for the quantitative model, tumor and blood-specific genes with differential NDR cfDNA degradation in their promoters and first exon-intron junctions in plasma samples were identified from healthy individuals and cancer patients. Using a machine learning and *in silico* cfDNA generation approach, a sparse linear model was trained and tested to predict ctDNA burden from NDR cfDNA coverage. To further explore how the approach could be useful for cost-effective monitoring ctDNA dynamics, a compact (<25 kb) capture-based sequencing assay targeting predictive NDRs was designed to explore the robustness of NDR-based targeted approach using independent plasma samples (n=53) from CRC patients, and applied to estimate ctDNA levels in longitudinally collected plasma samples from a cohort of five colorectal cancer patients.

Association of gene expression and cfDNA fragmentation patterns

Analysis of cfDNA from the healthy individuals revealed nucleosome depletion and reduced cfDNA protection flanked by a series of strongly positioned nucleosomes at gene promoter regions (FIG. 2a). Relative coverage at the promoter NDR was inversely correlated with gene expression in whole blood cells. Studies of nucleosome positioning in cells have found that, apart from promoters, exon-intron junctions are associated with NDRs. The inventors therefore systematically scanned these gene regions for association between gene expression and cfDNA relative coverage (FIG. 2a). Strikingly, it was found that the first exon-intron junction of transcripts showed a similar association between coverage and expression, where relative cfDNA coverage at the NDR ranging from -300 to -100 bp with respect to the end of the first exon exhibited a strong inverse correlation with transcript expression in whole blood cells. However, surprisingly, correlation between expression and cfDNA coverage was not observed at other exon-intron and intron-exon junctions as well as at gene ends (FIG. 2a and FIG. 6). As expected, when comparing highly-expressed (fpkm ≥ 30) and unexpressed gene groups, a strong positive correlation (Pearson $r = 0.81$; Spearman correlation, $\rho = 0.85$) was observed between the cfDNA relative coverage at promoter and first exon-intron junction NDRs across genes (FIG. 2b). While relative coverage at these NDRs correlated strongly with gene expression level, relative coverage could not perfectly separate unexpressed from expressed genes (FIG. 2b, c), suggesting that additional factors beyond gene expression contribute to NDR cfDNA degradation. To further explore the factors affecting cfDNA degradation at NDRs, the association between NDR relative coverage and a range of epigenetic features was explored (FIG. 7). In addition to gene expression levels (linear regression, promoter r = -0.23, junction r = -0.22), relative coverage was negatively correlated with DNase hypersensitivity (promoter r = -0.60, junction r = -0.55), H3K4me3 (promoter r = -0.59, junction r = -0.54), and H3K27ac (promoter r = -0.45, junction r = -0.41), which are markers of open chromatin, active promoters, and active enhancers respectively. In contrast, H3K36me3 (promoter r = 0.49, junction r = 0.46) and H3K9me3 (promoter r = 0.11, junction r = 0.10), markers of gene bodies and heterochromatin, were positively correlated with NDR relative coverage.

cfDNA coverage patterns at NDRs in colorectal cancer patients

To further explore the hypothesis that NDR cfDNA coverage in plasma samples from cancer patients is associated with the epigenetic state of tumor cells, a targeted sequencing panel was first used to screen plasma samples from CRC patients for cases of high ctDNA burden (VAF > 15% for known cancer driver mutations, FIG. 1). 8 plasma samples from 5 patients were initially identified and high-depth WGS was performed on these samples (~72x-101x, Sample ID: CRC-1 to 8 in Table S1). ctDNA fractions in these samples were inferred using four existing tissue-based estimation methods (see Methods) and the median tumor purity estimate from these methods was used as ctDNA fractions (in the range 35-86%, Table S1). Gene expression data from TCGA and GTEx was then used to identify genes specifically expressed in CRC tumors and whole blood (see methods, FIG. 8). As an example, *PPP1R16A* was identified as a CRC-specific gene with robust depletion of NDR cfDNA coverage in plasma samples from cancer patients as compared to healthy individuals, and *GMFG* was identified as a blood-specific gene with greater coverage depletion in healthy blood plasma (FIG. 3a). As expected, CRC-specific genes generally showed depletion of cfDNA at both promoter and junction NDRs in the plasma of CRC patients compared to healthy controls (FIG. 3b). In contrast, blood-specific genes showed higher cfDNA coverage at NDRs in the plasma of CRC patients compared to healthy controls. Furthermore, directly comparing CRC and blood-specific genes, CRC-specific genes had significantly greater cfDNA depletion at NDRs in plasma samples from CRC patients ($P < 2.2\times10^{-16}$, Wilcoxon rank-sum test, FIG. 3b).

Quantitative estimation of colorectal cancer ctDNA burden

With the insight that cfDNA coverage at NDRs is associated with the transcriptional state of DNA in the tumor cells, it was hypothesized that cfDNA coverage at a small set of NDRs could be used to infer the ctDNA burden (fraction of tumor DNA out of all cfDNA) in the blood plasma of a cancer patient. As training data, 8 deep WGS samples from 5 CRC patients were *in silico* "diluted" with data from healthy individuals, resulting in a training set of 231 samples of ctDNA proportions ranging from 0.5% up to the original undiluted fractions (FIG. 3c, Table S2). Candidate CRC-specific transcripts that were upregulated in CRC tumors ($fpkm_{CRC} > 10$, $fpkm_{blood} < 1$) and had a differential DNA degradation signal at both promoter and junction NDRs

(relative coverage score < -0.2) were shortlisted. Candidate blood-specific transcripts were shortlisted with similar criteria ($fpkm_{CRC} < 1$, $fpkm_{blood} > 10$, relative coverage score > 0.2). Relative coverages at the NDRs of these candidate transcripts were used as input features (total 529 unique tumor and 379 blood features, Table S3). Lasso L_1-regularization regression was then used in combination with a stability-based feature selection approach to a select a minimal set of 6 predictive NDRs (Table 1), which could predict the ctDNA fraction in the training data with a mean absolute error (MAE) of ~1.8% (FIG. 3d). The signs of coefficients for the 6 NDRs in the trained model corresponded to the sign of differential expression of the associated transcripts in tumor tissue relative to whole blood (Table S4). To evaluate the ability of the model to generalize to unseen data, 4 additional samples (CRC-9 to 12 in Table S1, WGS at ~80-95x) from 2 new CRC patients were sequenced and an *in silico* diluted test set of 113 samples was created (Table S2). The model accurately predicted the ctDNA proportion in this independent test set (FIG. 3e, MAE=3.4%). A direct comparison shows high similarity between the observed (predicted) and expected ctDNA fractions (FIG. 3f; Pearson $r = 0.96$; Spearman correlation, $\rho = 0.97$). To further explore the performance of more complex models, the inventors estimated the predictive error as a function of model complexity (number of top predictive features) and found that models with 4-10 NDR features were generally more accurate and better at generalizing to unseen data compared with models using fewer or more features (FIG. 9). Next, the lower limit for ctDNA detection in the NDR model was explored. Using a previous approach (Adalsteinsson VA, *et al.* Scalable whole-exome sequencing of cell-free DNA reveals high concordance with metastatic tumors. *Nature Communications* **8**, 1324 (2017)), the inventors evaluated the sensitivity and specificity of the model as a function of ctDNA fraction threshold. The 113 *in silico* test set CRC samples (FIG. 3e, CRC-9 to 12) were used as positives, and 40 random subsets (Table S5, ~80x each) from the data of plasma samples (n=29) from healthy individuals were used as negatives. At a 2% ctDNA fraction threshold, the model correctly predicted all positive and negative samples (100% sensitivity and specificity, Table S5). In comparison, at a 1% threshold, the sensitivity was maintained at 100% but the specificity dropped to 75%. FIG. 19 provides an overview of the machine learning feature selection, model fitting, and train/test set performance for colorectal cancer.

To further evaluate the robustness of the model when tested on *in silico* samples generated using healthy samples not seen during model training, the healthy samples (n=29) were split into two different groups to separately generate *in silico* training and test data. Reassuringly, this analysis showed robust model performance in the presence of independent train/test healthy samples (FIG. 10; test set median Pearson r = 0.92; median Spearman correlation, ρ = 0.93; median MAE = 5.3%).

Next, the predictive performance of the model was compared with ichorCNA (Adalsteinsson VA, *et al.* Scalable whole-exome sequencing of cell-free DNA reveals high concordance with metastatic tumors. *Nature Communications* **8**, 1324 (2017)), a method that estimates the ctDNA fraction on the basis of arm-level copy number alterations in low-pass WGS data. Overall, ichorCNA generally predicted comparable estimates of ctDNA burden (FIG. 11; Pearson r = 0.91; Spearman correlation, ρ = 0.92). However, while 31 out of 120 low burden samples (ctDNA burden ≤ 5%) were predicted as non-cancerous by ichorCNA (FIG. 12), only 4/120 were predicted as non-cancerous by the NDR approach. This is consistent with the reported 3% lower limit of detection using arm-level CNAs in ichorCNA (Adalsteinsson VA, *et al.* Scalable whole-exome sequencing of cell-free DNA reveals high concordance with metastatic tumors. *Nature Communications* **8**, 1324 (2017)).

Table 1

Gene	Transcript	Chr	Site	Region	Expr.	$FPKM_{blood}$	$FPKM_{CRC}$	Pr
SHKBP1	ENST00000599716	19	41082891	junction	blood	10.66	0.22	1.000
ACSL1	ENST00000454703	4	185747070	junction	blood	35.07	0.78	1.000
BCAR1	ENST00000162330	16	75285369	junction	tumor	0.00	16.86	1.000
RAB25	ENST00000361084	1	156030951	promoter	tumor	0.07	131.50	0.999
PRTN3	ENST00000234347	19	840960	promoter	blood	13.78	0.00	0.995
LSR	ENST00000605618	19	35739922	promoter	tumor	0.22	31.85	0.990

Table 1 NDR features predictive of ctDNA fraction in CRC. *The column Site is the position of the nucleosome-depleted site (GRCh37); Region is the annotated class of the nucleosome-depleted site (promoter or exon-intron junction); Expr. denotes whether the transcript is specifically expressed in CRC tumor tissue or whole blood cells; Pr is the probability/frequency with which the feature was selected in the Lasso stability-selection approach.*

Additional predictive features for colorectal cancer

Apart from the 6 robust features identified, there may exist other predictive features that correlate with ctDNA burden. A step-wise search with Lasso regression

on all 344 *in silico* samples was performed and the top stable 6 features in each step were extracted to estimate ctDNA fractions. The search was repeated for 100 independent times, followed by pooling all predictive features with a deviation threshold of 3% (FIG. 20). This analysis yielded 435 6-feature combinations with a predictive accuracy ≤3% (see Table S14), comprising a total of 158 unique features (see Table S15).

Targeted NDR assay to estimate ctDNA burden

Intriguingly, since the predictive models used data from only a few NDRs, it was hypothesized that a targeted sequencing approach could be deployed for robust and low-cost estimation of ctDNA burden. The CRC model only requires cfDNA relative coverages at 6 NDRs (Table 1). The inventors therefore designed capture probes for these 6 regions (total ~24 kb) and performed targeted sequencing (~300x) on 53 new plasma samples from CRC patients (FIG. 4a), followed by ctDNA burden estimation from the relative coverage of the NDRs using the existing CRC model. To examine the accuracy of the model on targeted NDR sequencing data, low-pass WGS (~4x) was also performed on the same plasma samples for ctDNA content estimation with the CNA-based method, ichorCNA. High concordance (Pearson r = 0.84; Spearman correlation, ρ = 0.79) of estimated ctDNA burden with the CNA and NDR-based approaches was observed (FIG. 4b and Table S6). Moreover, in the 53 samples (FIG. 4a, Table S6), targeted sequencing (~6000x) of a panel of 100 frequently mutated genes (~370 kb, Table S7) in colorectal cancer was performed. SNVs called by MuTect and VarScan were intersected and further filtered to minimize false positives (Table S8, see Methods). This analysis identified high-confidence somatic mutations in 27 plasma samples and revealed high correlation (Pearson r = 0.85; Spearman correlation, ρ = 0.88) between maximum VAFs and NDR-based ctDNA burden estimates across samples (FIG. 4c and Table S6). ctDNA was detected in 49 out of 53 (92%) samples with the targeted NDR approach, compared to 33/53 (62%) and 27/53 (51%) with ichorCNA and SNV calling approaches, respectively. The 4 ctDNA-negative samples identified with the NDR approach were also ctDNA-negative using ichorCNA and the SNV approach (Table S6). Overall, this demonstrates that the NDR-based estimation approach is robust and can be deployed with a compact and low-cost targeted sequencing approach.

NDR-based monitoring of ctDNA dynamics and disease progression

To further explore how NDR-based ctDNA burden estimation could be used for low-cost monitoring of cancer progression, targeted NDR assay was applied to serial plasma samples collected from five CRC patients (FIG. 4d). Overall, targeted NDR profiling showed concordant ctDNA burden dynamics when compared with SNV VAFs profiled in the same samples, with coinciding increases and decreases in ctDNA burden and VAFs over time. For example, patient C357 showed generally increasing ctDNA burden and VAFs over time, and patient C986 had an intermediate coinciding peak in both ctDNA burden and VAFs. Driver mutations in *TP53*, *PIK3CA* and *APC* were detected in patient C986. While VAFs of these mutations were highly correlated, they showed a between-mutation spread of ~0.1-0.2 VAF units across all timepoints. Similarly, patient C519 had *TP53* and *APC* mutations with a ~0.2-0.3 unit difference in VAFs. While such differences may be caused by both technical (e.g. capture efficiency) and biological (e.g. clonality or concomitant CNAs) bias, they demonstrate the challenge in estimating ctDNA burden levels based on VAFs alone.

It was noted that a number of plasma samples for which the NDR-based ctDNA burden was inferred to be positive, yet the variant calling pipeline identified no SNVs under default settings. To further understand this discordance, the raw sequencing data in these "mutation-free" plasma samples was manually inspected. Indeed, when searching for variants that were identified in other samples/timepoints from the same patients, the raw sequencing data supported presence of the expected SNVs in all the samples with positive NDR-quantified ctDNA burden (Table S9). In contrast, one plasma sample (patient C1531, day 191) was quantified with zero ctDNA burden by the NDR approach and manual screening confirmed absence of *TP53* and *APC* mutations in this sample (Table S9). Overall, these results highlight the robustness of the targeted NDR assay for ctDNA burden estimation.

It was next explored how ctDNA burden dynamics correlate with response to targeted or cytotoxic treatments. Patient C357 was treated with Regorafenib (days 821-842 after diagnosis) followed Trifluridine (days 979-1026). However, ctDNA burden estimation in this time interval (days 800-1056) showed no drop in ctDNA burden following either treatment, indicating tumor resistance to both drugs; end-treatment CT scans (Day 916 and 1056 respectively) confirmed progressive disease. In contrast, patients with positive response to treatment showed a marked reduction of ctDNA burden in plasma. For example, patient C1531 received the chemotherapy

regimen of FOLFOXIRI (days 82-175) and had on and post-treatment CT scans showing partial response. Strikingly, this patient showed a concomitant and marked drop in ctDNA burden both during (day 160) and after (day 191) treatment. In patient C575, *TP53* and *ATR* mutations were only identified at two out of four timepoints by the pipeline. In this patient, both CT scans and ctDNA burden estimation inferred stable disease during the first round of XELOX/bevacizumab treatment (days 612-833). However, during the second round of treatment, both the ctDNA burden increased (day 864) and CT scans confirmed progressive disease, indicating acquired drug resistance. Finally, discrepancies between tumor dynamics inferred from CT imaging and ctDNA burden has previously been reported. Patient C519 reflected one such example, where CT scans indicated progressive disease while both ctDNA burden estimates and mutation VAFs decreased.

Estimation of ctDNA burden across cancer types

The predictive model for CRC ctDNA burden included 3 (out of 6) NDR coverage features from genes overexpressed in whole blood. Intriguingly, a predictive model completely restricted to blood-specific genes could hypothetically quantify the extent that a cfDNA profile deviates from a healthy baseline profile, allowing prediction of ctDNA burden across different cancer types. Indeed, the inventors were able to identify genes overexpressed in whole blood compared to solid tumor tissue that also had decreased NDR coverage in plasma samples from healthy individuals as compared to patients of distinct cancer types (FIG. 5a). To further systematically test this idea, deep (~72-94x) cfDNA WGS sequencing of blood samples from 10 breast cancer patients was performed (Table S1) and *#in silico* diluted cfDNA samples of variable ctDNA burden were generated (Table S2, FIG. 5b). Since germline data was not available for the BRCA patients, ctDNA fractions were estimated in the 10 BRCA samples using ichorCNA. Transcripts highly overexpressed in whole blood compared to solid tumor tissues were then shortlisted (comprising 20 different solid tumor types, FIG. 5b), yielding 792 blood-specific candidate NDR features (Table S10). Using a training dataset comprising cfDNA samples from both CRC and BRCA patients, it was found that models comprising approximately 10 features were able to generalize well to unseen data from both cancer types (FIG. 13, Table 2).

Table 2

Gene	Transcript	Chr	Site	Region	Group	$FPKM_{blood}$
SLC11A1	ENST00000465984.5	2	219246911	promoter	blood	10.54
NLRP12	ENST00000324134.10	19	54327597	promoter	blood	9.17
PRTN3	ENST00000234347.9	19	840960	promoter	blood	13.78
HMBS	ENST00000392841.1	11	118958697	promoter	blood	7.28
LILRB3	ENST00000460208.1	19	54721567	promoter	blood	51.15
ACSL1	ENST00000513001.5	4	185678973	junction	blood	17.65
GP9	ENST00000307395.4	3	128779693	junction	blood	9.72
MX2	ENST00000398632.3	21	42774561	promoter	blood	7.28
RASGRP4	ENST00000615340.4	19	38916837	promoter	blood	6.88
ATG16L2	ENST00000542481.1	11	72534940	promoter	blood	25.18

***Table 2**: Pan-cancer top-10 features. Columns / Gene : gene name / Transcript : transcript ID / Chr : chromosome / Site : coordinate of nucleosome-depleted site (GRCh37) / Region : location of nucleosome-depleted site / Group : gene group based on its expression in blood and tumor / $FPKM_{blood}$: FPKM value in normal blood. Their FPKM values in tumors of 20 cancer types (BLCA, BRCA, CESC, CRC, ESCA, GBM, HNSC, KIRC, KIRP, LGG, LIHC, LUAD, LUSC, OV, PAAD, PRAD, SKCM, STAD, THCA, and UCEC) are all <1.*

A model fitted with the training data using the top 10 predictive features (Table 2) had a mean absolute error of 2.2%, with comparable accuracy in CRC and BRCA samples (FIG. 5c). In the unseen CRC and BRCA test data (FIG. 5d), the model achieved an overall accuracy (MAE=4.3%; Pearson r = 0.95; Spearman correlation, ρ = 0.97; FIG. 14), comparable to the CRC-specific model applied to CRC data (MAE=3.4%; Pearson r = 0.96; Spearman correlation, ρ = 0.97; FIG. 3e, f) and a BRCA-specific model applied to the BRCA data (MAE=6.1%; Pearson r = 0.97; Spearman correlation, ρ = 0.97; FIG. 15). A strong concordance was also observed between the CRC+BRCA and CRC-specific models in their predicted ctDNA fractions in the test set plasma samples from CRC patients (Pearson r = 0.95; Spearman correlation, ρ = 0.95; FIG. 16). The lower limit of detection for the CRC+BRCA model was analysed by evaluating the sensitivity and specificity of the model as a function of ctDNA fraction threshold. The 206 *in silico* test set samples (113 CRC + 93 BRCA, FIG. 5d) were used as positives and 40 random subsets (Table S11, ~80x each) from healthy individuals were used as negatives. At a 3% ctDNA fraction detection limit, the CRC+BRCA model achieved 100% sensitivity and specificity (Table S11). In comparison, at a 2% threshold, the sensitivity was almost maintained at 99.5% but the specificity dropped to 88%. These results support that a model based on a limited set of blood-specific NDR features can predict ctDNA fractions across two distinct cancer types. FIG. 21 provides an overview of the machine learning feature selection, model fitting, and train/test set performance for pan-cancer features.

Additional predictive features for pan-cancer

Lasso regression with all 792 blood features was employed to identify all potential predictive combination of pan-cancer features. A step-wise extensive search was carried out on all the 652 in silico samples (see Table S2), and the top 10 features in each step were extracted to estimate ctDNA content (FIG. 22). The inventors pooled all predictive features with a deviation threshold of 4% from 100 independent runs. This analysis yielded 385 10-feature combinations with a predictive accuracy ≤4% (Table S16), comprising a total of 132 unique features (Table S17).

Additional predictive feature combinations

An additional search for predictive and feature combinations for both the CRC and pan-cancer models was performed. While this search was implemented as previously described (FIGs. 22 and 24), a modified approach was used to generate in silico samples, which better preserved variability in cfDNA profiles across individuals: Each cancer cfDNA sample was in silico diluted by the normal data from a random subset (n=19) of all 29 healthy samples. In this analysis, the CRC model yielded 119 new 6-feature combinations with a predictive accuracy ≤4% (FIG. 23, Table S18), comprising a total of 68 unique features (Table S19). 61 out of these 68 features were also identified as predictive in the previous CRC model (Table S15). Similarly, the pan-cancer model yielded 217 new 10-feature combinations with a predictive accuracy ≤5% (FIG. 23, Table S20), comprising a total of 76 unique features (Table S21) with 63/76 identified in the previous pan-cancer model (Table S17).

Discussion

Monitoring of ctDNA offers a non-invasive approach to tracking disease progression and has been demonstrated as a valuable real-time tool for assessing therapeutic response. Here, it is shown that cfDNA coverage patterns at tumor and blood-specific NDRs can be used for quantitative estimation of the ctDNA burden in blood plasma samples. While SNV VAFs can be used as a proxy for the ctDNA burden, this only works for the subset of patients with known and measured clonal SNVs in a given targeted gene panel. SNV-based approximation of ctDNA burden may be further

challenged by clonal haematopoiesis, which is frequently observed in cancer patients. Additionally, absolute ctDNA fraction estimation from SNVs requires co-estimation of allele zygosity and clonality, which may be challenging to infer for metastatic patients with multiple independently evolving tumors contributing ctDNA to the blood circulation. Furthermore, in low ctDNA burden samples, which are common and clinically important, NDR-based burden estimation showed improved accuracy as compared to a lp-WGS-based estimation method. In contrast to lp-WGS and DNA methylation-based profiling, NDR-based estimation is directly compatible with targeted gene panel sequencing. Since the ctDNA burden estimation model requires data from 10 or less NDRs, these regions can be profiled at low cost by capturing <25 kb of genomic sequence. Targeted cfDNA assays often cover hundreds of genes and >1 Mb captured genomic sequence, with larger panels required for profiling across cancer types and tumour mutation burden estimation. It would be straightforward to co-profile NDRs in such assays, with only a minor increment in panel size. Furthermore, down-sampling analysis showed that the NDR approach is robust down to 100x sequence coverage (FIG. 17), imposing a sequencing demand equivalent to ~0.001x WGS, orders of magnitude lower than current lp-WGS approaches. Importantly, an integrated NDR/gene assay would be able to estimate ctDNA burden in patients without clonal mutations in targeted cancer genes, potentially corresponding to 5-70% of patients depending on cancer type. The approach could enable low-cost and simultaneous quantitative estimation of ctDNA burden and mutational profiling in response to treatment interventions. Indeed, given the estimated lower limit of detection (~2%) of the NDR approach, this application (i.e. simultaneous quantitative estimation of ctDNA burden and mutational profiling in response to treatment interventions) may be more relevant as compared to employing the NDR approach for screening of cancer in healthy/cancer-free individuals. Furthermore, critical for treatment decision support, independent ctDNA burden estimates could assist in classification of clonal and subclonal actionable mutations. Intriguingly, it was found that a model restricted to blood-specific NDRs could robustly predict ctDNA burden across both colorectal and breast cancer patients, suggesting it might be possible to estimate ctDNA burden independently of tumor types and metastatic lesions.

Nucleosome positioning across gene bodies, and its association with transcriptional activity, has been studied using both biochemical assays and cfDNA profiles. Unexpectedly, the systematic analysis across ordered exon-intron junctions

revealed that, in addition to the promoter, only the first exon-intron junction showed signatures of strong nucleosome and expression-dependent cfDNA degradation (FIG. 2a and FIG. 6). Interestingly, transcription and splicing are coupled processes, and it has been observed that H3K4me3 and H3K9ac chromatin marks of active transcription are concentrated specifically at both promoters and ends of first exons. The data further supports that nucleosome depletion and DNA accessibility at the first exon-intron splice junction is strongly associated with transcriptional activity, supporting a model where the first exon splice region may act as a transcriptional enhancer.

In summary, the inventors have shown how tissue and expression-specific cfDNA degradation at NDRs can be used to quantitatively estimate ctDNA burden in blood samples. The approach is directly compatible with targeted gene sequencing, allowing for low-cost and simultaneous discovery of actionable cancer mutations and accurate estimation of ctDNA burden. It is anticipated that next-generation cfDNA assays based on these findings will be useful for quantitatively tracking and analysing cancer disease progression across time and patients.

Materials and Methods

Plasma samples

Cancer patient and healthy volunteer samples were collected under studies 2013/110/B (now 2018/2795) and 2012/733/B approved by the Singhealth Centralised Institutional Review Board. Plasma was separated from blood within 2 hours of venipuncture via centrifugation at 10min x 300g and 10min x 9730g, and then stored at -80 °C. DNA was extracted from plasma using the QIAamp Circulating Nucleic Acid Kit following manufacturer's instructions. Sequencing libraries were made using the KAPA HyperPrep kit (Kapa Biosystems, now Roche) following manufacturer's instructions and paired-end sequenced (2x151 bp) on either an Illumina Hiseq4000 or HiseqX.

Whole genome sequencing

A targeted sequencing panel (Table S7) was first used to screen plasma samples from CRC patients and 12 samples (Table S1) of likely high ctDNA burden were selected, having maximum VAF > 15% for known CRC cancer driver mutations (Supplementary Data 1). Similarly, 10 BRCA plasma samples of high ctDNA burden

were selected, with either VAF > 15% based on a panel of 77 genes (Table S12) of common breast cancer mutations (Supplementary Data 2), or alternatively, significant proportions (>20%) of short (length < 150 bp) cfDNA fragments (Table S1). It has been reported that short cfDNA fragments below 150 bp are enriched in high-ctDNA plasma samples. Deep WGS (~90x) was performed on the 12 cfDNA samples from 7 CRC patients and 10 cfDNA samples from 10 BRCA patients (Table S1). For the 5 CRC patients with 2 samples each, there was at least a 12 months interval between the two samples. Bwa-mem (Li H. Aligning sequence reads, clone sequences and assembly contigs with BWA-MEM. *arXiv preprint arXiv:13033997*, (2013)) was used to align the WGS reads from healthy (n=29, ~5x coverage), cancer (CRC n=12, BRCA n=10, ~90x coverage), and germline samples (CRC n=12 ~30x coverage, not available for BRCA) were matched to the hg19 human genome. Duplicates were marked using biobambam (Tischler G, Leonard S. biobambam: tools for read pair collation based algorithms on BAM files. *Source Code for Biology and Medicine* **9**, 13 (2014)). It has been found that trimming reads from both ends increased the coverage signal of nucleosome positioning. Similarly, the original reads (~151 bp) were trimmed from the two ends and the central 61 bp was preserved to amplify the nucleosome-associated DNA degradation signal. BAM files of healthy individuals were merged using SAMtools merge function (Li H, *et al.* The sequence alignment/map format and SAMtools. *Bioinformatics* **25**, 2078-2079 (2009)). Low-pass WGS (~4x) was performed on 53 cfDNA samples from 23 CRC patients (Table S6).

Sample preparation for targeted sequencing

Plasma and patient-matched buffy coat samples were isolated from whole blood within six hours from collection and stored at -80°C. DNA was extracted with the QIAamp Circulating Nucleic Acid Kit, followed by library preparation using the KAPA HyperPrep kit. All libraries were tagged with custom dual indexes containing a random 8-mer unique molecular identifier. Targeted capture was performed on xGen custom panels (Integrated DNA Technologies) relevant to the experiment: a) panel of 100 genes selected based on literature review for relevance to colorectal and breast cancer, see Table S7, or b) capture probes (Supplementary Data 3) targeting genomic regions (4 kb centered at the sites in Table 1) related to the 6 NDRs predictive of ctDNA content in colorectal cancer. Paired-end sequencing (2 x 151 bp) was done on an Illumina Hiseq4000 machine.

Variant calling and allele frequency estimation

Sequencing data was analyzed using the bcbio-nextgen pipeline (Guimera RV. bcbio-nextgen: Automated, distributed next-gen sequencing pipeline. *EMBnetjournal* **17**, 30 (2012)), including read alignment with BWA mem, PCR duplicate marking with biobambam, as well as recalibration and realignment with GATK (DePristo MA, *et al.* A framework for variation discovery and genotyping using next-generation DNA sequencing data. *Nature genetics* **43**, 491 (2011)). Somatic variant calling was performed using MuTect (Cibulskis K, *et al.* Sensitive detection of somatic point mutations in impure and heterogeneous cancer samples. *Nature biotechnology* **31**, 213 (2013)) and VarScan (Koboldt DC, *et al.* VarScan: variant detection in massively parallel sequencing of individual and pooled samples. *Bioinformatics* **25**, 2283-2285 (2009)) with default parameters, and all calls were annotated with Variant Effect Predictor (McLaren W, *et al.* The ensembl variant effect predictor. *Genome biology* **17**, 122 (2016)). Variants were removed if they were outside coding regions. The inferred VAFs were either from one of the two callers if the variant was missed by one caller, or the mean if the variant was called by both callers (Table S8). Variants from HLA-A, KMT2C and MUC17 were filtered because the majority of variants in these genes were also found by at least one caller at >=0.005 VAF in buffy coat sequencing.

Gene expression analysis

Tissue-specific RNA-seq transcript expression data was obtained from GTEx (including 337 whole blood samples; Table S14). Tumor RNA-seq transcript expression was obtained from TCGA (Table S14). Because a gene usually comprises multiple alternative transcripts with different genomic positions, gene expression was studied at the transcript level for a precise mapping of promoter and junction locations. Transcripts of all coding genes were grouped on the basis of their expression level (fpkm) in whole blood. If a group (e.g. $0.1 < \text{fpkm} \leq 1$; 25155 transcripts) had more than 5000 transcripts, 5000 transcripts were randomly to represent the group. Unexpressed genes were defined as transcripts that were not expressed in ≥ 99% of all 7861 GTEx samples.

Relative cfDNA coverage estimation

Read coverage at promoter and junction regions was computed from BAM files with SAMtools *depth* function (Li H, *et al.* The sequence alignment/map format and SAMtools. *Bioinformatics* **25**, 2078-2079 (2009)). For the promoter region (-150 to 50 bp relative to TSS), the mean raw coverage across the region was divided (yielding "relative coverage") by the mean coverage of the upstream (-2000~-1000 bp relative to TSS) and downstream (1000~2000 bp relative to TSS) flanks (FIG. 18). Thus, the mean coverage of the combined upstream and downstream 2k bp flanks serves as a "normalization factor". A similar approach was used for exon-intron junctions (FIG. 18). To measure the difference of relative coverage at NDRs between plasma samples from CRC patients and healthy individuals, the relative coverage score was computed:

$$\text{score} = \frac{\text{mean(CRC)} - \text{mean(healthy)}}{\sqrt{\text{s.d.(CRC)}}}$$

where *mean(CRC)* and *mean(healthy)* are the mean of average relative coverages at NDRs across CRC plasma and healthy plasma samples respectively, and *s.d.(CRC)* is the standard deviation of average relative coverages at NDRs across CRC samples. The variance in healthy samples could not be estimated due to low sequencing depth (~5x). When computing average relative coverage of each NDR (either -150 to 50 bp relative to TSS, or -300 to -100 bp relative to first exon end), positions with relative coverage > 2 were truncated to reduce bias from potential outlier values.

To explore the association between relative coverage and a range of epigenetic features, linear regression was used to fit each candidate feature (covariate) with relative coverage (response). Whole blood gene expression (fpkm) was discretized into 6 bins [unexpressed, 0.01 < fpkm ≤ 0.1, 0.1 < fpkm ≤ 1, 1 < fpkm ≤ 5, 5 < fpkm ≤ 30, fpkm > 30] and fitted as a categorical covariate with the unexpressed group as the reference group. Peaks of epigenetic features [DNase, H3K4me3, H3K36me3, H3K27ac, H3K4me1, H3K9me3 and H3K27me3] from primary T-cells (E034) were obtained from the Roadmap Epigenomics Project. Epigenetic features were fitted as binary covariates with no signal as the reference group.

Estimation of ctDNA fractions from deep WGS cfDNA data

The ctDNA fractions in CRC plasma samples were quantified using four different methods: THetA2, TitanCNA, AbsCN-seq and PurBayes (Oesper L, Satas G,

Raphael BJ. Quantifying tumor heterogeneity in whole-genome and whole-exome sequencing data. *Bioinformatics* **30**, 3532-3540 (2014); Ha G, *et al.* TITAN: inference of copy number architectures in clonal cell populations from tumor whole-genome sequence data. *Genome research* **24**, 1881-1893 (2014); Bao L, Pu M, Messer K. AbsCN-seq: a statistical method to estimate tumor purity, ploidy and absolute copy numbers from next-generation sequencing data. *Bioinformatics* **30**, 1056-1063 (2014); Larson NB, Fridley BL. PurBayes: estimating tumor cellularity and subclonality in next-generation sequencing data. *Bioinformatics* **29**, 1888-1889 (2013)). These methods were originally developed to use matched tumor tissue and germline Exome/WGS data to estimate mutation and copy number tumor heterogeneity, including tumor purity. Here, these methods were applied to the ~90x cfDNA and ~30x matched germline (buffy coat) WGS data to estimate ctDNA fractions. Somatic mutations and copy number alterations, as input to AbsCN-seq and PurBayes, were called by SMuRF (Huang W, Guo YA, Muthukumar K, Baruah P, Chang MM, Skanderup AJ. SMuRF: Portable and accurate ensemble prediction of somatic mutations. *Bioinformatics (Oxford, England)*, (2019)) and CNVkit (Talevich E, Shain AH, Botton T, Bastian BC. CNVkit: genome-wide copy number detection and visualization from targeted DNA sequencing. *PLoS Comput Biol* **12**, e1004873 (2016)), respectively, using the bcbio-nextgen workflow (Guimera RV. bcbio-nextgen: Automated, distributed next-gen sequencing pipeline. *EMBnetjournal* **17**, 30 (2012)). The median of these four ctDNA fraction estimates for a given sample was used as the final consensus estimate of the ctDNA fraction. Since germline samples were not available for the BRCA patients, the ctDNA fractions of the BRCA plasma samples were estimated by ichorCNA (Adalsteinsson VA, *et al.* Scalable whole-exome sequencing of cell-free DNA reveals high concordance with metastatic tumors. *Nature Communications* **8**, 1324 (2017)).

***In silico* sample generation**

The cancer cfDNA samples were *in silico* diluted by mixing cancer cfDNA reads with reads from healthy samples, maintaining the same average coverage as the original undiluted cancer cfDNA sample. The *in silico* generated samples were diluted from ctDNA content ranging from 0.005 up to the original undiluted fractions, with a denser sampling of low fractions ≤ 0.05 (Table S2). The inventors generated a training set of 231 samples originating from 8 samples from 5 CRC patients, and a test set of 113 samples originating from 4 samples from 2 additional CRC patients. For BRCA,

the training set comprised 215 *in silico* generated samples from 7 patients/samples, and the test set had 93 samples from 3 patients/samples (Table S2).

Generation of NDR features

The relative coverage score (see above) of NDRs for all transcripts was computed and the relative coverage score was combined with expression data to shortlist tumor/blood-specific transcripts associated with differential tumor/blood NDR cfDNA coverage. For each transcript, the inventors calculated its median fpkm ($fpkm_{blood}$) across all whole blood samples, its median fpkm ($fpkm_{CRC}$) across all CRC samples, as well as its respective median fpkm values for other tumor types. Tumor transcripts were defined as being highly expressed in CRC tumor, lowly expressed in normal blood cell, and more highly degraded in CRC samples at both promoter and junction NDRs ($fpkm_{CRC} > 10$, $fpkm_{blood} < 1$, relative coverage score < -0.2). Blood transcripts were defined with similar rules ($fpkm_{CRC} < 1$, $fpkm_{blood} > 10$, relative coverage score > 0.2). This approach shortlisted 284 CRC and 210 blood transcripts, each transcript with two features (promoter and junction NDR coverage). After removing overlapping features (multiple transcripts sharing the same NDR), NDR coverages of the resulting 529 tumor and 379 blood features (total n=908) were used as input features for predictive modelling. For the CRC+BRCA model, only transcripts with blood-specific expression ($fpkm_{blood} > 5$) that were also lowly expressed (fpkm < 1) in tumors of all 20 tumor types were shortlisted (TCGA tumor type acronyms: BLCA, BRCA, CESC, CRC, ESCA, GBM, HNSC, KIRC, KIRP, LGG, LIHC, LUAD, LUSC, OV, PAAD, PRAD, SKCM, STAD, THCA, UCEC), leading to a total of 792 features.

Lasso regularized regression to predict ctDNA fraction

Lasso regularized linear regression using glmnet (Friedman J, Hastie T, Tibshirani R. Regularization paths for generalized linear models via coordinate descent. *Journal of statistical software* **33**, 1 (2010)) was used to select features and predict ctDNA content in plasma cfDNA samples. To select robust features, half of the training data was first extracted randomly and Lasso with ten-fold cross-validation was used to identify features predictive of ctDNA fractions. This procedure was repeated 1000 times and the top stable features (selection frequency ≥ 0.99) were extracted as the final predictive features, which resulted in 6 predictive features (Table 1) for the CRC-specific model and 10 predictive features (Table 2) for the CRC+BRCA model,

respectively. The inventors trained the final predictive model with ten-fold cross-validation on the full training set. The inventors also attempted to predict ctDNA fractions with log-transformed relative coverage, and tested the performance using a logistic regression model, both of which failed to outperform the current model in prediction accuracy (data not shown).

To evaluate the robustness of the model when was trained and tested on *in silico* samples generated using independent healthy samples, the normal samples were split evenly into 2 sets. The first set (N1) was used to perform *in silico* spike-ins/dilution of the training set, and the second set (N2) was used for *in silico* dilution of the test set. Briefly, the coefficients of the CRC model (comprising the 6 features in Table 1) were re-fitted using the training data (diluted with the N1 healthy samples), and the model accuracy on the withheld test samples (diluted with N2) were then evaluated. This procedure was repeated 10 times and the model accuracy on the test data generated using the independent normal samples was evaluated.

ichorCNA benchmarking

For the *in silico* samples, cfDNA reads from the 12 deep-WGS CRC samples were mixed with reads from healthy samples to generate *in silico* low-pass samples (~0.1x) for ctDNA content estimation using ichorCNA. The usage guidelines with default parameters were followed in the 2 step workflow: 1) read count coverage calculation with HMMcopy Suite, and 2) tumor content estimation with ichorCNA R package.

Data Availability

cfDNA sequencing data have been deposited at the European Genome-phenome Archive (EGA) under the accession code EGAS00001004657. The data is made available for academic research. Data will be released subject to a data transfer agreement.

Supplementary Tables and Data

Table S1. ctDNA burden estimation of plasma samples from cancer patients.

Table S2. The *in silico* samples of various ctDNA content.

Table S3. Information on all candidate features of nucleosome-depleted regions for colorectal cancer.

Table S4. Coefficients for the selected NDRs in the trained models.

Table S5. Observed ctDNA fractions in the LOD analysis for the CRC model.

Table S6. CRC plasma samples for lp-WGS and targeted sequencing.

Table S7. A panel of 100 genes frequently mutated in colorectal and breast cancer.

Table S8. Variant allele frequency estimation of CRC plasma samples.

Table S9. Mutations missed by the callers for the CRC patients with serial plasma samples.

Table S10. Information on all candidate pan-cancer features of nucleosome-depleted regions.

Table S11. Observed ctDNA fractions in the LOD analysis for the CRC+BRCA model.

Table S12. A panel of 77 genes for screening breast cancer samples.

Table S13. Transcript expression data.

Table S14. Information on all predictive features for colorectal cancer

Table S15. Information on predictive features for colorectal cancer

Table S16. Information on additional predictive pan-cancer features

Table S17. Information on predictive pan-cancer features

Table S18. All predictive feature combinations for CRC using in silico samples generated with random subsets of healthy samples.

Table S19. Information on predictive features for CRC using in silico samples generated with random subsets of healthy samples.

Table S20. All predictive pan-cancer feature combinations using in silico samples generated with random subsets of healthy samples.

Table S21. Information on predictive pan-cancer features using in silico samples generated with random subsets of healthy samples.

Supplementary Data 1

Supplementary Data 2

Supplementary Data 3

Table S1. ctDNA burden estimation of plasma samples from cancer patients.

sample name	sample ID	cancer type	coverage	tumor content estimation - repetition 1				tumor content estimation - repetition 2				tumor content estimation - repetition 3				mean ctDNA content	median ctDNA content
				theta2	titanCNA	abscnseq	PurBayes	theta2	titanCNA	abscnseq	PurBayes	theta2	titanCNA	abscnseq	PurBayes		
1014_180816	CRC-1	CRC	80.84	0.38	0.55	0.48	0.43	0.38	0.56	0.48	0.43	0.38	0.55	0.46	0.43	0.46	0.45
1279_221015	CRC-9	CRC	94.67	0.43	0.65	0.50	NA	0.43	0.65	0.50	NA	0.43	0.63	0.50	0.83	0.56	0.50
1279_241116	CRC-10	CRC	95.22	0.66	0.49	NA	0.40	0.66	0.49	NA	0.40	0.66	0.49	NA	0.40	0.52	0.49
1531_160616	CRC-2	CRC	90.65	0.86	NA	NA	0.93	0.86	0.82	NA	0.94	0.86	0.81	NA	0.93	0.87	0.86
1531_180119	CRC-3	CRC	100.63	0.67	0.48	0.32	0.30	0.75	0.48	0.32	0.83	0.75	0.50	0.32	0.79	0.54	0.49
512_051015	CRC-11	CRC	79.96	0.64	0.69	0.49	0.44	0.64	0.69	0.49	0.44	0.59	0.68	0.49	0.88	0.60	0.61
512_130114	CRC-12	CRC	79.90	0.27	0.51	0.44	0.35	0.27	0.51	0.44	0.35	0.27	0.52	0.56	0.35	0.40	0.39
519_210114	CRC-4	CRC	87.27	0.30	0.40	0.35	0.36	0.30	0.40	0.35	0.36	0.30	0.43	0.35	0.35	0.35	0.35
809_030915	CRC-5	CRC	75.76	0.45	0.64	0.59	0.44	0.45	0.64	0.59	0.44	0.45	0.63	0.59	0.94	0.57	0.59
809_110914	CRC-6	CRC	72.56	0.35	0.59	NA	NA	0.35	0.59	NA	NA	0.35	0.60	NA	0.47	0.47	0.47
986_100215	CRC-7	CRC	71.83	0.25	0.69	0.50	0.36	0.25	0.69	0.50	0.36	0.25	0.47	0.50	0.37	0.43	0.42
986_261016	CRC-8	CRC	76.72	0.34	0.54	0.51	0.37	0.34	0.54	0.51	0.37	0.34	0.54	0.51	0.37	0.44	0.44

sample name	sample ID	cancer type	coverage	ctDNA content estimated from ichorCNA
D14	BRCA-1	BRCA	86.98	0.70
D23	BRCA-2	BRCA	79.41	0.76
D7	BRCA-3	BRCA	94.33	0.13
D9	BRCA-4	BRCA	89.86	0.66
E10c	BRCA-5	BRCA	87.92	0.58
E7c	BRCA-6	BRCA	85.45	0.51
E8c	BRCA-7	BRCA	78.61	0.54
D19	BRCA-8	BRCA	76.67	0.74
E2c	BRCA-9	BRCA	71.80	0.41
E6c	BRCA-10	BRCA	71.50	0.54

Table S2. The *in silico* samples of various ctDNA content.

	patient ID	sample name	sample ID	ctDNA fraction	sample size
training set CRC	1014	1014_160816	CRC-1	0.005, 0.010, 0.015, 0.020, 0.025, 0.030, 0.035, 0.040, 0.045, 0.050, 0.075, 0.100, 0.125, 0.150, 0.175, 0.200, 0.225, 0.250, 0.275, 0.300, 0.325, 0.350, 0.375, 0.400, 0.425, 0.450, 0.465	27
	1531	1531_160616	CRC-2	0.005, 0.010, 0.015, 0.020, 0.025, 0.030, 0.035, 0.040, 0.045, 0.050, 0.075, 0.100, 0.125, 0.150, 0.175, 0.200, 0.225, 0.250, 0.275, 0.300, 0.325, 0.350, 0.375, 0.400, 0.425, 0.450, 0.475, 0.500, 0.525, 0.550, 0.575, 0.600, 0.625, 0.650, 0.675, 0.700, 0.725, 0.750, 0.775, 0.800, 0.825, 0.850, 0.868	43
	1531	1531_160119	CRC-3	0.005, 0.010, 0.015, 0.020, 0.025, 0.030, 0.035, 0.040, 0.045, 0.050, 0.075, 0.100, 0.125, 0.150, 0.175, 0.200, 0.225, 0.250, 0.275, 0.300, 0.325, 0.350, 0.375, 0.400, 0.425, 0.450, 0.475, 0.490	28
	519	519_210114	CRC-4	0.005, 0.010, 0.015, 0.020, 0.025, 0.030, 0.035, 0.040, 0.045, 0.050, 0.075, 0.100, 0.125, 0.150, 0.175, 0.200, 0.225, 0.250, 0.275, 0.300, 0.325, 0.350, 0.351	23
	809	809_030915	CRC-5	0.005, 0.010, 0.015, 0.020, 0.025, 0.030, 0.035, 0.040, 0.045, 0.050, 0.075, 0.100, 0.125, 0.150, 0.175, 0.200, 0.225, 0.250, 0.275, 0.300, 0.325, 0.350, 0.375, 0.400, 0.425, 0.450, 0.475, 0.500, 0.525, 0.550, 0.575, 0.590	32
	809	809_110914	CRC-6	0.005, 0.010, 0.015, 0.020, 0.025, 0.030, 0.035, 0.040, 0.045, 0.050, 0.075, 0.100, 0.125, 0.150, 0.175, 0.200, 0.225, 0.250, 0.275, 0.300, 0.325, 0.350, 0.375, 0.400, 0.425, 0.450, 0.469	27
	986	986_100215	CRC-7	0.005, 0.010, 0.015, 0.020, 0.025, 0.030, 0.035, 0.040, 0.045, 0.050, 0.075, 0.100, 0.125, 0.150, 0.175, 0.200, 0.225, 0.250, 0.275, 0.300, 0.325, 0.350, 0.375, 0.400, 0.419	25
	986	986_261016	CRC-8	0.005, 0.010, 0.015, 0.020, 0.025, 0.030, 0.035, 0.040, 0.045, 0.050, 0.075, 0.100, 0.125, 0.150, 0.175, 0.200, 0.225, 0.250, 0.275, 0.300, 0.325, 0.350, 0.375, 0.400, 0.425, 0.440	26
training set BRCA	BRCA-D14	D14	BRCA-1	0.005, 0.010, 0.015, 0.020, 0.025, 0.030, 0.035, 0.040, 0.045, 0.050, 0.075, 0.100, 0.125, 0.150, 0.175, 0.200, 0.225, 0.250, 0.275, 0.300, 0.325, 0.350, 0.375, 0.400, 0.425, 0.450, 0.475, 0.500, 0.525, 0.550, 0.575, 0.600, 0.625, 0.650, 0.675, 0.6967	36
	BRCA-D23	D23	BRCA-2	0.005, 0.010, 0.015, 0.020, 0.025, 0.030, 0.035, 0.040, 0.045, 0.050, 0.075, 0.100, 0.125, 0.150, 0.175, 0.200, 0.225, 0.250, 0.275, 0.300, 0.325, 0.350, 0.375, 0.400, 0.425, 0.450, 0.475, 0.500, 0.525, 0.550, 0.575, 0.600, 0.625, 0.650, 0.675, 0.700, 0.725, 0.750, 0.7567	39
	BRCA-D7	D7	BRCA-3	0.005, 0.010, 0.015, 0.020, 0.025, 0.030, 0.035, 0.040, 0.045, 0.050, 0.075, 0.100, 0.125, 0.1258	14
	BRCA-D9	D9	BRCA-4	0.005, 0.010, 0.015, 0.020, 0.025, 0.030, 0.035, 0.040, 0.045, 0.050, 0.075, 0.100, 0.125, 0.150, 0.175, 0.200, 0.225, 0.250, 0.275, 0.300, 0.325, 0.350, 0.375, 0.400, 0.425, 0.450, 0.475, 0.500, 0.525, 0.550, 0.575, 0.600, 0.625, 0.650, 0.6577	35
	BRCA-E10c	E10c	BRCA-5	0.005, 0.010, 0.015, 0.020, 0.025, 0.030, 0.035, 0.040, 0.045, 0.050, 0.075, 0.100, 0.125, 0.150, 0.175, 0.200, 0.225, 0.250, 0.275, 0.300, 0.325, 0.350, 0.375, 0.400, 0.425, 0.450, 0.475, 0.500, 0.525, 0.550, 0.575, 0.5831	32
	BRCA-E7c	E7c	BRCA-6	0.005, 0.010, 0.015, 0.020, 0.025, 0.030, 0.035, 0.040, 0.045, 0.050, 0.075, 0.100, 0.125, 0.150, 0.175, 0.200, 0.225, 0.250, 0.275, 0.300, 0.325, 0.350, 0.375, 0.400, 0.425, 0.450, 0.475, 0.500, 0.5076	29
	BRCA-E8c	E8c	BRCA-7	0.005, 0.010, 0.015, 0.020, 0.025, 0.030, 0.035, 0.040, 0.045, 0.050, 0.075, 0.100, 0.125, 0.150, 0.175, 0.200, 0.225, 0.250, 0.275, 0.300, 0.325, 0.350, 0.375, 0.400, 0.425, 0.450, 0.475, 0.500, 0.525, 0.5356	30

Table S2 (continued)

test set CRC	1279	1279_221015	CRC-9	0.005, 0.010, 0.015, 0.020, 0.025, 0.030, 0.035, 0.040, 0.045, 0.050, 0.075, 0.100, 0.125, 0.150, 0.175, 0.200, 0.225, 0.250, 0.275, 0.300, 0.325, 0.350, 0.375, 0.400, 0.425, 0.450, 0.475, 0.500	28
	1279	1279_241116	CRC-10	0.005, 0.010, 0.015, 0.020, 0.025, 0.030, 0.035, 0.040, 0.045, 0.050, 0.075, 0.100, 0.125, 0.150, 0.175, 0.200, 0.225, 0.250, 0.275, 0.300, 0.325, 0.350, 0.375, 0.400, 0.425, 0.450, 0.475, 0.490	28
	512	512_051015	CRC-11	0.005, 0.010, 0.015, 0.020, 0.025, 0.030, 0.035, 0.040, 0.045, 0.050, 0.075, 0.100, 0.125, 0.150, 0.175, 0.200, 0.225, 0.250, 0.275, 0.300, 0.325, 0.350, 0.375, 0.400, 0.425, 0.450, 0.475, 0.500, 0.525, 0.550, 0.575, 0.600, 0.614	33
	512	512_130114	CRC-12	0.005, 0.010, 0.015, 0.020, 0.025, 0.030, 0.035, 0.040, 0.045, 0.050, 0.075, 0.100, 0.125, 0.150, 0.175, 0.200, 0.225, 0.250, 0.275, 0.300, 0.325, 0.350, 0.375, 0.394	24
test set BRCA	D19	D19	BRCA-8	0.005, 0.010, 0.015, 0.020, 0.025, 0.030, 0.035, 0.040, 0.045, 0.050, 0.075, 0.100, 0.125, 0.150, 0.175, 0.200, 0.225, 0.250, 0.275, 0.300, 0.325, 0.350, 0.375, 0.400, 0.425, 0.450, 0.475, 0.500, 0.525, 0.550, 0.575, 0.600, 0.625, 0.650, 0.675, 0.700, 0.725, 0.7363	38
	E2c	E2c	BRCA-9	0.005, 0.010, 0.015, 0.020, 0.025, 0.030, 0.035, 0.040, 0.045, 0.050, 0.075, 0.100, 0.125, 0.150, 0.175, 0.200, 0.225, 0.250, 0.275, 0.300, 0.325, 0.350, 0.375, 0.400, 0.4122	25
	E6c	E6c	BRCA-10	0.005, 0.010, 0.015, 0.020, 0.025, 0.030, 0.035, 0.040, 0.045, 0.050, 0.075, 0.100, 0.125, 0.150, 0.175, 0.200, 0.225, 0.250, 0.275, 0.300, 0.325, 0.350, 0.375, 0.400, 0.425, 0.450, 0.475, 0.500, 0.525, 0.5386	30

Table S3. Information on all candidate features of nucleosome-depleted regions for colorectal cancer.

Columns
ID: feature index
Transcript: transcript ID
Gene: gene name
Chr: chromosome
Site: coordinate of nucleosome-depleted site (GRCh37)
Region: location of nucleosome-depleted site
Group: gene group based on its expression in blood and tumor
$FPKM_{blood}$: FPKM value in normal blood
$FPKM_{tumor}$: FPKM value in tumor of colorectal cancer

ID	Transcript	Gene	Chr	Site	Region	Group	$FPKM_{blood}$	$FPKM_{tumor}$
1	ENST00000003084.10	CFTR	7	117120017	promoter	tumor	0.00	30.20
2	ENST00000027335.7	CDH17	8	95220815	promoter	tumor	0.00	149.83
3	ENST00000161006.7	PRSS22	16	2908171	promoter	tumor	0.00	10.29
4	ENST00000162330.9	BCAR1	16	75285507	promoter	tumor	0.00	16.86
5	ENST00000201586.6	SULT2B1	19	49055332	promoter	tumor	0.03	16.67
6	ENST00000211314.4	TMEM14A	6	52535907	promoter	tumor	0.67	25.17
7	ENST00000215582.7	MISP	19	751126	promoter	tumor	0.00	116.54
8	ENST00000215743.7	MMP11	22	24115006	promoter	tumor	0.08	42.41
9	ENST00000216968.4	PROCR	20	33759876	promoter	tumor	0.36	28.48
10	ENST00000221992.10	CEACAM5	19	42212537	promoter	tumor	0.00	1235.90
11	ENST00000223271.7	RARRES2	7	150038763	promoter	tumor	0.41	46.30
12	ENST00000226230.7	TMEM97	17	26646121	promoter	tumor	0.39	20.84
13	ENST00000226760.5	WFS1	4	6271577	promoter	tumor	0.35	15.01
14	ENST00000227868.8	PDHX	11	34938119	promoter	tumor	0.99	13.52
15	ENST00000228916.6	SCNN1A	12	6484715	promoter	tumor	0.05	32.36
16	ENST00000230588.8	MEP1A	6	46761127	promoter	tumor	0.00	21.95
17	ENST00000232458.9	ECT2	3	172468472	promoter	tumor	0.28	12.07
18	ENST00000245451.8	BMP4	14	54423529	promoter	tumor	0.00	16.43
19	ENST00000245907.10	C3	19	6720693	promoter	tumor	0.37	15.08
20	ENST00000250405.9	BCL2L2	14	23775971	promoter	tumor	1.00	11.63
21	ENST00000254260.7	RHPN2	19	33555794	promoter	tumor	0.03	23.49
22	ENST00000255681.6	MACROD1	11	63933533	promoter	tumor	0.54	22.18
23	ENST00000256585.9	REG4	1	120354283	promoter	tumor	0.09	37.82
24	ENST00000256951.9	EMP1	12	13349650	promoter	tumor	0.39	14.17
25	ENST00000260227.4	MMP7	11	102401484	promoter	tumor	0.00	29.38
26	ENST00000261769.9	CDH1	16	68771128	promoter	tumor	0.00	123.30
27	ENST00000262429.8	ATP2C2	16	84402133	promoter	tumor	0.34	16.47
28	ENST00000262753.8	POF1B	X	84634748	promoter	tumor	0.02	40.41
29	ENST00000263629.8	MTIF2	2	55496384	promoter	tumor	0.85	13.76
30	ENST00000263735.8	EPCAM	2	47596287	promoter	tumor	0.11	594.54
31	ENST00000263895.8	RND3	2	151344208	promoter	tumor	0.00	10.29
32	ENST00000264144.4	LAMC2	1	183155423	promoter	tumor	0.01	31.46
33	ENST00000264748.6	FGFRL1	4	1006239	promoter	tumor	0.82	17.03
34	ENST00000266980.8	SLC39A5	12	56624436	promoter	tumor	0.00	20.87
35	ENST00000267101.7	ERBB3	12	56473645	promoter	tumor	0.00	40.98
36	ENST00000267814.13	SORD	15	45315302	promoter	tumor	0.93	13.70

37	ENST00000267996.11	TPM1	15	63334957	promoter	tumor	0.87	32.98
38	ENST00000269571.9	ERBB2	17	37856333	promoter	tumor	0.00	11.47
39	ENST00000270560.3	TM4SF5	17	4675187	promoter	tumor	0.00	18.39
40	ENST00000271064.11	TINAGL1	1	32042136	promoter	tumor	0.10	42.75
41	ENST00000278559.7	CAPN5	11	76777988	promoter	tumor	0.52	27.31
42	ENST00000278937.6	MPZL2	11	118134997	promoter	tumor	0.37	17.05
43	ENST00000288937.6	MRPL17	11	6704632	promoter	tumor	0.85	16.44
44	ENST00000290130.3	MIS18A	21	33651380	promoter	tumor	0.49	12.76
45	ENST00000290913.7	CHCHD6	3	126423063	promoter	tumor	0.65	15.07
46	ENST00000291525.11	TFF3	21	43735463	promoter	tumor	0.00	209.02
47	ENST00000292401.8	AZGP1	7	99573780	promoter	tumor	0.14	45.24
48	ENST00000292408.8	FGFR4	5	176513887	promoter	tumor	0.07	25.86
49	ENST00000295092.2	FAM84A	2	14772810	promoter	tumor	0.00	13.18
50	ENST00000296129.5	CDCP1	3	45187914	promoter	tumor	0.11	15.27
51	ENST00000296252.8	LIPH	3	185270401	promoter	tumor	0.03	12.23
52	ENST00000296424.8	BDH2	4	104021040	promoter	tumor	0.99	14.16
53	ENST00000296666.12	PRRC1	5	126853301	promoter	tumor	0.95	11.62
54	ENST00000297205.6	STEAP1	7	89783689	promoter	tumor	0.00	14.91
55	ENST00000299610.4	MFAP4	17	19290553	promoter	tumor	0.39	15.19
56	ENST00000299714.7	SEC11C	18	56807107	promoter	tumor	0.62	11.38
57	ENST00000300119.7	MYO1A	12	57443901	promoter	tumor	0.00	15.11
58	ENST00000300283.10	CKMT1B	15	43885252	promoter	tumor	0.00	35.88
59	ENST00000300557.2	PRR15L	17	46035244	promoter	tumor	0.03	96.21
60	ENST00000301395.7	GGT6	17	4463876	promoter	tumor	0.00	16.81
61	ENST00000301887.8	BATF2	11	64764517	promoter	tumor	0.43	11.12
62	ENST00000307078.9	AXIN2	17	63557765	promoter	tumor	0.09	14.10
63	ENST00000308302.3	GOLT1A	1	204183220	promoter	tumor	0.03	12.22
64	ENST00000308631.6	RHOD	11	66824289	promoter	tumor	0.07	10.41
65	ENST00000310398.6	AGR3	7	16921611	promoter	tumor	0.00	33.08
66	ENST00000310706.9	JUP	17	39942950	promoter	tumor	0.87	86.21
67	ENST00000310836.10	UGT8	4	115519611	promoter	tumor	0.04	14.08
68	ENST00000311160.13	TNS3	7	47621742	promoter	tumor	0.68	16.18
69	ENST00000311381.7	C6orf203	6	107349417	promoter	tumor	0.93	14.55
70	ENST00000311620.6	ANKS4B	16	21244986	promoter	tumor	0.00	10.61
71	ENST00000316673.8	HNF4A	20	42984340	promoter	tumor	0.00	10.78
72	ENST00000317508.10	PRSS8	16	31147083	promoter	tumor	0.11	143.22
73	ENST00000318024.8	USH1C	11	17565963	promoter	tumor	0.00	46.62
74	ENST00000318407.4	BOK	2	242498136	promoter	tumor	0.57	13.75
75	ENST00000318443.9	CD276	15	73976554	promoter	tumor	0.00	11.45
76	ENST00000318683.6	B3GNT3	19	17905919	promoter	tumor	0.00	57.75
77	ENST00000319838.9	GPR35	2	241544848	promoter	tumor	0.31	30.59
78	ENST00000322536.7	DDX10	11	108535752	promoter	tumor	0.75	10.84
79	ENST00000324038.6	FAM101A	12	124773710	promoter	tumor	0.00	10.08
80	ENST00000325307.11	HMGB3	X	150151759	promoter	tumor	0.30	14.09
81	ENST00000325568.9	IL32	16	3115298	promoter	tumor	0.93	14.52
82	ENST00000326587.11	MAGED1	X	51636698	promoter	tumor	0.60	16.14
83	ENST00000329875.12	PYCR1	17	79894755	promoter	tumor	0.12	36.33
84	ENST00000331243.4	FAM84A	2	14772824	promoter	tumor	0.01	33.07
85	ENST00000331595.8	BGN	X	152760397	promoter	tumor	0.60	74.92
86	ENST00000332149.9	TMPRSS2	21	42880086	promoter	tumor	0.02	43.57
87	ENST00000333090.4	TSKU	11	76494283	promoter	tumor	0.00	17.21
88	ENST00000334047.11	F3	1	95007356	promoter	tumor	0.08	13.07

89	ENST00000334869.8	LGMN	14	93215047	promoter	tumor	0.94	45.73
90	ENST00000337682.8	FAM60A	12	31479306	promoter	tumor	0.97	25.73
91	ENST00000338660.5	VWA1	1	1370903	promoter	tumor	0.06	21.82
92	ENST00000339276.5	SFN	1	27189629	promoter	tumor	0.60	113.82
93	ENST00000340556.10	MORN2	2	39103103	promoter	tumor	0.33	11.41
94	ENST00000344616.3	S100A14	1	153568808	promoter	tumor	0.00	143.55
95	ENST00000350051.7	BIRC5	17	76210279	promoter	tumor	0.63	18.32
96	ENST00000352551.9	UBE2C	20	44441313	promoter	tumor	0.00	10.99
97	ENST00000354624.5	HKDC1	10	70980059	promoter	tumor	0.14	20.07
98	ENST00000354900.7	LSR	19	35739675	promoter	tumor	0.75	31.22
99	ENST00000355097.6	ENTPD2	9	139948497	promoter	tumor	0.03	10.14
100	ENST00000355808.9	PDHA1	X	19362068	promoter	tumor	0.25	16.21
101	ENST00000355899.7	PLS3	X	114795509	promoter	tumor	0.00	12.05
102	ENST00000356509.7	GMNN	6	24775159	promoter	tumor	0.57	11.97
103	ENST00000356762.7	CRB3	19	6464294	promoter	tumor	0.00	12.29
104	ENST00000357166.10	ZDHHC9	X	128977860	promoter	tumor	0.29	20.11
105	ENST00000357602.7	IPO5	13	98612503	promoter	tumor	0.80	15.40
106	ENST00000358278.7	TPM1	15	63334884	promoter	tumor	0.43	69.53
107	ENST00000358432.7	EPHA2	1	16482582	promoter	tumor	0.03	23.85
108	ENST00000358813.4	CCL20	2	228678570	promoter	tumor	0.00	33.26
109	ENST00000358867.10	TMEM126B	11	85339629	promoter	tumor	0.47	17.68
110	ENST00000360325.11	CLDN7	17	7165797	promoter	tumor	0.09	133.65
111	ENST00000360605.8	URI1	19	30414551	promoter	tumor	0.44	12.86
112	ENST00000360760.9	SPATS2L	2	201171247	promoter	tumor	0.73	32.04
113	ENST00000360779.3	SDCBP2	20	1309883	promoter	tumor	0.00	17.84
114	ENST00000360798.7	LSR	19	35739668	promoter	tumor	0.30	55.63
115	ENST00000361084.9	RAB25	1	156030951	promoter	tumor	0.07	131.50
116	ENST00000361852.8	EPS8L3	1	110306546	promoter	tumor	0.00	26.64
117	ENST00000361901.6	CALD1	7	134464429	promoter	tumor	0.42	33.93
118	ENST00000366787.7	THBS2	6	169654139	promoter	tumor	0.07	14.23
119	ENST00000366999.8	NEK2	1	211848960	promoter	tumor	0.16	11.93
120	ENST00000367274.8	UBE2T	1	202311108	promoter	tumor	0.63	29.13
121	ENST00000367283.7	ELF3	1	201979715	promoter	tumor	0.07	135.46
122	ENST00000367284.9	ELF3	1	201979645	promoter	tumor	0.02	50.55
123	ENST00000367313.4	LAD1	1	201368676	promoter	tumor	0.05	100.09
124	ENST00000367976.3	CTGF	6	132272513	promoter	tumor	0.32	44.18
125	ENST00000368408.3	EFNA3	1	155051348	promoter	tumor	0.36	18.08
126	ENST00000368554.8	PRAP1	10	135122914	promoter	tumor	0.00	32.41
127	ENST00000369406.7	HMGCS2	1	120311517	promoter	tumor	0.00	17.63
128	ENST00000370481.8	GBP3	1	89488565	promoter	tumor	0.66	12.56
129	ENST00000370828.3	GPC4	X	132549518	promoter	tumor	0.03	13.27
130	ENST00000371221.3	ALDH18A1	10	97416463	promoter	tumor	0.04	29.55
131	ENST00000372486.5	NTMT1	9	132371163	promoter	tumor	0.00	14.12
132	ENST00000372966.7	NOX1	X	100129334	promoter	tumor	0.00	48.52
133	ENST00000373255.8	H2AFY2	10	71812552	promoter	tumor	0.42	12.60
134	ENST00000373290.6	TSPAN15	10	71211229	promoter	tumor	0.30	60.96
135	ENST00000373669.6	PIN4	X	71401529	promoter	tumor	0.87	13.81
136	ENST00000373699.5	PPIL1	6	36842800	promoter	tumor	0.85	17.26
137	ENST00000373944.7	ZWINT	10	58121036	promoter	tumor	0.38	16.27
138	ENST00000374183.4	BSPRY	9	116111821	promoter	tumor	0.22	15.59
139	ENST00000374214.3	UQCC2	6	33679504	promoter	tumor	1.00	17.77
140	ENST00000374837.7	MAP1LC3A	20	33134658	promoter	tumor	0.87	16.45

141	ENST00000375431.8	GRTP1	13	114018441	promoter	tumor	0.05	18.16
142	ENST00000376569.7	DDR1	6	30851846	promoter	tumor	0.08	11.00
143	ENST00000376652.8	ENTPD6	20	25176356	promoter	tumor	0.44	14.06
144	ENST00000378115.2	ARHGEF35	7	143892748	promoter	tumor	0.10	13.16
145	ENST00000378378.8	ARHGEF16	1	3370990	promoter	tumor	0.00	12.12
146	ENST00000378427.5	FAM213B	1	2516237	promoter	tumor	0.59	12.06
147	ENST00000379046.6	NQO1	16	69760487	promoter	tumor	0.07	39.35
148	ENST00000379047.7	NQO1	16	69760571	promoter	tumor	0.09	34.23
149	ENST00000379715.9	EEF1E1	6	8102811	promoter	tumor	0.59	17.82
150	ENST00000379742.4	POSTN	13	38172895	promoter	tumor	0.01	11.69
151	ENST00000379805.3	PDHA1	X	19362086	promoter	tumor	0.76	11.58
152	ENST00000379923.5	ACO1	9	32384618	promoter	tumor	0.81	16.28
153	ENST00000380071.7	RFC3	13	34392186	promoter	tumor	0.48	15.11
154	ENST00000381134.7	ARSE	X	2882311	promoter	tumor	0.00	24.51
155	ENST00000382648.4	GJB2	13	20767037	promoter	tumor	0.09	18.88
156	ENST00000389614.5	GPX2	14	65409531	promoter	tumor	0.10	652.10
157	ENST00000391967.6	LAD1	1	201368736	promoter	tumor	0.00	16.64
158	ENST00000393316.7	BCL2L15	1	114430169	promoter	tumor	0.11	11.11
159	ENST00000393366.6	ATP5G1	17	46970179	promoter	tumor	0.63	40.08
160	ENST00000393725.6	KIAA1191	5	175788768	promoter	tumor	0.75	11.70
161	ENST00000394201.8	SCOC	4	141294797	promoter	tumor	0.53	14.61
162	ENST00000394265.5	PPP1R1B	17	37784751	promoter	tumor	0.00	81.30
163	ENST00000395641.2	NUPR1	16	28550329	promoter	tumor	0.45	37.05
164	ENST00000397542.6	CDHR5	11	625067	promoter	tumor	0.02	18.38
165	ENST00000397714.6	SEPTIN10	2	110371504	promoter	tumor	0.14	14.96
166	ENST00000397995.2	RNASE4	14	21152742	promoter	tumor	0.56	10.20
167	ENST00000398599.8	CEACAM5	19	42212504	promoter	tumor	0.00	74.52
168	ENST00000401412.5	AGR2	7	16844611	promoter	tumor	0.00	103.38
169	ENST00000403444.7	CEACAM1	19	43032630	promoter	tumor	0.00	33.67
170	ENST00000405271.5	EPCAM	2	47572297	promoter	tumor	0.00	20.99
171	ENST00000405816.5	CEACAM5	19	42212568	promoter	tumor	0.00	10.92
172	ENST00000409189.7	CCL20	2	228678558	promoter	tumor	0.00	20.73
173	ENST00000410036.2	MZT2A	2	132250316	promoter	tumor	0.00	12.64
174	ENST00000416348.1	ADIRF	10	88728189	promoter	tumor	0.00	22.43
175	ENST00000419304.6	AGR2	7	16844704	promoter	tumor	0.00	257.72
176	ENST00000419308.6	FOXA2	20	22565101	promoter	tumor	0.00	13.51
177	ENST00000420892.1	HTRA1	10	124266207	promoter	tumor	0.98	24.46
178	ENST00000423485.5	TOP2A	17	38574202	promoter	tumor	0.44	31.06
179	ENST00000425042.6	HID1	17	72968829	promoter	tumor	0.23	13.99
180	ENST00000425340.2	FUT2	19	49199232	promoter	tumor	0.02	13.10
181	ENST00000427250.5	LSR	19	35739905	promoter	tumor	0.00	13.66
182	ENST00000428445.1	VARS	6	31750366	promoter	tumor	0.78	10.22
183	ENST00000428849.6	KIFC1	6	33359313	promoter	tumor	0.60	17.24
184	ENST00000429772.6	TMEM106C	12	48357403	promoter	tumor	0.70	34.02
185	ENST00000430118.1	HMGB3	X	150154004	promoter	tumor	0.52	12.82
186	ENST00000433307.2	PLEKHA1	10	124152644	promoter	tumor	0.98	13.38
187	ENST00000439109.6	NQO1	16	69760463	promoter	tumor	0.00	10.97
188	ENST00000440815.7	IL32	16	3115370	promoter	tumor	0.34	22.19
189	ENST00000441275.5	BDH1	3	197282858	promoter	tumor	0.87	17.80
190	ENST00000444124.6	DDC	7	50633154	promoter	tumor	0.00	21.66
191	ENST00000446188.1	ELF3	1	201979772	promoter	tumor	0.00	13.93
192	ENST00000448599.2	PHGR1	15	40643234	promoter	tumor	0.00	289.14

193	ENST00000450427.1	PRR15	7	29605066	promoter	tumor	0.00	10.59
194	ENST00000450894.7	ITGB4	17	73717577	promoter	tumor	0.14	50.86
195	ENST00000452441.5	DDR1	6	30852327	promoter	tumor	0.07	51.62
196	ENST00000455712.5	POLR2H	3	184080403	promoter	tumor	0.94	11.92
197	ENST00000463201.2	PRAP1	10	135164879	promoter	tumor	0.00	54.46
198	ENST00000467415.5	TMEM14C	6	10723358	promoter	tumor	0.69	26.73
199	ENST00000467905.5	AK2	1	33502487	promoter	tumor	0.00	11.87
200	ENST00000469862.1	CENPF	1	214828491	promoter	tumor	0.39	10.26
201	ENST00000472782.1	ATP5G3	2	176046423	promoter	tumor	0.62	10.87
202	ENST00000473336.5	RAB25	1	156031174	promoter	tumor	0.00	17.65
203	ENST00000476587.1	NDUFB5	3	179334763	promoter	tumor	0.89	14.92
204	ENST00000478194.1	FERMT1	20	6074819	promoter	tumor	0.00	27.00
205	ENST00000478869.1	WDR12	2	203765843	promoter	tumor	0.71	14.50
206	ENST00000479419.1	IFT172	2	27669072	promoter	tumor	0.00	37.10
207	ENST00000484713.1	LAMB2	3	49159029	promoter	tumor	0.41	13.87
208	ENST00000489477.1	NDUFAF4	6	97345750	promoter	tumor	0.66	10.30
209	ENST00000489523.5	AGR2	7	16844623	promoter	tumor	0.00	64.63
210	ENST00000490807.5	NTPCR	1	233086360	promoter	tumor	0.77	10.54
211	ENST00000494163.1	IFT172	2	27669063	promoter	tumor	0.00	11.52
212	ENST00000494446.1	FN1	2	216230399	promoter	tumor	0.79	52.10
213	ENST00000494801.5	TCEAL4	X	102840491	promoter	tumor	0.60	13.59
214	ENST00000495558.1	VWA1	1	1370241	promoter	tumor	0.00	13.92
215	ENST00000495848.1	ELF3	1	201979722	promoter	tumor	0.00	17.88
216	ENST00000496195.1	GLRX3	10	131977638	promoter	tumor	0.98	10.30
217	ENST00000497734.5	SRC	20	35973088	promoter	tumor	0.00	12.44
218	ENST00000507614.1	TIMM8B	11	111957446	promoter	tumor	0.80	10.54
219	ENST00000507699.1	PALLD	4	169819128	promoter	tumor	0.31	14.56
220	ENST00000514985.5	SEPP1	5	42812181	promoter	tumor	0.59	49.95
221	ENST00000520271.5	COX6C	8	100905850	promoter	tumor	0.51	12.86
222	ENST00000523677.5	C1orf210	1	43751250	promoter	tumor	0.00	13.49
223	ENST00000524832.5	CHID1	11	902322	promoter	tumor	0.42	10.82
224	ENST00000525657.1	C1QTNF5	11	119211508	promoter	tumor	0.05	17.27
225	ENST00000526202.5	LMO7	13	76334795	promoter	tumor	0.09	23.11
226	ENST00000527020.5	USH1C	11	17565947	promoter	tumor	0.00	10.90
227	ENST00000527106.5	FUT6	19	5836771	promoter	tumor	0.00	13.22
228	ENST00000528430.2	PPP1R16A	8	145726472	promoter	tumor	0.92	22.33
229	ENST00000530094.5	CTNND1	11	57529269	promoter	tumor	0.00	26.61
230	ENST00000532203.1	MRPL17	11	6704547	promoter	tumor	0.65	21.73
231	ENST00000533827.5	VPS51	11	64876763	promoter	tumor	0.00	12.01
232	ENST00000534378.5	ILVBL	19	15236533	promoter	tumor	0.64	11.41
233	ENST00000537496.5	MMAB	12	110011308	promoter	tumor	0.93	12.43
234	ENST00000541754.1	NNMT	11	114168085	promoter	tumor	0.72	23.55
235	ENST00000542056.1	GPRC5A	12	13044513	promoter	tumor	0.00	23.91
236	ENST00000543445.5	LDHA	11	18416107	promoter	tumor	0.00	71.47
237	ENST00000543623.5	PLCD3	17	43192496	promoter	tumor	0.27	14.58
238	ENST00000544913.2	HMGCS2	1	120311528	promoter	tumor	0.03	21.61
239	ENST00000546314.5	STARD10	11	72493404	promoter	tumor	0.00	31.66
240	ENST00000546485.5	RPL41	12	56510416	promoter	tumor	0.75	48.15
241	ENST00000547281.5	CDK4	12	58146059	promoter	tumor	0.83	30.31
242	ENST00000547838.2	FAM109A	12	111801553	promoter	tumor	0.94	11.49
243	ENST00000548169.2	ATP2A2	12	110729854	promoter	tumor	0.34	13.63
244	ENST00000552128.2	TSPAN8	12	71533055	promoter	tumor	0.00	15.81

245	ENST00000552561.5	TMEM106C	12	48357388	promoter	tumor	0.38	17.25
246	ENST00000553237.5	CDK4	12	58146109	promoter	tumor	0.06	16.39
247	ENST00000554989.1	CKB	14	103987659	promoter	tumor	0.75	83.82
248	ENST00000557049.1	GPX2	14	65409438	promoter	tumor	0.00	18.28
249	ENST00000558580.1	SORD	15	45328434	promoter	tumor	0.95	15.73
250	ENST00000561504.1	ADIRF	10	88728247	promoter	tumor	0.75	46.05
251	ENST00000562684.5	HN1L	16	1728278	promoter	tumor	0.25	19.21
252	ENST00000581920.1	TYMS	18	667721	promoter	tumor	0.88	11.79
253	ENST00000583327.2	ITGB4	17	73747894	promoter	tumor	0.12	32.84
254	ENST00000586005.5	SMIM22	16	4845422	promoter	tumor	0.00	103.03
255	ENST00000587251.5	LGALS3BP	17	76976005	promoter	tumor	0.00	48.36
256	ENST00000588605.5	C19orf33	19	38794804	promoter	tumor	0.22	18.46
257	ENST00000588606.5	SMIM22	16	4845379	promoter	tumor	0.00	148.57
258	ENST00000589378.5	TJP3	19	3721735	promoter	tumor	0.13	11.74
259	ENST00000591778.5	LGALS3BP	17	76976000	promoter	tumor	0.21	30.24
260	ENST00000591795.1	DENND1C	19	6469662	promoter	tumor	0.56	11.26
261	ENST00000594443.5	FBL	19	40337010	promoter	tumor	0.00	19.57
262	ENST00000594605.5	STAP2	19	4338874	promoter	tumor	0.06	27.33
263	ENST00000595110.1	FAM83E	19	49118098	promoter	tumor	0.00	13.13
264	ENST00000597153.5	LGALS4	19	39303585	promoter	tumor	0.00	20.51
265	ENST00000600229.5	CRB3	19	6464290	promoter	tumor	0.08	20.31
266	ENST00000600324.5	STAP2	19	4338818	promoter	tumor	0.02	13.85
267	ENST00000601623.5	LSR	19	35740250	promoter	tumor	0.21	24.39
268	ENST00000605618.5	LSR	19	35739922	promoter	tumor	0.22	31.85
269	ENST00000610552.4	SLC2A8	9	130159417	promoter	tumor	0.65	11.38
270	ENST00000612794.1	GPX2	14	65409623	promoter	tumor	0.00	23.73
271	ENST00000612809.4	C8orf59	8	86132604	promoter	tumor	0.94	54.53
272	ENST00000616154.1	CDX1	5	149546453	promoter	tumor	0.00	138.07
273	ENST00000616727.4	MUC13	3	124653595	promoter	tumor	0.01	221.05
274	ENST00000618855.4	TMPRSS4	11	117947727	promoter	tumor	0.00	10.45
275	ENST00000619895.4	TMC4	19	54676865	promoter	tumor	0.35	33.05
276	ENST00000620753.4	EI24	11	125439354	promoter	tumor	0.63	12.17
277	ENST00000008938.4	PGLYRP1	19	46526323	promoter	blood	148.76	0.05
278	ENST00000199708.2	HBQ1	16	230452	promoter	blood	45.79	0.00
279	ENST00000216338.8	GZMH	14	25078864	promoter	blood	15.58	0.99
280	ENST00000221515.5	RETN	19	7733930	promoter	blood	72.49	0.19
281	ENST00000221954.6	CEACAM4	19	42133442	promoter	blood	32.81	0.13
282	ENST00000225538.3	P2RX1	17	3819794	promoter	blood	15.55	0.30
283	ENST00000232014.8	BCL6	3	187454357	promoter	blood	19.07	0.18
284	ENST00000234347.9	PRTN3	19	840960	promoter	blood	13.78	0.00
285	ENST00000236826.7	MMP8	11	102595685	promoter	blood	20.68	0.04
286	ENST00000244709.8	TREM1	6	41254457	promoter	blood	67.12	0.63
287	ENST00000246115.4	S1PR4	19	3178766	promoter	blood	127.44	0.94
288	ENST00000246549.2	FFAR2	19	35940617	promoter	blood	58.85	0.34
289	ENST00000246657.2	CCR7	17	38721724	promoter	blood	11.89	0.75
290	ENST00000259396.8	ORM1	9	117085336	promoter	blood	34.89	0.14
291	ENST00000262407.5	ITGA2B	17	42466873	promoter	blood	12.34	0.04
292	ENST00000264972.9	ZAP70	2	98330023	promoter	blood	15.69	0.72
293	ENST00000279452.10	CD44	11	35198175	promoter	blood	10.76	0.00
294	ENST00000281703.10	GLT1D1	12	129338081	promoter	blood	22.75	0.02
295	ENST00000290075.10	SLC25A37	8	23386469	promoter	blood	45.08	0.87
296	ENST00000292432.9	HK3	5	176326333	promoter	blood	98.07	0.60

297	ENST00000295683.2	CXCR1	2	219031718	promoter	blood	355.57	0.18
298	ENST00000296435.2	CAMP	3	48264837	promoter	blood	27.17	0.06
299	ENST00000296487.8	PPM1M	3	52280186	promoter	blood	13.09	0.41
300	ENST00000297239.10	SYTL3	6	159082351	promoter	blood	10.79	0.54
301	ENST00000299663.7	CLEC4E	12	8693559	promoter	blood	29.27	0.20
302	ENST00000302017.3	ZNF467	7	149470568	promoter	blood	25.10	0.54
303	ENST00000303531.11	PRKCB	16	23847345	promoter	blood	16.08	0.36
304	ENST00000303757.12	LST1	6	31554977	promoter	blood	11.09	0.23
305	ENST00000307564.8	AKNA	9	117156685	promoter	blood	11.95	0.38
306	ENST00000310544.8	PHOSPHO1	17	47307890	promoter	blood	30.92	0.08
307	ENST00000318507.6	CXCR2	2	218990727	promoter	blood	157.27	0.28
308	ENST00000326165.10	CD300LF	17	72709117	promoter	blood	18.99	0.70
309	ENST00000328118.7	FMNL1	17	43299444	promoter	blood	11.80	0.41
310	ENST00000329021.9	NFAM1	22	42828401	promoter	blood	43.63	0.94
311	ENST00000329410.3	C16orf54	16	29757327	promoter	blood	24.31	0.49
312	ENST00000332549.7	IL1R2	2	102608306	promoter	blood	112.29	0.55
313	ENST00000334475.10	TREM1	6	41254420	promoter	blood	11.13	0.19
314	ENST00000336577.8	MMP25	16	3096682	promoter	blood	194.37	0.54
315	ENST00000336906.4	HBG2	11	5276041	promoter	blood	104.85	0.00
316	ENST00000338372.6	VSTM1	19	54567207	promoter	blood	10.71	0.00
317	ENST00000342571.7	MKNK1	1	47051643	promoter	blood	14.42	0.02
318	ENST00000343534.9	C1orf162	1	112016414	promoter	blood	37.68	0.74
319	ENST00000346667.8	IKZF1	7	50344378	promoter	blood	11.73	0.24
320	ENST00000352818.8	CD44	11	35160851	promoter	blood	14.11	0.00
321	ENST00000354352.9	SLC11A1	2	219246971	promoter	blood	111.80	0.63
322	ENST00000355524.7	FCAR	19	55385736	promoter	blood	53.04	0.07
323	ENST00000356815.3	HBM	16	215977	promoter	blood	163.82	0.00
324	ENST00000356838.7	TMEM71	8	133772828	promoter	blood	16.78	0.36
325	ENST00000356864.3	TNFRSF10C	8	22960103	promoter	blood	108.86	0.56
326	ENST00000357198.8	DOK3	5	176936858	promoter	blood	66.68	0.74
327	ENST00000357260.5	FAM212B	1	112282046	promoter	blood	12.23	0.67
328	ENST00000358375.8	OSCAR	19	54604129	promoter	blood	18.93	0.28
329	ENST00000367025.7	TRAF3IP3	1	209929394	promoter	blood	17.52	0.64
330	ENST00000367053.5	CR1	1	207669502	promoter	blood	10.47	0.02
331	ENST00000367535.7	NCF2	1	183559716	promoter	blood	75.23	0.98
332	ENST00000367568.4	STX11	6	144471663	promoter	blood	24.42	0.79
333	ENST00000367972.8	FCGR2A	1	161475220	promoter	blood	27.69	0.40
334	ENST00000368015.1	ARHGAP30	1	161039760	promoter	blood	20.61	0.58
335	ENST00000368732.5	S100A8	1	153363452	promoter	blood	53.91	0.00
336	ENST00000368737.4	S100A12	1	153348125	promoter	blood	1099.02	0.31
337	ENST00000371806.3	FCN1	9	137809809	promoter	blood	379.64	0.88
338	ENST00000373103.5	CSF3R	1	36948879	promoter	blood	61.20	0.04
339	ENST00000373925.5	THEMIS2	1	28199055	promoter	blood	12.15	0.53
340	ENST00000374005.7	FGR	1	27961788	promoter	blood	32.42	0.29
341	ENST00000374163.5	RPS6KA1	1	26872333	promoter	blood	17.41	0.87
342	ENST00000375448.4	PADI4	1	17634692	promoter	blood	95.04	0.03
343	ENST00000375862.6	HCK	20	30640000	promoter	blood	20.11	0.09
344	ENST00000376670.7	GATA1	X	48644962	promoter	blood	11.17	0.01
345	ENST00000377497.7	RASGRP2	11	64512306	promoter	blood	48.02	0.55
346	ENST00000378023.8	FAM65B	6	24877583	promoter	blood	15.67	0.00
347	ENST00000379400.7	RASSF2	20	4804291	promoter	blood	13.75	0.82
348	ENST00000380299.3	HBD	11	5255878	promoter	blood	138.84	0.07

349	ENST00000381112.7	CCM2	7	45067233	promoter	blood	17.78	0.00
350	ENST00000381153.7	C11orf21	11	2323290	promoter	blood	11.33	0.09
351	ENST00000381603.7	SIRPB1	20	1600642	promoter	blood	26.01	0.00
352	ENST00000381605.8	SIRPB1	20	1600655	promoter	blood	24.72	0.12
353	ENST00000391750.5	LILRB3	19	54727378	promoter	blood	65.61	0.41
354	ENST00000391761.5	OSCAR	19	54604083	promoter	blood	35.99	0.46
355	ENST00000393450.5	MYL4	17	45286714	promoter	blood	22.77	0.00
356	ENST00000393847.5	DPEP2	16	68033356	promoter	blood	24.04	0.44
357	ENST00000394991.7	SNCA	4	90758379	promoter	blood	32.19	0.35
358	ENST00000397147.6	NCF4	22	37257030	promoter	blood	154.32	0.92
359	ENST00000398421.6	NCF1	7	74188358	promoter	blood	11.04	0.04
360	ENST00000399173.5	FGR	1	27952751	promoter	blood	101.05	0.26
361	ENST00000399753.2	MSRB1	16	1993196	promoter	blood	11.22	0.15
362	ENST00000409220.5	ARHGAP25	2	69001933	promoter	blood	23.89	0.31
363	ENST00000409930.3	IL1RN	2	113885138	promoter	blood	21.18	0.85
364	ENST00000413580.5	PHOSPHO1	17	47308128	promoter	blood	42.76	0.05
365	ENST00000416215.6	PTPN6	12	7060519	promoter	blood	12.72	0.88
366	ENST00000418089.5	NCF2	1	183559739	promoter	blood	12.55	0.12
367	ENST00000419510.6	BCL6	3	187454876	promoter	blood	45.28	0.23
368	ENST00000422400.6	VNN2	6	133079022	promoter	blood	14.59	0.10
369	ENST00000423345.4	PRAM1	19	8567996	promoter	blood	25.32	0.30
370	ENST00000425428.6	CD44	11	35160729	promoter	blood	17.51	0.00
371	ENST00000433194.6	CDK5RAP2	9	123165730	promoter	blood	22.55	0.52
372	ENST00000434472.6	CD44	11	35160840	promoter	blood	11.65	0.58
373	ENST00000441002.1	IL1R2	2	102624977	promoter	blood	16.30	0.00
374	ENST00000442111.6	GLT1D1	12	129338039	promoter	blood	20.30	0.01
375	ENST00000445347.1	LILRB3	19	54726959	promoter	blood	49.26	0.10
376	ENST00000445961.5	RPS9	19	54704740	promoter	blood	14.72	0.89
377	ENST00000447110.5	PIK3R5	17	8869029	promoter	blood	12.89	0.29
378	ENST00000449131.6	BEST1	11	61717842	promoter	blood	13.35	0.54
379	ENST00000454703.6	ACSL1	4	185747273	promoter	blood	35.07	0.78
380	ENST00000460442.5	ZDHHC19	3	195925781	promoter	blood	22.43	0.04
381	ENST00000464431.1	ABTB1	3	127394329	promoter	blood	20.22	0.70
382	ENST00000464465.6	CSF3R	1	36937075	promoter	blood	259.11	0.50
383	ENST00000465814.5	ARAP1	11	72433133	promoter	blood	10.09	0.58
384	ENST00000465984.5	SLC11A1	2	219246911	promoter	blood	10.54	0.03
385	ENST00000467786.1	FGD3	9	95737532	promoter	blood	43.15	0.29
386	ENST00000474085.5	IL1R2	2	102638525	promoter	blood	24.35	0.04
387	ENST00000475225.5	SLC11A1	2	219247025	promoter	blood	37.49	0.19
388	ENST00000475226.1	HBB	11	5248053	promoter	blood	2709.48	0.00
389	ENST00000475472.5	FGR	1	27961645	promoter	blood	49.95	0.18
390	ENST00000477801.1	S100A8	1	153363547	promoter	blood	161.47	0.07
391	ENST00000480395.5	TRIM22	11	5717722	promoter	blood	17.36	0.70
392	ENST00000481568.2	C10orf54	10	73521701	promoter	blood	31.27	0.90
393	ENST00000483750.5	WAS	X	48542217	promoter	blood	34.49	0.17
394	ENST00000484747.5	ZNF467	7	149470308	promoter	blood	14.36	0.44
395	ENST00000485743.1	HBB	11	5248302	promoter	blood	128.52	0.00
396	ENST00000485928.5	PHC2	1	33815412	promoter	blood	11.05	0.73
397	ENST00000486097.1	NCF1	7	74197786	promoter	blood	12.51	0.06
398	ENST00000487540.6	CSF3R	1	36937988	promoter	blood	47.30	0.17
399	ENST00000488171.5	CD55	1	207495032	promoter	blood	25.43	0.43
400	ENST00000488945.5	GNLY	2	85912298	promoter	blood	11.68	0.09

401	ENST00000489358.5	NAMPT	7	105925396	promoter	blood	30.07	0.00
402	ENST00000489551.5	CSF3R	1	36948535	promoter	blood	106.01	0.10
403	ENST00000491955.5	MPP1	X	154011509	promoter	blood	10.84	0.42
404	ENST00000492413.5	SLC11A1	2	219247010	promoter	blood	17.89	0.00
405	ENST00000493242.1	LILRB2	19	54784952	promoter	blood	22.65	0.13
406	ENST00000494185.1	LMNB1	5	126147405	promoter	blood	10.53	0.00
407	ENST00000496823.1	BCL6	3	187463247	promoter	blood	21.33	0.20
408	ENST00000497259.5	ARHGAP25	2	69034363	promoter	blood	25.49	0.72
409	ENST00000497920.1	ARID5A	2	97213127	promoter	blood	11.90	0.30
410	ENST00000509314.5	FBXL5	4	15661487	promoter	blood	10.24	0.00
411	ENST00000509339.1	MXD3	5	176735063	promoter	blood	30.07	0.08
412	ENST00000510784.6	FAM65B	6	25042396	promoter	blood	61.47	0.19
413	ENST00000513001.5	ACSL1	4	185680030	promoter	blood	17.65	0.10
414	ENST00000517558.1	TNFRSF10C	8	22960434	promoter	blood	45.94	0.13
415	ENST00000519192.1	SLC25A37	8	23386488	promoter	blood	357.35	0.55
416	ENST00000520174.5	DMTN	8	21914416	promoter	blood	16.02	0.00
417	ENST00000520553.5	HCK	20	30640045	promoter	blood	87.74	0.73
418	ENST00000520654.1	SLC25A37	8	23386566	promoter	blood	18.30	0.77
419	ENST00000523022.5	CA1	8	86290342	promoter	blood	40.92	0.11
420	ENST00000523829.5	TMEM71	8	133772807	promoter	blood	11.05	0.22
421	ENST00000525270.5	VNN2	6	133084586	promoter	blood	38.37	0.12
422	ENST00000526980.5	CSF3R	1	36948500	promoter	blood	184.80	0.10
423	ENST00000527146.1	IFITM2	11	308320	promoter	blood	18.56	0.63
424	ENST00000528780.5	IFITM1	11	313506	promoter	blood	47.88	0.31
425	ENST00000529635.5	TBC1D10C	11	67171600	promoter	blood	16.89	0.34
426	ENST00000533968.1	SPI1	11	47400038	promoter	blood	12.90	0.22
427	ENST00000534862.5	HCK	20	30639991	promoter	blood	16.31	0.23
428	ENST00000535669.6	CD37	19	49838684	promoter	blood	33.70	0.19
429	ENST00000539932.5	SLC11A1	2	219246926	promoter	blood	50.32	0.02
430	ENST00000540998.5	CDC42SE1	1	151032125	promoter	blood	10.52	0.00
431	ENST00000542481.1	ATG16L2	11	72534940	promoter	blood	25.18	0.37
432	ENST00000542590.1	TBC1D10C	11	67171660	promoter	blood	43.95	0.92
433	ENST00000543576.5	DENND1C	19	6481798	promoter	blood	12.06	0.00
434	ENST00000544232.5	TMEM91	19	41882645	promoter	blood	12.57	0.20
435	ENST00000544665.7	ITGAM	16	31271315	promoter	blood	56.38	0.99
436	ENST00000546704.1	ARHGAP9	12	57868923	promoter	blood	19.20	0.13
437	ENST00000550399.5	ARHGAP9	12	57868717	promoter	blood	14.44	0.45
438	ENST00000552370.5	TMBIM6	12	50144403	promoter	blood	26.69	0.00
439	ENST00000553070.5	NFE2	12	54694799	promoter	blood	23.61	0.00
440	ENST00000558012.5	PSTPIP1	15	77287426	promoter	blood	26.47	0.31
441	ENST00000559750.5	PSTPIP1	15	77287513	promoter	blood	16.39	0.12
442	ENST00000564662.1	COTL1	16	84651681	promoter	blood	10.13	0.81
443	ENST00000564905.1	XPO6	16	28145246	promoter	blood	12.98	0.47
444	ENST00000568763.1	CORO1A	16	30194926	promoter	blood	45.17	0.63
445	ENST00000570106.6	SIGLEC5	19	52133588	promoter	blood	40.53	0.18
446	ENST00000572782.1	ARRB2	17	4617846	promoter	blood	16.63	0.33
447	ENST00000576628.1	ACAP1	17	7239916	promoter	blood	20.20	0.18
448	ENST00000577894.1	EVI2B	17	29641123	promoter	blood	14.34	0.00
449	ENST00000578067.5	LIMD2	17	61777468	promoter	blood	10.86	0.22
450	ENST00000578402.5	LIMD2	17	61778045	promoter	blood	31.49	0.77
451	ENST00000585901.6	TYROBP	19	36399149	promoter	blood	13.40	0.19
452	ENST00000586946.1	TYROBP	19	36399197	promoter	blood	23.56	0.61

453	ENST00000587259.5	VMP1	17	57807076	promoter	blood	10.58	0.05
454	ENST00000587856.1	FMNL1	17	43311251	promoter	blood	22.20	0.28
455	ENST00000588673.3	OAZ1	19	2270290	promoter	blood	24.28	0.69
456	ENST00000589614.5	TREM1	6	41254403	promoter	blood	31.20	0.54
457	ENST00000589900.5	ICAM3	19	10450305	promoter	blood	21.24	0.00
458	ENST00000592860.2	CFD	19	859664	promoter	blood	16.53	0.85
459	ENST00000595042.5	FPR1	19	52255146	promoter	blood	63.93	0.18
460	ENST00000595217.1	NKG7	19	51875955	promoter	blood	33.26	0.52
461	ENST00000595325.5	MYO1F	19	8642322	promoter	blood	13.66	0.09
462	ENST00000595636.1	GMFG	19	39826664	promoter	blood	10.44	0.68
463	ENST00000595725.5	CD37	19	49838657	promoter	blood	20.04	0.12
464	ENST00000595840.1	LRRC25	19	18508421	promoter	blood	36.84	0.88
465	ENST00000596426.5	CD37	19	49838691	promoter	blood	55.55	0.57
466	ENST00000596764.5	VAV1	19	6772739	promoter	blood	12.25	0.59
467	ENST00000597852.5	CD37	19	49838675	promoter	blood	13.98	0.20
468	ENST00000598034.5	GMFG	19	39826646	promoter	blood	43.77	0.45
469	ENST00000599180.2	FFAR2	19	35939203	promoter	blood	24.79	0.00
470	ENST00000599716.5	SHKBP1	19	41082793	promoter	blood	10.66	0.22
471	ENST00000600626.1	C5AR2	19	47840371	promoter	blood	12.99	0.11
472	ENST00000600972.1	JUND	19	18391739	promoter	blood	17.49	0.60
473	ENST00000602185.5	GMFG	19	39826645	promoter	blood	14.09	0.00
474	ENST00000602569.1	IFITM2	11	308217	promoter	blood	3175.79	0.00
475	ENST00000605039.5	BIN2	12	51717938	promoter	blood	11.02	0.11
476	ENST00000611028.2	FOLR3	11	71846798	promoter	blood	11.13	0.00
477	ENST00000612844.4	FOLR3	11	71846756	promoter	blood	13.11	0.00
478	ENST00000615439.4	RASGRP4	19	38916945	promoter	blood	10.11	0.00
479	ENST00000615825.1	MME	3	154801957	promoter	blood	12.37	0.88
480	ENST00000616356.4	FCN1	9	137809723	promoter	blood	16.99	0.07
481	ENST00000618265.4	CD177	19	43857811	promoter	blood	222.54	0.73
482	ENST00000620541.4	RIN3	14	92980137	promoter	blood	17.39	0.84
483	ENST00000620888.4	HBG2	11	5276011	promoter	blood	161.14	0.00
484	ENST00000003084.10	CFTR	7	117120201	junction	tumor	0.00	30.20
485	ENST00000027335.7	CDH17	8	95220711	junction	tumor	0.00	149.83
486	ENST00000161006.7	PRSS22	16	2908024	junction	tumor	0.00	10.29
487	ENST00000162330.9	BCAR1	16	75285369	junction	tumor	0.00	16.86
488	ENST00000201586.6	SULT2B1	19	49055580	junction	tumor	0.03	16.67
489	ENST00000211314.4	TMEM14A	6	52536043	junction	tumor	0.67	25.17
490	ENST00000215582.7	MISP	19	751171	junction	tumor	0.00	116.54
491	ENST00000215743.7	MMP11	22	24115165	junction	tumor	0.08	42.41
492	ENST00000216968.4	PROCR	20	33760027	junction	tumor	0.36	28.48
493	ENST00000221992.10	CEACAM5	19	42212714	junction	tumor	0.00	1235.90
494	ENST00000223271.7	RARRES2	7	150038667	junction	tumor	0.41	46.30
495	ENST00000226230.7	TMEM97	17	26646391	junction	tumor	0.39	20.84
496	ENST00000226760.5	WFS1	4	6271741	junction	tumor	0.35	15.01
497	ENST00000227868.8	PDHX	11	34938362	junction	tumor	0.99	13.52
498	ENST00000228916.6	SCNN1A	12	6484671	junction	tumor	0.05	32.36
499	ENST00000230588.8	MEP1A	6	46761204	junction	tumor	0.00	21.95
500	ENST00000232458.9	ECT2	3	172468647	junction	tumor	0.28	12.07
501	ENST00000245451.8	BMP4	14	54423268	junction	tumor	0.00	16.43
502	ENST00000245907.10	C3	19	6720527	junction	tumor	0.37	15.08
503	ENST00000250405.9	BCL2L2	14	23776103	junction	tumor	1.00	11.63
504	ENST00000254260.7	RHPN2	19	33555690	junction	tumor	0.03	23.49

505	ENST00000255681.6	MACROD1	11	63933169	junction	tumor	0.54	22.18
506	ENST00000256585.9	REG4	1	120354032	junction	tumor	0.09	37.82
507	ENST00000256951.9	EMP1	12	13349806	junction	tumor	0.39	14.17
508	ENST00000260227.4	MMP7	11	102401324	junction	tumor	0.00	29.38
509	ENST00000261769.9	CDH1	16	68771366	junction	tumor	0.00	123.30
510	ENST00000262429.8	ATP2C2	16	84402320	junction	tumor	0.34	16.47
511	ENST00000262753.8	POF1B	X	84634644	junction	tumor	0.02	40.41
512	ENST00000263629.8	MTIF2	2	55496305	junction	tumor	0.85	13.76
513	ENST00000263735.8	EPCAM	2	47596720	junction	tumor	0.11	594.54
514	ENST00000263895.8	RND3	2	151344063	junction	tumor	0.00	10.29
515	ENST00000264144.4	LAMC2	1	183155566	junction	tumor	0.01	31.46
516	ENST00000264748.6	FGFRL1	4	1006352	junction	tumor	0.82	17.03
517	ENST00000266980.8	SLC39A5	12	56624657	junction	tumor	0.00	20.87
518	ENST00000267101.7	ERBB3	12	56474166	junction	tumor	0.00	40.98
519	ENST00000267814.13	SORD	15	45315547	junction	tumor	0.93	13.70
520	ENST00000267996.11	TPM1	15	63335142	junction	tumor	0.87	32.98
521	ENST00000269571.9	ERBB2	17	37856564	junction	tumor	0.00	11.47
522	ENST00000270560.3	TM4SF5	17	4675394	junction	tumor	0.00	18.39
523	ENST00000271064.11	TINAGL1	1	32042196	junction	tumor	0.10	42.75
524	ENST00000278559.7	CAPN5	11	76778141	junction	tumor	0.52	27.31
525	ENST00000278937.6	MPZL2	11	118134811	junction	tumor	0.37	17.05
526	ENST00000288937.6	MRPL17	11	6704354	junction	tumor	0.85	16.44
527	ENST00000290130.3	MIS18A	21	33650992	junction	tumor	0.49	12.76
528	ENST00000290913.7	CHCHD6	3	126423242	junction	tumor	0.65	15.07
529	ENST00000291525.11	TFF3	21	43735403	junction	tumor	0.00	209.02
530	ENST00000292401.8	AZGP1	7	99573568	junction	tumor	0.14	45.24
531	ENST00000292408.8	FGFR4	5	176514078	junction	tumor	0.07	25.86
532	ENST00000295092.2	FAM84A	2	14773061	junction	tumor	0.00	13.18
533	ENST00000296129.5	CDCP1	3	45187698	junction	tumor	0.11	15.27
534	ENST00000296252.8	LIPH	3	185270211	junction	tumor	0.03	12.23
535	ENST00000296424.8	BDH2	4	104020940	junction	tumor	0.99	14.16
536	ENST00000296666.12	PRRC1	5	126853468	junction	tumor	0.95	11.62
537	ENST00000297205.6	STEAP1	7	89783857	junction	tumor	0.00	14.91
538	ENST00000299610.4	MFAP4	17	19290463	junction	tumor	0.39	15.19
539	ENST00000299714.7	SEC11C	18	56807267	junction	tumor	0.62	11.38
540	ENST00000300119.7	MYO1A	12	57443671	junction	tumor	0.00	15.11
541	ENST00000300283.10	CKMT1B	15	43885469	junction	tumor	0.00	35.88
542	ENST00000300557.2	PRR15L	17	46035023	junction	tumor	0.03	96.21
543	ENST00000301395.7	GGT6	17	4463677	junction	tumor	0.00	16.81
544	ENST00000301887.8	BATF2	11	64764348	junction	tumor	0.43	11.12
545	ENST00000307078.9	AXIN2	17	63557568	junction	tumor	0.09	14.10
546	ENST00000308302.3	GOLT1A	1	204183010	junction	tumor	0.03	12.22
547	ENST00000308831.6	RHOD	11	66824505	junction	tumor	0.07	10.41
548	ENST00000310398.6	AGR3	7	16921568	junction	tumor	0.00	33.08
549	ENST00000310706.9	JUP	17	39942840	junction	tumor	0.87	86.21
550	ENST00000310836.10	UGT8	4	115520130	junction	tumor	0.04	14.08
551	ENST00000311160.13	TNS3	7	47621649	junction	tumor	0.68	16.18
552	ENST00000311381.7	C6orf203	6	107349475	junction	tumor	0.93	14.55
553	ENST00000311620.6	ANKS4B	16	21245222	junction	tumor	0.00	10.61
554	ENST00000316673.8	HNF4A	20	42984493	junction	tumor	0.00	10.78
555	ENST00000317508.10	PRSS8	16	31146735	junction	tumor	0.11	143.22
556	ENST00000318024.8	USH1C	11	17565819	junction	tumor	0.00	46.62

557	ENST00000318407.4	BOK	2	242498408	junction	tumor	0.57	13.75
558	ENST00000318443.9	CD276	15	73976801	junction	tumor	0.00	11.45
559	ENST00000318683.6	B3GNT3	19	17906015	junction	tumor	0.00	57.75
560	ENST00000319838.9	GPR35	2	241544987	junction	tumor	0.31	30.59
561	ENST00000322536.7	DDX10	11	108536066	junction	tumor	0.75	10.84
562	ENST00000324038.6	FAM101A	12	124773916	junction	tumor	0.00	10.08
563	ENST00000325307.11	HMGB3	X	150151849	junction	tumor	0.30	14.09
564	ENST00000325568.9	IL32	16	3115495	junction	tumor	0.93	14.52
565	ENST00000326587.11	MAGED1	X	51636851	junction	tumor	0.60	16.14
566	ENST00000329875.12	PYCR1	17	79894624	junction	tumor	0.12	36.33
567	ENST00000331595.8	BGN	X	152760571	junction	tumor	0.60	74.92
568	ENST00000332149.9	TMPRSS2	21	42880008	junction	tumor	0.02	43.57
569	ENST00000333090.4	TSKU	11	76494448	junction	tumor	0.00	17.21
570	ENST00000334047.11	F3	1	95007093	junction	tumor	0.08	13.07
571	ENST00000334869.8	LGMN	14	93214834	junction	tumor	0.94	45.73
572	ENST00000337682.8	FAM60A	12	31478958	junction	tumor	0.97	25.73
573	ENST00000338660.5	VWA1	1	1371201	junction	tumor	0.06	21.82
574	ENST00000339276.5	SFN	1	27190948	junction	tumor	0.60	113.82
575	ENST00000340556.10	MORN2	2	39103251	junction	tumor	0.33	11.41
576	ENST00000344616.3	S100A14	1	153588771	junction	tumor	0.00	143.55
577	ENST00000350051.7	BIRC5	17	76210508	junction	tumor	0.63	18.32
578	ENST00000352551.9	UBE2C	20	44441435	junction	tumor	0.00	10.99
579	ENST00000354624.5	HKDC1	10	70980254	junction	tumor	0.14	20.07
580	ENST00000354900.7	LSR	19	35740034	junction	tumor	0.75	31.22
581	ENST00000355097.6	ENTPD2	9	139948333	junction	tumor	0.03	10.14
582	ENST00000355808.9	PDHA1	X	19362212	junction	tumor	0.25	16.21
583	ENST00000355899.7	PLS3	X	114795587	junction	tumor	0.00	12.05
584	ENST00000356509.7	GMNN	6	24775340	junction	tumor	0.57	11.97
585	ENST00000356762.7	CRB3	19	6464361	junction	tumor	0.00	12.29
586	ENST00000357166.10	ZDHHC9	X	128977672	junction	tumor	0.29	20.11
587	ENST00000357602.7	IPO5	13	98612657	junction	tumor	0.80	15.40
588	ENST00000358432.7	EPHA2	1	16482343	junction	tumor	0.03	23.85
589	ENST00000358813.4	CCL20	2	228678703	junction	tumor	0.00	33.26
590	ENST00000358867.10	TMEM126B	11	85339732	junction	tumor	0.47	17.68
591	ENST00000360325.11	CLDN7	17	7165140	junction	tumor	0.09	133.65
592	ENST00000360605.8	URI1	19	30414661	junction	tumor	0.44	12.86
593	ENST00000360760.9	SPATS2L	2	201171324	junction	tumor	0.73	32.04
594	ENST00000360779.3	SDCBP2	20	1309729	junction	tumor	0.00	17.84
595	ENST00000361084.9	RAB25	1	156031234	junction	tumor	0.07	131.50
596	ENST00000361852.8	EPS8L3	1	110306444	junction	tumor	0.00	26.64
597	ENST00000361901.6	CALD1	7	134464500	junction	tumor	0.42	33.93
598	ENST00000366787.7	THBS2	6	169654085	junction	tumor	0.07	14.23
599	ENST00000366999.8	NEK2	1	211848726	junction	tumor	0.16	11.93
600	ENST00000367274.8	UBE2T	1	202311023	junction	tumor	0.63	29.13
601	ENST00000367283.7	ELF3	1	201979948	junction	tumor	0.07	135.46
602	ENST00000367284.9	ELF3	1	201979834	junction	tumor	0.02	50.55
603	ENST00000367313.4	LAD1	1	201368538	junction	tumor	0.05	100.09
604	ENST00000367976.3	CTGF	6	132272247	junction	tumor	0.32	44.18
605	ENST00000368408.3	EFNA3	1	155051545	junction	tumor	0.36	18.08
606	ENST00000368554.8	PRAP1	10	135122967	junction	tumor	0.00	32.41
607	ENST00000369406.7	HMGCS2	1	120311364	junction	tumor	0.00	17.63
608	ENST00000370481.8	GBP3	1	89488367	junction	tumor	0.66	12.56

609	ENST00000370828.3	GPC4	X	132548834	junction	tumor	0.03	13.27
610	ENST00000371221.3	ALDH18A1	10	97416354	junction	tumor	0.04	29.55
611	ENST00000372486.5	NTMT1	9	132371457	junction	tumor	0.00	14.12
612	ENST00000372966.7	NOX1	X	100129084	junction	tumor	0.00	48.52
613	ENST00000373255.8	H2AFY2	10	71812756	junction	tumor	0.42	12.60
614	ENST00000373290.6	TSPAN15	10	71211446	junction	tumor	0.30	60.96
615	ENST00000373669.6	PIN4	X	71401678	junction	tumor	0.87	13.81
616	ENST00000373699.5	PPIL1	6	36842493	junction	tumor	0.85	17.26
617	ENST00000373944.7	ZWINT	10	58120957	junction	tumor	0.38	16.27
618	ENST00000374183.4	BSPRY	9	116112060	junction	tumor	0.22	15.59
619	ENST00000374214.3	UQCC2	6	33679326	junction	tumor	1.00	17.77
620	ENST00000374837.7	MAP1LC3A	20	33134720	junction	tumor	0.87	16.45
621	ENST00000375431.8	GRTP1	13	114018335	junction	tumor	0.05	18.16
622	ENST00000376569.7	DDR1	6	30851922	junction	tumor	0.08	11.00
623	ENST00000376652.8	ENTPD6	20	25176503	junction	tumor	0.44	14.06
624	ENST00000378115.2	ARHGEF35	7	143892631	junction	tumor	0.10	13.16
625	ENST00000378378.8	ARHGEF16	1	3371375	junction	tumor	0.00	12.12
626	ENST00000378427.5	FAM213B	1	2518387	junction	tumor	0.59	12.06
627	ENST00000379046.6	NQO1	16	69760336	junction	tumor	0.07	39.35
628	ENST00000379715.9	EEF1E1	6	8102668	junction	tumor	0.59	17.82
629	ENST00000379742.4	POSTN	13	38172745	junction	tumor	0.01	11.69
630	ENST00000379923.5	ACO1	9	32384733	junction	tumor	0.81	16.28
631	ENST00000380071.7	RFC3	13	34392402	junction	tumor	0.48	15.11
632	ENST00000381134.7	ARSE	X	2882265	junction	tumor	0.00	24.51
633	ENST00000382848.4	GJB2	13	20766922	junction	tumor	0.09	18.88
634	ENST00000389614.5	GPX2	14	65409223	junction	tumor	0.10	652.10
635	ENST00000391967.6	LAD1	1	201368397	junction	tumor	0.00	16.64
636	ENST00000393316.7	BCL2L15	1	114429871	junction	tumor	0.11	11.11
637	ENST00000393366.6	ATP5G1	17	46970272	junction	tumor	0.63	40.08
638	ENST00000393725.6	KIAA1191	5	175788605	junction	tumor	0.75	11.70
639	ENST00000394201.8	SCOC	4	141294871	junction	tumor	0.53	14.61
640	ENST00000394265.5	PPP1R1B	17	37784875	junction	tumor	0.00	81.30
641	ENST00000394267.2	PPP1R1B	17	37784959	junction	tumor	0.00	87.42
642	ENST00000395641.2	NUPR1	16	28550117	junction	tumor	0.45	37.05
643	ENST00000397542.6	CDHR5	11	624818	junction	tumor	0.02	18.38
644	ENST00000397714.6	SEPTIN10	2	110371375	junction	tumor	0.14	14.96
645	ENST00000397995.2	RNASE4	14	21152855	junction	tumor	0.56	10.20
646	ENST00000401412.5	AGR2	7	16844577	junction	tumor	0.00	103.38
647	ENST00000403444.7	CEACAM1	19	43032463	junction	tumor	0.00	33.67
648	ENST00000405271.5	EPCAM	2	47572362	junction	tumor	0.00	20.99
649	ENST00000410036.2	MZT2A	2	132250293	junction	tumor	0.00	12.64
650	ENST00000416348.1	ADIRF	10	88728362	junction	tumor	0.00	22.43
651	ENST00000419304.6	AGR2	7	16844559	junction	tumor	0.00	257.72
652	ENST00000419308.6	FOXA2	20	22564830	junction	tumor	0.00	13.51
653	ENST00000420892.1	HTRA1	10	124266401	junction	tumor	0.98	24.46
654	ENST00000423485.5	TOP2A	17	38574023	junction	tumor	0.44	31.06
655	ENST00000425042.6	HID1	17	72968686	junction	tumor	0.23	13.99
656	ENST00000425340.2	FUT2	19	49199346	junction	tumor	0.02	13.10
657	ENST00000428445.1	VARS	6	31750307	junction	tumor	0.78	10.22
658	ENST00000428649.6	KIFC1	6	33359774	junction	tumor	0.60	17.24
659	ENST00000429772.6	TMEM106C	12	48357487	junction	tumor	0.70	34.02
660	ENST00000430118.1	HMGB3	X	150154222	junction	tumor	0.52	12.82

661	ENST00000433307.2	PLEKHA1	10	124152857	junction	tumor	0.98	13.38
662	ENST00000441275.5	BDH1	3	197282652	junction	tumor	0.87	17.80
663	ENST00000444124.6	DDC	7	50632982	junction	tumor	0.00	21.66
664	ENST00000448599.2	PHGR1	15	40643263	junction	tumor	0.00	289.14
665	ENST00000450427.1	PRR15	7	29605369	junction	tumor	0.00	10.59
666	ENST00000450894.7	ITGB4	17	73717692	junction	tumor	0.14	50.86
667	ENST00000452441.5	DDR1	6	30852487	junction	tumor	0.07	51.62
668	ENST00000455712.5	POLR2H	3	184080512	junction	tumor	0.94	11.92
669	ENST00000463201.2	PRAP1	10	135164937	junction	tumor	0.00	54.46
670	ENST00000467415.5	TMEM14C	6	10723474	junction	tumor	0.69	26.73
671	ENST00000467905.5	AK2	1	33502337	junction	tumor	0.00	11.87
672	ENST00000469862.1	CENPF	1	214828746	junction	tumor	0.39	10.26
673	ENST00000472782.1	ATP5G3	2	176046384	junction	tumor	0.62	10.87
674	ENST00000476587.1	NDUFB5	3	179334832	junction	tumor	0.89	14.92
675	ENST00000478194.1	FERMT1	20	6074721	junction	tumor	0.00	27.00
676	ENST00000478869.1	WDR12	2	203765748	junction	tumor	0.71	14.50
677	ENST00000479419.1	IFT172	2	27668796	junction	tumor	0.00	37.10
678	ENST00000484713.1	LAMB2	3	49158866	junction	tumor	0.41	13.87
679	ENST00000489477.1	NDUFAF4	6	97345542	junction	tumor	0.66	10.30
680	ENST00000490807.5	NTPCR	1	233086490	junction	tumor	0.77	10.54
681	ENST00000494446.1	FN1	2	216230228	junction	tumor	0.79	52.10
682	ENST00000494801.5	TCEAL4	X	102840552	junction	tumor	0.60	13.59
683	ENST00000495558.1	VWA1	1	1370526	junction	tumor	0.00	13.92
684	ENST00000496195.1	GLRX3	10	131977684	junction	tumor	0.98	10.30
685	ENST00000497734.5	SRC	20	35973290	junction	tumor	0.00	12.44
686	ENST00000507614.1	TIMM8B	11	111957364	junction	tumor	0.80	10.54
687	ENST00000507699.1	PALLD	4	169819865	junction	tumor	0.31	14.56
688	ENST00000514985.5	SEPP1	5	42811938	junction	tumor	0.59	49.95
689	ENST00000520271.5	COX6C	8	100905671	junction	tumor	0.51	12.86
690	ENST00000523677.5	C1orf210	1	43751115	junction	tumor	0.00	13.49
691	ENST00000524832.5	CHID1	11	902198	junction	tumor	0.42	10.82
692	ENST00000525657.1	C1QTNF5	11	119211405	junction	tumor	0.05	17.27
693	ENST00000526202.5	LMO7	13	76334967	junction	tumor	0.09	23.11
694	ENST00000527106.5	FUT6	19	5838688	junction	tumor	0.00	13.22
695	ENST00000528430.2	PPP1R16A	8	145726677	junction	tumor	0.92	22.33
696	ENST00000530094.5	CTNND1	11	57529518	junction	tumor	0.00	26.61
697	ENST00000533827.5	VPS51	11	64877063	junction	tumor	0.00	12.01
698	ENST00000534378.5	ILVBL	19	15236467	junction	tumor	0.64	11.41
699	ENST00000537496.5	MMAB	12	110011152	junction	tumor	0.93	12.43
700	ENST00000541754.1	NNMT	11	114168120	junction	tumor	0.72	23.55
701	ENST00000542056.1	GPRC5A	12	13044598	junction	tumor	0.00	23.91
702	ENST00000543445.5	LDHA	11	18416188	junction	tumor	0.00	71.47
703	ENST00000543623.5	PLCD3	17	43192462	junction	tumor	0.27	14.58
704	ENST00000546314.5	STARD10	11	72493311	junction	tumor	0.00	31.66
705	ENST00000546485.5	RPL41	12	56510443	junction	tumor	0.75	48.15
706	ENST00000547281.5	CDK4	12	58145958	junction	tumor	0.83	30.31
707	ENST00000547838.2	FAM109A	12	111801492	junction	tumor	0.94	11.49
708	ENST00000548169.2	ATP2A2	12	110729929	junction	tumor	0.34	13.63
709	ENST00000552128.2	TSPAN8	12	71532931	junction	tumor	0.00	15.81
710	ENST00000552561.5	TMEM106C	12	48357416	junction	tumor	0.38	17.25
711	ENST00000554989.1	CKB	14	103987600	junction	tumor	0.75	83.82
712	ENST00000557049.1	GPX2	14	65409385	junction	tumor	0.00	18.28

713	ENST00000558580.1	SORD	15	45328542	junction	tumor	0.95	15.73
714	ENST00000559087.5	BMP4	14	54423477	junction	tumor	0.00	13.08
715	ENST00000562684.5	HN1L	16	1728357	junction	tumor	0.25	19.21
716	ENST00000564043.1	NQO1	16	69760404	junction	tumor	0.32	89.24
717	ENST00000581920.1	TYMS	18	667752	junction	tumor	0.88	11.79
718	ENST00000583327.2	ITGB4	17	73747929	junction	tumor	0.12	32.84
719	ENST00000586005.5	SMIM22	16	4845450	junction	tumor	0.00	103.03
720	ENST00000587251.5	LGALS3BP	17	76975906	junction	tumor	0.00	48.36
721	ENST00000588605.5	C19orf33	19	38794923	junction	tumor	0.22	18.46
722	ENST00000589378.5	TJP3	19	3721908	junction	tumor	0.13	11.74
723	ENST00000591795.1	DENND1C	19	6469607	junction	tumor	0.56	11.26
724	ENST00000594443.5	FBL	19	40336931	junction	tumor	0.00	19.57
725	ENST00000594605.5	STAP2	19	4338649	junction	tumor	0.06	27.33
726	ENST00000595110.1	FAM83E	19	49117965	junction	tumor	0.00	13.13
727	ENST00000597153.5	LGALS4	19	39303482	junction	tumor	0.00	20.51
728	ENST00000601623.5	LSR	19	35740271	junction	tumor	0.21	24.39
729	ENST00000610552.4	SLC2A8	9	130159565	junction	tumor	0.65	11.38
730	ENST00000612794.1	GPX2	14	65409328	junction	tumor	0.00	23.73
731	ENST00000612809.4	C8orf59	8	86132535	junction	tumor	0.94	54.53
732	ENST00000616154.1	CDX1	5	149546475	junction	tumor	0.00	138.07
733	ENST00000616727.4	MUC13	3	124653505	junction	tumor	0.01	221.05
734	ENST00000618855.4	TMPRSS4	11	117948020	junction	tumor	0.00	10.45
735	ENST00000619895.4	TMC4	19	54676734	junction	tumor	0.35	33.05
736	ENST00000620753.4	EI24	11	125439410	junction	tumor	0.63	12.17
737	ENST00000008938.4	PGLYRP1	19	46525993	junction	blood	148.76	0.05
738	ENST00000199708.2	HBQ1	16	230580	junction	blood	45.79	0.00
739	ENST00000216338.8	GZMH	14	25078765	junction	blood	15.58	0.99
740	ENST00000221515.5	RETN	19	7734007	junction	blood	72.49	0.19
741	ENST00000221954.6	CEACAM4	19	42133268	junction	blood	32.81	0.13
742	ENST00000225538.3	P2RX1	17	3819383	junction	blood	15.55	0.30
743	ENST00000232014.8	BCL6	3	187453878	junction	blood	19.07	0.18
744	ENST00000234347.9	PRTN3	19	841069	junction	blood	13.78	0.00
745	ENST00000236826.7	MMP8	11	102595485	junction	blood	20.68	0.04
746	ENST00000244709.8	TREM1	6	41254345	junction	blood	67.12	0.63
747	ENST00000246115.4	S1PR4	19	3180330	junction	blood	127.44	0.94
748	ENST00000246549.2	FFAR2	19	35942667	junction	blood	58.85	0.34
749	ENST00000246657.2	CCR7	17	38721652	junction	blood	11.89	0.75
750	ENST00000259396.8	ORM1	9	117085527	junction	blood	34.89	0.14
751	ENST00000262407.5	ITGA2B	17	42466654	junction	blood	12.34	0.04
752	ENST00000264972.9	ZAP70	2	98330137	junction	blood	15.69	0.72
753	ENST00000279452.10	CD44	11	35198287	junction	blood	10.76	0.00
754	ENST00000281703.10	GLT1D1	12	129338194	junction	blood	22.75	0.02
755	ENST00000290075.10	SLC25A37	8	23386725	junction	blood	45.08	0.87
756	ENST00000292432.9	HK3	5	176326268	junction	blood	98.07	0.60
757	ENST00000295683.2	CXCR1	2	219031631	junction	blood	355.57	0.18
758	ENST00000296435.2	CAMP	3	48265202	junction	blood	27.17	0.06
759	ENST00000296487.8	PPM1M	3	52280330	junction	blood	13.09	0.41
760	ENST00000297239.10	SYTL3	6	159082417	junction	blood	10.79	0.54
761	ENST00000299663.7	CLEC4E	12	8693357	junction	blood	29.27	0.20
762	ENST00000302017.3	ZNF467	7	149470197	junction	blood	25.10	0.54
763	ENST00000303531.11	PRKCB	16	23847669	junction	blood	16.08	0.36
764	ENST00000303757.12	LST1	6	31555095	junction	blood	11.09	0.23

765	ENST00000307564.8	AKNA	9	17156637	junction	blood	11.95	0.38
766	ENST00000310544.8	PHOSPHO1	17	47307830	junction	blood	30.92	0.08
767	ENST00000318507.6	CXCR2	2	218991076	junction	blood	157.27	0.28
768	ENST00000326165.10	CD300LF	17	72708963	junction	blood	18.99	0.70
769	ENST00000328118.7	FMNL1	17	43299554	junction	blood	11.80	0.41
770	ENST00000329021.9	NFAM1	22	42828243	junction	blood	43.63	0.94
771	ENST00000329410.3	C16orf54	16	29757232	junction	blood	24.31	0.49
772	ENST00000332549.7	IL1R2	2	102608473	junction	blood	112.29	0.55
773	ENST00000336577.8	MMP25	16	3097017	junction	blood	194.37	0.54
774	ENST00000336906.4	HBG2	11	5275867	junction	blood	104.85	0.00
775	ENST00000338372.6	VSTM1	19	54566998	junction	blood	10.71	0.00
776	ENST00000342571.7	MKNK1	1	47051546	junction	blood	14.42	0.02
777	ENST00000343534.9	C1orf162	1	112016652	junction	blood	37.68	0.74
778	ENST00000346667.8	IKZF1	7	50344518	junction	blood	11.73	0.24
779	ENST00000352818.8	CD44	11	35160917	junction	blood	14.11	0.00
780	ENST00000354352.9	SLC11A1	2	219247098	junction	blood	111.80	0.63
781	ENST00000355524.7	FCAR	19	55385779	junction	blood	53.04	0.07
782	ENST00000356815.3	HBM	16	216088	junction	blood	163.82	0.00
783	ENST00000356838.7	TMEM71	8	133772722	junction	blood	16.78	0.36
784	ENST00000356864.3	TNFRSF10C	8	22960694	junction	blood	108.86	0.56
785	ENST00000357198.8	DOK3	5	176936803	junction	blood	66.68	0.74
786	ENST00000357260.5	FAM212B	1	112281808	junction	blood	12.23	0.67
787	ENST00000358375.8	OSCAR	19	54604047	junction	blood	18.93	0.28
788	ENST00000367025.7	TRAF3IP3	1	209929654	junction	blood	17.52	0.64
789	ENST00000367053.5	CR1	1	207669733	junction	blood	10.47	0.02
790	ENST00000367535.7	NCF2	1	183559291	junction	blood	75.23	0.98
791	ENST00000367568.4	STX11	6	144471840	junction	blood	24.42	0.79
792	ENST00000367972.8	FCGR2A	1	161475342	junction	blood	27.69	0.40
793	ENST00000368015.1	ARHGAP30	1	161039410	junction	blood	20.61	0.58
794	ENST00000368732.5	S100A8	1	153363333	junction	blood	53.91	0.00
795	ENST00000368737.4	S100A12	1	153348028	junction	blood	1099.02	0.31
796	ENST00000371806.3	FCN1	9	137809615	junction	blood	379.64	0.88
797	ENST00000373103.5	CSF3R	1	36948412	junction	blood	61.20	0.04
798	ENST00000373925.5	THEMIS2	1	28199176	junction	blood	12.15	0.53
799	ENST00000374005.7	FGR	1	27961576	junction	blood	32.42	0.29
800	ENST00000374163.5	RPS6KA1	1	26872526	junction	blood	17.41	0.87
801	ENST00000375448.4	PADI4	1	17634809	junction	blood	95.04	0.03
802	ENST00000375862.6	HCK	20	30640289	junction	blood	20.11	0.09
803	ENST00000376670.7	GATA1	X	48645053	junction	blood	11.17	0.01
804	ENST00000377497.7	RASGRP2	11	64512214	junction	blood	48.02	0.55
805	ENST00000378023.8	FAM65B	6	24877179	junction	blood	15.67	0.00
806	ENST00000379400.7	RASSF2	20	4804203	junction	blood	13.75	0.82
807	ENST00000380299.3	HBD	11	5255572	junction	blood	138.84	0.07
808	ENST00000381112.7	CCM2	7	45067396	junction	blood	17.78	0.00
809	ENST00000381153.7	C11orf21	11	2322986	junction	blood	11.33	0.09
810	ENST00000381603.7	SIRPB1	20	1600515	junction	blood	26.01	0.00
811	ENST00000391750.5	LILRB3	19	54727293	junction	blood	65.61	0.41
812	ENST00000393450.5	MYL4	17	45286923	junction	blood	22.77	0.00
813	ENST00000393847.5	DPEP2	16	68033278	junction	blood	24.04	0.44
814	ENST00000394991.7	SNCA	4	90758113	junction	blood	32.19	0.35
815	ENST00000397147.6	NCF4	22	37257245	junction	blood	154.32	0.92
816	ENST00000398421.6	NCF1	7	74188450	junction	blood	11.04	0.04

817	ENST00000399173.5	FGR	1	27952557	junction	blood	101.05	0.26
818	ENST00000399753.2	MSRB1	16	1993103	junction	blood	11.22	0.15
819	ENST00000409220.5	ARHGAP25	2	69002552	junction	blood	23.89	0.31
820	ENST00000409930.3	IL1RN	2	113885317	junction	blood	21.18	0.85
821	ENST00000416215.6	PTPN6	12	7060683	junction	blood	12.72	0.88
822	ENST00000422400.6	VNN2	6	133078810	junction	blood	14.59	0.10
823	ENST00000423345.4	PRAM1	19	8567449	junction	blood	25.32	0.30
824	ENST00000433194.6	CDK5RAP2	9	123165594	junction	blood	22.55	0.52
825	ENST00000441002.1	IL1R2	2	102625104	junction	blood	16.30	0.00
826	ENST00000445347.1	LILRB3	19	54726815	junction	blood	49.26	0.10
827	ENST00000445961.5	RPS9	19	54704829	junction	blood	14.72	0.89
828	ENST00000447110.5	PIK3R5	17	8868913	junction	blood	12.89	0.29
829	ENST00000449131.6	BEST1	11	61717899	junction	blood	13.35	0.54
830	ENST00000454703.6	ACSL1	4	185747070	junction	blood	35.07	0.78
831	ENST00000460442.5	ZDHHC19	3	195925660	junction	blood	22.43	0.04
832	ENST00000464431.1	ABTB1	3	127395274	junction	blood	20.22	0.70
833	ENST00000464465.6	CSF3R	1	36937034	junction	blood	259.11	0.50
834	ENST00000465814.5	ARAP1	11	72432895	junction	blood	10.09	0.58
835	ENST00000467786.1	FGD3	9	95737687	junction	blood	43.15	0.29
836	ENST00000474085.5	IL1R2	2	102638711	junction	blood	24.35	0.04
837	ENST00000475226.1	HBB	11	5247807	junction	blood	2709.48	0.00
838	ENST00000477801.1	S100A8	1	153362871	junction	blood	161.47	0.07
839	ENST00000480395.5	TRIM22	11	5717885	junction	blood	17.36	0.70
840	ENST00000481568.2	C10orf54	10	73521355	junction	blood	31.27	0.90
841	ENST00000483750.5	WAS	X	48542374	junction	blood	34.49	0.17
842	ENST00000485743.1	HBB	11	5248160	junction	blood	128.52	0.00
843	ENST00000485928.5	PHC2	1	33815198	junction	blood	11.05	0.73
844	ENST00000486097.1	NCF1	7	74197975	junction	blood	12.51	0.06
845	ENST00000487540.6	CSF3R	1	36937839	junction	blood	47.30	0.17
846	ENST00000488171.5	CD55	1	207495210	junction	blood	25.43	0.43
847	ENST00000488945.5	GNLY	2	85912344	junction	blood	11.68	0.09
848	ENST00000489358.5	NAMPT	7	105925274	junction	blood	30.07	0.00
849	ENST00000491955.5	MPP1	X	154009875	junction	blood	10.84	0.42
850	ENST00000493242.1	LILRB2	19	54784816	junction	blood	22.65	0.13
851	ENST00000494185.1	LMNB1	5	126147590	junction	blood	10.53	0.00
852	ENST00000496823.1	BCL6	3	187463198	junction	blood	21.33	0.20
853	ENST00000497259.5	ARHGAP25	2	69034612	junction	blood	25.49	0.72
854	ENST00000497920.1	ARID5A	2	97213254	junction	blood	11.90	0.30
855	ENST00000509314.5	FBXL5	4	15661350	junction	blood	10.24	0.00
856	ENST00000509339.1	MXD3	5	176734782	junction	blood	30.07	0.08
857	ENST00000510784.6	FAM65B	6	25042079	junction	blood	61.47	0.19
858	ENST00000513001.5	ACSL1	4	185678973	junction	blood	17.65	0.10
859	ENST00000520174.5	DMTN	8	21914647	junction	blood	16.02	0.00
860	ENST00000523022.5	CA1	8	86290275	junction	blood	40.92	0.11
861	ENST00000525270.5	VNN2	6	133084522	junction	blood	38.37	0.12
862	ENST00000527146.1	IFITM2	11	308438	junction	blood	18.56	0.63
863	ENST00000528780.5	IFITM1	11	313691	junction	blood	47.88	0.31
864	ENST00000529635.5	TBC1D10C	11	67171825	junction	blood	16.89	0.34
865	ENST00000533968.1	SPI1	11	47399860	junction	blood	12.90	0.22
866	ENST00000535669.6	CD37	19	49838866	junction	blood	33.70	0.19
867	ENST00000540998.5	CDC42SE1	1	151031955	junction	blood	10.52	0.00
868	ENST00000542481.1	ATG16L2	11	72535167	junction	blood	25.18	0.37

869	ENST00000543576.5	DENND1C	19	6481690	junction	blood	12.06	0.00
870	ENST00000544232.5	TMEM91	19	41882759	junction	blood	12.57	0.20
871	ENST00000544665.7	ITGAM	16	31271413	junction	blood	56.38	0.99
872	ENST00000546704.1	ARHGAP9	12	57868658	junction	blood	19.20	0.13
873	ENST00000552370.5	TMBIM6	12	50144488	junction	blood	26.69	0.00
874	ENST00000553070.5	NFE2	12	54694585	junction	blood	23.61	0.00
875	ENST00000558012.5	PSTPIP1	15	77287950	junction	blood	26.47	0.31
876	ENST00000564662.1	COTL1	16	84651107	junction	blood	10.13	0.81
877	ENST00000564905.1	XPO6	16	28145162	junction	blood	12.98	0.47
878	ENST00000568763.1	CORO1A	16	30195046	junction	blood	45.17	0.63
879	ENST00000570106.6	SIGLEC5	19	52133552	junction	blood	40.53	0.18
880	ENST00000572782.1	ARRB2	17	4618338	junction	blood	16.63	0.33
881	ENST00000576628.1	ACAP1	17	7240106	junction	blood	20.20	0.18
882	ENST00000577894.1	EVI2B	17	29640997	junction	blood	14.34	0.00
883	ENST00000578067.5	LIMD2	17	61776617	junction	blood	10.86	0.22
884	ENST00000578402.5	LIMD2	17	61777729	junction	blood	31.49	0.77
885	ENST00000585901.6	TYROBP	19	36399070	junction	blood	13.40	0.19
886	ENST00000586946.1	TYROBP	19	36399077	junction	blood	23.56	0.61
887	ENST00000587259.5	VMP1	17	57807378	junction	blood	10.58	0.05
888	ENST00000587856.1	FMNL1	17	43311567	junction	blood	22.20	0.28
889	ENST00000588673.3	OAZ1	19	2270675	junction	blood	24.28	0.69
890	ENST00000589900.5	ICAM3	19	10450215	junction	blood	21.24	0.00
891	ENST00000592860.2	CFD	19	859765	junction	blood	16.53	0.85
892	ENST00000595042.5	FPR1	19	52255067	junction	blood	63.93	0.18
893	ENST00000595217.1	NKG7	19	51875633	junction	blood	33.26	0.52
894	ENST00000595325.5	MYO1F	19	8642191	junction	blood	13.66	0.09
895	ENST00000595636.1	GMFG	19	39826614	junction	blood	10.44	0.68
896	ENST00000595840.1	LRRC25	19	18508263	junction	blood	36.84	0.88
897	ENST00000596764.5	VAV1	19	6773022	junction	blood	12.25	0.59
898	ENST00000597852.5	CD37	19	49838832	junction	blood	13.98	0.20
899	ENST00000599180.2	FFAR2	19	35939281	junction	blood	24.79	0.00
900	ENST00000599716.5	SHKBP1	19	41082891	junction	blood	10.66	0.22
901	ENST00000600626.1	C5AR2	19	47840426	junction	blood	12.99	0.11
902	ENST00000600972.1	JUND	19	18391266	junction	blood	17.49	0.60
903	ENST00000605039.5	BIN2	12	51717806	junction	blood	11.02	0.11
904	ENST00000611028.2	FOLR3	11	71846814	junction	blood	11.13	0.00
905	ENST00000615439.4	RASGRP4	19	38916709	junction	blood	10.11	0.00
906	ENST00000615825.1	MME	3	154802116	junction	blood	12.37	0.88
907	ENST00000618265.4	CD177	19	43857918	junction	blood	222.54	0.73
908	ENST00000620541.4	RIN3	14	92980320	junction	blood	17.39	0.84

Table S4 Coefficients for the selected NDRs in the trained models (CRC model and CRC + BRCA model).

Columns
Gene: gene name
Transcript: transcript ID
Region: location of nucleosome-depleted site
Group: gene group based on its expression in blood and tumor
Coefficient: value of the regression coefficient. The intercept value is 0.4368.

CRC model					
Feature	**Gene**	**Transcript**	**Region**	**Group**	**Coefficient**
1	SHKBP1	ENST00000599716	junction	blood	0.607
2	ACSL1	ENST00000454703	junction	blood	0.431
3	BCAR1	ENST00000162330	junction	tumor	-0.321
4	RAB25	ENST00000361084	promoter	tumor	-0.213
5	PRTN3	ENST00000234347	promoter	blood	0.062
6	LSR	ENST00000605618	promoter	tumor	-0.174

Columns
Gene: gene name
Transcript: transcript ID
Region: location of nucleosome-depleted site
Group: gene group based on its expression in blood and tumor
Coefficient: value of the regression coefficient. The intercept value is -1.3719.

CRC+BRCA model					
Feature	**Gene**	**Transcript**	**Region**	**Group**	**Coefficient**
1	SLC11A1	ENST00000465984	promoter	blood	0.150
2	NLRP12	ENST00000324134	promoter	blood	0.181
3	PRTN3	ENST00000234347	promoter	blood	0.124
4	HMBS	ENST00000392841	promoter	blood	0.251
5	LILRB3	ENST00000460208	promoter	blood	0.140
6	ACSL1	ENST00000513001	junction	blood	0.106
7	GP9	ENST00000307395	junction	blood	0.251
8	MX2	ENST00000398632	promoter	blood	0.106
9	RASGRP4	ENST00000615340	promoter	blood	0.222
10	ATG16L2	ENST00000542481	promoter	blood	0.166

Table S5 Observed ctDNA fractions in the LOD analysis for the CRC model.

Sample	**Group**	**Expected ctDNA fraction**	**Observed ctDNA fraction**
1279_221015-0.005	positive	0.0050	0.0015
1279_221015-0.010	positive	0.0100	0.0192
1279_221015-0.015	positive	0.0150	0.0170
1279_221015-0.020	positive	0.0200	0.0246
1279_221015-0.025	positive	0.0250	0.0250
1279_221015-0.030	positive	0.0300	0.0389
1279_221015-0.035	positive	0.0350	0.0426
1279_221015-0.040	positive	0.0400	0.0471

1279_221015-0.045	positive	0.0450	0.0750
1279_221015-0.050	positive	0.0500	0.0692
1279_221015-0.075	positive	0.0750	0.0964
1279_221015-0.100	positive	0.1000	0.1093
1279_221015-0.125	positive	0.1250	0.1210
1279_221015-0.150	positive	0.1500	0.1381
1279_221015-0.175	positive	0.1750	0.1250
1279_221015-0.200	positive	0.2000	0.1452
1279_221015-0.225	positive	0.2250	0.1590
1279_221015-0.250	positive	0.2500	0.2252
1279_221015-0.275	positive	0.2750	0.2856
1279_221015-0.300	positive	0.3000	0.3152
1279_221015-0.325	positive	0.3250	0.3456
1279_221015-0.350	positive	0.3500	0.3587
1279_221015-0.375	positive	0.3750	0.3994
1279_221015-0.400	positive	0.4000	0.4318
1279_221015-0.425	positive	0.4250	0.4363
1279_221015-0.450	positive	0.4500	0.4634
1279_221015-0.475	positive	0.4750	0.4652
1279_221015-0.500	positive	0.5000	0.4776
1279_241116-0.005	positive	0.0050	0.0033
1279_241116-0.010	positive	0.0100	0.0150
1279_241116-0.015	positive	0.0150	0.0420
1279_241116-0.020	positive	0.0200	0.0368
1279_241116-0.025	positive	0.0250	0.0396
1279_241116-0.030	positive	0.0300	0.0439
1279_241116-0.035	positive	0.0350	0.0439
1279_241116-0.040	positive	0.0400	0.0576
1279_241116-0.045	positive	0.0450	0.0574
1279_241116-0.050	positive	0.0500	0.0692
1279_241116-0.075	positive	0.0750	0.0508
1279_241116-0.100	positive	0.1000	0.0707
1279_241116-0.125	positive	0.1250	0.1357
1279_241116-0.150	positive	0.1500	0.1457
1279_241116-0.175	positive	0.1750	0.1366
1279_241116-0.200	positive	0.2000	0.1632
1279_241116-0.225	positive	0.2250	0.2000
1279_241116-0.250	positive	0.2500	0.2310
1279_241116-0.275	positive	0.2750	0.2914
1279_241116-0.300	positive	0.3000	0.3281
1279_241116-0.325	positive	0.3250	0.3622
1279_241116-0.350	positive	0.3500	0.3690
1279_241116-0.375	positive	0.3750	0.3762
1279_241116-0.400	positive	0.4000	0.4185
1279_241116-0.425	positive	0.4250	0.4311
1279_241116-0.450	positive	0.4500	0.4618
1279_241116-0.475	positive	0.4750	0.4958
1279_241116-0.490	positive	0.4900	0.4937
512_051015-0.005	positive	0.0050	0.0049

512_051015-0.010	positive	0.0100	0.0077
512_051015-0.015	positive	0.0150	0.0133
512_051015-0.020	positive	0.0200	0.0163
512_051015-0.025	positive	0.0250	0.0235
512_051015-0.030	positive	0.0300	0.0311
512_051015-0.035	positive	0.0350	0.0322
512_051015-0.040	positive	0.0400	0.0330
512_051015-0.045	positive	0.0450	0.0371
512_051015-0.050	positive	0.0500	0.0296
512_051015-0.075	positive	0.0750	0.0388
512_051015-0.100	positive	0.1000	0.0500
512_051015-0.125	positive	0.1250	0.0682
512_051015-0.150	positive	0.1500	0.0881
512_051015-0.175	positive	0.1750	0.0743
512_051015-0.200	positive	0.2000	0.0948
512_051015-0.225	positive	0.2250	0.1386
512_051015-0.250	positive	0.2500	0.1762
512_051015-0.275	positive	0.2750	0.2095
512_051015-0.300	positive	0.3000	0.2319
512_051015-0.325	positive	0.3250	0.2451
512_051015-0.350	positive	0.3500	0.2761
512_051015-0.375	positive	0.3750	0.2971
512_051015-0.400	positive	0.4000	0.3063
512_051015-0.425	positive	0.4250	0.3056
512_051015-0.450	positive	0.4500	0.3568
512_051015-0.475	positive	0.4750	0.4021
512_051015-0.500	positive	0.5000	0.4009
512_051015-0.525	positive	0.5250	0.4008
512_051015-0.550	positive	0.5500	0.4460
512_051015-0.575	positive	0.5750	0.4464
512_051015-0.600	positive	0.6000	0.4736
512_051015-0.614	positive	0.6140	0.4474
512_130114-0.005	positive	0.0050	0.0136
512_130114-0.010	positive	0.0100	0.0167
512_130114-0.015	positive	0.0150	0.0198
512_130114-0.020	positive	0.0200	0.0363
512_130114-0.025	positive	0.0250	0.0352
512_130114-0.030	positive	0.0300	0.0402
512_130114-0.035	positive	0.0350	0.0285
512_130114-0.040	positive	0.0400	0.0309
512_130114-0.045	positive	0.0450	0.0374
512_130114-0.050	positive	0.0500	0.0406
512_130114-0.075	positive	0.0750	0.0492
512_130114-0.100	positive	0.1000	0.0904
512_130114-0.125	positive	0.1250	0.1008
512_130114-0.150	positive	0.1500	0.1432
512_130114-0.175	positive	0.1750	0.2025
512_130114-0.200	positive	0.2000	0.2242
512_130114-0.225	positive	0.2250	0.2376

512_130114-0.250	positive	0.2500	0.2570
512_130114-0.275	positive	0.2750	0.3262
512_130114-0.300	positive	0.3000	0.3659
512_130114-0.325	positive	0.3250	0.3947
512_130114-0.350	positive	0.3500	0.4564
512_130114-0.375	positive	0.3750	0.4838
512_130114-0.394	positive	0.3940	0.4822
sub-healthy-1	negative	0.0000	0.0000
sub-healthy-2	negative	0.0000	0.0024
sub-healthy-3	negative	0.0000	0.0001
sub-healthy-4	negative	0.0000	0.0005
sub-healthy-5	negative	0.0000	0.0000
sub-healthy-6	negative	0.0000	0.0162
sub-healthy-7	negative	0.0000	0.0065
sub-healthy-8	negative	0.0000	0.0000
sub-healthy-9	negative	0.0000	0.0084
sub-healthy-10	negative	0.0000	0.0071
sub-healthy-11	negative	0.0000	0.0000
sub-healthy-12	negative	0.0000	0.0124
sub-healthy-13	negative	0.0000	0.0013
sub-healthy-14	negative	0.0000	0.0118
sub-healthy-15	negative	0.0000	0.0109
sub-healthy-16	negative	0.0000	0.0069
sub-healthy-17	negative	0.0000	0.0116
sub-healthy-18	negative	0.0000	0.0076
sub-healthy-19	negative	0.0000	0.0049
sub-healthy-20	negative	0.0000	0.0000
sub-healthy-21	negative	0.0000	0.0000
sub-healthy-22	negative	0.0000	0.0095
sub-healthy-23	negative	0.0000	0.0106
sub-healthy-24	negative	0.0000	0.0121
sub-healthy-25	negative	0.0000	0.0085
sub-healthy-26	negative	0.0000	0.0000
sub-healthy-27	negative	0.0000	0.0176
sub-healthy-28	negative	0.0000	0.0099
sub-healthy-29	negative	0.0000	0.0000
sub-healthy-30	negative	0.0000	0.0076
sub-healthy-31	negative	0.0000	0.0002
sub-healthy-32	negative	0.0000	0.0076
sub-healthy-33	negative	0.0000	0.0078
sub-healthy-34	negative	0.0000	0.0071
sub-healthy-35	negative	0.0000	0.0077
sub-healthy-36	negative	0.0000	0.0110
sub-healthy-37	negative	0.0000	0.0074
sub-healthy-38	negative	0.0000	0.0000
sub-healthy-39	negative	0.0000	0.0000
sub-healthy-40	negative	0.0000	0.0105

Table S6 CRC plasma samples for lp-WGS and targeted sequencing.

sample name	patient ID	sample ID	cancer type	lp-WGS coverage	ichorCNA-estimated ctDNA content	max VAF	NDR-estimated ctDNA content
069_020913	69	CRC-13	CRC	1.97	0.00	undetected	0.00
069_310316	69	CRC-14	CRC	7.01	0.09	undetected	0.08
095_100913	95	CRC-15	CRC	5.77	0.38	0.54	0.37
095_150513	95	CRC-16	CRC	6.18	0.43	0.55	0.47
1014_140616	1014	CRC-17	CRC	1.82	0.39	0.56	0.38
1176_040815	1176	CRC-18	CRC	2.96	0.05	undetected	0.21
1176_111116	1176	CRC-19	CRC	1.35	0.00	undetected	0.06
1176_240715	1176	CRC-20	CRC	1.27	0.00	0.11	0.06
1179_160316	1179	CRC-21	CRC	1.96	0.16	0.29	0.25
1179_270715	1179	CRC-22	CRC	3.78	0.18	0.20	0.34
1429_141116	1429	CRC-23	CRC	0.42	0.20	undetected	0.08
1429_170316	1429	CRC-24	CRC	5.83	0.39	0.36	0.36
1490_050516	1490	CRC-25	CRC	2.12	0.49	0.72	0.49
1490_171116	1490	CRC-26	CRC	2.08	0.00	undetected	0.33
149_100613	149	CRC-27	CRC	2.43	0.00	undetected	0.19
149_130214	149	CRC-28	CRC	3.72	0.05	undetected	0.18
1531_010716	1531	CRC-29	CRC	1.38	0.48	0.77	0.49
1531_111016	1531	CRC-30	CRC	4.23	0.00	undetected	0.07
1531_111116	1531	CRC-31	CRC	1.93	0.00	undetected	0.00
330_091115	330	CRC-32	CRC	5.93	0.23	0.38	0.25
330_170414	330	CRC-33	CRC	6.93	0.00	undetected	0.00
357_110716	357	CRC-34	CRC	3.48	0.51	0.56	0.49
357_230913	357	CRC-35	CRC	2.06	0.00	undetected	0.11
357_290216	357	CRC-36	CRC	4.28	0.57	0.49	0.39
357_291015	357	CRC-37	CRC	5.94	0.37	0.29	0.38
375_021116	375	CRC-38	CRC	3.13	0.00	undetected	0.10
375_210115	375	CRC-39	CRC	2.90	0.00	undetected	0.17
386_091214	386	CRC-40	CRC	0.70	0.09	0.22	0.21
386_180516	386	CRC-41	CRC	3.86	0.32	0.49	0.38
476_050916	476	CRC-42	CRC	1.09	0.11	0.19	0.09
476_110315	476	CRC-43	CRC	3.32	0.12	0.27	0.20
519_020715	519	CRC-44	CRC	6.30	0.15	0.17	0.29
519_140116	519	CRC-45	CRC	2.31	0.06	undetected	0.14
519_240314	519	CRC-46	CRC	4.88	0.29	0.51	0.33
571_261114	571	CRC-47	CRC	2.64	0.00	undetected	0.06
571_291015	571	CRC-48	CRC	2.07	0.05	undetected	0.15
575_191015	575	CRC-49	CRC	2.63	0.11	0.12	0.10
575_270214	575	CRC-50	CRC	1.40	0.19	0.11	0.18
575_270516	575	CRC-51	CRC	2.13	0.00	0.11	0.11
575_270616	575	CRC-52	CRC	6.88	0.05	undetected	0.21

592_171116	592	CRC-53	CRC	2.42	0.00	undetected	0.08
592_280316	592	CRC-54	CRC	3.01	0.00	undetected	0.09
741_091116	741	CRC-55	CRC	1.50	0.00	undetected	0.07
741_150415	741	CRC-56	CRC	4.26	0.00	undetected	0.10
834_090715	834	CRC-57	CRC	2.71	0.00	undetected	0.00
834_241116	834	CRC-58	CRC	4.41	0.13	undetected	0.09
836_090415	836	CRC-59	CRC	1.27	0.00	undetected	0.04
836_090715	836	CRC-60	CRC	4.39	0.00	undetected	0.17
836_180416	836	CRC-61	CRC	4.23	0.39	0.25	0.22
897_200815	897	CRC-62	CRC	6.55	0.34	0.47	0.26
897_220316	897	CRC-63	CRC	8.03	0.07	0.16	0.07
986_060315	986	CRC-64	CRC	6.37	0.19	0.19	0.31
986_260916	986	CRC-65	CRC	4.52	0.28	0.73	0.47

Table S7 A panel of 100 genes frequently mutated in colorectal and breast cancer.

ABL1	BCL9L	CSF1R	ERBB3	GNA11	JAK2	MDM2	NPM1	PTPN11	SRC
ACVR2A	BRAF	CTCF	ERBB4	GNAQ	JAK3	MDM4	NRAS	RB1	STK11
AKT1	BRCA1	CTNNB1	ESR1	GNAS	KDR	MET	PDGFRA	RBM10	TAP1
ALK	BRCA2	DCC	EZH2	HLA-A	KIT	MLH1	PDIA3	RET	TAPBP
APC	CALR	DDR2	FBXW7	HNF1A	KMT2C	MPL	PIK3CA	RNF43	TP53
ARID1A	CANX	DMD	FGFR1	HRAS	KRAS	MTOR	PIK3R1	SMAD2	TSC1
ATM	CDH1	DOT1L	FGFR2	HSPA5	MAGI3	MUC17	POLD1	SMAD4	TSC2
ATR	CDKN1B	EGFR	FGFR3	IDH1	MAP2K1	NF1	POLD2	SMARCB1	VHL
AURKA	CDKN2A	EP300	FLT3	IDH2	MAP2K4	NOTCH1	POLE	SMO	ZFP36L2
B2M	CHD4	ERBB2	GATA3	JAK1	MAP3K1	NOTCH4	PTEN	SOX9	ZNRF3

Table S8 Variant allele frequency estimation of CRC plasma samples.

Sample	Chr	Pos (GRCh38)	Ref	Alt	Codon	AA	Gene	Symbol/Gene	Feature	Exon	mutect_VAF Tumour	varscan_VAFTumour	mutect_VAF Normal	varscan_VAFNormal	MedianVAF
T095_100913	chr12	25245350	C	T	gGt/gAt	G/D	ENSG00000133703	KRAS	ENST00000256078	2/6	0.211	0.212	0	0	0.2115
T095_100913	chr17	72124084	-	+C	-/C	-/X	ENSG00000125398	SOX9	ENST00000245479	3/3		0.202		0	0.202
T095_100913	chr17	7674230	C	T	Ggc/Agc	G/S	ENSG00000141510	TP53	ENST00000269305	7/11	0.539		0		0.539
T095_150513	chr12	25245350	C	T	gGt/gAt	G/D	ENSG00000133703	KRAS	ENST00000256078	2/6	0.234	0.221	0	0	0.2275
T095_150513	chr17	72124084	-	+C	-/C	-/X	ENSG00000125398	SOX9	ENST00000245479	3/3		0.187		0	0.187
T095_150513	chr17	7674230	C	T	Ggc/Agc	G/S	ENSG00000141510	TP53	ENST00000269305	7/11	0.553		0		0.553
T1014_110115	chr2	147926116-7	-	-A	Aaa/aa	K/X	ENSG00000121989	ACVR2A	ENST00000241416	10/11		0.285		0.005	0.285
T1014_140616	chr14	104773077	C	A	Gac/Tac	D/Y	ENSG00000142208	AKT1	ENST00000554581	10/13	0.199	0.199	0	0	0.199
T1014_140616	chr17	72122793	A	T	cAc/cTc	H/L	ENSG00000125398	SOX9	ENST00000245479	2/3	0.367		0		0.367
T1014_140616	chr5	112839783	G	T	Gag/Tag	E/*	ENSG00000134982	APC	ENST00000257430	16/16	0.559		0		0.559
T1014_180816	chr14	104773077	C	A	Gac/Tac	D/Y	ENSG00000142208	AKT1	ENST00000554581	10/13	0.246	0.256	0	0	0.251
T1014_180816	chr17	72122793	A	T	cAc/cTc	H/L	ENSG00000125398	SOX9	ENST00000245479	2/3	0.305	0.284	0	0	0.2945
T1014_180816	chr5	112839783	G	T	Gag/Tag	E/*	ENSG00000134982	APC	ENST00000257430	16/16	0.458		0.002		0.458
T1176_240715	chr3	142555897-8	-	-T	Ata/ta	I/X	ENSG00000175054	ATR	ENST00000350721	10/47		0.108		0.037	0.108
T1179_160316	chr12	25245351	C	A	Ggt/Tgt	G/C	ENSG00000133703	KRAS	ENST00000256078	2/6	0.289	0.288	0.001	0	0.2885
T1179_160316	chr17	7674250	C	A	tGt/tTt	C/F	ENSG00000141510	TP53	ENST00000269305	7/11	0.275	0.265	0	0.001	0.27
T1179_160316	chr4	153329715	G	T	tCt/tAt	S/Y	ENSG00000109670	FBXW7	ENST00000281708	8/12	0.119	0.104	0	0	0.1115
T1179_160316	chr5	112839826-7	-	-T	agT/ag	S/X	ENSG00000134982	APC	ENST00000257430	16/16		0.241		0.001	0.241
T1179_270715	chr12	25245351	C	A	Ggt/Tgt	G/C	ENSG00000133703	KRAS	ENST00000256078	2/6	0.203	0.196	0.001	0	0.2005
T1179_270715	chr17	7674250	C	A	tGt/tTt	C/F	ENSG00000141510	TP53	ENST00000269305	7/11	0.14	0.143	0	0.001	0.1415

T1179_270715	chr5	112839826-7	-	-T	agT/ag	S/X	ENSG00000134982	APC	ENST00000257430	16/16		0.185		0.001	0.185
T1279_221015	chr10	87933148	G	A	cGa/cAa	R/Q	ENSG00000171862	PTEN	ENST00000371953	5/9	0.515		0		0.515
T1279_221015	chr5	112839240	G	T	Gag/Tag	E/*	ENSG00000134982	APC	ENST00000257430	16/16	0.54		0.001		0.54
T1279_241116	chr10	87933148	G	A	cGa/cAa	R/Q	ENSG00000171862	PTEN	ENST00000371953	5/9	0.378		0		0.378
T1279_241116	chr5	112839240	G	T	Gag/Tag	E/*	ENSG00000134982	APC	ENST00000257430	16/16	0.447		0.001		0.447
T1429_141116	chr1	114716126	C	T	gCt/gAt	C/D	ENSG00000213281	NRAS	ENST00000369535	2/7	0.108	0.135	0	0	0.1215
T1429_141116	chr11	108297326	A	G	aAt/aGt	N/S	ENSG00000149311	ATM	ENST00000278616	33/63	0.465		0		0.465
T1429_141116	chr12	132641691	G	A	gcC/gcT	A	ENSG00000177084	POLE	ENST00000320574	39/49	0.547		0		0.547
T1429_141116	chr12	6581743	C	T	aaG/aaA	K	ENSG00000111642	CHD4	ENST00000357038	31/40	0.45		0.001		0.45
T1429_141116	chr13	32332043	A	C	Aat/Cat	N/H	ENSG00000139618	BRCA2	ENST00000380152	10/27	0.403		0		0.403
T1429_141116	chr13	32332843	A	G	tcA/tcG	S	ENSG00000139618	BRCA2	ENST00000380152	10/27	0.41		0		0.41
T1429_141116	chr13	32336584	T	C	caT/caC	H	ENSG00000139618	BRCA2	ENST00000380152	11/27	0.465		0		0.465
T1429_141116	chr13	32337326	A	G	Aac/Gac	N/D	ENSG00000139618	BRCA2	ENST00000380152	11/27	0.451		0		0.451
T1429_141116	chr17	43071077	T	C	Agt/Ggt	S/G	ENSG00000012048	BRCA1	ENST00000471181	16/24	0.521		0.001		0.521
T1429_141116	chr17	43082453	A	G	tcT/tcC	S	ENSG00000012048	BRCA1	ENST00000471181	12/24	0.456		0		0.456
T1429_141116	chr17	43091983	T	C	aAa/aGa	K/R	ENSG00000012048	BRCA1	ENST00000471181	10/24	0.495		0.001		0.495
T1429_141116	chr17	43092418	T	C	gAa/gGa	E/G	ENSG00000012048	BRCA1	ENST00000471181	10/24	0.461		0.002		0.461
T1429_141116	chr17	43093220	A	G	Ttg/Ctg	L	ENSG00000012048	BRCA1	ENST00000471181	10/24	0.489		0.001		0.489
T1429_141116	chr17	43093449	G	A	agC/agT	S	ENSG00000012048	BRCA1	ENST00000471181	10/24	0.483		0.001		0.483
T1429_141116	chr17	58362569	C	T	cGg/cAg	R/Q	ENSG00000108375	RNF43	ENST00000584437	5/9	0.435		0.001		0.435
T1429_141116	chr17	7675088	C	T	cGc/cAc	R/H	ENSG00000141510	TP53	ENST00000269305	5/11		0.109		0.001	0.109

T1429_141116	chr4	54736599	G	C	cGGdoC	L	ENSG00000157404	KIT	ENST00000288135	18/21	0.443		0		0.443
T1429_141116	chr4	55113321	G	A	aCaTaTa	T/I	ENSG00000128052	KDR	ENST00000263923	7/30	0.479		0		0.479
T1429_141116	chr6	32221646	G	A	tCgtTg	S/L	ENSG00000204901	NOTCH4	ENST00000375023	4/30	0.35	0.341	0	0	0.3455
T1429_141116	chr6	32847198	T	C	gAcgGc	D/G	ENSG00000166394	TAP1	ENST00000364258	10/11	0.661		0.001		0.661
T1429_170316	chr1	114713908	T	A	cAgCTa	Q/L	ENSG00000213281	NRAS	ENST00000369535	3/7	0.348	0.322	0	0	0.335
T1429_170316	chr10	8059488	C	T	tCgtTg	S/L	ENSG00000107485	GATA3	ENST00000379328	3/6	0.2	0.199	0	0	0.1995
T1429_170316	chr16	68815631	T	C	gaTgaC	D	ENSG00000099968	CDH1	ENST00000261769	10/16	0.357		0.001		0.357
T1429_170316	chr17	7674230	C	T	CgcAgc	G/S	ENSG00000141510	TP53	ENST00000269305	7/11	0.345	0.341	0	0	0.343
T1429_170316	chr22	29649585	C	T	CggTgg	R/W	ENSG00000183579	ZNRF3	ENST00000544604	8/9	0.233	0.232	0	0.001	0.2325
T1429_170316	chr5	112782446	C	T	CgaTga	R/*	ENSG00000134982	APC	ENST00000257430	7/16	0.268	0.231	0	0	0.2495
T1490_050516	chr1	11240292	G	A	gCdgTc	A/V	ENSG00000198793	MTOR	ENST00000361445	11/58	0.164	0.145	0	0	0.1545
T1490_050516	chr17	7675088	C	T	cGrcAc	R/H	ENSG00000141510	TP53	ENST00000269305	5/11	0.719		0		0.719
T1490_050516	chr19	2226938	C	T	CagTag	Q/*	ENSG00000104885	DOT1L	ENST00000398665	27/28	0.24	0.267	0.001	0	0.2635
T1490_050516	chr4	55118645	C	T	cGgcAg	R/Q	ENSG00000128052	KDR	ENST00000263923	3/30	0.362		0		0.362
T1490_050516	chr5	112838070	-	+TGAATACTACA	tAgtTGAATACTACAtg	L/LNTTX	ENSG00000134982	APC	ENST00000257430	16/16		0.185		0	0.185
T1490_050516	chr5	112839474	C	T	CagTag	Q/*	ENSG00000134982	APC	ENST00000257430	16/16	0.526		0		0.526
T1531_030716	chr17	7675088	C	T	cGrcAc	R/H	ENSG00000141510	TP53	ENST00000269305	5/11	0.747		0.001		0.747
T1531_030716	chr2	43224452	T	G	gAcgGc	D/A	ENSG00000152518	ZFP36L2	ENST00000282388	2/2		0.309		0	0.309
T1531_030716	chr5	112839439	C	A	tCatAa	S/*	ENSG00000134982	APC	ENST00000257430	16/16	0.77		0		0.77
T1531_030716	chr17	7675088	C	T	cGrcAc	R/H	ENSG00000141510	TP53	ENST00000269305	5/11	0.788		0		0.788
T1531_160616	chr5	112839439	C	A	tCatAa	S/*	ENSG00000134982	APC	ENST00000257430	16/16	0.79		0		0.79
T330_091116	chr11	118908483	-	+G	-/C	-/X	ENSG00000186174	BCL9L	ENST00000334681	2/6		0.224		0	0.224

T330_091115	chr19	50409156	G	A	Ggg/Agg	G/R	ENSG00000 062822	POLD1	ENST00000 440232	16/27	0.259	0.256	0	0	0.2575
T330_091115	chr4	152326137	G	A	Cgc/Tgc	R/C	ENSG00000 109670	FBXW7	ENST00000 281708	10/12	0.362		0		0.362
T330_091115	chr5	112839576	C	T	Cag/Tag	Q/*	ENSG00000 134982	APC	ENST00000 257430	16/16	0.366		0		0.366
T330_091115	chr5	150080316	C	T	Gtg/Atg	V/M	ENSG00000 182578	CSF1R	ENST00000 286301	4/22	0.169	0.161	0.001	0	0.165
T357_110716	chr12	25245350	C	T	gCt/gAt	G/D	ENSG00000 133703	KRAS	ENST00000 256078	2/6	0.496		0		0.496
T357_110716	chr13	32362670	G	T	agG/agT	R/S	ENSG00000 139618	BRCA2	ENST00000 380152	17/27	0.233	0.256	0	0	0.2445
T357_110716	chr17	7674945	G	A	Cga/Tga	R/*	ENSG00000 141510	TP53	ENST00000 269305	6/11	0.56		0		0.56
T357_110716	chr2	211657762	T	G	caA/caC	Q/H	ENSG00000 178568	ERBB4	ENST00000 342788	16/28		0.172		0.001	0.172
T357_110716	chr2	43224819-36	-	- CGCGGCC GCCGCGGA GG	gCCTCCGC GGCGGCC GCCg	ASAAAA/X	ENSG00000 152518	ZFP36L2	ENST00000 282388	2/2		0.324		0.001	0.324
T357_290216	chr12	25245350	C	T	gCt/gAt	G/D	ENSG00000 133703	KRAS	ENST00000 256078	2/6	0.494		0		0.494
T357_290216	chr13	32362670	G	T	agG/agT	R/S	ENSG00000 139618	BRCA2	ENST00000 380152	17/27	0.181	0.174	0	0	0.1775
T357_290216	chr17	7674945	G	A	Cga/Tga	R/*	ENSG00000 141510	TP53	ENST00000 269305	6/11	0.488		0		0.488
T357_290216	chr2	211657762	T	G	caA/caC	Q/H	ENSG00000 178568	ERBB4	ENST00000 342788	16/28		0.142		0.001	0.142
T357_290216	chr2	43224819-36	-	- CGCGGCC GCCGCGGA GG	gCCTCCGC GGCGGCC GCCg	ASAAAA/X	ENSG00000 152518	ZFP36L2	ENST00000 282388	2/2		0.271		0.001	0.271
T357_291015	chr12	25245350	C	T	gCt/gAt	G/D	ENSG00000 133703	KRAS	ENST00000 256078	2/6	0.291	0.297	0	0	0.294
T357_291015	chr13	32362670	G	T	agG/agT	R/S	ENSG00000 139618	BRCA2	ENST00000 380152	17/27	0.132	0.135	0	0	0.1335
T357_291015	chr17	7674945	G	A	Cga/Tga	R/*	ENSG00000 141510	TP53	ENST00000 269305	6/11	0.247	0.248	0	0	0.2475
T357_291015	chr2	211657762	T	G	caA/caC	Q/H	ENSG00000 178568	ERBB4	ENST00000 342788	16/28		0.106		0.001	0.106
T357_291015	chr2	43224819-36	-	- CGCGGCC GCCGCGGA GG	gCCTCCGC GGCGGCC GCCg	ASAAAA/X	ENSG00000 152518	ZFP36L2	ENST00000 282388	2/2		0.17		0.001	0.17

T386_091214	chr17	7675088	C	T	cGc/cAc	R/H	ENSG00000141510	TP53	ENST00000269305	5/11	0.228	0.218	0.001	0.001	0.273
T386_091214	chr3	179218367	A	C	cAg/cCg	Q/P	ENSG00000121879	PIK3CA	ENST00000263967	10/21	0.164	0.15	0.001	0.001	0.152
T386_091214	chr5	112837953	C	T	CagTag	Q*	ENSG00000134982	APC	ENST00000257430	15/16	0.111	0.11	0.001	0	0.1105
T386_091214	chrX	33020165	A	G	gTt/gCt	V/A	ENSG00000186847	DMD	ENST00000357033	2/79	0.11	0.113	0	0	0.1115
T386_180516	chr10	121503837	G	C	tCg/tGg	S/W	ENSG00000066468	FGFR2	ENST00000457416	10/18	0.135	0.177	0	0	0.156
T386_180516	chr12	11250416	A	T	agA/agT	R/S	ENSG00000179295	PTPN11	ENST00000351677	15/16	0.223	0.236	0	0	0.2295
T386_180516	chr17	7675088	C	T	cGc/cAc	R/H	ENSG00000141510	TP53	ENST00000269305	5/11	0.494	0.001			0.494
T386_180516	chr3	179218367	A	C	cAg/cCg	Q/P	ENSG00000121879	PIK3CA	ENST00000263967	10/21	0.384		0.001		0.384
T386_180516	chr5	112837953	C	T	CagTag	Q*	ENSG00000134982	APC	ENST00000257430	15/16	0.292	0.288	0.001	0	0.29
T386_180516	chr5	112839543	G	T	GaaTaa	E*	ENSG00000134982	APC	ENST00000257430	15/16	0.23	0.244	0	0	0.237
T386_180516	chr8	38421931	A	T	gTt/gAt	V/D	ENSG00000077782	FGFR1	ENST00000425967	9/19	0.188	0.192	0	0	0.19
T386_180516	chrX	33020165	A	G	gTt/gCt	V/A	ENSG00000186847	DMD	ENST00000357033	2/79	0.274	0.308	0	0	0.291
T476_050916	chr17	7675088	C	T	cGc/cAc	R/H	ENSG00000141510	TP53	ENST00000269305	5/11	0.183	0.195	0	0.001	0.189
T476_050916	chr2	43225892	-	+C	-/G	-/X	ENSG00000152518	ZFP36L2	ENST00000282388	2/2		0.176		0	0.176
T476_110315	chr17	7675088	C	T	cGc/cAc	R/H	ENSG00000141510	TP53	ENST00000269305	5/11	0.243	0.264	0	0.001	0.2535
T476_110315	chr2	43225892	-	+C	-/G	-/X	ENSG00000152518	ZFP36L2	ENST00000282388	2/2		0.272		0	0.272
T476_110315	chr3	179221162	A	T	aAg/aTg	K/M	ENSG00000121879	PIK3CA	ENST00000263967	14/21	0.12	0.113	0	0	0.1165
T512_051015	chr15	43768557	A	C	aAg/aCg	K/T	ENSG00000167034	PDIA3	ENST00000300289	9/13	0.085	0.104	0	0	0.0995
T512_051015	chr18	51065534	C	T	cCt/cTt	P/L	ENSG00000141646	SMAD4	ENST00000342988	9/12	0.614		0		0.614
T512_051015	chr5	112839729	G	T	GagTag	E/*	ENSG00000134982	APC	ENST00000257430	16/16	0.684		0		0.684
T512_130114	chr18	51065534	C	T	cCt/cTt	P/L	ENSG00000141646	SMAD4	ENST00000342988	9/12	0.371		0		0.371
T512_130114	chr5	112839729	G	T	GagTag	E/*	ENSG00000134982	APC	ENST00000257430	16/16	0.464		0		0.464

T519_020715	chr17	7673803	G	A	Cgt/Tgt	R/C	ENSG00000141510	TP53	ENST00000269305	8/11	0.173	0.166	0	0	0.1695
T519_210114	chr17	7673803	G	A	Cgt/Tgt	R/C	ENSG00000141510	TP53	ENST00000269305	8/11	0.43		0		0.43
T519_210114	chr20	58903555	C	A	gaC/gaA	D/E	ENSG00000087460	GNAS	ENST00000371100	4/13	0.111	0.12	0	0	0.1155
T519_210114	chr5	112839465	C	T	Cag/Tag	Q/*	ENSG00000134982	APC	ENST00000257430	16/16	0.195	0.189	0	0.001	0.192
T519_210114	chr5	56871965	G	T	Gaa/Taa	E/*	ENSG00000095015	MAP3K1	ENST00000399503	7/20	0.192	0.194	0	0	0.193
T519_240314	chr17	7673803	G	A	Cgt/Tgt	R/C	ENSG00000141510	TP53	ENST00000269305	8/11	0.513		0		0.513
T519_240314	chr20	58903555	C	A	gaC/gaA	D/E	ENSG00000087460	GNAS	ENST00000371100	4/13	0.12	0.109	0	0	0.1145
T519_240314	chr5	112839465	C	T	Cag/Tag	Q/*	ENSG00000134982	APC	ENST00000257430	16/16	0.215	0.223	0	0.001	0.219
T519_240314	chr5	56871965	G	T	Gaa/Taa	E/*	ENSG00000095015	MAP3K1	ENST00000399503	7/20	0.205	0.205	0	0	0.205
T575_191015	chr17	7673811	A	G	tTt/tCt	F/S	ENSG00000141510	TP53	ENST00000269305	8/11	0.104	0.103	0.001	0	0.1035
T575_191015	chr3	142555897-8	-	-T	Ata/ta	i/X	ENSG00000175054	ATR	ENST00000350721	10/47		0.116		0.028	0.116
T575_270214	chr17	7673811	A	G	tTt/tCt	F/S	ENSG00000141510	TP53	ENST00000269305	8/11	0.109	0.107	0.001	0	0.108
T575_270515	chr3	142555897-8	-	-T	Ata/ta	i/X	ENSG00000175054	ATR	ENST00000350721	10/47		0.109		0.028	0.109
T809_030915	chr1	64869346	C	A	aaG/aaT	K/N	ENSG00000162434	JAK1	ENST00000342505	6/25	0.123	0.135	0	0	0.129
T809_030915	chr17	7675088	C	T	cGc/cAc	R/H	ENSG00000141510	TP53	ENST00000269305	5/11	0.544		0		0.544
T809_030915	chr5	112839693	C	T	Cag/Tag	Q/*	ENSG00000134982	APC	ENST00000257430	16/16	0.542		0.001		0.542
T809_110914	chr1	64869346	C	A	aaG/aaT	K/N	ENSG00000162434	JAK1	ENST00000342505	6/25	0.186	0.172	0	0	0.179
T809_110914	chr17	7675088	C	T	cGc/cAc	R/H	ENSG00000141510	TP53	ENST00000269305	5/11	0.727		0		0.727
T809_110914	chr5	112839693	C	T	Cag/Tag	Q/*	ENSG00000134982	APC	ENST00000257430	16/16	0.744		0.001		0.744
T836_180416	chr17	7674939	C	A	Gaa/Taa	E/*	ENSG00000141510	TP53	ENST00000269305	6/11	0.224	0.222	0	0	0.223
T836_180416	chr5	112839474	C	T	Cag/Tag	Q/*	ENSG00000134982	APC	ENST00000257430	16/16	0.248	0.259	0	0	0.2535
T897_200815	chr12	25245347	C	T	gGc/gAc	G/D	ENSG00000133703	KRAS	ENST00000256078	2/6	0.171	0.17	0	0	0.1705

T897_200815	chr17	72126097	-	+CG	tcg/tCGcg	S/SX	ENSG00000 125398	SOX9	ENST00000 245479	3/3		0.213		0	0.213
T897_200815	chr17	7675967-8	-	-A	Tgc/gc	C/X	ENSG00000 141510	TP53	ENST00000 269305	5/11		0.327		0.001	0.327
T897_200815	chr18	51965549	G	A	cGc/cAc	R/H	ENSG00000 141646	SMAD4	ENST00000 342988	9/12	0.128	0.115	0	0.001	0.122
T897_200815	chr18	51978285	A	T	gAtg/Tt	D/V	ENSG00000 141646	SMAD4	ENST00000 342988	12/12	0.236	0.229	0.001	0	0.2325
T897_200815	chr22	29050710	C	T	ccC/ccT	P	ENSG00000 183579	ZNRF3	ENST00000 544604	8/9	0.204	0.229	0	0	0.2165
T897_200815	chr3	179199688	G	A	cGa/cAa	R/Q	ENSG00000 121879	PIK3CA	ENST00000 263967	2/21	0.286	0.304	0	0.001	0.295
T897_200815	chr4	152329695-6	-	-T	aaA/aa	K/X	ENSG00000 109670	FBXW7	ENST00000 281708	8/12		0.214		0	0.214
T897_200815	chr5	112059714	G	I	Gaa/Iaa	E/*	ENSG00000 134982	APC	ENST00000 257430	16/16	0.467		0		0.467
T897_220316	chr5	112059714	G	T	Gaa/Taa	E/*	ENSG00000 134982	APC	ENST00000 257430	16/16	0.173	0.156	0	0.001	0.1645
T986_060315	chr17	7675076	T	C	cAt/cGt	H/R	ENSG00000 141510	TP53	ENST00000 269305	5/11	0.189	0.198	0.001	0.001	0.1935
T986_060315	chr3	179218304	A	G	gAg/gGg	E/G	ENSG00000 121879	PIK3CA	ENST00000 263967	10/21	0.164	0.186	0	0	0.175
T986_060315	chr5	112792446	C	T	Cga/Tga	R/*	ENSG00000 134982	APC	ENST00000 257430	7/16	0.102	0.107	0	0.001	0.1045
T986_060315	chr17	7675076	T	C	cAt/cGt	H/R	ENSG00000 141510	TP53	ENST00000 269305	5/11	0.305	0.315	0.001	0.001	0.31
T986_100215	chr3	179218304	A	G	gAg/gGg	E/G	ENSG00000 121879	PIK3CA	ENST00000 263967	10/21	0.232	0.222	0	0	0.227
T986_100215	chr5	112792446	C	T	Cga/Tga	R/*	ENSG00000 134982	APC	ENST00000 257430	7/16	0.175	0.174	0	0.001	0.1765
T986_260916	chr17	72126617	-	+GA	cga/cGAga	R/RX	ENSG00000 125398	SOX9	ENST00000 245479	3/3		0.311		0.001	0.311
T986_260916	chr17	7675075	T	C	cAt/cGt	H/R	ENSG00000 141510	TP53	ENST00000 269305	5/11	0.726		0.001		0.726
T986_260916	chr3	179218301	A	G	gAg/gGg	E/G	ENSG00000 121879	PIK3CA	ENST00000 263967	10/21	0.65		0		0.65
T986_260916	chr5	112792446	C	T	Cga/Tga	R/*	ENSG00000 134982	APC	ENST00000 257430	7/16	0.559		0		0.559
T986_261016	chr17	72126617	-	+GA	cga/cGAga	R/RX	ENSG00000 125398	SOX9	ENST00000 245479	3/3		0.206		0.001	0.206
T986_261016	chr17	7675075	T	C	cAt/cGt	H/R	ENSG00000 141510	TP53	ENST00000 269305	5/11	0.413		0.001		0.413
T986_261016	chr3	179218304	A	G	gAg/gGg	E/G	ENSG00000 121879	PIK3CA	ENST00000 263967	10/21	0.351		0		0.351

19986_261016	chr6	112792446	C	T	CgaTga	Y	ENSG00000134962	APC	ENST00000257430	7/16	0.261	0.268	0	0.001	0.2645
19986_261016	chr7	55165435	C	T	taCtaT	Y	ENSG00000146648	EGFR	ENST00000275493	15/28	0.164	0.161	0	0	0.1625

Table S9 Mutations missed by the callers for the CRC patients with serial plasma samples.

Patient	Sample	Day	chr	Pos (GRCh38)	Ref	Alt	Symbol/Gene	VAF-Mutect	VAF-Varscan	VAF-manual	ctDNA detection - ichorCNA	ctDNA detection - NDR
357	357_230913	34	chr13	32362670	G	T	BRCA2	undetected	undetected	0	negative	positive
			chr2	211657762	T	G	ERBB4	undetected	undetected	0		
			chr12	25245350	C	T	KRAS	undetected	undetected	0.0105		
			chr17	7674945	G	A	TP53	undetected	undetected	0		
			chr2	43224819-36	-	- GGCGGCC GCCGCGGA GG	ZFP36L2	undetected	undetected	0		
1531	1531_111016	160	chr5	112839439	C	A	APC	undetected	undetected	0	negative	positive
			chr17	7675088	C	T	TP53	undetected	undetected	0.0012		
1531	1531_111116	191	chr5	112839439	C	A	APC	undetected	undetected	0	negative	negative
			chr17	7675088	C	T	TP53	undetected	undetected	0		
575	575_270616	864	chr3	142555897-8	-	-T	ATR	undetected	undetected	0.0579	positive	positive
			chr17	7673811	A	G	TP53	undetected	undetected	0.0546		
519	519_140116	726	chr5	112839465	C	T	APC	undetected	undetected	0.0247	positive	positive
			chr20	58903555	C	A	GNAS	undetected	undetected	0.0232		
			chr5	56871965	G	T	MAP3K1	undetected	undetected	0.0177		
			chr17	7673803	G	A	TP53	undetected	undetected	0.0448		

Table S10. Information on all candidate pan-cancer features of nucleosome-depleted regions.

Columns
ID: feature index
Transcript: transcript ID
Gene: gene name
Chr: chromosome
Site: coordinate of nucleosome-depleted site (GRCh37)
Region: location of nucleosome-depleted site
Group: gene group based on its expression in blood and tumor
$FPKM_{blood}$: FPKM value in normal blood. Their FPKM values in tumors of 20 cancer types are all <1.

ID	Transcript	Gene	Chr	Site	Region	Group	$FPKM_{blood}$
1	ENST00000008938.4	PGLYRP1	19	46526323	promoter	blood	148.76
2	ENST00000177694.1	TBX21	17	45810610	promoter	blood	5.98
3	ENST00000194097.8	NAIP	5	70316737	promoter	blood	10.22
4	ENST00000199708.2	HBQ1	16	230452	promoter	blood	45.79
5	ENST00000217133.1	TUBB1	20	57594309	promoter	blood	6.01
6	ENST00000219596.5	MEFV	16	3306627	promoter	blood	19.19
7	ENST00000221804.4	CLC	19	40228668	promoter	blood	19.65
8	ENST00000221954.6	CEACAM4	19	42133442	promoter	blood	32.81
9	ENST00000225275.3	MPO	17	56358296	promoter	blood	7.23
10	ENST00000233997.3	AZU1	19	827836	promoter	blood	14.03
11	ENST00000234347.9	PRTN3	19	840960	promoter	blood	13.78
12	ENST00000236826.7	MMP8	11	102595685	promoter	blood	20.68
13	ENST00000245620.13	LILRB3	19	54726850	promoter	blood	22.83
14	ENST00000258104.7	DYSF	2	71680852	promoter	blood	6.76
15	ENST00000262407.5	ITGA2B	17	42466873	promoter	blood	12.34
16	ENST00000262651.3	HCK	20	30640045	promoter	blood	8.74
17	ENST00000262865.8	BPI	20	36932525	promoter	blood	18.06
18	ENST00000263621.1	ELANE	19	852291	promoter	blood	21.67
19	ENST00000264260.6	IL18RAP	2	103035149	promoter	blood	42.11
20	ENST00000264834.4	KLF1	19	12997995	promoter	blood	8.95
21	ENST00000267396.8	REM2	14	23352374	promoter	blood	6.91
22	ENST00000287497.12	ITGAM	16	31271311	promoter	blood	6.52
23	ENST00000294800.7	FCGR3B	1	161601252	promoter	blood	13.85
24	ENST00000295619.3	PROK2	3	71834212	promoter	blood	12.98
25	ENST00000295683.2	CXCR1	2	219031718	promoter	blood	355.57
26	ENST00000296028.3	PPBP	4	74853914	promoter	blood	50.15
27	ENST00000296435.2	CAMP	3	48264837	promoter	blood	27.17
28	ENST00000297435.2	DEFA4	8	6795860	promoter	blood	34.98
29	ENST00000299663.7	CLEC4E	12	8693559	promoter	blood	29.27
30	ENST00000299665.2	CLEC4D	12	8666136	promoter	blood	10.47
31	ENST00000302312.8	AHSP	16	31539185	promoter	blood	85.51
32	ENST00000304076.6	VAV1	19	6772725	promoter	blood	7.61
33	ENST00000304361.8	CLEC12A	12	10124014	promoter	blood	10.23
34	ENST00000307395.4	GP9	3	128779610	promoter	blood	9.72
35	ENST00000307564.8	AKNA	9	117156685	promoter	blood	11.95

36	ENST00000310544.8	PHOSPHO1	17	47307890	promoter	blood	30.92
37	ENST00000312156.8	NFE2	12	54689544	promoter	blood	11.15
38	ENST00000314412.6	FUT7	9	139927462	promoter	blood	16.90
39	ENST00000314446.9	LILRB2	19	54785039	promoter	blood	7.87
40	ENST00000318507.6	CXCR2	2	218990727	promoter	blood	157.27
41	ENST00000324134.10	NLRP12	19	54327597	promoter	blood	9.17
42	ENST00000326965.6	TAGAP	6	159466184	promoter	blood	5.94
43	ENST00000327857.6	DEFA3	8	6875823	promoter	blood	355.10
44	ENST00000329800.7	TMCC2	1	205225329	promoter	blood	10.64
45	ENST00000330597.3	HBG1	11	5271122	promoter	blood	5.07
46	ENST00000330807.9	ALAS2	X	55057497	promoter	blood	142.66
47	ENST00000331941.6	CSF3R	1	36945120	promoter	blood	16.12
48	ENST00000335854.8	ALAS2	X	55057410	promoter	blood	101.19
49	ENST00000336906.4	HBG2	11	5276041	promoter	blood	104.85
50	ENST00000338372.6	VSTM1	19	54567207	promoter	blood	10.71
51	ENST00000340023.6	FPR2	19	52264104	promoter	blood	34.71
52	ENST00000342063.4	C19orf35	19	2282175	promoter	blood	8.64
53	ENST00000342571.7	MKNK1	1	47051643	promoter	blood	14.42
54	ENST00000344138.8	GRAP2	22	40297086	promoter	blood	5.60
55	ENST00000348343.10	BMX	X	15518952	promoter	blood	6.99
56	ENST00000353065.7	PROK2	3	71834357	promoter	blood	82.89
57	ENST00000355524.7	FCAR	19	55385736	promoter	blood	53.04
58	ENST00000356815.3	HBM	16	215977	promoter	blood	163.82
59	ENST00000357396.7	CEACAM3	19	42300369	promoter	blood	16.26
60	ENST00000367053.5	CR1	1	207669502	promoter	blood	10.47
61	ENST00000367964.6	FCGR3B	1	161601753	promoter	blood	465.71
62	ENST00000368034.8	CD244	1	160832645	promoter	blood	6.27
63	ENST00000373103.5	CSF3R	1	36948879	promoter	blood	61.20
64	ENST00000375448.4	PADI4	1	17634692	promoter	blood	95.04
65	ENST00000375809.7	C6orf25	6	31691150	promoter	blood	5.36
66	ENST00000375862.6	HCK	20	30640000	promoter	blood	20.11
67	ENST00000376092.7	LST1	6	31554977	promoter	blood	5.01
68	ENST00000376670.7	GATA1	X	48644962	promoter	blood	11.17
69	ENST00000377901.8	TMEM71	8	133772828	promoter	blood	6.74
70	ENST00000378023.8	FAM65B	6	24877583	promoter	blood	15.67
71	ENST00000378625.5	NADK	1	1711508	promoter	blood	13.09
72	ENST00000379595.7	PSTPIP1	15	77287472	promoter	blood	5.90
73	ENST00000380299.3	HBD	11	5255878	promoter	blood	138.84
74	ENST00000380315.2	HBB	11	5250625	promoter	blood	5.45
75	ENST00000381153.7	C11orf21	11	2323290	promoter	blood	11.33
76	ENST00000381603.7	SIRPB1	20	1600642	promoter	blood	26.01
77	ENST00000381605.8	SIRPB1	20	1600655	promoter	blood	24.72
78	ENST00000382689.7	DEFA1B	8	6856717	promoter	blood	118.00
79	ENST00000382692.2	DEFA1	8	6837602	promoter	blood	996.76
80	ENST00000391726.7	FCAR	19	55385704	promoter	blood	6.00
81	ENST00000392619.1	CD300E	17	72619877	promoter	blood	24.98
82	ENST00000392621.5	CD300LB	17	72527605	promoter	blood	7.72
83	ENST00000392841.1	HMBS	11	118958697	promoter	blood	7.28
84	ENST00000393450.5	MYL4	17	45286714	promoter	blood	22.77
85	ENST00000394430.5	RASGRP2	11	64512061	promoter	blood	17.61
86	ENST00000394432.7	RASGRP2	11	64511650	promoter	blood	9.91

87	ENST00000397497.8	PTK2B	8	27288416	promoter	blood	5.81
88	ENST00000397797.1	HBA1	16	226703	promoter	blood	25.27
89	ENST00000398421.6	NCF1	7	74188358	promoter	blood	11.04
90	ENST00000398632.3	MX2	21	42774561	promoter	blood	7.28
91	ENST00000399753.2	MSRB1	16	1993196	promoter	blood	11.22
92	ENST00000402255.5	APOBEC3A	22	39348756	promoter	blood	11.96
93	ENST00000402280.5	NLRC4	2	32489949	promoter	blood	5.84
94	ENST00000404054.3	TACC3	4	1741078	promoter	blood	5.17
95	ENST00000409369.1	IL18RAP	2	103036146	promoter	blood	46.86
96	ENST00000410026.6	NABP1	2	192542862	promoter	blood	7.35
97	ENST00000413580.5	PHOSPHO1	17	47308128	promoter	blood	42.76
98	ENST00000414723.1	GCA	2	163212948	promoter	blood	9.14
99	ENST00000415495.5	CEACAM3	19	42300549	promoter	blood	14.84
100	ENST00000418507.6	LST1	6	31553901	promoter	blood	6.17
101	ENST00000421556.5	RASGRP2	11	64511594	promoter	blood	5.27
102	ENST00000421702.2	FCGR3B	1	161600948	promoter	blood	18.36
103	ENST00000425417.1	ARHGAP26	5	142586765	promoter	blood	5.74
104	ENST00000425515.6	VNN3	6	133055904	promoter	blood	8.73
105	ENST00000426897.6	CD37	19	49838653	promoter	blood	7.43
106	ENST00000427321.1	C1orf228	1	45189457	promoter	blood	8.41
107	ENST00000427466.1	THEMIS2	1	28199067	promoter	blood	7.94
108	ENST00000430041.6	ARHGAP9	12	57871981	promoter	blood	22.12
109	ENST00000436504.2	LILRB3	19	54723224	promoter	blood	69.95
110	ENST00000436693.6	TLR6	4	38858438	promoter	blood	5.83
111	ENST00000441002.1	IL1R2	2	102624977	promoter	blood	16.30
112	ENST00000441045.5	NAMPT	7	105925397	promoter	blood	5.42
113	ENST00000441366.6	EPB42	15	43513249	promoter	blood	11.69
114	ENST00000442948.3	FOLR3	11	71846989	promoter	blood	9.64
115	ENST00000444257.5	PLB1	2	28827594	promoter	blood	7.51
116	ENST00000445347.1	LILRB3	19	54726959	promoter	blood	49.26
117	ENST00000448367.5	FES	15	91432780	promoter	blood	6.30
118	ENST00000452208.1	RGL4	22	24038671	promoter	blood	64.94
119	ENST00000453777.1	LILRA1	19	55105125	promoter	blood	6.64
120	ENST00000455062.2	NCF1	7	74191615	promoter	blood	15.11
121	ENST00000456013.5	PTPN6	12	7060434	promoter	blood	7.47
122	ENST00000460045.1	IMPDH1	7	128035225	promoter	blood	8.72
123	ENST00000460208.1	LILRB3	19	54721567	promoter	blood	51.15
124	ENST00000460442.5	ZDHHC19	3	195925781	promoter	blood	22.43
125	ENST00000460650.5	SELL	1	169673894	promoter	blood	5.03
126	ENST00000462275.5	TBXAS1	7	139529072	promoter	blood	6.07
127	ENST00000462927.5	CYTH4	22	37678566	promoter	blood	26.95
128	ENST00000463153.1	ABHD5	3	43759160	promoter	blood	5.85
129	ENST00000463516.5	MYO1G	7	45014814	promoter	blood	5.23
130	ENST00000464329.1	CD53	1	111440292	promoter	blood	10.28
131	ENST00000464526.1	LST1	6	31553971	promoter	blood	9.98
132	ENST00000464591.1	C1orf162	1	112017190	promoter	blood	7.62
133	ENST00000464994.5	IL1R2	2	102608422	promoter	blood	12.24
134	ENST00000465814.5	ARAP1	11	72433133	promoter	blood	10.09
135	ENST00000465984.5	SLC11A1	2	219246911	promoter	blood	10.54
136	ENST00000466138.1	CSF3R	1	36933410	promoter	blood	32.37
137	ENST00000466151.1	PADI2	1	17409921	promoter	blood	7.13

138	ENST00000466612.5	ABTB1	3	127391857	promoter	blood	6.18
139	ENST00000467001.1	PADI4	1	17675225	promoter	blood	24.03
140	ENST00000467525.5	FCGR2A	1	161476123	promoter	blood	8.40
141	ENST00000467786.1	FGD3	9	95737532	promoter	blood	43.15
142	ENST00000467972.5	SLC12A9	7	100454416	promoter	blood	6.80
143	ENST00000468221.5	SLC11A1	2	219246752	promoter	blood	42.34
144	ENST00000468945.1	PADI4	1	17672529	promoter	blood	17.46
145	ENST00000469273.1	LILRB3	19	54724660	promoter	blood	16.30
146	ENST00000469280.1	NCF2	1	183533186	promoter	blood	13.91
147	ENST00000469349.1	NBEAL2	3	47049253	promoter	blood	7.54
148	ENST00000469380.1	CSF3R	1	36939431	promoter	blood	5.77
149	ENST00000469449.1	SLC11A1	2	219248410	promoter	blood	5.27
150	ENST00000469532.1	RAC2	22	37640318	promoter	blood	9.83
151	ENST00000469799.5	SLC11A1	2	219247002	promoter	blood	8.27
152	ENST00000469886.5	CYTH4	22	37678556	promoter	blood	6.16
153	ENST00000470579.5	ARID5A	2	97202480	promoter	blood	7.93
154	ENST00000471466.5	RAB24	5	176730706	promoter	blood	6.58
155	ENST00000471836.1	PARVG	22	44577630	promoter	blood	6.53
156	ENST00000472694.1	HBA1	16	226697	promoter	blood	64.74
157	ENST00000473070.1	FAM65B	6	24843364	promoter	blood	19.03
158	ENST00000473156.5	LILRA1	19	55105047	promoter	blood	7.68
159	ENST00000473883.5	HCLS1	3	121363030	promoter	blood	36.16
160	ENST00000474129.1	ABTB1	3	127395815	promoter	blood	8.59
161	ENST00000475225.5	SLC11A1	2	219247025	promoter	blood	37.49
162	ENST00000475472.5	FGR	1	27961645	promoter	blood	49.95
163	ENST00000475683.1	TUBA4A	2	220118638	promoter	blood	10.51
164	ENST00000476050.5	TRAF3IP3	1	209941940	promoter	blood	5.61
165	ENST00000476408.1	CD53	1	111422859	promoter	blood	10.54
166	ENST00000476492.1	LAPTM5	1	31230604	promoter	blood	6.02
167	ENST00000476532.1	SASH3	X	128913955	promoter	blood	9.72
168	ENST00000477720.1	LILRA5	19	54822933	promoter	blood	16.70
169	ENST00000478298.5	ABTB1	3	127395379	promoter	blood	6.71
170	ENST00000478902.1	ZDHHC18	1	27177620	promoter	blood	12.52
171	ENST00000479534.5	PADI2	1	17401846	promoter	blood	5.78
172	ENST00000479996.1	RGS19	20	62710778	promoter	blood	9.02
173	ENST00000480467.5	CDK5RAP2	9	123165773	promoter	blood	16.88
174	ENST00000480825.6	CSF3R	1	36941928	promoter	blood	127.36
175	ENST00000481215.1	RAC2	22	37627543	promoter	blood	7.04
176	ENST00000481314.5	HCLS1	3	121379748	promoter	blood	13.32
177	ENST00000481517.1	STAT5B	17	40369889	promoter	blood	8.48
178	ENST00000481789.1	KCNAB2	1	6156316	promoter	blood	8.66
179	ENST00000482429.1	LTB	6	31550183	promoter	blood	5.85
180	ENST00000482543.1	PTK2B	8	27310374	promoter	blood	9.94
181	ENST00000483487.2	SLC11A1	2	219248890	promoter	blood	5.23
182	ENST00000483665.6	FCGR2A	1	161475247	promoter	blood	6.60
183	ENST00000483722.1	TREML2	6	41168932	promoter	blood	15.58
184	ENST00000483750.5	WAS	X	48542217	promoter	blood	34.49
185	ENST00000484216.1	HBA2	16	222943	promoter	blood	296.56
186	ENST00000484762.1	CSF3R	1	36933677	promoter	blood	8.26
187	ENST00000485335.1	IL1R2	2	102639852	promoter	blood	12.15
188	ENST00000485341.5	LSP1	11	1901907	promoter	blood	5.48

189	ENST00000485583.1	LRCH4	7	100183752	promoter	blood	5.95
190	ENST00000485743.1	HBB	11	5248302	promoter	blood	128.52
191	ENST00000485991.5	CFP	X	47489294	promoter	blood	5.10
192	ENST00000486097.1	NCF1	7	74197786	promoter	blood	12.51
193	ENST00000486327.6	DHX34	19	47870370	promoter	blood	6.88
194	ENST00000486742.2	LILRA5	19	54824344	promoter	blood	17.29
195	ENST00000486749.5	SLC2A3	12	8088763	promoter	blood	9.53
196	ENST00000486935.2	SEMA4D	9	91996758	promoter	blood	5.98
197	ENST00000487283.5	ZAP70	2	98349392	promoter	blood	7.23
198	ENST00000487290.5	HCLS1	3	121379745	promoter	blood	6.41
199	ENST00000487445.6	GCA	2	163200669	promoter	blood	12.82
200	ENST00000487651.5	SLC12A9	7	100456358	promoter	blood	6.67
201	ENST00000487761.5	GPSM3	6	32160645	promoter	blood	14.37
202	ENST00000487791.1	HBA1	16	226747	promoter	blood	29.54
203	ENST00000487871.1	SMAP2	1	40879649	promoter	blood	36.53
204	ENST00000488945.5	GNLY	2	85912298	promoter	blood	11.68
205	ENST00000488970.1	BTK	X	100609209	promoter	blood	7.40
206	ENST00000489175.1	KCNE1	21	35884505	promoter	blood	6.75
207	ENST00000489358.5	NAMPT	7	105925396	promoter	blood	30.07
208	ENST00000489551.5	CSF3R	1	36948535	promoter	blood	106.01
209	ENST00000489980.5	GNLY	2	85921465	promoter	blood	14.53
210	ENST00000490763.1	SLC2A3	12	8082631	promoter	blood	5.93
211	ENST00000490872.1	SLC11A1	2	219254688	promoter	blood	26.15
212	ENST00000491376.5	IMPDH1	7	128050036	promoter	blood	6.59
213	ENST00000492413.5	SLC11A1	2	219247010	promoter	blood	17.89
214	ENST00000493242.1	LILRB2	19	54784952	promoter	blood	22.65
215	ENST00000493288.1	PGD	1	10472891	promoter	blood	9.99
216	ENST00000493365.5	ABTB1	3	127391795	promoter	blood	6.22
217	ENST00000493632.5	INPP5D	2	234078206	promoter	blood	17.01
218	ENST00000493871.1	MPP1	X	154014500	promoter	blood	6.09
219	ENST00000494080.5	CCDC88B	11	64109078	promoter	blood	7.88
220	ENST00000494268.1	MSL3	X	11778341	promoter	blood	6.22
221	ENST00000495406.1	CDK5RAP2	9	123152555	promoter	blood	10.53
222	ENST00000495458.5	RAB24	5	176730682	promoter	blood	11.72
223	ENST00000495988.1	APOBEC3A	22	39348746	promoter	blood	40.03
224	ENST00000496379.5	FES	15	91433070	promoter	blood	7.77
225	ENST00000496915.1	PREX1	20	47259276	promoter	blood	5.23
226	ENST00000497441.5	RASGRP2	11	64504726	promoter	blood	12.78
227	ENST00000497615.1	NADK	1	1686335	promoter	blood	9.43
228	ENST00000497747.5	NADK	1	1686305	promoter	blood	9.33
229	ENST00000498461.1	ALOX5	10	45938869	promoter	blood	13.87
230	ENST00000498666.5	ITGB2	21	46340875	promoter	blood	13.12
231	ENST00000500323.2	DOK3	5	176935878	promoter	blood	10.88
232	ENST00000502380.1	DOK3	5	176937383	promoter	blood	8.44
233	ENST00000504910.1	HK3	5	176318392	promoter	blood	6.36
234	ENST00000505207.5	UBE2D3	4	103746937	promoter	blood	7.43
235	ENST00000508794.6	NAIP	5	70316601	promoter	blood	11.43
236	ENST00000509314.5	FBXL5	4	15661487	promoter	blood	10.24
237	ENST00000509339.1	MXD3	5	176735063	promoter	blood	30.07
238	ENST00000512426.5	CCND3	6	41908323	promoter	blood	7.01
239	ENST00000512747.3	IL2RG	X	70331456	promoter	blood	6.21

240	ENST00000513001.5	ACSL1	4	185680030	promoter	blood	17.65
241	ENST00000517804.5	DMTN	8	21914477	promoter	blood	7.30
242	ENST00000517813.1	DENND3	8	142194587	promoter	blood	13.47
243	ENST00000517985.5	DENND3	8	142188220	promoter	blood	9.36
244	ENST00000518135.1	TNFRSF10C	8	22972020	promoter	blood	5.06
245	ENST00000518249.5	DENND3	8	142151302	promoter	blood	9.51
246	ENST00000518806.1	DENND3	8	142187186	promoter	blood	11.76
247	ENST00000519594.5	LCP2	5	169724731	promoter	blood	5.37
248	ENST00000520174.5	DMTN	8	21914416	promoter	blood	16.02
249	ENST00000520322.1	LCP2	5	169678696	promoter	blood	5.68
250	ENST00000520450.5	DOCK2	5	169483442	promoter	blood	11.23
251	ENST00000520571.1	DENND3	8	142198997	promoter	blood	8.57
252	ENST00000520887.1	FAM49B	8	130859563	promoter	blood	7.15
253	ENST00000521442.1	ATP6V1B2	8	20075693	promoter	blood	8.33
254	ENST00000523015.1	DENND3	8	142154013	promoter	blood	7.05
255	ENST00000523022.5	CA1	8	86290342	promoter	blood	40.92
256	ENST00000523066.1	DENND3	8	142183604	promoter	blood	6.75
257	ENST00000523266.5	DMTN	8	21916717	promoter	blood	6.93
258	ENST00000523369.1	LCP2	5	169685502	promoter	blood	9.88
259	ENST00000523530.1	DENND3	8	142201373	promoter	blood	7.23
260	ENST00000523615.1	STK10	5	171488634	promoter	blood	12.61
261	ENST00000523829.5	TMEM71	8	133772807	promoter	blood	11.05
262	ENST00000526387.5	TBC1D10C	11	67171386	promoter	blood	7.10
263	ENST00000526474.1	TBC1D10C	11	67172719	promoter	blood	8.87
264	ENST00000526980.5	CSF3R	1	36948500	promoter	blood	184.80
265	ENST00000527031.5	JAK3	19	17958800	promoter	blood	6.17
266	ENST00000527146.1	IFITM2	11	308320	promoter	blood	18.56
267	ENST00000527525.5	SIPA1	11	65407337	promoter	blood	5.39
268	ENST00000528086.5	CD44	11	35160718	promoter	blood	8.17
269	ENST00000528780.5	IFITM1	11	313506	promoter	blood	47.88
270	ENST00000530119.5	TALDO1	11	747464	promoter	blood	7.74
271	ENST00000530226.1	SIPA1	11	65413282	promoter	blood	6.84
272	ENST00000530587.5	PHF21A	11	45959815	promoter	blood	6.25
273	ENST00000531221.5	FCGR3B	1	161600996	promoter	blood	57.18
274	ENST00000531334.1	ECE1	1	21548574	promoter	blood	5.78
275	ENST00000532028.1	PHF21A	11	45967420	promoter	blood	5.50
276	ENST00000532362.1	CMTM2	16	66620812	promoter	blood	114.27
277	ENST00000532897.5	MKNK1	1	47037972	promoter	blood	6.23
278	ENST00000533815.2	BTNL8	5	180336564	promoter	blood	5.72
279	ENST00000533968.1	SPI1	11	47400038	promoter	blood	12.90
280	ENST00000534261.3	SIGLEC5	19	52148798	promoter	blood	6.14
281	ENST00000534754.5	SORL1	11	121481961	promoter	blood	9.84
282	ENST00000535615.5	CARS2	13	111318077	promoter	blood	5.33
283	ENST00000535841.2	DEFA1B	8	6875811	promoter	blood	962.74
284	ENST00000536885.1	ARAP1	11	72399526	promoter	blood	7.74
285	ENST00000536995.5	ATG16L2	11	72532933	promoter	blood	11.55
286	ENST00000538842.1	ATG16L2	11	72527790	promoter	blood	6.35
287	ENST00000539134.1	RELT	11	73104289	promoter	blood	6.58
288	ENST00000539932.5	SLC11A1	2	219246926	promoter	blood	50.32
289	ENST00000540182.5	NLRC5	16	57074600	promoter	blood	6.20
290	ENST00000540513.1	ACRBP	12	6748017	promoter	blood	9.23

291	ENST00000541206.6	RNF166	16	88770025	promoter	blood	11.36
292	ENST00000541623.5	ARAP1	11	72399582	promoter	blood	8.01
293	ENST00000541800.6	PLBD1	12	14689059	promoter	blood	6.78
294	ENST00000542481.1	ATG16L2	11	72534940	promoter	blood	25.18
295	ENST00000542587.5	LPAR2	19	19739739	promoter	blood	10.95
296	ENST00000543576.5	DENND1C	19	6481798	promoter	blood	12.06
297	ENST00000544490.5	ATG16L2	11	72525472	promoter	blood	30.13
298	ENST00000544997.5	FERMT3	11	63974150	promoter	blood	7.56
299	ENST00000546200.5	ARHGAP9	12	57871634	promoter	blood	66.03
300	ENST00000546704.1	ARHGAP9	12	57868923	promoter	blood	19.20
301	ENST00000548139.5	ARHGAP9	12	57871842	promoter	blood	15.20
302	ENST00000551000.1	ARHGAP9	12	57871650	promoter	blood	8.28
303	ENST00000552953.5	ARHGAP9	12	57870424	promoter	blood	24.58
304	ENST00000553070.5	NFE2	12	54694799	promoter	blood	23.61
305	ENST00000553872.1	PYGL	14	51388246	promoter	blood	8.64
306	ENST00000554736.5	GNG2	14	52328042	promoter	blood	9.30
307	ENST00000556418.1	RIN3	14	93118846	promoter	blood	12.65
308	ENST00000558177.5	ANPEP	15	90345967	promoter	blood	11.96
309	ENST00000558332.3	IL16	15	81591757	promoter	blood	7.66
310	ENST00000558588.5	PLCB2	15	40599894	promoter	blood	12.82
311	ENST00000559341.5	MAN2A2	15	91459225	promoter	blood	8.61
312	ENST00000559750.5	PSTPIP1	15	77287513	promoter	blood	16.39
313	ENST00000560064.1	PSTPIP1	15	77328035	promoter	blood	5.96
314	ENST00000560377.5	PSTPIP1	15	77287726	promoter	blood	8.38
315	ENST00000561175.1	ADAM8	10	135086080	promoter	blood	6.86
316	ENST00000562129.1	CORO1A	16	30199396	promoter	blood	14.38
317	ENST00000562759.1	ST20	15	80200378	promoter	blood	5.59
318	ENST00000562918.5	ITGAX	16	31366495	promoter	blood	10.15
319	ENST00000563269.1	PLCG2	16	81964866	promoter	blood	6.38
320	ENST00000563526.5	CYBA	16	88717396	promoter	blood	7.13
321	ENST00000564072.1	SLCO3A1	15	92704805	promoter	blood	8.74
322	ENST00000564572.1	CNN2	19	1036798	promoter	blood	5.34
323	ENST00000564632.1	ITGAL	16	30531077	promoter	blood	12.98
324	ENST00000564707.1	AHSP	16	31539298	promoter	blood	6.85
325	ENST00000564768.1	CORO1A	16	30198003	promoter	blood	6.01
326	ENST00000564894.1	RNF166	16	88768058	promoter	blood	7.90
327	ENST00000564905.1	XPO6	16	28145246	promoter	blood	12.98
328	ENST00000565076.1	SIRPB1	20	1552558	promoter	blood	5.74
329	ENST00000565284.5	XPO6	16	28164239	promoter	blood	14.84
330	ENST00000565497.5	CORO1A	16	30194940	promoter	blood	6.42
331	ENST00000566082.1	USB1	16	58049017	promoter	blood	6.82
332	ENST00000567034.5	CORO1A	16	30197253	promoter	blood	11.54
333	ENST00000567038.1	XPO6	16	28113307	promoter	blood	8.97
334	ENST00000567178.1	ITGAM	16	31339358	promoter	blood	23.09
335	ENST00000568760.5	DEF8	16	90023661	promoter	blood	7.24
336	ENST00000568982.5	CORO1A	16	30194930	promoter	blood	7.54
337	ENST00000570106.6	SIGLEC5	19	52133588	promoter	blood	40.53
338	ENST00000570439.1	ACAP1	17	7248650	promoter	blood	5.27
339	ENST00000570473.5	TRIM25	17	54981704	promoter	blood	5.32
340	ENST00000570755.1	MMP25	16	3097532	promoter	blood	31.89
341	ENST00000571206.1	ARRB2	17	4618884	promoter	blood	26.58

342	ENST00000571220.1	ACAP1	17	7246254	promoter	blood	29.18
343	ENST00000571303.1	MLKL	16	74725367	promoter	blood	5.93
344	ENST00000571791.5	ARRB2	17	4613977	promoter	blood	13.94
345	ENST00000572418.1	P2RX1	17	3819746	promoter	blood	9.95
346	ENST00000572666.5	CORO7	16	4411903	promoter	blood	7.67
347	ENST00000572782.1	ARRB2	17	4617846	promoter	blood	16.63
348	ENST00000574548.1	RNF167	17	4847675	promoter	blood	6.40
349	ENST00000574888.5	ARRB2	17	4613950	promoter	blood	7.24
350	ENST00000575131.5	ARRB2	17	4613956	promoter	blood	11.97
351	ENST00000575441.1	MMP25	16	3106795	promoter	blood	88.59
352	ENST00000576594.1	ACAP1	17	7250448	promoter	blood	17.88
353	ENST00000576628.1	ACAP1	17	7239916	promoter	blood	20.20
354	ENST00000576769.1	SLC43A2	17	1486992	promoter	blood	5.40
355	ENST00000578574.1	SLC16A3	17	80186938	promoter	blood	7.93
356	ENST00000581287.5	SLC16A3	17	80191563	promoter	blood	11.97
357	ENST00000581974.1	DHRS13	17	27226541	promoter	blood	5.97
358	ENST00000582174.5	FLOT2	17	27224672	promoter	blood	6.46
359	ENST00000582812.5	NDEL1	17	8316449	promoter	blood	9.15
360	ENST00000583093.5	SECTM1	17	80291639	promoter	blood	7.78
361	ENST00000583810.5	PIK3R5	17	8785825	promoter	blood	8.43
362	ENST00000584445.5	NARF	17	80438344	promoter	blood	11.89
363	ENST00000585852.5	FMNL1	17	43308036	promoter	blood	19.81
364	ENST00000586080.1	R3HDM4	19	901236	promoter	blood	5.15
365	ENST00000587259.5	VMP1	17	57807076	promoter	blood	10.58
366	ENST00000587265.1	CA4	17	58235469	promoter	blood	5.45
367	ENST00000587287.1	RASGRP4	19	38902036	promoter	blood	6.80
368	ENST00000587444.1	VASP	19	46029052	promoter	blood	6.41
369	ENST00000587856.1	FMNL1	17	43311251	promoter	blood	22.20
370	ENST00000588708.5	RASGRP4	19	38907787	promoter	blood	24.68
371	ENST00000589261.5	ICAM3	19	10450295	promoter	blood	6.41
372	ENST00000589900.5	ICAM3	19	10450305	promoter	blood	21.24
373	ENST00000589911.1	FMNL1	17	43322691	promoter	blood	7.99
374	ENST00000590227.5	DNAH17	17	76446380	promoter	blood	5.85
375	ENST00000590856.1	UNC13D	17	73826742	promoter	blood	6.33
376	ENST00000590974.1	LYL1	19	13213975	promoter	blood	5.48
377	ENST00000591616.1	UNC13D	17	73831353	promoter	blood	7.12
378	ENST00000592527.1	FMNL1	17	43310229	promoter	blood	7.31
379	ENST00000594221.5	STXBP2	19	7706716	promoter	blood	6.21
380	ENST00000594696.1	PRAM1	19	8556907	promoter	blood	17.63
381	ENST00000594743.1	CD37	19	49840472	promoter	blood	8.07
382	ENST00000595046.1	MYO1F	19	8642326	promoter	blood	6.90
383	ENST00000595325.5	MYO1F	19	8642322	promoter	blood	13.66
384	ENST00000595596.1	GRAMD1A	19	35503892	promoter	blood	5.53
385	ENST00000595725.5	CD37	19	49838657	promoter	blood	20.04
386	ENST00000596937.1	MYO1F	19	8615297	promoter	blood	6.21
387	ENST00000597222.1	MYO1F	19	8604936	promoter	blood	29.52
388	ENST00000597611.7	FKBP8	19	18654887	promoter	blood	9.25
389	ENST00000597852.5	CD37	19	49838675	promoter	blood	13.98
390	ENST00000598005.1	MYO1F	19	8606840	promoter	blood	17.89
391	ENST00000598201.5	SHKBP1	19	41086073	promoter	blood	12.36
392	ENST00000598529.5	MYO1F	19	8619448	promoter	blood	16.08

393	ENST00000598907.5	SHKBP1	19	41084102	promoter	blood	14.71
394	ENST00000598953.1	FPR2	19	52264465	promoter	blood	37.43
395	ENST00000599123.1	MYO1F	19	8620661	promoter	blood	7.54
396	ENST00000599180.2	FFAR2	19	35939203	promoter	blood	24.79
397	ENST00000599662.1	CEACAM3	19	42312851	promoter	blood	9.48
398	ENST00000599694.1	RASAL3	19	15567410	promoter	blood	6.37
399	ENST00000599716.5	SHKBP1	19	41082793	promoter	blood	10.66
400	ENST00000600463.1	IFI30	19	18284979	promoter	blood	6.41
401	ENST00000600885.1	MYO1F	19	8592271	promoter	blood	5.95
402	ENST00000601502.1	MYO1F	19	8610602	promoter	blood	8.05
403	ENST00000602101.6	RASAL3	19	15575325	promoter	blood	7.16
404	ENST00000602136.1	MYO1F	19	8612931	promoter	blood	7.01
405	ENST00000602142.5	VAV1	19	6772737	promoter	blood	8.46
406	ENST00000602166.1	EGLN2	19	41312824	promoter	blood	5.19
407	ENST00000602612.5	KCNAB2	1	6086380	promoter	blood	5.03
408	ENST00000605039.5	BIN2	12	51717938	promoter	blood	11.02
409	ENST00000607855.5	CD177	19	43857843	promoter	blood	5.94
410	ENST00000609870.5	CELF2	10	11207447	promoter	blood	12.41
411	ENST00000611028.2	FOLR3	11	71846798	promoter	blood	11.13
412	ENST00000612844.4	FOLR3	11	71846756	promoter	blood	13.11
413	ENST00000614135.4	RASGRP4	19	38916945	promoter	blood	8.18
414	ENST00000614254.1	AOAH	7	36570290	promoter	blood	14.33
415	ENST00000615340.4	RASGRP4	19	38916837	promoter	blood	6.88
416	ENST00000616356.4	FCN1	9	137809723	promoter	blood	16.99
417	ENST00000619100.4	SLC38A5	X	48325880	promoter	blood	10.86
418	ENST00000620888.4	HBG2	11	5276011	promoter	blood	161.14
419	ENST00000621510.1	AOAH	7	36554282	promoter	blood	19.27
420	ENST00000622764.1	SAP25	7	100171443	promoter	blood	5.94
421	ENST00000008938.4	PGLYRP1	19	46525993	junction	blood	148.76
422	ENST00000177694.1	TBX21	17	45811311	junction	blood	5.98
423	ENST00000194097.8	NAIP	5	70316486	junction	blood	10.22
424	ENST00000199708.2	HBQ1	16	230580	junction	blood	45.79
425	ENST00000217133.1	TUBB1	20	57594634	junction	blood	6.01
426	ENST00000219596.5	MEFV	16	3306311	junction	blood	19.19
427	ENST00000221804.4	CLC	19	40228578	junction	blood	19.65
428	ENST00000221954.6	CEACAM4	19	42133268	junction	blood	32.81
429	ENST00000225275.3	MPO	17	56357966	junction	blood	7.23
430	ENST00000233997.3	AZU1	19	827904	junction	blood	14.03
431	ENST00000234347.9	PRTN3	19	841069	junction	blood	13.78
432	ENST00000236826.7	MMP8	11	102595485	junction	blood	20.68
433	ENST00000245620.13	LILRB3	19	54726815	junction	blood	22.83
434	ENST00000258104.7	DYSF	2	71681216	junction	blood	6.76
435	ENST00000262407.5	ITGA2B	17	42466654	junction	blood	12.34
436	ENST00000262651.3	HCK	20	30640289	junction	blood	8.74
437	ENST00000262865.8	BPI	20	36932755	junction	blood	18.06
438	ENST00000263621.1	ELANE	19	852395	junction	blood	21.67
439	ENST00000264260.6	IL18RAP	2	103035400	junction	blood	42.11
440	ENST00000264834.4	KLF1	19	12997868	junction	blood	8.95
441	ENST00000267396.8	REM2	14	23352599	junction	blood	6.91
442	ENST00000287497.12	ITGAM	16	31271413	junction	blood	6.52
443	ENST00000294800.7	FCGR3B	1	161600845	junction	blood	13.85

444	ENST00000295619.3	PROK2	3	71834108	junction	blood	12.98
445	ENST00000295683.2	CXCR1	2	219031631	junction	blood	355.57
446	ENST00000296028.3	PPBP	4	74853673	junction	blood	50.15
447	ENST00000296435.2	CAMP	3	48265202	junction	blood	27.17
448	ENST00000297435.2	DEFA4	8	6795748	junction	blood	34.98
449	ENST00000299663.7	CLEC4E	12	8693357	junction	blood	29.27
450	ENST00000299665.2	CLEC4D	12	8666356	junction	blood	10.47
451	ENST00000302312.8	AHSP	16	31539283	junction	blood	85.51
452	ENST00000304076.6	VAV1	19	6773022	junction	blood	7.61
453	ENST00000304361.8	CLEC12A	12	10124286	junction	blood	10.23
454	ENST00000307395.4	GP9	3	128779693	junction	blood	9.72
455	ENST00000307564.8	AKNA	9	117156637	junction	blood	11.95
456	ENST00000310544.8	PHOSPHO1	17	47307830	junction	blood	30.92
457	ENST00000312156.8	NFE2	12	54689328	junction	blood	11.15
458	ENST00000314412.6	FUT7	9	139926431	junction	blood	16.90
459	ENST00000314446.9	LILRB2	19	54784816	junction	blood	7.87
460	ENST00000318507.6	CXCR2	2	218991076	junction	blood	157.27
461	ENST00000324134.10	NLRP12	19	54327140	junction	blood	9.17
462	ENST00000326965.6	TAGAP	6	159465911	junction	blood	5.94
463	ENST00000327857.6	DEFA3	8	6875744	junction	blood	355.10
464	ENST00000329800.7	TMCC2	1	205225544	junction	blood	10.64
465	ENST00000330597.3	HBG1	11	5270943	junction	blood	5.07
466	ENST00000330807.9	ALAS2	X	55057375	junction	blood	142.66
467	ENST00000331941.6	CSF3R	1	36945034	junction	blood	16.12
468	ENST00000336906.4	HBG2	11	5275867	junction	blood	104.85
469	ENST00000338372.6	VSTM1	19	54566998	junction	blood	10.71
470	ENST00000340023.6	FPR2	19	52264483	junction	blood	34.71
471	ENST00000342063.4	C19orf35	19	2282086	junction	blood	8.64
472	ENST00000342571.7	MKNK1	1	47051546	junction	blood	14.42
473	ENST00000344138.8	GRAP2	22	40297334	junction	blood	5.60
474	ENST00000348343.10	BMX	X	15519063	junction	blood	6.99
475	ENST00000355524.7	FCAR	19	55385779	junction	blood	53.04
476	ENST00000356815.3	HBM	16	216088	junction	blood	163.82
477	ENST00000357396.7	CEACAM3	19	42300673	junction	blood	16.26
478	ENST00000367053.5	CR1	1	207669733	junction	blood	10.47
479	ENST00000367964.6	FCGR3B	1	161601676	junction	blood	465.71
480	ENST00000368034.8	CD244	1	160832407	junction	blood	6.27
481	ENST00000373103.5	CSF3R	1	36948412	junction	blood	61.20
482	ENST00000375448.4	PADI4	1	17634809	junction	blood	95.04
483	ENST00000375809.7	C6orf25	6	31691221	junction	blood	5.36
484	ENST00000376092.7	LST1	6	31555095	junction	blood	5.01
485	ENST00000376670.7	GATA1	X	48645053	junction	blood	11.17
486	ENST00000377901.8	TMEM71	8	133772722	junction	blood	6.74
487	ENST00000378023.8	FAM65B	6	24877179	junction	blood	15.67
488	ENST00000378625.5	NADK	1	1711344	junction	blood	13.09
489	ENST00000379595.7	PSTPIP1	15	77287950	junction	blood	5.90
490	ENST00000380299.3	HBD	11	5255572	junction	blood	138.84
491	ENST00000380315.2	HBB	11	5250482	junction	blood	5.45
492	ENST00000381153.7	C11orf21	11	2322986	junction	blood	11.33
493	ENST00000381603.7	SIRPB1	20	1600515	junction	blood	26.01
494	ENST00000382689.7	DEFA1B	8	6856645	junction	blood	118.00

495	ENST00000382692.2	DEFA1	8	6837535	junction	blood	996.76
496	ENST00000392619.1	CD300E	17	72619721	junction	blood	24.98
497	ENST00000392621.5	CD300LB	17	72527450	junction	blood	7.72
498	ENST00000392841.1	HMBS	11	118958788	junction	blood	7.28
499	ENST00000393450.5	MYL4	17	45286923	junction	blood	22.77
500	ENST00000394430.5	RASGRP2	11	64510266	junction	blood	17.61
501	ENST00000394432.7	RASGRP2	11	64511475	junction	blood	9.91
502	ENST00000397497.8	PTK2B	8	27288969	junction	blood	5.81
503	ENST00000397797.1	HBA1	16	226761	junction	blood	25.27
504	ENST00000398421.6	NCF1	7	74188450	junction	blood	11.04
505	ENST00000398632.3	MX2	21	42775563	junction	blood	7.28
506	ENST00000399753.2	MSRB1	16	1993103	junction	blood	11.22
507	ENST00000402255.5	APOBEC3A	22	39348855	junction	blood	11.96
508	ENST00000402280.5	NLRC4	2	32489807	junction	blood	5.84
509	ENST00000404054.3	TACC3	4	1743848	junction	blood	5.17
510	ENST00000409369.1	IL18RAP	2	103036257	junction	blood	46.86
511	ENST00000410026.6	NABP1	2	192542967	junction	blood	7.35
512	ENST00000414723.1	GCA	2	163212991	junction	blood	9.14
513	ENST00000418507.6	LST1	6	31554092	junction	blood	6.17
514	ENST00000425417.1	ARHGAP26	5	142586873	junction	blood	5.74
515	ENST00000425515.6	VNN3	6	133055619	junction	blood	8.73
516	ENST00000426897.6	CD37	19	49838832	junction	blood	7.43
517	ENST00000427321.1	C1orf228	1	45189578	junction	blood	8.41
518	ENST00000427466.1	THEMIS2	1	28199176	junction	blood	7.94
519	ENST00000430041.6	ARHGAP9	12	57871568	junction	blood	22.12
520	ENST00000436504.2	LILRB3	19	54722998	junction	blood	69.95
521	ENST00000436693.6	TLR6	4	38858382	junction	blood	5.83
522	ENST00000441002.1	IL1R2	2	102625104	junction	blood	16.30
523	ENST00000441045.5	NAMPT	7	105925274	junction	blood	5.42
524	ENST00000441366.6	EPB42	15	43513014	junction	blood	11.69
525	ENST00000442948.3	FOLR3	11	71847166	junction	blood	9.64
526	ENST00000444257.5	PLB1	2	28827626	junction	blood	7.51
527	ENST00000448367.5	FES	15	91432866	junction	blood	6.30
528	ENST00000452208.1	RGL4	22	24038875	junction	blood	64.94
529	ENST00000453777.1	LILRA1	19	55105246	junction	blood	6.64
530	ENST00000455062.2	NCF1	7	74191693	junction	blood	15.11
531	ENST00000456013.5	PTPN6	12	7060683	junction	blood	7.47
532	ENST00000460045.1	IMPDH1	7	128035185	junction	blood	8.72
533	ENST00000460208.1	LILRB3	19	54721188	junction	blood	51.15
534	ENST00000460442.5	ZDHHC19	3	195925660	junction	blood	22.43
535	ENST00000460650.5	SELL	1	169673709	junction	blood	5.03
536	ENST00000462275.5	TBXAS1	7	139529278	junction	blood	6.07
537	ENST00000462927.5	CYTH4	22	37678629	junction	blood	26.95
538	ENST00000463153.1	ABHD5	3	43759349	junction	blood	5.85
539	ENST00000463516.5	MYO1G	7	45014773	junction	blood	5.23
540	ENST00000464329.1	CD53	1	111440514	junction	blood	10.28
541	ENST00000464591.1	C1orf162	1	112018687	junction	blood	7.62
542	ENST00000464994.5	IL1R2	2	102608495	junction	blood	12.24
543	ENST00000465814.5	ARAP1	11	72432895	junction	blood	10.09
544	ENST00000465984.5	SLC11A1	2	219247098	junction	blood	10.54
545	ENST00000466138.1	CSF3R	1	36933159	junction	blood	32.37

546	ENST00000466151.1	PADI2	1	17409731	junction	blood	7.13
547	ENST00000466612.5	ABTB1	3	127392451	junction	blood	6.18
548	ENST00000467001.1	PADI4	1	17675280	junction	blood	24.03
549	ENST00000467525.5	FCGR2A	1	161476381	junction	blood	8.40
550	ENST00000467786.1	FGD3	9	95737687	junction	blood	43.15
551	ENST00000467972.5	SLC12A9	7	100456564	junction	blood	6.80
552	ENST00000468945.1	PADI4	1	17672634	junction	blood	17.46
553	ENST00000469273.1	LILRB3	19	54724398	junction	blood	16.30
554	ENST00000469280.1	NCF2	1	183532569	junction	blood	13.91
555	ENST00000469349.1	NBEAL2	3	47049676	junction	blood	7.54
556	ENST00000469380.1	CSF3R	1	36939365	junction	blood	5.77
557	ENST00000469449.1	SLC11A1	2	219249088	junction	blood	5.27
558	ENST00000469532.1	RAC2	22	37640154	junction	blood	9.83
559	ENST00000470579.5	ARID5A	2	97202567	junction	blood	7.93
560	ENST00000471466.5	RAB24	5	176730010	junction	blood	6.58
561	ENST00000471636.1	PARVG	22	44577797	junction	blood	6.53
562	ENST00000472694.1	HBA1	16	227132	junction	blood	64.74
563	ENST00000473070.1	FAM65B	6	24843090	junction	blood	19.03
564	ENST00000473883.5	HCLS1	3	121361774	junction	blood	36.16
565	ENST00000474129.1	ABTB1	3	127395926	junction	blood	8.59
566	ENST00000475472.5	FGR	1	27961576	junction	blood	49.95
567	ENST00000475683.1	TUBA4A	2	220118578	junction	blood	10.51
568	ENST00000476050.5	TRAF3IP3	1	209942005	junction	blood	5.61
569	ENST00000476408.1	CD53	1	111422954	junction	blood	10.54
570	ENST00000476492.1	LAPTM5	1	31230506	junction	blood	6.02
571	ENST00000476532.1	SASH3	X	128914130	junction	blood	9.72
572	ENST00000477720.1	LILRA5	19	54822684	junction	blood	16.70
573	ENST00000478298.5	ABTB1	3	127395424	junction	blood	6.71
574	ENST00000478902.1	ZDHHC18	1	27177722	junction	blood	12.52
575	ENST00000479534.5	PADI2	1	17401351	junction	blood	5.78
576	ENST00000479996.1	RGS19	20	62710647	junction	blood	9.02
577	ENST00000480467.5	CDK5RAP2	9	123165521	junction	blood	16.88
578	ENST00000480825.6	CSF3R	1	36940978	junction	blood	127.36
579	ENST00000481215.1	RAC2	22	37627271	junction	blood	7.04
580	ENST00000481314.5	HCLS1	3	121379667	junction	blood	13.32
581	ENST00000481517.1	STAT5B	17	40369395	junction	blood	8.48
582	ENST00000481789.1	KCNAB2	1	6156816	junction	blood	8.66
583	ENST00000482429.1	LTB	6	31549336	junction	blood	5.85
584	ENST00000482543.1	PTK2B	8	27310677	junction	blood	9.94
585	ENST00000483665.6	FCGR2A	1	161475342	junction	blood	6.60
586	ENST00000483722.1	TREML2	6	41168692	junction	blood	15.58
587	ENST00000483750.5	WAS	X	48542374	junction	blood	34.49
588	ENST00000484216.1	HBA2	16	223006	junction	blood	296.56
589	ENST00000484762.1	CSF3R	1	36933423	junction	blood	8.26
590	ENST00000485335.1	IL1R2	2	102640083	junction	blood	12.15
591	ENST00000485341.5	LSP1	11	1902593	junction	blood	5.48
592	ENST00000485583.1	LRCH4	7	100183504	junction	blood	5.95
593	ENST00000485743.1	HBB	11	5248160	junction	blood	128.52
594	ENST00000485991.5	CFP	X	47489168	junction	blood	5.10
595	ENST00000486097.1	NCF1	7	74197975	junction	blood	12.51
596	ENST00000486327.6	DHX34	19	47870412	junction	blood	6.88

597	ENST00000486742.2	LILRA5	19	54824287	junction	blood	17.29
598	ENST00000486749.5	SLC2A3	12	8088616	junction	blood	9.53
599	ENST00000486935.2	SEMA4D	9	91996089	junction	blood	5.98
600	ENST00000487283.5	ZAP70	2	98349484	junction	blood	7.23
601	ENST00000487445.6	GCA	2	163200785	junction	blood	12.82
602	ENST00000487651.5	SLC12A9	7	100459206	junction	blood	6.67
603	ENST00000487761.5	GPSM3	6	32160249	junction	blood	14.37
604	ENST00000487791.1	HBA1	16	226810	junction	blood	29.54
605	ENST00000487871.1	SMAP2	1	40879912	junction	blood	36.53
606	ENST00000488945.5	GNLY	2	85912344	junction	blood	11.68
607	ENST00000488970.1	BTK	X	100608858	junction	blood	7.40
608	ENST00000489175.1	KCNE1	21	35884325	junction	blood	6.75
609	ENST00000489980.5	GNLY	2	85922546	junction	blood	14.53
610	ENST00000490763.1	SLC2A3	12	8082280	junction	blood	5.93
611	ENST00000490872.1	SLC11A1	2	219254751	junction	blood	26.15
612	ENST00000491376.5	IMPDH1	7	128049810	junction	blood	6.59
613	ENST00000493288.1	PGD	1	10473308	junction	blood	9.99
614	ENST00000493365.5	ABTB1	3	127391924	junction	blood	6.22
615	ENST00000493632.5	INPP5D	2	234078810	junction	blood	17.01
616	ENST00000493871.1	MPP1	X	154014479	junction	blood	6.09
617	ENST00000494080.5	CCDC88B	11	64109214	junction	blood	7.88
618	ENST00000494268.1	MSL3	X	11778428	junction	blood	6.22
619	ENST00000495406.1	CDK5RAP2	9	123152019	junction	blood	10.53
620	ENST00000496379.5	FES	15	91433192	junction	blood	7.77
621	ENST00000496915.1	PREX1	20	47258945	junction	blood	5.23
622	ENST00000497441.5	RASGRP2	11	64504225	junction	blood	12.78
623	ENST00000497615.1	NADK	1	1685983	junction	blood	9.43
624	ENST00000498461.1	ALOX5	10	45938985	junction	blood	13.87
625	ENST00000498666.5	ITGB2	21	46340736	junction	blood	13.12
626	ENST00000500323.2	DOK3	5	176935238	junction	blood	10.88
627	ENST00000502380.1	DOK3	5	176937261	junction	blood	8.44
628	ENST00000504910.1	HK3	5	176318389	junction	blood	6.36
629	ENST00000505207.5	UBE2D3	4	103746879	junction	blood	7.43
630	ENST00000509314.5	FBXL5	4	15661350	junction	blood	10.24
631	ENST00000509339.1	MXD3	5	176734782	junction	blood	30.07
632	ENST00000512426.5	CCND3	6	41908108	junction	blood	7.01
633	ENST00000512747.3	IL2RG	X	70331275	junction	blood	6.21
634	ENST00000513001.5	ACSL1	4	185678973	junction	blood	17.65
635	ENST00000517804.5	DMTN	8	21914647	junction	blood	7.30
636	ENST00000517813.1	DENND3	8	142195377	junction	blood	13.47
637	ENST00000517985.5	DENND3	8	142188295	junction	blood	9.36
638	ENST00000518135.1	TNFRSF10C	8	22972283	junction	blood	5.06
639	ENST00000518249.5	DENND3	8	142151423	junction	blood	9.51
640	ENST00000519594.5	LCP2	5	169724538	junction	blood	5.37
641	ENST00000520322.1	LCP2	5	169677734	junction	blood	5.68
642	ENST00000520450.5	DOCK2	5	169484670	junction	blood	11.23
643	ENST00000520571.1	DENND3	8	142199245	junction	blood	8.57
644	ENST00000520887.1	FAM49B	8	130859050	junction	blood	7.15
645	ENST00000521442.1	ATP6V1B2	8	20075793	junction	blood	8.33
646	ENST00000523015.1	DENND3	8	142154358	junction	blood	7.05
647	ENST00000523022.5	CA1	8	86290275	junction	blood	40.92

648	ENST00000523066.1	DENND3	8	142183840	junction	blood	6.75
649	ENST00000523266.5	DMTN	8	21917007	junction	blood	6.93
650	ENST00000523369.1	LCP2	5	169685041	junction	blood	9.88
651	ENST00000523530.1	DENND3	8	142202548	junction	blood	7.23
652	ENST00000523615.1	STK10	5	171488143	junction	blood	12.61
653	ENST00000526387.5	TBC1D10C	11	67171411	junction	blood	7.10
654	ENST00000526474.1	TBC1D10C	11	67172977	junction	blood	8.87
655	ENST00000527031.5	JAK3	19	17958755	junction	blood	6.17
656	ENST00000527146.1	IFITM2	11	308438	junction	blood	18.56
657	ENST00000527525.5	SIPA1	11	65407492	junction	blood	5.39
658	ENST00000528086.5	CD44	11	35160917	junction	blood	8.17
659	ENST00000528780.5	IFITM1	11	313691	junction	blood	47.88
660	ENST00000530119.5	TALDO1	11	747578	junction	blood	7.74
661	ENST00000530226.1	SIPA1	11	65413428	junction	blood	6.84
662	ENST00000530587.5	PHF21A	11	45959708	junction	blood	6.25
663	ENST00000531334.1	ECE1	1	21548240	junction	blood	5.78
664	ENST00000532028.1	PHF21A	11	45967391	junction	blood	5.50
665	ENST00000532362.1	CMTM2	16	66621001	junction	blood	114.27
666	ENST00000532897.5	MKNK1	1	47037735	junction	blood	6.23
667	ENST00000533815.2	BTNL8	5	180336697	junction	blood	5.72
668	ENST00000533968.1	SPI1	11	47399860	junction	blood	12.90
669	ENST00000534261.3	SIGLEC5	19	52148730	junction	blood	6.14
670	ENST00000534754.5	SORL1	11	121483541	junction	blood	9.84
671	ENST00000535615.5	CARS2	13	111317875	junction	blood	5.33
672	ENST00000536885.1	ARAP1	11	72399500	junction	blood	7.74
673	ENST00000536995.5	ATG16L2	11	72533340	junction	blood	11.55
674	ENST00000538842.1	ATG16L2	11	72527872	junction	blood	6.35
675	ENST00000539134.1	RELT	11	73104962	junction	blood	6.58
676	ENST00000540182.5	NLRC5	16	57074630	junction	blood	6.20
677	ENST00000540513.1	ACRBP	12	6747841	junction	blood	9.23
678	ENST00000541206.6	RNF166	16	88769198	junction	blood	11.36
679	ENST00000541800.6	PLBD1	12	14688593	junction	blood	6.78
680	ENST00000542481.1	ATG16L2	11	72535167	junction	blood	25.18
681	ENST00000542587.5	LPAR2	19	19739237	junction	blood	10.95
682	ENST00000543576.5	DENND1C	19	6481690	junction	blood	12.06
683	ENST00000544490.5	ATG16L2	11	72525608	junction	blood	30.13
684	ENST00000544997.5	FERMT3	11	63974286	junction	blood	7.56
685	ENST00000546704.1	ARHGAP9	12	57868658	junction	blood	19.20
686	ENST00000548139.5	ARHGAP9	12	57871784	junction	blood	15.20
687	ENST00000552953.5	ARHGAP9	12	57870373	junction	blood	24.58
688	ENST00000553070.5	NFE2	12	54694585	junction	blood	23.61
689	ENST00000553872.1	PYGL	14	51387674	junction	blood	8.64
690	ENST00000554736.5	GNG2	14	52328108	junction	blood	9.30
691	ENST00000556418.1	RIN3	14	93119420	junction	blood	12.65
692	ENST00000558177.5	ANPEP	15	90345638	junction	blood	11.96
693	ENST00000558332.3	IL16	15	81592816	junction	blood	7.66
694	ENST00000558588.5	PLCB2	15	40599790	junction	blood	12.82
695	ENST00000559341.5	MAN2A2	15	91459486	junction	blood	8.61
696	ENST00000560064.1	PSTPIP1	15	77328276	junction	blood	5.96
697	ENST00000561175.1	ADAM8	10	135085920	junction	blood	6.86
698	ENST00000562129.1	CORO1A	16	30199570	junction	blood	14.38

699	ENST00000562759.1	ST20	15	80199971	junction	blood	5.59
700	ENST00000562918.5	ITGAX	16	31366612	junction	blood	10.15
701	ENST00000563269.1	PLCG2	16	81965259	junction	blood	6.38
702	ENST00000563526.5	CYBA	16	88717364	junction	blood	7.13
703	ENST00000564072.1	SLCO3A1	15	92706776	junction	blood	8.74
704	ENST00000564572.1	CNN2	19	1039063	junction	blood	5.34
705	ENST00000564632.1	ITGAL	16	30531288	junction	blood	12.98
706	ENST00000564707.1	AHSP	16	31539335	junction	blood	6.85
707	ENST00000564768.1	CORO1A	16	30198544	junction	blood	6.01
708	ENST00000564894.1	RNF166	16	88767670	junction	blood	7.90
709	ENST00000564905.1	XPO6	16	28145162	junction	blood	12.98
710	ENST00000565076.1	SIRPB1	20	1552366	junction	blood	5.74
711	ENST00000565284.5	XPO6	16	28163980	junction	blood	14.84
712	ENST00000565497.5	CORO1A	16	30195046	junction	blood	6.42
713	ENST00000566082.1	USB1	16	58051343	junction	blood	6.82
714	ENST00000567034.5	CORO1A	16	30198041	junction	blood	11.54
715	ENST00000567038.1	XPO6	16	28113168	junction	blood	8.97
716	ENST00000567178.1	ITGAM	16	31339551	junction	blood	23.09
717	ENST00000568760.5	DEF8	16	90024068	junction	blood	7.24
718	ENST00000570106.6	SIGLEC5	19	52133552	junction	blood	40.53
719	ENST00000570439.1	ACAP1	17	7253547	junction	blood	5.27
720	ENST00000570473.5	TRIM25	17	54981616	junction	blood	5.32
721	ENST00000570755.1	MMP25	16	3097548	junction	blood	31.89
722	ENST00000571206.1	ARRB2	17	4619328	junction	blood	26.58
723	ENST00000571220.1	ACAP1	17	7246881	junction	blood	29.18
724	ENST00000571303.1	MLKL	16	74725175	junction	blood	5.93
725	ENST00000571791.5	ARRB2	17	4614039	junction	blood	13.94
726	ENST00000572418.1	P2RX1	17	3819383	junction	blood	9.95
727	ENST00000572666.5	CORO7	16	4411362	junction	blood	7.67
728	ENST00000572782.1	ARRB2	17	4618338	junction	blood	16.63
729	ENST00000574548.1	RNF167	17	4847933	junction	blood	6.40
730	ENST00000575441.1	MMP25	16	3107210	junction	blood	88.59
731	ENST00000576594.1	ACAP1	17	7250561	junction	blood	17.88
732	ENST00000576628.1	ACAP1	17	7240106	junction	blood	20.20
733	ENST00000576769.1	SLC43A2	17	1486498	junction	blood	5.40
734	ENST00000578574.1	SLC16A3	17	80186982	junction	blood	7.93
735	ENST00000581287.5	SLC16A3	17	80194107	junction	blood	11.97
736	ENST00000581974.1	DHRS13	17	27226145	junction	blood	5.97
737	ENST00000582174.5	FLOT2	17	27224544	junction	blood	6.46
738	ENST00000582812.5	NDEL1	17	8316587	junction	blood	9.15
739	ENST00000583093.5	SECTM1	17	80291576	junction	blood	7.78
740	ENST00000583810.5	PIK3R5	17	8785105	junction	blood	8.43
741	ENST00000584445.5	NARF	17	80439087	junction	blood	11.89
742	ENST00000585852.5	FMNL1	17	43308054	junction	blood	19.81
743	ENST00000586080.1	R3HDM4	19	900829	junction	blood	5.15
744	ENST00000587259.5	VMP1	17	57807378	junction	blood	10.58
745	ENST00000587265.1	CA4	17	58235488	junction	blood	5.45
746	ENST00000587287.1	RASGRP4	19	38901755	junction	blood	6.80
747	ENST00000587444.1	VASP	19	46029261	junction	blood	6.41
748	ENST00000587856.1	FMNL1	17	43311567	junction	blood	22.20
749	ENST00000588708.5	RASGRP4	19	38907692	junction	blood	24.68

750	ENST00000589261.5	ICAM3	19	10450215	junction	blood	6.41
751	ENST00000589911.1	FMNL1	17	43322783	junction	blood	7.99
752	ENST00000590227.5	DNAH17	17	76445496	junction	blood	5.85
753	ENST00000590856.1	UNC13D	17	73826659	junction	blood	6.33
754	ENST00000590974.1	LYL1	19	13213345	junction	blood	5.48
755	ENST00000591616.1	UNC13D	17	73831001	junction	blood	7.12
756	ENST00000592527.1	FMNL1	17	43310664	junction	blood	7.31
757	ENST00000594221.5	STXBP2	19	7706739	junction	blood	6.21
758	ENST00000594696.1	PRAM1	19	8555984	junction	blood	17.63
759	ENST00000594743.1	CD37	19	49840478	junction	blood	8.07
760	ENST00000595046.1	MYO1F	19	8641326	junction	blood	6.90
761	ENST00000595325.5	MYO1F	19	8642191	junction	blood	13.66
762	ENST00000595596.1	GRAMD1A	19	35504595	junction	blood	5.53
763	ENST00000595725.5	CD37	19	49838866	junction	blood	20.04
764	ENST00000596937.1	MYO1F	19	8615044	junction	blood	6.21
765	ENST00000597222.1	MYO1F	19	8604831	junction	blood	29.52
766	ENST00000597611.7	FKBP8	19	18654719	junction	blood	9.25
767	ENST00000598005.1	MYO1F	19	8606797	junction	blood	17.89
768	ENST00000598201.5	SHKBP1	19	41086391	junction	blood	12.36
769	ENST00000598529.5	MYO1F	19	8619361	junction	blood	16.08
770	ENST00000598907.5	SHKBP1	19	41084448	junction	blood	14.71
771	ENST00000599123.1	MYO1F	19	8620543	junction	blood	7.54
772	ENST00000599180.2	FFAR2	19	35939281	junction	blood	24.79
773	ENST00000599662.1	CEACAM3	19	42312968	junction	blood	9.48
774	ENST00000599694.1	RASAL3	19	15567313	junction	blood	6.37
775	ENST00000599716.5	SHKBP1	19	41082891	junction	blood	10.66
776	ENST00000600463.1	IFI30	19	18286032	junction	blood	6.41
777	ENST00000600885.1	MYO1F	19	8592222	junction	blood	5.95
778	ENST00000601502.1	MYO1F	19	8610534	junction	blood	8.05
779	ENST00000602101.6	RASAL3	19	15575316	junction	blood	7.16
780	ENST00000602136.1	MYO1F	19	8612920	junction	blood	7.01
781	ENST00000602166.1	EGLN2	19	41313179	junction	blood	5.19
782	ENST00000602612.5	KCNAB2	1	6086505	junction	blood	5.03
783	ENST00000605039.5	BIN2	12	51717806	junction	blood	11.02
784	ENST00000607855.5	CD177	19	43857918	junction	blood	5.94
785	ENST00000609870.5	CELF2	10	11207645	junction	blood	12.41
786	ENST00000611028.2	FOLR3	11	71846814	junction	blood	11.13
787	ENST00000614135.4	RASGRP4	19	38916709	junction	blood	8.18
788	ENST00000614254.1	AOAH	7	36570024	junction	blood	14.33
789	ENST00000616356.4	FCN1	9	137809615	junction	blood	16.99
790	ENST00000619100.4	SLC38A5	X	48325349	junction	blood	10.86
791	ENST00000621510.1	AOAH	7	36554078	junction	blood	19.27
792	ENST00000622764.1	SAP25	7	100171220	junction	blood	5.94

Table S11 Observed ctDNA fractions in the LOD analysis for the CRC+BRCA model.

Sample	Group	Expected ctDNA fractions	Observed ctDNA fraction
1279_221015-0.005	positive	0.0050	0.0194
1279_221015-0.010	positive	0.0100	0.0245
1279_221015-0.015	positive	0.0150	0.0364
1279_221015-0.020	positive	0.0200	0.0361
1279_221015-0.025	positive	0.0250	0.0482
1279_221015-0.030	positive	0.0300	0.0515
1279_221015-0.035	positive	0.0350	0.0597
1279_221015-0.040	positive	0.0400	0.0721
1279_221015-0.045	positive	0.0450	0.0631
1279_221015-0.050	positive	0.0500	0.0652
1279_221015-0.075	positive	0.0750	0.0837
1279_221015-0.100	positive	0.1000	0.1084
1279_221015-0.125	positive	0.1250	0.1332
1279_221015-0.150	positive	0.1500	0.1566
1279_221015-0.175	positive	0.1750	0.1561
1279_221015-0.200	positive	0.2000	0.1770
1279_221015-0.225	positive	0.2250	0.1910
1279_221015-0.250	positive	0.2500	0.2421
1279_221015-0.275	positive	0.2750	0.2313
1279_221015-0.300	positive	0.3000	0.2821
1279_221015-0.325	positive	0.3250	0.3011
1279_221015-0.350	positive	0.3500	0.3237
1279_221015-0.375	positive	0.3750	0.3630
1279_221015-0.400	positive	0.4000	0.3893
1279_221015-0.425	positive	0.4250	0.4190
1279_221015-0.450	positive	0.4500	0.4658
1279_221015-0.475	positive	0.4750	0.4764
1279_221015-0.500	positive	0.5000	0.4699
1279_241116-0.005	positive	0.0050	0.0252
1279_241116-0.010	positive	0.0100	0.0143
1279_241116-0.015	positive	0.0150	0.0230
1279_241116-0.020	positive	0.0200	0.0242
1279_241116-0.025	positive	0.0250	0.0385
1279_241116-0.030	positive	0.0300	0.0310
1279_241116-0.035	positive	0.0350	0.0426
1279_241116-0.040	positive	0.0400	0.0407
1279_241116-0.045	positive	0.0450	0.0418
1279_241116-0.050	positive	0.0500	0.0457
1279_241116-0.075	positive	0.0750	0.0761
1279_241116-0.100	positive	0.1000	0.1275
1279_241116-0.125	positive	0.1250	0.1369
1279_241116-0.150	positive	0.1500	0.1199
1279_241116-0.175	positive	0.1750	0.1242
1279_241116-0.200	positive	0.2000	0.1394
1279_241116-0.225	positive	0.2250	0.1577
1279_241116-0.250	positive	0.2500	0.1860
1279_241116-0.275	positive	0.2750	0.2301

1279_241116-0.300	positive	0.3000	0.2666
1279_241116-0.325	positive	0.3250	0.3036
1279_241116-0.350	positive	0.3500	0.2946
1279_241116-0.375	positive	0.3750	0.3256
1279_241116-0.400	positive	0.4000	0.3788
1279_241116-0.425	positive	0.4250	0.4033
1279_241116-0.450	positive	0.4500	0.4591
1279_241116-0.475	positive	0.4750	0.4359
1279_241116-0.490	positive	0.4900	0.4611
512_051015-0.005	positive	0.0050	0.0273
512_051015-0.010	positive	0.0100	0.0221
512_051015-0.015	positive	0.0150	0.0301
512_051015-0.020	positive	0.0200	0.0252
512_051015-0.025	positive	0.0250	0.0283
512_051015-0.030	positive	0.0300	0.0233
512_051015-0.035	positive	0.0350	0.0485
512_051015-0.040	positive	0.0400	0.0712
512_051015-0.045	positive	0.0450	0.0793
512_051015-0.050	positive	0.0500	0.0947
512_051015-0.075	positive	0.0750	0.1269
512_051015-0.100	positive	0.1000	0.1528
512_051015-0.125	positive	0.1250	0.1788
512_051015-0.150	positive	0.1500	0.2018
512_051015-0.175	positive	0.1750	0.2097
512_051015-0.200	positive	0.2000	0.2359
512_051015-0.225	positive	0.2250	0.2709
512_051015-0.250	positive	0.2500	0.2759
512_051015-0.275	positive	0.2750	0.2731
512_051015-0.300	positive	0.3000	0.2930
512_051015-0.325	positive	0.3250	0.3230
512_051015-0.350	positive	0.3500	0.3364
512_051015-0.375	positive	0.3750	0.3723
512_051015-0.400	positive	0.4000	0.4192
512_051015-0.425	positive	0.4250	0.4303
512_051015-0.450	positive	0.4500	0.4825
512_051015-0.475	positive	0.4750	0.4897
512_051015-0.500	positive	0.5000	0.5015
512_051015-0.525	positive	0.5250	0.5312
512_051015-0.550	positive	0.5500	0.5683
512_051015-0.575	positive	0.5750	0.5989
512_051015-0.600	positive	0.6000	0.6028
512_051015-0.614	positive	0.6140	0.5969
512_130114-0.005	positive	0.0050	0.0308
512_130114-0.010	positive	0.0100	0.0283
512_130114-0.015	positive	0.0150	0.0118
512_130114-0.020	positive	0.0200	0.0000
512_130114-0.025	positive	0.0250	0.0167
512_130114-0.030	positive	0.0300	0.0283
512_130114-0.035	positive	0.0350	0.0565

512_130114-0.040	positive	0.0400	0.0616
512_130114-0.045	positive	0.0450	0.0454
512_130114-0.050	positive	0.0500	0.0398
512_130114-0.075	positive	0.0750	0.0774
512_130114-0.100	positive	0.1000	0.0893
512_130114-0.125	positive	0.1250	0.1541
512_130114-0.150	positive	0.1500	0.1891
512_130114-0.175	positive	0.1750	0.1988
512_130114-0.200	positive	0.2000	0.2222
512_130114-0.225	positive	0.2250	0.2824
512_130114-0.250	positive	0.2500	0.3523
512_130114-0.275	positive	0.2750	0.3871
512_130114-0.300	positive	0.3000	0.4119
512_130114-0.325	positive	0.3250	0.4908
512_130114-0.350	positive	0.3500	0.5099
512_130114-0.375	positive	0.3750	0.5502
512_130114-0.394	positive	0.3940	0.5966
D19-0.005	positive	0.0050	0.0226
D19-0.010	positive	0.0100	0.0232
D19-0.015	positive	0.0150	0.0205
D19-0.020	positive	0.0200	0.0316
D19-0.025	positive	0.0250	0.0438
D19-0.030	positive	0.0300	0.0458
D19-0.035	positive	0.0350	0.0525
D19-0.040	positive	0.0400	0.0458
D19-0.045	positive	0.0450	0.0405
D19-0.050	positive	0.0500	0.0400
D19-0.075	positive	0.0750	0.0745
D19-0.100	positive	0.1000	0.1132
D19-0.125	positive	0.1250	0.1275
D19-0.150	positive	0.1500	0.1471
D19-0.175	positive	0.1750	0.1751
D19-0.200	positive	0.2000	0.1870
D19-0.225	positive	0.2250	0.1984
D19-0.250	positive	0.2500	0.2162
D19-0.275	positive	0.2750	0.2241
D19-0.300	positive	0.3000	0.2362
D19-0.325	positive	0.3250	0.2530
D19-0.350	positive	0.3500	0.3078
D19-0.375	positive	0.3750	0.3103
D19-0.400	positive	0.4000	0.3277
D19-0.425	positive	0.4250	0.3472
D19-0.450	positive	0.4500	0.3787
D19-0.475	positive	0.4750	0.3919
D19-0.500	positive	0.5000	0.4156
D19-0.525	positive	0.5250	0.4327
D19-0.550	positive	0.5500	0.4640
D19-0.575	positive	0.5750	0.4798
D19-0.600	positive	0.6000	0.5154

D19-0.625	positive	0.6250	0.5406
D19-0.650	positive	0.6500	0.5359
D19-0.675	positive	0.6750	0.5388
D19-0.700	positive	0.7000	0.5457
D19-0.725	positive	0.7250	0.5634
D19-0.7363	positive	0.7363	0.5554
E2c-0.005	positive	0.0050	0.0033
E2c-0.010	positive	0.0100	0.0041
E2c-0.015	positive	0.0150	0.0371
E2c-0.020	positive	0.0200	0.0500
E2c-0.025	positive	0.0250	0.0740
E2c-0.030	positive	0.0300	0.0815
E2c-0.035	positive	0.0350	0.0885
E2c-0.040	positive	0.0400	0.0859
E2c-0.045	positive	0.0450	0.0961
E2c-0.050	positive	0.0500	0.1203
E2c-0.075	positive	0.0750	0.1333
E2c-0.100	positive	0.1000	0.1525
E2c-0.125	positive	0.1250	0.1676
E2c-0.150	positive	0.1500	0.1783
E2c-0.175	positive	0.1750	0.2136
E2c-0.200	positive	0.2000	0.2138
E2c-0.225	positive	0.2250	0.2539
E2c-0.250	positive	0.2500	0.3305
E2c-0.275	positive	0.2750	0.3979
E2c-0.300	positive	0.3000	0.4422
E2c-0.325	positive	0.3250	0.4868
E2c-0.350	positive	0.3500	0.5341
E2c-0.375	positive	0.3750	0.5800
E2c-0.400	positive	0.4000	0.5747
E2c-0.4122	positive	0.4122	0.5703
E6c-0.005	positive	0.0050	0.0165
E6c-0.010	positive	0.0100	0.0221
E6c-0.015	positive	0.0150	0.0206
E6c-0.020	positive	0.0200	0.0395
E6c-0.025	positive	0.0250	0.0451
E6c-0.030	positive	0.0300	0.0589
E6c-0.035	positive	0.0350	0.0643
E6c-0.040	positive	0.0400	0.0687
E6c-0.045	positive	0.0450	0.0750
E6c-0.050	positive	0.0500	0.0744
E6c-0.075	positive	0.0750	0.1185
E6c-0.100	positive	0.1000	0.1275
E6c-0.125	positive	0.1250	0.1787
E6c-0.150	positive	0.1500	0.2008
E6c-0.175	positive	0.1750	0.2179
E6c-0.200	positive	0.2000	0.2374
E6c-0.225	positive	0.2250	0.2570
E6c-0.250	positive	0.2500	0.3111

E6c-0.275	positive	0.2750	0.3204
E6c-0.300	positive	0.3000	0.3706
E6c-0.325	positive	0.3250	0.4481
E6c-0.350	positive	0.3500	0.4578
E6c-0.375	positive	0.3750	0.4920
E6c-0.400	positive	0.4000	0.5168
E6c-0.425	positive	0.4250	0.5272
E6c-0.450	positive	0.4500	0.5648
E6c-0.475	positive	0.4750	0.5723
E6c-0.500	positive	0.5000	0.6091
E6c-0.525	positive	0.5250	0.6031
E6c-0.5386	positive	0.5386	0.5896
sub-healthy-1	negative	0.0000	0.0187
sub-healthy-2	negative	0.0000	0.0122
sub-healthy-3	negative	0.0000	0.0193
sub-healthy-4	negative	0.0000	0.0179
sub-healthy-5	negative	0.0000	0.0040
sub-healthy-6	negative	0.0000	0.0188
sub-healthy-7	negative	0.0000	0.0155
sub-healthy-8	negative	0.0000	0.0157
sub-healthy-9	negative	0.0000	0.0151
sub-healthy-10	negative	0.0000	0.0148
sub-healthy-11	negative	0.0000	0.0099
sub-healthy-12	negative	0.0000	0.0241
sub-healthy-13	negative	0.0000	0.0136
sub-healthy-14	negative	0.0000	0.0129
sub-healthy-15	negative	0.0000	0.0020
sub-healthy-16	negative	0.0000	0.0050
sub-healthy-17	negative	0.0000	0.0128
sub-healthy-18	negative	0.0000	0.0087
sub-healthy-19	negative	0.0000	0.0084
sub-healthy-20	negative	0.0000	0.0012
sub-healthy-21	negative	0.0000	0.0067
sub-healthy-22	negative	0.0000	0.0218
sub-healthy-23	negative	0.0000	0.0208
sub-healthy-24	negative	0.0000	0.0138
sub-healthy-25	negative	0.0000	0.0227
sub-healthy-26	negative	0.0000	0.0079
sub-healthy-27	negative	0.0000	0.0178
sub-healthy-28	negative	0.0000	0.0262
sub-healthy-29	negative	0.0000	0.0157
sub-healthy-30	negative	0.0000	0.0195
sub-healthy-31	negative	0.0000	0.0075
sub-healthy-32	negative	0.0000	0.0011
sub-healthy-33	negative	0.0000	0.0114
sub-healthy-34	negative	0.0000	0.0045
sub-healthy-35	negative	0.0000	0.0143
sub-healthy-36	negative	0.0000	0.0131
sub-healthy-37	negative	0.0000	0.0168

sub-healthy-38	negative	0.0000	0.0065
sub-healthy-39	negative	0.0000	0.0026
sub-healthy-40	negative	0.0000	0.0028

Table S12 A panel of 77 genes for screening breast cancer samples.

CDH1	ARID1A	MAGI3	FLT3	SMARCB1	RNF43	FGFR2
CDKN2A	ATR	MDM2	GNA11	SMO	APC	MET
HRAS	AURKA	MDM4	GNAQ	VHL	EGFR	FGFR3
JAK2	BRCA1	KMT2C	GNAS	BRAF	ZNRF3	ALK
JAK3	BRCA2	NOTCH4	HNF1A	KRAS	ATM	MAP2K1
NF1	CDKN1B	TSC1	IDH1	NRAS	PTEN	MTOR
NOTCH1	DOT1L	TSC2	IDH2	PIK3CA	CTNNB1	MAP2K4
RB1	ERBB3	ABL1	KDR	PIK3R1	MLH1	MAP3K1
RET	ESR1	CSF1R	MPL	SMAD4	ERBB2	AKT1
SRC	GATA3	DDR2	NPM1	TP53	ERBB4	PDGFRA
STK11	JAK1	EZH2	PTPN11	FBXW7	FGFR1	KIT

Table S13. Transcript expression data.

source	**tissue**	**sample size**	**download URLs**
GTEx	whole blood	337	https://toil.xenahubs.net/download/gtex_RSEM_isoform_fpkm.gz
TCGA	tumor of colorectal cancer (CRC)	372	https://toil.xenahubs.net/download/tcga_RSEM_isoform_fpkm.gz

Table S14. Information on all predictive features for colorectal cancer

Columns
Feature ID : feature index (see Table S3 for feature details)
MAE : mean absolute error between observed and calculated ctDNA fractions from 344 samples

Feature ID	MAE
59 86 475 703 760 790	0.017
70 256 268 322 379 903	0.019
72 86 703 760 790 900	0.019
70 78 268 322 364 475	0.020
86 555 703 760 790 900	0.020
59 86 703 760 790 900	0.020
72 86 760 790 900 905	0.020
256 268 322 379 475 553	0.020
70 268 322 364 571 903	0.021
70 161 268 322 571 903	0.021
161 268 322 359 553 903	0.021
86 703 760 790 900 905	0.021
78 268 284 322 571 903	0.021
256 268 284 322 359 379	0.021
115 161 268 744 903 905	0.021
70 78 268 284 322 903	0.021
161 268 284 359 553 903	0.021
70 115 268 322 571 903	0.021
284 359 379 475 571 788	0.021
70 268 284 322 571 903	0.021
59 78 126 154 181 639	0.021
86 703 760 788 790 900	0.021
70 161 181 322 480 903	0.021
59 86 703 760 790 905	0.021
124 181 256 485 744 905	0.021
70 161 268 284 322 903	0.022
70 115 161 268 359 903	0.022
115 161 268 553 884 905	0.022
124 161 268 553 673 905	0.022
70 268 284 322 364 903	0.022
59 124 126 153 161 250	0.022
70 124 161 268 322 903	0.022
115 161 181 553 673 905	0.022
161 268 322 359 553 571	0.022
124 161 268 485 553 673	0.022
70 268 571 839 903 905	0.022
78 268 284 322 884 903	0.022
268 322 359 379 475 553	0.022
124 181 485 571 673 744	0.022
268 284 322 553 884 903	0.022
78 115 124 268 322 903	0.022
124 284 475 480 673 788	0.022
126 568 604 714 777 830	0.022
70 161 268 284 903 905	0.022
59 86 553 703 760 790	0.022
268 322 379 475 553 905	0.022
67 124 161 181 284 673	0.022
268 359 379 475 553 905	0.023
70 268 284 322 884 903	0.023
115 284 359 485 571 777	0.023
268 284 359 379 475 553	0.023
268 322 777 788 884 903	0.023
70 181 322 475 480 884	0.023
78 161 268 284 322 903	0.023

Feature ID	MAE
115 161 268 284 903 905	0.023
115 124 181 284 447 485	0.023
115 181 284 571 824 903	0.023
70 124 161 268 673 903	0.023
67 124 181 485 673 744	0.023
67 124 181 673 830 839	0.023
70 268 284 322 673 903	0.023
70 124 161 268 903 905	0.023
70 161 268 839 903 905	0.023
70 115 124 268 903 905	0.023
59 86 703 760 788 790	0.023
39 447 466 595 604 639	0.023
124 161 181 256 673 744	0.023
70 470 480 485 639 858	0.023
70 115 181 475 571 684	0.023
268 359 379 475 553 788	0.023
70 115 268 373 571 900	0.023
70 124 161 181 903 905	0.023
72 154 284 777 788 884	0.024
124 161 268 553 903 905	0.024
336 540 632 714 793 874	0.024
70 181 336 830 839 884	0.024
70 115 124 268 571 903	0.024
2 256 336 529 632 682	0.024
161 256 268 336 475 905	0.024
379 553 571 788 858 900	0.024
268 284 322 673 788 903	0.024
115 124 161 181 284 447	0.024
70 268 284 788 903 905	0.024
115 284 480 485 529 777	0.024
359 475 553 571 788 900	0.024
70 161 181 571 864 903	0.024
161 181 744 884 903 905	0.024
70 161 181 284 884 903	0.024
115 124 268 322 379 673	0.024
268 284 322 788 884 903	0.024
82 217 477 487 629 717	0.024
268 359 379 475 571 788	0.024
161 268 284 322 673 903	0.024
126 496 470 658 793 858	0.024
2 39 256 395 619 839	0.024
124 126 161 181 284 673	0.024
2 115 124 181 359 830	0.025
359 379 475 553 571 900	0.025
124 161 181 673 744 830	0.025
70 161 268 284 673 903	0.025
124 181 256 359 485 830	0.025
124 181 364 673 788 903	0.025
115 161 181 359 485 673	0.025
480 485 673 721 744 858	0.025
70 475 571 788 900 905	0.025
284 379 475 788 900 905	0.025
78 153 322 568 830 884	0.025
70 379 475 571 788 900	0.025

Feature ID	MAE
124 161 181 284 364 673	0.025
115 124 161 181 673 744	0.025
2 337 384 395 839 899	0.025
161 256 268 359 379 673	0.025
284 322 788 884 903 905	0.025
115 161 268 284 673 903	0.025
364 410 525 542 793 839	0.025
70 115 124 161 181 905	0.025
124 268 284 322 788 903	0.025
115 154 359 480 485 830	0.025
78 154 364 542 619 796	0.025
84 336 359 466 632 858	0.025
359 379 475 553 788 884	0.025
379 553 571 788 900 905	0.025
72 126 204 542 714 796	0.025
78 124 181 359 485 830	0.025
181 256 359 485 777 830	0.025
268 359 379 475 788 884	0.025
115 124 161 268 903 905	0.025
78 115 154 364 604 830	0.025
359 379 475 553 571 788	0.025
181 256 485 555 673 744	0.025
124 181 256 284 673 830	0.025
115 126 161 284 903 905	0.025
78 154 364 485 568 830	0.025
39 256 525 568 619 839	0.025
115 154 181 256 485 905	0.026
181 202 284 322 673 884	0.026
78 204 364 525 542 632	0.026
181 284 322 673 777 884	0.026
115 161 181 673 744 884	0.026
364 568 619 830 858 884	0.026
284 322 571 788 884 903	0.026
181 284 322 480 903 905	0.026
115 124 161 181 284 673	0.026
32 122 202 286 487 594	0.026
115 161 268 322 884 903	0.026
72 153 247 250 591 594	0.026
70 115 161 268 284 903	0.026
70 181 478 721 744 884	0.026
115 124 181 673 744 830	0.026
70 124 181 788 903 905	0.026
284 359 379 475 553 571	0.026
78 154 542 568 721 830	0.026
78 126 256 522 542 639	0.026
161 268 284 322 359 903	0.026
124 161 268 322 379 673	0.026
67 332 455 580 704 904	0.026
268 322 359 571 788 903	0.026
2 256 464 540 568 874	0.026
154 480 485 568 673 744	0.026
124 161 268 673 788 903	0.026
70 395 410 540 702 874	0.026
161 268 322 364 673 903	0.026

Feature ID	MAE
124 181 256 359 744 830	0.026
181 284 322 485 721 903	0.026
59 336 470 632 721 858	0.026
39 256 337 407 702 839	0.026
67 124 181 284 364 903	0.026
359 619 721 744 830 884	0.026
181 284 322 359 485 884	0.026
268 284 322 359 379 903	0.026
124 181 284 359 364 485	0.026
268 379 475 571 788 900	0.026
70 124 126 256 470 830	0.026
2 115 154 604 619 830	0.026
115 154 359 480 721 777	0.026
153 256 336 359 410 639	0.026
84 359 604 619 830 858	0.026
39 204 632 793 858 901	0.026
67 78 124 126 256 364	0.026
322 359 379 475 788 884	0.027
59 161 181 673 744 884	0.027
181 364 673 721 744 903	0.027
181 284 322 485 673 777	0.027
78 204 632 682 721 858	0.027
161 181 322 675 744 884	0.027
115 124 161 181 673 905	0.027
70 364 480 542 619 721	0.027
70 379 475 788 900 905	0.027
268 322 359 379 673 903	0.027
96 122 202 447 675 695	0.027
59 78 115 525 619 744	0.027
322 359 379 553 571 788	0.027
59 124 161 181 322 903	0.027
78 154 250 478 777 796	0.027
322 359 379 475 571 788	0.027
284 359 379 475 553 788	0.027
154 181 284 322 673 777	0.027
124 268 359 379 475 571	0.027
161 268 284 322 884 903	0.027
70 480 542 639 682 721	0.027
161 181 202 284 884 903	0.027
78 124 161 268 284 903	0.027
78 124 181 673 744 830	0.027
115 322 604 744 777 830	0.027
70 124 181 256 284 903	0.027
124 359 379 475 788 905	0.027
139 250 336 364 542 796	0.027
322 359 480 673 721 744	0.027
154 364 480 485 542 619	0.027
78 126 364 632 777 796	0.027
59 639 682 793 796 858	0.027
204 478 542 639 721 793	0.027
67 468 487 721 780 899	0.027
451 522 525 542 619 793	0.027
126 161 181 673 903 905	0.027
39 217 384 702 727 796	0.027
124 161 268 571 673 903	0.027
124 161 181 359 485 744	0.027
126 154 466 639 682 858	0.027

Feature ID	MAE
115 410 525 744 777 830	0.027
59 161 181 202 480 744	0.027
379 475 553 571 788 900	0.027
35 39 153 464 540 796	0.027
161 181 485 673 744 884	0.027
59 78 126 153 154 884	0.027
126 336 348 466 721 852	0.027
115 124 480 673 744 905	0.027
115 181 485 673 744 839	0.027
78 126 154 485 568 777	0.027
78 181 284 322 485 777	0.027
78 154 181 284 485 777	0.027
322 359 475 553 571 788	0.027
59 161 268 322 364 903	0.027
2 39 337 702 766 899	0.027
204 364 542 619 714 796	0.027
70 379 475 571 900 905	0.027
67 153 429 540 568 874	0.027
359 379 475 788 884 905	0.027
59 124 161 181 673 903	0.027
78 154 364 568 777 830	0.027
70 115 124 268 485 903	0.027
359 379 475 571 788 905	0.027
72 109 202 348 410 473	0.027
256 447 468 469 568 717	0.028
18 217 391 455 480 717	0.028
268 284 379 475 788 900	0.028
42 407 522 568 721 896	0.028
70 72 542 639 744 796	0.028
70 126 181 478 571 839	0.028
70 126 470 480 639 858	0.028
59 124 161 359 485 830	0.028
2 18 410 525 632 839	0.028
59 475 553 673 703 788	0.028
204 256 525 568 682 793	0.028
181 284 322 485 777 884	0.028
70 153 322 568 830 884	0.028
115 124 447 702 830 858	0.028
78 126 154 639 793 858	0.028
67 451 455 470 568 766	0.028
395 540 632 714 793 874	0.028
39 204 480 542 632 793	0.028
59 379 475 571 673 788	0.028
379 475 553 788 884 905	0.028
78 115 256 470 788 830	0.028
161 268 673 788 903 905	0.028
124 181 322 364 485 673	0.028
359 379 475 553 571 884	0.028
126 529 632 639 793 858	0.028
18 466 639 744 858 884	0.028
268 379 475 788 900 905	0.028
410 466 470 480 525 744	0.028
78 115 154 485 744 830	0.028
115 154 181 359 485 903	0.028
447 468 529 704 841 867	0.028
39 337 714 766 793 842	0.028
70 256 336 395 632 839	0.028

Feature ID	MAE
161 268 284 485 673 903	0.028
78 154 181 485 777 839	0.028
139 384 455 525 568 830	0.028
78 154 359 455 480 830	0.028
154 395 466 555 639 796	0.028
67 197 270 429 632 761	0.028
78 154 322 364 568 777	0.028
32 179 473 753 780 904	0.028
115 124 161 268 364 839	0.028
72 154 284 485 673 777	0.028
154 359 480 485 673 830	0.028
204 466 470 480 639 858	0.028
59 126 410 619 639 744	0.028
161 268 284 322 379 903	0.028
256 407 473 555 824 874	0.028
2 522 525 529 721 793	0.028
359 379 475 553 571 673	0.028
78 256 632 682 777 858	0.028
67 115 124 256 284 485	0.028
59 480 485 744 830 884	0.028
78 115 153 322 721 777	0.028
153 525 542 714 721 796	0.028
379 475 553 571 788 884	0.028
78 115 154 181 284 777	0.028
115 284 485 571 673 884	0.028
115 284 485 529 777 884	0.028
126 466 470 714 796 858	0.028
84 204 466 470 604 858	0.028
115 154 284 364 571 884	0.028
70 115 181 478 744 777	0.028
181 336 480 702 721 744	0.028
115 154 673 744 830 858	0.028
322 359 379 475 553 788	0.028
78 115 154 256 777 830	0.028
78 250 256 364 410 796	0.028
204 364 470 568 721 830	0.029
70 364 470 480 639 793	0.029
78 204 542 632 766 858	0.029
78 126 153 154 529 830	0.029
115 124 126 161 485 555	0.029
447 451 522 721 793 842	0.029
59 78 126 154 744 777	0.029
59 126 714 839 874 884	0.029
18 256 522 555 632 682	0.029
115 480 485 619 744 830	0.029
359 379 475 553 673 788	0.029
466 528 540 717 824 904	0.029
264 270 412 447 842 856	0.029
395 451 470 568 604 656	0.029
39 337 384 466 639 824	0.029
540 604 632 688 780 904	0.029
364 485 542 796 839 905	0.029
379 475 571 788 900 905	0.029
79 96 217 336 717 753	0.029
126 154 256 359 830 884	0.029
78 126 154 571 639 858	0.029
379 475 673 788 884 905	0.029

Feature ID	MAE
332 580 704 796 841 904	0.029
96 204 256 384 466 470	0.029
115 124 161 181 485 673	0.029
78 153 410 542 632 766	0.029
124 268 379 571 788 900	0.029
78 154 485 744 777 858	0.029
18 139 325 407 466 632	0.029
115 154 364 480 619 858	0.029
337 429 555 714 822 824	0.029
2 70 395 540 632 682	0.029
161 181 284 485 673 721	0.029
79 336 455 466 632 702	0.029
72 96 468 477 590 855	0.029
359 379 475 553 788 905	0.029
161 268 788 884 903 905	0.029
2 395 540 632 714 874	0.029
249 337 522 704 749 780	0.029
2 39 337 478 525 540	0.029
79 204 429 522 525 529	0.029
35 270 293 555 632 896	0.029
153 154 480 568 682 884	0.029
284 485 571 673 777 884	0.029
115 124 161 268 364 903	0.029
126 395 451 542 714 793	0.029
18 153 447 528 632 904	0.029
359 379 475 788 900 905	0.029
88 293 412 428 632 685	0.029
412 464 466 632 704 842	0.029
35 79 249 704 780 896	0.029
78 115 126 154 256 777	0.029
4 85 202 217 249 465	0.029
153 568 604 714 727 766	0.029
379 475 553 571 673 788	0.029
2 391 466 632 735 858	0.029
78 154 364 604 777 858	0.029
35 67 270 384 412 727	0.029
2 18 96 193 555 842	0.029
67 522 529 540 688 842	0.029
202 204 466 470 639 682	0.029
18 204 384 466 639 899	0.029
249 395 487 594 841 899	0.029
70 153 336 455 568 721	0.029
67 336 429 451 470 480	0.029
124 161 268 364 571 903	0.029
59 115 126 485 744 830	0.029
322 359 379 475 553 571	0.029
78 115 124 256 322 485	0.029
67 217 230 249 465 487	0.029
466 528 540 555 717 824	0.030
39 204 525 542 619 793	0.030
2 256 451 568 824 874	0.030
202 256 469 473 528 717	0.030
115 181 256 284 364 903	0.030
176 266 407 447 522 727	0.030
39 256 395 447 555 748	0.030
115 124 161 268 744 830	0.030
67 395 412 451 464 727	0.030

Feature ID	MAE
39 337 456 766 842 899	0.030
154 181 322 673 788 884	0.030
2 126 359 777 796 858	0.030
70 284 322 364 571 903	0.030
78 115 153 154 721 777	0.030
67 75 217 465 511 899	0.030
42 391 407 451 466 717	0.030
18 153 204 542 568 796	0.030
124 181 284 485 777 884	0.030
256 478 632 766 777 796	0.030
126 395 447 632 714 793	0.030
407 466 522 528 604 639	0.030
78 124 181 364 485 673	0.030
78 124 364 542 639 714	0.030
379 475 553 571 788 905	0.030
39 153 395 540 721 727	0.030
70 395 470 485 766 899	0.030
39 204 395 528 604 839	0.030
79 337 395 528 555 727	0.030
379 475 571 673 788 884	0.030
379 475 571 673 788 905	0.030
153 154 480 542 721 793	0.030
35 391 540 586 717 793	0.030
475 553 571 788 884 905	0.030
275 359 485 619 796 830	0.030
18 122 202 270 688 761	0.030
67 72 410 429 704 901	0.030
82 154 364 793 796 858	0.030
124 268 379 553 788 905	0.030
466 528 568 721 727 766	0.030
35 57 632 634 655 904	0.030
18 154 470 540 639 796	0.030
57 82 202 410 594 632	0.030
179 249 270 293 337 515	0.030
204 504 619 714 777 796	0.030
70 126 364 542 619 796	0.030
217 467 477 478 717 841	0.030
18 67 487 529 701 904	0.030
2 115 181 256 744 777	0.030
18 395 456 555 721 727	0.030
204 480 542 682 721 793	0.030
72 179 247 594 685 841	0.030
42 122 217 270 822 899	0.030
359 379 475 553 571 905	0.030
115 268 284 487 830 900	0.024

Table S15. Information on predictive features for colorectal cancer

Columns
ID : feature index, same as Table S3
Transcript : transcript ID
Gene : gene name
Chr : chromosome
Site : coordinate of nucleosome-depleted site (GRCh37)
Region : location of nucleosome-depleted site
Group : gene group based on its expression in blood and tumor
$FPKM_{blood}$: FPKM value in normal blood
$FPKM_{tumor}$: FPKM value in tumor of colorectal cancer

ID	Transcript	Gene	Chr	Site	Region	Group	$FPKM_{blood}$	$FPKM_{tumor}$
2	ENST00000027335.7	CDH17	8	95220815	promoter	tumor	0.00	149.83
4	ENST00000162330.9	BCAR1	16	75285507	promoter	tumor	0.00	16.86
18	ENST00000245451.8	BMP4	14	54423529	promoter	tumor	0.00	16.43
32	ENST00000264144.4	LAMC2	1	183155423	promoter	tumor	0.01	31.46
35	ENST00000267101.7	ERBB3	12	56473645	promoter	tumor	0.00	40.98
39	ENST00000270560.3	TM4SF5	17	4675187	promoter	tumor	0.00	18.39
42	ENST00000278937.6	MPZL2	11	118134997	promoter	tumor	0.37	17.05
57	ENST00000300119.7	MYO1A	12	57443901	promoter	tumor	0.00	15.11
59	ENST00000300557.2	PRR15L	17	46035244	promoter	tumor	0.03	96.21
67	ENST00000310836.10	UGT8	4	115519611	promoter	tumor	0.04	14.08
70	ENST00000311620.6	ANKS4B	16	21244986	promoter	tumor	0.00	10.61
72	ENST00000317508.10	PRSS8	16	31147083	promoter	tumor	0.11	143.22
75	ENST00000318443.9	CD276	15	73976554	promoter	tumor	0.00	11.45
78	ENST00000322536.7	DDX10	11	108535752	promoter	tumor	0.75	10.84
79	ENST00000324038.6	FAM101A	12	124773710	promoter	tumor	0.00	10.08
82	ENST00000326587.11	MAGED1	X	51636698	promoter	tumor	0.60	16.14
84	ENST00000331243.4	FAM84A	2	14772824	promoter	tumor	0.01	33.07
85	ENST00000331595.8	BGN	X	152760397	promoter	tumor	0.60	74.92
86	ENST00000332149.9	TMPRSS2	21	42880086	promoter	tumor	0.02	43.57
88	ENST00000334047.11	F3	1	95007356	promoter	tumor	0.08	13.07
96	ENST00000352551.9	UBE2C	20	44441313	promoter	tumor	0.00	10.99
109	ENST00000358867.10	TMEM126B	11	85339629	promoter	tumor	0.47	17.68
115	ENST00000361084.9	RAB25	1	156030951	promoter	tumor	0.07	131.50
122	ENST00000367284.9	ELF3	1	201979645	promoter	tumor	0.02	50.55
124	ENST00000367976.3	CTGF	6	132272513	promoter	tumor	0.32	44.18
126	ENST00000368554.8	PRAP1	10	135122914	promoter	tumor	0.00	32.41
139	ENST00000374214.3	UQCC2	6	33679504	promoter	tumor	1.00	17.77
153	ENST00000380071.7	RFC3	13	34392186	promoter	tumor	0.48	15.11
154	ENST00000381134.7	ARSE	X	2882311	promoter	tumor	0.00	24.51
161	ENST00000394201.8	SCOC	4	141294797	promoter	tumor	0.53	14.61
176	ENST00000419308.6	FOXA2	20	22585101	promoter	tumor	0.00	13.51
179	ENST00000425042.6	HID1	17	72968829	promoter	tumor	0.23	13.99
181	ENST00000427250.5	LSR	19	35739905	promoter	tumor	0.00	13.66
197	ENST00000463201.2	PRAP1	10	135164879	promoter	tumor	0.00	54.46
202	ENST00000473336.5	RAB25	1	156031174	promoter	tumor	0.00	17.65
204	ENST00000478194.1	FERMT1	20	6074819	promoter	tumor	0.00	27.00
217	ENST00000497734.5	SRC	20	35973088	promoter	tumor	0.00	12.44
230	ENST00000532203.1	MRPL17	11	6704547	promoter	tumor	0.65	21.73
247	ENST00000554989.1	CKB	14	103987659	promoter	tumor	0.75	83.82
249	ENST00000558580.1	SORD	15	45328434	promoter	tumor	0.95	15.73
250	ENST00000561504.1	ADIRF	10	88728247	promoter	tumor	0.75	46.05
256	ENST00000588605.5	C19orf33	19	38794804	promoter	tumor	0.22	18.46
264	ENST00000597153.5	LGALS4	19	39303585	promoter	tumor	0.00	20.51
266	ENST00000600324.5	STAP2	19	4338818	promoter	tumor	0.02	13.85
268	ENST00000605618.5	LSR	19	35739922	promoter	tumor	0.22	31.85
270	ENST00000612794.1	GPX2	14	65409623	promoter	tumor	0.00	23.73
275	ENST00000619895.4	TMC4	19	54676865	promoter	tumor	0.35	33.05
284	ENST00000234347.9	PRTN3	19	840960	promoter	blood	13.78	0.00
286	ENST00000244709.8	TREM1	6	41254457	promoter	blood	67.12	0.63
293	ENST00000279452.10	CD44	11	35198175	promoter	blood	10.76	0.00
322	ENST00000355524.7	FCAR	19	55385736	promoter	blood	53.04	0.07
325	ENST00000356864.3	TNFRSF10C	8	22960103	promoter	blood	108.86	0.56
332	ENST00000367568.4	STX11	6	144471663	promoter	blood	24.42	0.79
336	ENST00000368737.4	S100A12	1	153348125	promoter	blood	1099.02	0.31
337	ENST00000371806.3	FCN1	9	137609809	promoter	blood	379.64	0.88

348	ENST00000380299.3	HBD	11	5255878	promoter	blood	138.84	0.07
359	ENST00000398421.6	NCF1	7	74188358	promoter	blood	11.04	0.04
364	ENST00000413580.5	PHOSPHO1	17	47308128	promoter	blood	42.76	0.05
379	ENST00000454703.6	ACSL1	4	185747273	promoter	blood	35.07	0.78
384	ENST00000465984.5	SLC11A1	2	219246911	promoter	blood	10.54	0.03
391	ENST00000480395.5	TRIM22	11	5717722	promoter	blood	17.36	0.70
395	ENST00000485743.1	HBB	11	5248302	promoter	blood	128.52	0.00
407	ENST00000496823.1	BCL6	3	187463247	promoter	blood	21.33	0.20
410	ENST00000509314.5	FBXL5	4	15661487	promoter	blood	10.24	0.00
412	ENST00000510784.6	FAM65B	6	25042396	promoter	blood	61.47	0.19
428	ENST00000535669.6	CD37	19	49838684	promoter	blood	33.70	0.19
429	ENST00000539932.5	SLC11A1	2	219246926	promoter	blood	50.32	0.02
447	ENST00000576628.1	ACAP1	17	7239916	promoter	blood	20.20	0.18
451	ENST00000585901.6	TYROBP	19	36399149	promoter	blood	13.40	0.19
455	ENST00000588673.3	OAZ1	19	2270290	promoter	blood	24.28	0.69
464	ENST00000595840.1	LRRC25	19	18508421	promoter	blood	36.84	0.88
465	ENST00000596426.5	CD37	19	49838691	promoter	blood	55.55	0.57
466	ENST00000596764.5	VAV1	19	6772739	promoter	blood	12.25	0.59
467	ENST00000597852.5	CD37	19	49838675	promoter	blood	13.98	0.20
468	ENST00000598034.5	GMFG	19	39826646	promoter	blood	43.77	0.45
469	ENST00000599180.2	FFAR2	19	35939203	promoter	blood	24.79	0.00
470	ENST00000599716.5	SHKBP1	19	41082793	promoter	blood	10.66	0.22
473	ENST00000602185.5	GMFG	19	39826645	promoter	blood	14.09	0.00
475	ENST00000605039.5	BIN2	12	51717938	promoter	blood	11.02	0.11
477	ENST00000612844.4	FOLR3	11	71846756	promoter	blood	13.11	0.00
478	ENST00000615439.4	RASGRP4	19	38916945	promoter	blood	10.11	0.00
480	ENST00000616356.4	FCN1	9	137809723	promoter	blood	16.99	0.07
485	ENST00000027335.7	CDH17	8	95220711	junction	tumor	0.00	149.83
487	ENST00000162330.9	BCAR1	16	75285369	junction	tumor	0.00	16.86
511	ENST00000262753.8	POF1B	X	84634644	junction	tumor	0.02	40.41
515	ENST00000264144.4	LAMC2	1	183155586	junction	tumor	0.01	31.46
522	ENST00000270560.3	TM4SF5	17	4675394	junction	tumor	0.00	18.39
525	ENST00000278937.6	MPZL2	11	118134811	junction	tumor	0.37	17.05
528	ENST00000290913.7	CHCHD6	3	126423242	junction	tumor	0.65	15.07
529	ENST00000291525.11	TFF3	21	43735403	junction	tumor	0.00	209.02
540	ENST00000300119.7	MYO1A	12	57443671	junction	tumor	0.00	15.11
542	ENST00000300557.2	PRR15L	17	46035023	junction	tumor	0.03	96.21
553	ENST00000311620.6	ANKS4B	16	21245222	junction	tumor	0.00	10.61
555	ENST00000317508.10	PRSS8	16	31146735	junction	tumor	0.11	143.22
568	ENST00000332149.9	TMPRSS2	21	42880008	junction	tumor	0.02	43.57
571	ENST00000334869.8	LGMN	14	93214834	junction	tumor	0.94	45.73
580	ENST00000354900.7	LSR	19	35740034	junction	tumor	0.75	31.22
586	ENST00000357166.10	ZDHHC9	X	128977672	junction	tumor	0.29	20.11
590	ENST00000358867.10	TMEM126B	11	85339732	junction	tumor	0.47	17.68
591	ENST00000360325.11	CLDN7	17	7165140	junction	tumor	0.09	133.65
594	ENST00000360779.3	SDCBP2	20	1309729	junction	tumor	0.00	17.84
595	ENST00000361084.9	RAB25	1	156031234	junction	tumor	0.07	131.50
604	ENST00000367976.3	CTGF	6	132272247	junction	tumor	0.32	44.18
619	ENST00000374214.3	UQCC2	6	33679326	junction	tumor	1.00	17.77
629	ENST00000379742.4	POSTN	13	38172745	junction	tumor	0.01	11.69
632	ENST00000381134.7	ARSE	X	2862265	junction	tumor	0.00	24.51
634	ENST00000389614.5	GPX2	14	65409223	junction	tumor	0.10	652.10
639	ENST00000394201.8	SCOC	4	141294871	junction	tumor	0.53	14.61
655	ENST00000425042.6	HID1	17	72968686	junction	tumor	0.23	13.99
656	ENST00000425340.2	FUT2	19	49199346	junction	tumor	0.02	13.10
673	ENST00000472782.1	ATP5G3	2	176046384	junction	tumor	0.62	10.87
675	ENST00000478194.1	FERMT1	20	6074721	junction	tumor	0.00	27.00
682	ENST00000494801.5	TCEAL4	X	102840552	junction	tumor	0.60	13.59
685	ENST00000497734.5	SRC	20	35973290	junction	tumor	0.00	12.44
688	ENST00000514985.5	SEPP1	5	42811938	junction	tumor	0.59	49.95
695	ENST00000528430.2	PPP1R16A	8	145726677	junction	tumor	0.92	22.33
701	ENST00000542056.1	GPRC5A	12	13044598	junction	tumor	0.00	23.91
702	ENST00000543445.5	LDHA	11	18416188	junction	tumor	0.00	71.47
703	ENST00000543623.5	PLCD3	17	43192462	junction	tumor	0.27	14.58
704	ENST00000546314.5	STARD10	11	72493311	junction	tumor	0.00	31.66
714	ENST00000559087.5	BMP4	14	54423477	junction	tumor	0.00	13.08
717	ENST00000581920.1	TYMS	18	637752	junction	tumor	0.88	11.79
721	ENST00000588605.5	C19orf33	19	38794923	junction	tumor	0.22	18.46
727	ENST00000597153.5	LGALS4	19	39303482	junction	tumor	0.00	20.51
735	ENST00000619895.4	TMC4	19	54676734	junction	tumor	0.35	33.05
744	ENST00000234347.9	PRTN3	19	841069	junction	blood	13.78	0.00

748	ENST00000246549.2	FFAR2	19	35942667	junction	blood	58.85	0.34
749	ENST00000246657.2	CCR7	17	38721652	junction	blood	11.89	0.75
753	ENST00000279452.10	CD44	11	35198287	junction	blood	10.76	0.00
760	ENST00000297239.10	SYTL3	6	159082417	junction	blood	10.79	0.54
761	ENST00000299663.7	CLEC4E	12	8693357	junction	blood	29.27	0.20
766	ENST00000310544.8	PHOSPHO1	17	47307830	junction	blood	30.92	0.08
777	ENST00000343534.9	C1orf162	1	112016652	junction	blood	37.68	0.74
780	ENST00000354352.9	SLC11A1	2	219247098	junction	blood	111.80	0.63
788	ENST00000367025.7	TRAF3IP3	1	209929654	junction	blood	17.52	0.64
790	ENST00000367535.7	NCF2	1	183559291	junction	blood	75.23	0.98
793	ENST00000368015.1	ARHGAP30	1	161039410	junction	blood	20.61	0.58
796	ENST00000371806.3	FCN1	9	137809615	junction	blood	379.64	0.88
822	ENST00000422400.6	VNN2	6	133078810	junction	blood	14.59	0.10
824	ENST00000433194.6	CDK5RAP2	9	123165594	junction	blood	22.55	0.52
830	ENST00000454703.6	ACSL1	4	185747070	junction	blood	35.07	0.78
839	ENST00000480395.5	TRIM22	11	5717885	junction	blood	17.36	0.70
841	ENST00000483750.5	WAS	X	48542374	junction	blood	34.49	0.17
842	ENST00000485743.1	HBB	11	5248160	junction	blood	128.52	0.00
852	ENST00000496823.1	BCL6	3	187463198	junction	blood	21.33	0.20
855	ENST00000509314.5	FBXL5	4	15661350	junction	blood	10.24	0.00
856	ENST00000509339.1	MXD3	5	176734782	junction	blood	30.07	0.08
858	ENST00000513001.5	ACSL1	4	185678973	junction	blood	17.65	0.10
867	ENST00000540998.5	CDC42SE1	1	151031955	junction	blood	10.52	0.00
874	ENST00000553070.5	NFE2	12	54694585	junction	blood	23.61	0.00
884	ENST00000578402.5	LIMD2	17	61777729	junction	blood	31.49	0.77
896	ENST00000595840.1	LRRC25	19	18508263	junction	blood	36.84	0.88
899	ENST00000599180.2	FFAR2	19	35939281	junction	blood	24.79	0.00
900	ENST00000599716.5	SHKBP1	19	41082891	junction	blood	10.66	0.22
901	ENST00000600626.1	C5AR2	19	47840426	junction	blood	12.99	0.11
903	ENST00000605039.5	BIN2	12	51717806	junction	blood	11.02	0.11
904	ENST00000611028.2	FOLR3	11	71846814	junction	blood	11.13	0.00
905	ENST00000615439.4	RASGRP4	19	38916709	junction	blood	10.11	0.00

Table S16. Information on additional predictive pan-cancer features

Columns
Feature ID: feature index (see Table S10 for feature details)
MAE: mean absolute error between observed and calculated ctDNA fractions from 652 samples

Feature ID	MAE	Feature ID	MAE	Feature ID	MAE
34 41 73 83 90 123 294 415 452 742	0.024	34 41 83 90 123 126 294 667 742 789	0.033	34 135 137 242 278 415 428 621 680 768	0.035
34 41 73 83 90 123 126 294 415 667	0.025	34 41 83 90 123 126 294 634 667 789	0.033	34 135 242 278 311 415 428 621 634 680	0.035
34 41 83 90 123 126 259 294 415 667	0.025	15 29 89 152 288 299 357 388 674 736	0.033	52 206 258 288 296 338 403 435 547 656	0.035
34 41 83 90 123 294 415 452 667 789	0.026	37 64 97 201 236 242 453 454 735 772	0.033	205 278 376 428 454 621 634 680 768 789	0.035
41 73 83 90 123 294 376 415 452 742	0.026	52 64 201 236 242 258 388 421 621 772	0.033	205 376 428 454 621 634 667 680 768 789	0.035
34 41 73 83 90 123 126 294 415 789	0.026	34 41 73 83 90 123 126 279 294 376	0.033	34 89 205 278 428 621 634 680 768 789	0.035
34 64 135 201 278 415 653 735 772 778	0.026	34 41 73 83 90 123 126 259 294 789	0.033	15 29 170 171 299 402 606 682 766 797	0.035
41 73 83 90 123 126 294 375 415 452	0.026	89 242 278 428 561 621 680 742 768 789	0.033	34 89 135 236 278 311 428 449 768 789	0.035
34 52 201 415 653 666 735 763 772 776	0.026	34 41 73 83 90 123 126 294 376 789	0.033	170 262 296 412 435 608 644 703 708 766	0.035
41 73 83 90 123 126 294 452 634 667	0.027	34 52 201 236 242 268 415 453 742 772	0.033	37 64 152 201 206 242 302 454 666 742	0.035
41 73 83 90 123 126 294 415 634 667	0.027	34 41 73 83 90 123 126 259 294 376	0.033	37 52 64 73 201 242 258 421 674 772	0.035
41 73 83 90 123 126 294 375 415 667	0.027	52 288 259 304 357 386 402 449 630 674	0.033	170 296 302 406 416 429 460 607 636 708	0.035
34 41 73 83 90 123 126 294 376 415	0.027	9 34 89 135 238 242 428 742 768 789	0.033	37 52 201 205 236 242 387 735 745 772	0.035
41 83 90 123 126 294 376 415 634 667	0.027	41 83 90 123 126 259 294 634 667 789	0.033	9 37 52 64 135 242 304 621 742 772	0.035
41 83 90 123 126 294 415 634 667 742	0.027	34 41 83 90 123 126 294 376 742 789	0.033	34 89 135 137 205 278 428 763 768 789	0.035
41 73 83 90 123 294 376 452 634 667	0.027	9 52 201 288 357 388 453 547 630 674	0.033	52 64 126 201 205 288 415 454 742 772	0.036
41 73 83 90 123 126 294 452 667 789	0.028	8 152 259 299 328 435 544 735 775 778	0.033	137 201 242 259 288 421 454 621 680 772	0.036
41 73 83 90 123 126 294 452 742 789	0.029	73 137 415 421 428 454 621 634 667 680	0.033	89 135 206 236 259 338 357 435 547 776	0.035
41 83 90 123 126 259 294 452 667 742	0.029	9 37 64 201 236 258 415 574 735 778	0.034	29 52 201 259 357 388 402 454 544 607	0.036
41 73 83 90 123 126 259 294 421 452	0.029	41 73 83 90 123 294 634 667 742 789	0.034	8 27 64 236 258 304 338 387 376 594	0.036
41 73 83 90 123 126 259 294 376 415	0.029	15 29 127 206 302 306 358 402 544 655	0.034	29 127 306 368 402 412 544 607 653 655	0.036
41 73 83 90 123 126 294 376 452 742	0.029	41 83 90 123 126 294 634 667 742 789	0.034	37 97 236 242 276 311 454 634 735 772	0.036
97 137 205 454 634 653 667 680 778 787	0.029	34 89 135 242 276 428 680 742 768 789	0.034	15 89 152 206 259 288 357 388 482 724	0.036
41 73 83 90 123 126 259 273 294 667	0.029	37 205 236 302 311 336 454 621 666 742	0.034	34 152 201 242 258 259 288 298 547 666	0.036
34 41 73 83 90 123 126 294 452 789	0.030	41 73 83 90 123 126 294 376 742 789	0.034	34 135 137 201 242 278 314 735 772 778	0.036
34 41 73 83 90 123 259 294 452 667	0.030	37 64 201 206 236 258 338 415 666 763	0.034	152 171 308 402 544 608 653 655 766 775	0.036
34 41 73 83 90 123 126 259 294 452	0.030	41 83 90 123 126 259 294 634 667 742	0.034	89 135 428 621 634 667 680 742 768 789	0.036
34 41 73 83 90 123 126 294 376 452	0.030	279 376 428 454 498 621 634 680 763 789	0.034	137 201 205 311 415 421 454 621 666 772	0.036
41 83 90 126 259 294 415 634 667 742	0.030	41 73 83 90 123 126 259 294 742 789	0.034	9 201 236 242 304 621 667 674 772 778	0.036
41 83 90 123 294 415 634 667 742 789	0.030	8 126 135 152 206 299 306 357 775 778	0.034	137 206 299 357 388 435 544 653 666 778	0.036
41 73 83 90 123 294 376 452 667 789	0.030	89 242 311 428 454 634 680 742 768 789	0.034	9 37 64 201 205 206 258 367 630 735	0.036
41 73 83 90 123 126 259 294 376 452	0.030	9 52 135 242 259 357 388 392 435 745	0.034	37 52 64 201 242 338 421 454 735 772	0.036
41 73 83 90 123 259 294 376 634 667	0.030	9 52 64 89 236 258 288 338 376 435	0.034	73 278 421 428 454 621 634 680 742 768	0.036
34 41 73 83 90 123 126 135 294 376	0.030	52 73 201 242 302 464 621 666 736 772	0.034	206 262 311 336 367 415 436 482 544 778	0.036
97 137 201 236 278 348 415 454 772 778	0.031	52 64 201 236 242 311 454 666 742 772	0.034	89 201 236 242 259 278 735 768 772 778	0.036
41 73 83 90 123 126 294 375 452 789	0.031	9 89 258 259 288 302 388 621 630 674	0.034	9 52 64 201 242 258 278 304 367 778	0.036
41 73 83 90 123 126 294 376 634 667	0.031	37 64 258 314 338 454 630 666 763 787	0.034	9 135 137 236 258 388 482 542 594 621	0.036
41 73 83 90 123 126 294 376 421 742	0.031	135 201 236 242 276 304 645 653 772 776	0.034	258 338 367 376 388 435 456 482 544 775	0.036
34 41 73 83 90 123 126 294 376 667	0.031	89 135 137 206 311 426 464 680 768 789	0.034	9 29 288 298 299 386 402 453 630 775	0.036
34 41 83 90 123 126 294 375 667 742	0.031	73 137 278 421 428 454 621 634 680 768	0.034	211 308 376 408 490 544 645 655 708 724	0.036
9 34 89 135 278 428 621 680 768 789	0.031	52 64 137 201 236 242 259 454 666 772	0.034	89 135 428 454 634 667 680 742 768 788	0.036
41 73 83 90 123 126 294 634 667 789	0.032	34 137 415 421 428 621 634 667 680 768	0.034	137 311 428 454 498 621 634 667 680 742	0.036
73 83 90 123 126 135 259 294 376 452	0.032	34 89 135 276 428 560 742 763 768 789	0.034	29 127 306 357 378 402 435 544 655 766	0.036
34 135 236 278 428 621 680 763 768 789	0.032	171 299 306 408 544 608 644 645 663 724	0.034	89 137 152 259 376 388 644 674 708 776	0.036
52 137 236 258 288 304 338 388 674 778	0.032	8 29 52 288 304 336 402 607 630 655	0.034	205 376 428 454 498 621 634 667 680 768	0.036
41 73 83 90 123 126 294 634 667 742	0.032	15 29 299 357 415 453 630 674 682 786	0.034	37 64 258 338 376 454 594 630 666 763	0.036
34 137 201 236 242 278 415 735 772 778	0.032	9 29 152 236 258 259 288 304 388 547	0.034	37 64 201 205 236 311 454 666 742 772	0.036
41 73 83 90 123 126 294 375 667 742	0.032	89 205 428 454 634 653 667 680 768 789	0.034	8 52 135 201 278 367 376 768 772 778	0.036
41 73 83 90 123 126 259 294 376 667	0.032	127 137 206 306 402 412 415 653 655 786	0.034	135 205 278 428 454 621 634 680 766 789	0.036
41 73 83 90 123 126 294 667 742 789	0.032	41 73 83 90 123 126 259 294 376 742	0.034	137 242 278 376 428 454 634 680 768 789	0.036
34 89 135 205 242 428 621 680 768 789	0.032	9 259 288 296 357 328 547 630 655 674	0.034	37 236 242 258 311 338 454 621 668 742	0.036
34 41 73 83 90 123 126 294 667 742	0.032	64 137 278 304 621 634 645 653 772 778	0.034	29 89 152 299 357 388 392 435 544 594	0.036
34 41 73 83 90 123 126 294 667 789	0.032	152 357 376 415 435 544 574 736 763 776	0.034	89 205 278 428 454 634 680 742 768 789	0.036
34 37 52 135 201 236 242 415 735 772	0.032	34 73 97 135 276 421 428 763 768 772	0.034	34 52 201 205 236 242 415 653 735 772	0.036
41 73 83 90 123 126 294 375 667 789	0.032	89 205 278 311 428 454 634 680 768 789	0.034	9 29 135 152 258 304 388 542 594 630	0.036
34 41 73 83 90 123 126 294 634 667	0.032	9 34 97 137 201 236 242 735 772 778	0.035	89 201 288 357 376 388 392 402 655 775	0.036
34 73 123 135 278 428 621 680 768 789	0.032	89 152 201 236 288 338 378 392 655 775	0.035	41 73 83 90 123 259 294 667 742 789	0.036
37 52 64 97 201 205 242 421 454 772	0.032	37 201 236 242 304 376 621 634 667 742	0.035	127 299 306 357 388 435 544 608 655 775	0.036
89 428 449 454 634 667 680 742 768 789	0.032	29 52 89 152 259 266 299 309 357 358	0.035	8 29 64 89 152 205 288 336 454 666	0.036
8 52 135 259 304 314 336 454 666 778	0.032	34 89 135 137 276 428 621 680 768 772	0.035	34 135 137 205 242 428 621 680 768 789	0.037
34 89 135 278 428 621 680 768 772 789	0.032	8 52 309 435 544 607 630 735 775 776	0.035	205 278 311 428 454 621 634 680 768 789	0.037
34 41 73 83 90 123 126 294 742 789	0.032	8 29 52 236 357 386 435 453 454 674	0.035	64 137 278 288 415 453 645 742 772 778	0.037
34 89 135 242 278 428 621 680 768 789	0.033	52 152 205 268 388 630 735 745 775 787	0.035	37 52 64 236 242 258 421 621 674 772	0.037
34 41 73 83 90 123 126 259 294 667	0.033	73 135 242 276 421 428 454 621 680 768	0.035	73 137 242 278 428 454 634 680 768 789	0.037
97 311 428 454 621 634 667 680 742 768	0.033	29 89 135 152 236 331 482 547 634 742	0.035	29 52 259 288 338 357 388 456 547 674	0.037
34 73 135 137 421 428 621 680 768 772	0.033	52 174 331 338 435 454 466 544 621 634	0.035	126 127 170 171 299 655 666 724 766 775	0.037

Feature ID	MAE
89 137 205 428 454 621 667 680 742 789	0.037
9 37 52 97 236 242 402 621 667 772	0.037
29 135 152 201 258 415 630 735 772 778	0.037
9 37 52 89 201 258 594 630 735 778	0.037
8 29 152 286 299 357 388 435 482 778	0.037
34 89 205 278 311 428 680 742 786 789	0.037
37 52 64 201 205 236 311 346 742 772	0.037
29 295 299 304 366 402 412 453 665 735	0.037
37 64 201 205 415 594 630 666 735 766	0.037
37 52 64 201 236 242 269 367 735 772	0.037
52 201 258 288 357 386 402 547 607 653	0.037
128 170 299 393 412 435 645 717 735 736	0.037
152 206 236 415 435 460 630 665 708 786	0.037
8 52 152 201 299 357 435 745 766 778	0.037
15 89 127 142 288 311 388 416 724 778	0.037
8 52 89 135 235 258 304 338 547 674	0.037
37 52 89 258 314 338 421 594 638 674	0.037
8 37 64 242 278 304 367 421 772 778	0.037
8 37 135 205 258 259 304 314 338 656	0.037
89 242 278 311 428 454 621 680 768 789	0.037
29 127 171 299 306 357 402 544 665 766	0.037
9 34 37 64 201 205 634 663 735 772	0.037
37 52 278 314 338 388 403 456 630 656	0.037
8 62 138 236 288 311 483 621 742 772	0.037
89 152 286 306 376 435 544 607 709 766	0.037
9 52 89 258 259 288 304 338 456 630	0.037
73 137 428 454 621 634 667 680 735 768	0.037
127 170 171 205 296 302 402 412 766 775	0.037
137 288 296 306 314 388 415 663 735 778	0.037
29 152 206 299 357 435 544 630 765 775	0.037
170 232 367 489 492 527 594 636 644 717	0.037
127 171 206 299 311 402 412 415 655 786	0.037
8 37 52 64 201 338 490 547 666 674	0.037
34 135 137 276 376 428 634 680 768 772	0.037
206 211 302 306 408 490 646 666 724 763	0.037
52 152 202 264 388 416 490 674 736 775	0.037
37 52 64 242 338 463 484 634 735 772	0.037
170 171 299 416 449 585 594 653 736 766	0.037
89 137 311 428 454 634 667 680 768 789	0.037
34 135 265 278 421 428 621 634 680 768	0.037
152 201 206 242 268 357 388 392 655 775	0.037
152 206 236 306 314 357 402 544 766 775	0.037
8 52 64 89 258 259 288 338 463 742	0.037
9 64 242 278 304 367 421 547 772 778	0.037
206 259 286 304 336 435 607 663 666 778	0.037
151 171 306 314 408 490 544 715 735 763	0.037
34 137 265 278 415 428 621 680 768 772	0.037
34 52 205 236 242 311 666 735 745 772	0.037
89 277 450 490 636 645 675 708 745 776	0.038
34 37 64 89 258 288 338 463 621 674	0.038
40 211 231 277 306 314 402 403 456 636	0.038
135 236 242 278 428 454 621 680 768 789	0.038
29 171 206 296 338 415 585 645 655 766	0.038
29 152 302 358 392 453 454 544 666 703	0.038
9 29 152 306 402 450 466 544 606 645	0.038
34 135 278 311 428 621 680 742 768 772	0.038
9 64 89 201 242 304 621 667 674 778	0.038
9 34 37 137 201 242 288 663 735 772	0.038
9 135 236 242 258 278 304 621 742 772	0.038
9 52 64 242 278 547 634 735 768 772	0.038
127 288 296 367 393 415 435 665 768 778	0.038
9 52 64 278 367 547 634 663 735 772	0.038
8 37 52 64 201 236 258 745 772 778	0.038
152 201 402 415 498 653 674 735 745 786	0.038
89 242 311 428 454 667 680 742 768 789	0.038
9 259 288 357 388 456 630 674 735 778	0.038
52 127 201 435 544 607 630 735 766 778	0.038
9 64 135 278 311 428 680 742 768 789	0.038
37 52 137 201 205 236 454 735 745 772	0.038

Feature ID	MAE
152 171 205 299 357 388 415 435 665 682	0.038
127 174 206 286 304 392 438 630 665 708	0.038
8 52 89 309 376 388 392 435 493 745	0.038
8 52 64 258 302 338 463 621 666 674	0.038
8 29 64 236 253 259 338 454 665 763	0.038
37 52 64 201 236 242 258 304 742 772	0.038
34 73 135 137 276 421 428 763 768 772	0.038
29 152 206 258 357 392 430 594 621 766	0.038
127 171 206 286 415 436 544 665 768 775	0.038
73 171 206 277 286 314 544 558 665 775	0.038
9 170 408 421 527 542 544 644 646 775	0.038
8 37 64 206 258 259 338 454 630 763	0.038
137 278 311 428 454 621 634 680 742 786	0.038
8 9 64 135 201 338 435 630 745 778	0.038
127 302 435 490 544 547 644 646 724 775	0.038
171 286 314 412 544 644 645 665 735 768	0.038
15 152 211 231 232 305 415 708 734 766	0.038
171 299 357 408 459 544 645 665 724 776	0.038
37 52 64 201 205 236 242 454 735 772	0.038
34 73 137 205 278 428 634 680 768 789	0.038
52 64 206 236 258 367 376 621 674 772	0.038
8 137 205 259 309 454 621 636 668 735	0.038
137 205 278 375 415 428 621 634 680 768	0.038
89 137 152 206 236 259 268 309 435 463	0.038
170 171 412 415 453 482 594 666 682 768	0.039
8 9 52 89 258 286 304 338 388 630	0.039
37 64 236 258 392 454 621 636 668 674	0.039
206 277 357 402 408 435 449 456 558 644	0.039
9 89 135 152 205 259 294 376 630 742	0.039
8 37 52 64 258 311 314 338 454 666	0.039
9 52 89 126 258 286 304 338 454 630	0.039
15 206 302 306 402 412 636 648 663 735	0.039
15 89 137 152 288 296 357 388 415 674	0.039
15 49 127 171 206 408 415 544 554 705	0.039
8 201 288 331 357 392 547 674 766 778	0.039
41 89 205 415 421 428 680 742 768 789	0.039
37 52 64 236 258 304 348 421 742 772	0.039
37 64 89 205 258 338 367 376 630 674	0.039
64 137 205 236 304 621 667 674 772 778	0.039
15 152 507 608 644 655 682 736 745 787	0.039
8 37 135 304 338 630 674 735 766 778	0.039
135 137 242 428 454 621 634 667 680 768	0.039
89 127 171 286 299 357 388 490 655 666	0.039
29 52 288 296 314 338 392 403 674 735	0.039
52 152 205 206 268 304 338 348 388 655	0.039
29 89 152 206 259 268 357 388 655 674	0.039
41 73 89 90 123 259 294 376 742 789	0.039
37 52 127 259 286 314 338 666 735 765	0.039
137 205 278 311 428 454 654 680 768 789	0.039
8 258 259 288 338 415 594 630 735 778	0.039
89 286 304 338 388 392 547 666 674 778	0.039
97 137 205 311 376 428 454 680 742 768	0.039
37 137 201 205 236 345 454 568 786 772	0.039
9 37 52 64 201 242 278 304 772 775	0.039
89 152 268 338 376 388 392 435 655 778	0.039
89 135 205 278 428 621 634 680 742 768	0.039
15 170 171 302 402 449 453 594 682 786	0.039
29 62 221 259 286 357 388 630 666 674	0.039
8 15 29 89 152 171 206 299 766 775	0.039
8 9 37 201 205 547 630 668 674 735	0.039
137 242 428 454 498 621 634 667 680 742	0.039
9 34 135 242 278 428 621 680 768 772	0.039
9 52 152 268 304 396 367 388 453 490	0.039
201 236 258 259 286 482 547 674 735 778	0.039
170 171 232 296 299 450 505 708 724 736	0.039
127 137 268 296 302 392 392 402 435 655	0.039
152 201 206 258 268 482 547 630 655 666	0.039
8 126 302 402 453 544 630 653 768 775	0.039
64 201 258 278 338 415 453 607 630 634	0.039

Feature ID	MAE
15 29 73 152 201 206 268 299 724 766	0.039
64 89 236 258 278 304 653 742 772 778	0.039
9 9 304 357 435 544 653 666 742 778	0.039
89 135 137 242 428 454 680 742 768 778	0.039
89 135 205 259 428 454 680 742 768 778	0.039
152 268 258 258 306 309 314 357 435 607	0.039
127 171 206 252 408 415 450 544 644 766	0.039
15 302 393 408 412 450 635 653 682 756	0.039
89 135 201 259 338 482 607 630 735 775	0.039
8 9 137 304 376 388 392 435 544 778	0.039
37 52 135 201 236 242 268 454 621 772	0.039
127 170 171 206 302 306 412 734 746 768	0.040
8 9 89 135 242 278 367 621 674 772	0.040
9 34 137 205 376 428 634 667 680 768	0.040
8 89 137 152 288 336 367 415 674 778	0.040
34 137 205 278 428 680 763 768 772 789	0.040
34 137 205 278 376 428 621 680 765 789	0.040
8 64 258 402 454 634 666 667 674 767	0.040
8 37 89 152 205 206 258 304 665 674	0.040
137 205 278 428 454 621 634 680 768 786	0.040
262 367 527 574 585 619 675 708 776 787	0.040
97 137 311 428 454 634 667 680 742 768	0.040
36 213 367 406 527 568 619 628 682 787	0.040
37 52 64 206 236 242 269 367 735 772	0.040
206 259 277 286 306 402 412 645 655 724	0.040
206 211 262 296 412 630 644 674 708 766	0.040
8 37 52 64 236 242 258 338 421 772	0.040
36 151 206 302 367 392 408 703 715 763	0.040
15 29 127 368 544 547 594 630 655 724	0.040
89 206 259 268 306 357 376 435 655 666	0.040
34 37 201 236 242 278 311 735 772 778	0.040
127 171 206 304 306 482 544 653 666 766	0.040
52 64 201 236 242 304 421 621 674 772	0.040
304 306 393 406 435 605 645 703 708 724	0.040
37 64 201 205 242 259 311 454 742 772	0.040
137 205 278 376 428 496 621 634 680 768	0.040
127 231 314 357 402 544 644 682 756 775	0.040
15 127 232 302 306 311 402 682 724 756	0.040
8 29 288 304 386 392 435 630 655 778	0.040
29 296 306 314 388 402 415 435 544 653	0.040
8 127 171 206 309 490 544 655 708 775	0.040
9 34 137 276 376 426 621 680 768 789	0.040
151 174 232 357 408 546 644 682 715 763	0.040
127 205 302 402 412 415 435 653 656 786	0.040
8 52 89 256 288 304 338 357 630 674	0.040
89 171 288 306 357 376 392 449 453 655	0.040
37 64 256 258 338 464 490 666 670 674	0.040
221 259 268 306 368 402 435 450 655 735	0.040
11 41 89 90 123 135 294 415 454 634	0.029

Table S17. Information on predictive pan-cancer features

Columns
ID: feature index
Transcript: transcript ID
Gene: gene name
Chr: chromosome
Site: coordinate of nucleosome-depleted site (GRCh37)
Region: location of nucleosome-depleted site
Group: gene group based on its expression in blood and tumor
$FPKM_{blood}$: FPKM value in normal blood. Their FPKM values in tumors of 20 cancer types are all <1.

ID	Transcript	Gene	Chr	Site	Region	Group	$FPKM_{blood}$
8	ENST00000221954.6	CEACAM4	19	42133442	promoter	blood	32.81
9	ENST00000225275.3	MPO	17	56358296	promoter	blood	7.23
11	ENST00000234347.9	PRTN3	19	840960	promoter	blood	13.78
15	ENST00000262407.5	ITGA2B	17	42466873	promoter	blood	12.34
29	ENST00000299663.7	CLEC4E	12	8693559	promoter	blood	29.27
34	ENST00000307395.4	GP9	3	128779610	promoter	blood	9.72
37	ENST00000312156.8	NFE2	12	54689544	promoter	blood	11.15
38	ENST00000314412.6	FUT7	9	139927462	promoter	blood	16.90
39	ENST00000314446.9	LILRB2	19	54785039	promoter	blood	7.87
40	ENST00000318507.6	CXCR2	2	218990727	promoter	blood	157.27
41	ENST00000324134.10	NLRP12	19	54327597	promoter	blood	9.17
52	ENST00000342063.4	C19orf35	19	2282175	promoter	blood	8.64
64	ENST00000375448.4	PADI4	1	17634692	promoter	blood	95.04
73	ENST00000380299.3	HBD	11	5255878	promoter	blood	138.84
83	ENST00000392841.1	HMBS	11	118958697	promoter	blood	7.28
89	ENST00000398421.6	NCF1	7	74188358	promoter	blood	11.04
90	ENST00000398632.3	MX2	21	42774561	promoter	blood	7.28
97	ENST00000413580.5	PHOSPHO1	17	47308128	promoter	blood	42.76
123	ENST00000460208.1	LILRB3	19	54721567	promoter	blood	51.15
126	ENST00000462275.5	TBXAS1	7	139529072	promoter	blood	5.07
127	ENST00000462927.5	CYTH4	22	37678566	promoter	blood	26.95
135	ENST00000465984.5	SLC11A1	2	219246911	promoter	blood	10.54
137	ENST00000466151.1	PADI2	1	17409921	promoter	blood	7.13
142	ENST00000467972.5	SLC12A9	7	100454416	promoter	blood	6.80
151	ENST00000469799.5	SLC11A1	2	219247002	promoter	blood	8.27
152	ENST00000469886.5	CYTH4	22	37678556	promoter	blood	6.16
170	ENST00000478902.1	ZDHHC18	1	27177620	promoter	blood	12.52
171	ENST00000479534.5	PADI2	1	17401846	promoter	blood	5.78
174	ENST00000480825.6	CSF3R	1	36941928	promoter	blood	127.36
201	ENST00000487761.5	GPSM3	6	32160645	promoter	blood	14.37
205	ENST00000488970.1	BTK	X	100609209	promoter	blood	7.40
206	ENST00000489175.1	KCNE1	21	35884505	promoter	blood	6.75
211	ENST00000490872.1	SLC11A1	2	219254688	promoter	blood	26.15
213	ENST00000492413.5	SLC11A1	2	219247010	promoter	blood	17.89
221	ENST00000495406.1	CDK5RAP2	9	123152555	promoter	blood	10.53
231	ENST00000500323.2	DOK3	5	176935878	promoter	blood	10.88

232	ENST00000502380.1	DOK3	5	176937383	promoter	blood	8.44
236	ENST00000509314.5	FBXL5	4	15661487	promoter	blood	10.24
242	ENST00000517813.1	DENND3	8	142194587	promoter	blood	13.47
258	ENST00000523369.1	LCP2	5	169685502	promoter	blood	9.88
259	ENST00000523530.1	DENND3	8	142201373	promoter	blood	7.23
262	ENST00000526387.5	TBC1D10C	11	67171386	promoter	blood	7.10
264	ENST00000526980.5	CSF3R	1	36948500	promoter	blood	184.80
277	ENST00000532897.5	MKNK1	1	47037972	promoter	blood	6.23
278	ENST00000533815.2	BTNL8	5	180336564	promoter	blood	5.72
279	ENST00000533968.1	SPI1	11	47400038	promoter	blood	12.90
288	ENST00000539932.5	SLC11A1	2	219246926	promoter	blood	50.32
294	ENST00000542481.1	ATG16L2	11	72534940	promoter	blood	25.18
296	ENST00000543576.5	DENND1C	19	6481798	promoter	blood	12.06
299	ENST00000546200.5	ARHGAP9	12	57871634	promoter	blood	66.03
302	ENST00000551000.1	ARHGAP9	12	57871650	promoter	blood	8.28
304	ENST00000553070.5	NFE2	12	54694799	promoter	blood	23.61
306	ENST00000554736.5	GNG2	14	52328042	promoter	blood	9.30
309	ENST00000558332.3	IL16	15	81591757	promoter	blood	7.66
311	ENST00000559341.5	MAN2A2	15	91459225	promoter	blood	9.61
314	ENST00000560377.5	PSTPIP1	15	77287726	promoter	blood	8.38
331	ENST00000566082.1	USB1	16	58049017	promoter	blood	6.82
338	ENST00000570439.1	ACAP1	17	7248650	promoter	blood	5.27
348	ENST00000574548.1	RNF167	17	4847675	promoter	blood	6.40
357	ENST00000581974.1	DHRS13	17	27226541	promoter	blood	5.97
367	ENST00000587287.1	RASGRP4	19	38902036	promoter	blood	6.80
376	ENST00000590974.1	LYL1	19	13213975	promoter	blood	5.48
388	ENST00000597611.7	FKBP8	19	18654887	promoter	blood	9.25
392	ENST00000598529.5	MYO1F	19	8619448	promoter	blood	16.08
393	ENST00000598907.5	SHKBP1	19	41084102	promoter	blood	14.71
402	ENST00000601502.1	MYO1F	19	8610602	promoter	blood	8.05
403	ENST00000602101.6	RASAL3	19	15575325	promoter	blood	7.16
408	ENST00000605039.5	BIN2	12	51717938	promoter	blood	11.02
412	ENST00000612844.4	FOLR3	11	71846756	promoter	blood	13.11
415	ENST00000615340.4	RASGRP4	19	38916837	promoter	blood	6.88
416	ENST00000616356.4	FCN1	9	137809723	promoter	blood	16.99
421	ENST00000008938.4	PGLYRP1	19	46525993	junction	blood	148.76
428	ENST00000221954.6	CEACAM4	19	42133268	junction	blood	32.81
429	ENST00000225275.3	MPO	17	56357966	junction	blood	7.23
435	ENST00000262407.5	ITGA2B	17	42466654	junction	blood	12.34
449	ENST00000299663.7	CLEC4E	12	8693357	junction	blood	29.27
450	ENST00000299665.2	CLEC4D	12	8666356	junction	blood	10.47
452	ENST00000304076.6	VAV1	19	6773022	junction	blood	7.61
453	ENST00000304361.8	CLEC12A	12	10124286	junction	blood	10.23
454	ENST00000307395.4	GP9	3	128779693	junction	blood	9.72
456	ENST00000310544.8	PHOSPHO1	17	47307830	junction	blood	30.92
469	ENST00000336372.6	VSTM1	19	54566998	junction	blood	10.71
482	ENST00000375448.4	PADI4	1	17634809	junction	blood	95.04
490	ENST00000380299.3	HBD	11	5255572	junction	blood	138.84
498	ENST00000392841.1	HMBS	11	118958788	junction	blood	7.28

527	ENST00000448367.5	FES	15	91432866	junction	blood	6.30
542	ENST00000464994.5	IL1R2	2	102608495	junction	blood	12.24
544	ENST00000465984.5	SLC11A1	2	219247098	junction	blood	10.54
546	ENST00000466151.1	PADI2	1	17409731	junction	blood	7.13
547	ENST00000466612.5	ABTB1	3	127392451	junction	blood	6.18
558	ENST00000469532.1	RAC2	22	37640154	junction	blood	9.83
561	ENST00000471836.1	PARVG	22	44577797	junction	blood	6.53
574	ENST00000478902.1	ZDHHC18	1	27177722	junction	blood	12.52
585	ENST00000483665.6	FCGR2A	1	161475342	junction	blood	6.60
594	ENST00000485991.5	CFP	X	47489168	junction	blood	5.10
607	ENST00000488970.1	BTK	X	100608858	junction	blood	7.40
608	ENST00000489175.1	KCNE1	21	35884325	junction	blood	6.75
619	ENST00000495406.1	CDK5RAP2	9	123152019	junction	blood	10.53
621	ENST00000496915.1	PREX1	20	47258945	junction	blood	5.23
628	ENST00000504910.1	HK3	5	176318389	junction	blood	6.36
630	ENST00000509314.5	FBXL5	4	15661350	junction	blood	10.24
634	ENST00000513001.5	ACSL1	4	185678973	junction	blood	17.65
636	ENST00000517813.1	DENND3	8	142195377	junction	blood	13.47
644	ENST00000520887.1	FAM49B	8	130859050	junction	blood	7.15
645	ENST00000521442.1	ATP6V1B2	8	20075793	junction	blood	8.33
653	ENST00000526387.5	TBC1D10C	11	67171411	junction	blood	7.10
655	ENST00000527031.5	JAK3	19	17958755	junction	blood	6.17
666	ENST00000532897.5	MKNK1	1	47037735	junction	blood	6.23
667	ENST00000533815.2	BTNL8	5	180336697	junction	blood	5.72
670	ENST00000534754.5	SORL1	11	121483541	junction	blood	9.84
674	ENST00000538842.1	ATG16L2	11	72527872	junction	blood	6.35
675	ENST00000539134.1	RELT	11	73104962	junction	blood	6.58
680	ENST00000542481.1	ATG16L2	11	72535167	junction	blood	25.18
682	ENST00000543576.5	DENND1C	19	6481690	junction	blood	12.06
703	ENST00000564072.1	SLCO3A1	15	92706776	junction	blood	8.74
708	ENST00000564894.1	RNF166	16	88767670	junction	blood	7.90
715	ENST00000567038.1	XPO6	16	28113168	junction	blood	8.97
717	ENST00000568760.5	DEF8	16	90024068	junction	blood	7.24
724	ENST00000571303.1	MLKL	16	74725175	junction	blood	5.93
735	ENST00000581287.5	SLC16A3	17	80194107	junction	blood	11.97
736	ENST00000581974.1	DHRS13	17	27226145	junction	blood	5.97
742	ENST00000585852.5	FMNL1	17	43308054	junction	blood	19.81
745	ENST00000587265.1	CA4	17	58235488	junction	blood	5.45
763	ENST00000595725.5	CD37	19	49838866	junction	blood	20.04
766	ENST00000597611.7	FKBP8	19	18654719	junction	blood	9.25
768	ENST00000598201.5	SHKBP1	19	41086391	junction	blood	12.36
772	ENST00000599180.2	FFAR2	19	35939281	junction	blood	24.79
775	ENST00000599716.5	SHKBP1	19	41082891	junction	blood	10.66
776	ENST00000600463.1	IFI30	19	18286032	junction	blood	6.41
778	ENST00000601502.1	MYO1F	19	8610534	junction	blood	8.05
787	ENST00000614135.4	RASGRP4	19	38916709	junction	blood	8.18
789	ENST00000616356.4	FCN1	9	137809615	junction	blood	16.99

Table S18. All predictive feature combinations for CRC using in silico samples generated with random subsets of healthy samples.

Columns
Feature ID: feature index (see Table S3 for feature details)
MAE: mean absolute error between observed and calculated ctDNA fractions from 344 samples

Feature ID	MAE
364 379 475 788 790 905	0.030
284 364 475 788 790 905	0.031
284 364 379 475 788 905	0.031
284 364 379 475 790 905	0.032
179 407 788 830 900 905	0.032
364 379 760 790 852 903	0.033
39 540 760 788 830 900	0.035
35 39 410 540 760 830	0.035
284 364 475 760 788 905	0.033
364 540 760 830 903 905	0.033
364 379 475 703 788 905	0.033
284 364 475 703 788 905	0.033
364 476 760 785 790 905	0.034
35 476 673 830 852 890	0.034
364 379 540 760 790 903	0.034
364 379 476 703 760 790	0.034
364 379 407 760 790 903	0.034
39 126 379 476 852 903	0.034
39 364 476 788 790 905	0.034
364 379 476 788 900 905	0.034
39 379 410 540 703 760	0.034
39 379 407 540 760 790	0.034
364 476 540 788 790 905	0.034
364 760 790 830 900 903	0.035
410 476 540 688 760 830	0.035
476 760 788 830 900 903	0.035
379 407 476 788 790 905	0.035
364 476 703 785 790 905	0.036
39 364 476 703 788 905	0.035
364 476 788 790 900 905	0.036
35 39 301 540 690 903	0.035
378 476 540 788 790 905	0.036
379 476 703 788 790 905	0.035
364 379 760 790 900 903	0.036
116 126 486 629 830 903	0.036
284 410 469 540 571 830	0.036
39 379 407 703 790 903	0.036
364 379 540 703 793 903	0.035
39 322 469 476 830 903	0.036
284 364 476 703 790 905	0.036
364 407 476 788 790 905	0.036
126 284 410 480 830 890	0.036
39 364 379 407 540 903	0.036
39 116 379 407 790 903	0.036
364 379 476 790 900 903	0.037
39 67 379 703 900 903	0.037
39 379 407 540 703 903	0.037

Feature ID	MAE
407 476 760 788 830 890	0.037
39 116 379 407 703 790	0.037
39 116 284 379 540 703	0.037
86 284 476 760 830 903	0.037
364 476 540 788 900 905	0.037
407 760 788 830 900 903	0.037
39 379 407 703 793 903	0.037
86 364 379 410 900 903	0.037
301 470 473 553 629 890	0.037
364 476 760 788 900 905	0.037
35 39 476 540 673 830	0.037
379 407 476 703 790 905	0.037
39 284 379 703 793 903	0.037
126 364 379 407 476 760	0.037
39 126 476 830 852 903	0.038
364 379 407 410 760 903	0.038
126 284 410 469 540 830	0.038
284 369 410 469 540 830	0.038
364 476 703 788 900 905	0.038
295 476 364 727 830 852	0.038
364 407 476 703 788 905	0.038
39 126 379 410 469 476	0.038
379 407 476 703 788 905	0.038
364 407 476 703 790 905	0.038
86 407 410 760 830 900	0.038
39 364 703 830 903 903	0.038
375 476 703 788 790 900	0.038
39 284 540 594 727 830	0.038
35 284 410 571 793 830	0.038
703 760 790 830 900 903	0.038
86 470 656 842 859 890	0.038
35 284 410 540 571 830	0.038
39 476 703 786 790 905	0.038
284 379 407 410 469 571	0.038
379 540 760 790 900 903	0.038
379 407 760 790 900 903	0.038
86 116 126 469 553 721	0.039
284 322 410 469 540 830	0.039
35 39 470 478 540 830	0.039
284 469 476 540 571 890	0.039
407 760 790 830 900 903	0.039
284 410 480 540 571 830	0.039
35 86 284 469 478 830	0.039
284 410 469 629 540 830	0.039
116 284 379 407 760 790	0.039
39 266 308 322 485 744	0.039
284 410 476 540 571 830	0.039

Feature ID	MAE
35 86 306 673 793 852	0.039
407 703 760 790 830 903	0.039
116 364 379 407 760 903	0.039
284 410 480 629 760 830	0.039
284 476 540 571 830 852	0.039
72 197 256 395 473 856	0.039
364 476 760 830 900 903	0.039
284 379 410 673 760 852	0.039
39 284 379 407 703 903	0.039
39 379 407 410 760 900	0.039
364 540 760 830 900 903	0.040
39 407 476 703 788 905	0.040
35 364 379 540 703 903	0.040
72 204 301 451 473 639	0.040
18 70 256 439 467 777	0.040
98 359 391 395 456 890	0.040
35 476 540 673 760 830	0.040
364 379 407 476 540 903	0.040
67 364 379 407 760 903	0.040
39 379 407 703 900 903	0.040
18 72 276 393 468 842	0.040
284 476 540 727 830 890	0.040
35 39 703 793 852 903	0.040
468 469 553 559 652 842	0.040
407 540 760 790 830 900	0.040

Table S19. Information on predictive features for CRC using in silico samples generated with random subsets of healthy samples.

Columns
ID: feature index, same as Table S3
Transcript: transcript ID
Gene: gene name
Chr: chromosome
Site: coordinate of nucleosome-depleted site (GRCh37)
Region: location of nucleosome-depleted site
Group: gene group based on its expression in blood and tumor
$FPKM_{blood}$: FPKM value in normal blood
$FPKM_{tumor}$: FPKM value in tumor of colorectal cancer

ID	Transcript	Gene	Chr	Site	Region	Group	$FPKM_{blood}$	$FPKM_{tumor}$
18	ENST00000245451.8	BMP4	14	54423529	promoter	tumor	0	16.43
35	ENST00000267101.7	ERBB3	12	56473645	promoter	tumor	0	40.98
39	ENST00000270560.3	TM4SF5	17	4675187	promoter	tumor	0	18.39
67	ENST00000310836.10	UGT8	4	115519611	promoter	tumor	0.04	14.08
70	ENST00000311620.6	ANKS4B	16	21244986	promoter	tumor	0	10.61
72	ENST00000317508.10	PRSS8	16	31147083	promoter	tumor	0.11	143.22
86	ENST00000332149.9	TMPRSS2	21	42880086	promoter	tumor	0.02	43.57
115	ENST00000361084.9	RAB25	1	156030951	promoter	tumor	0.07	131.5
126	ENST00000368554.8	PRAP1	10	135122914	promoter	tumor	0	32.41
179	ENST00000425042.6	HID1	17	72968829	promoter	tumor	0.23	13.99
197	ENST00000463201.2	PRAP1	10	135164879	promoter	tumor	0	54.46
204	ENST00000478194.1	FERMT1	20	6074819	promoter	tumor	0	27
256	ENST00000588605.5	C19orf33	19	38794804	promoter	tumor	0.22	18.46
268	ENST00000605618.5	LSR	19	35739922	promoter	tumor	0.22	31.85
275	ENST00000619895.4	TMC4	19	54676865	promoter	tumor	0.35	33.05
284	ENST00000234347.9	PRTN3	19	840960	promoter	blood	13.78	0
301	ENST00000299663.7	CLEC4E	12	8693559	promoter	blood	29.27	0.2
306	ENST00000310544.8	PHOSPHO1	17	47307890	promoter	blood	30.92	0.08
322	ENST00000355524.7	FCAR	19	55385736	promoter	blood	53.04	0.07
359	ENST00000398421.6	NCF1	7	74188358	promoter	blood	11.04	0.04
364	ENST00000413580.5	PHOSPHO1	17	47308128	promoter	blood	42.76	0.05
379	ENST00000454703.6	ACSL1	4	185747273	promoter	blood	35.07	0.78
391	ENST00000480395.5	TRIM22	11	5717722	promoter	blood	17.36	0.7
393	ENST00000483750.5	WAS	X	48542217	promoter	blood	34.49	0.17
395	ENST00000485743.1	HBB	11	5248302	promoter	blood	128.52	0
407	ENST00000496823.1	BCL6	3	187463247	promoter	blood	21.33	0.2
410	ENST00000509314.5	FBXL5	4	15661487	promoter	blood	10.24	0
439	ENST00000553070.5	NFE2	12	54694799	promoter	blood	23.61	0
451	ENST00000585901.6	TYROBP	19	36399149	promoter	blood	13.4	0.19
455	ENST00000588673.3	OAZ1	19	2270290	promoter	blood	24.26	0.69
466	ENST00000596764.5	VAV1	19	6772739	promoter	blood	12.25	0.59
467	ENST00000597852.5	CD37	19	49838675	promoter	blood	13.98	0.2
468	ENST00000598034.5	GMFG	19	39826646	promoter	blood	43.77	0.45

469	ENST00000599180.2	FFAR2	19	35939203	promoter	blood	24.79	0
470	ENST00000599716.5	SHKBP1	19	41082793	promoter	blood	10.66	0.22
473	ENST00000602185.5	GMFG	19	39826645	promoter	blood	14.09	0
475	ENST00000605039.5	BIN2	12	51717938	promoter	blood	11.02	0.11
478	ENST00000615439.4	RASGRP4	19	38916945	promoter	blood	10.11	0
480	ENST00000616356.4	FCN1	9	137809723	promoter	blood	16.99	0.07
529	ENST00000291525.11	TFF3	21	43735403	junction	tumor	0	209.02
540	ENST00000300119.7	MYO1A	12	57443671	junction	tumor	0	15.11
553	ENST00000311620.6	ANKS4B	16	21245222	junction	tumor	0	10.61
559	ENST00000318683.6	B3GNT3	19	17906015	junction	tumor	0	57.75
571	ENST00000334869.8	LGMN	14	93214834	junction	tumor	0.94	45.73
594	ENST00000360779.3	SDCBP2	20	1309729	junction	tumor	0	17.84
639	ENST00000394201.8	SCOC	4	141294871	junction	tumor	0.53	14.61
652	ENST00000419308.6	FOXA2	20	22564830	junction	tumor	0	13.51
655	ENST00000425042.6	HID1	17	72968686	junction	tumor	0.23	13.99
673	ENST00000472782.1	ATP5G3	2	176046384	junction	tumor	0.62	10.87
688	ENST00000514985.5	SEPP1	5	42811938	junction	tumor	0.59	49.95
703	ENST00000543623.5	PLCD3	17	43192462	junction	tumor	0.27	14.58
721	ENST00000588605.5	C19orf33	19	38794923	junction	tumor	0.22	18.46
727	ENST00000597153.5	LGALS4	19	39303482	junction	tumor	0	20.51
744	ENST00000234347.9	PRTN3	19	841069	junction	blood	13.78	0
760	ENST00000297239.10	SYTL3	6	159082417	junction	blood	10.79	0.54
777	ENST00000343534.9	C1orf162	1	112016652	junction	blood	37.68	0.74
788	ENST00000367025.7	TRAF3IP3	1	209929654	junction	blood	17.52	0.64
790	ENST00000367535.7	NCF2	1	183559291	junction	blood	75.23	0.98
793	ENST00000368015.1	ARHGAP30	1	161039410	junction	blood	20.61	0.58
830	ENST00000454703.6	ACSL1	4	185747070	junction	blood	35.07	0.78
842	ENST00000485743.1	HBB	11	5248160	junction	blood	128.52	0
852	ENST00000496823.1	BCL6	3	187463198	junction	blood	21.33	0.2
856	ENST00000509339.1	MXD3	5	176734782	junction	blood	30.07	0.08
858	ENST00000513001.5	ACSL1	4	185678973	junction	blood	17.65	0.1
890	ENST00000589900.5	ICAM3	19	10450215	junction	blood	21.24	0
900	ENST00000599716.5	SHKBP1	19	41082891	junction	blood	10.66	0.22
903	ENST00000605039.5	BIN2	12	51717806	junction	blood	11.02	0.11
905	ENST00000615439.4	RASGRP4	19	38916709	junction	blood	10.11	0

Table S20. All predictive pan-cancer feature combinations using in silico samples generated with random subsets of healthy samples.

Columns
Feature ID: feature index (see Table S10 for feature details)
MAE: mean absolute error between observed and calculated ctDNA fractions from 652 samples

Feature ID	MAE
34 41 90 126 294 376 388 415 742 772	0.034
34 41 90 126 294 376 388 415 500 772	0.034
34 41 90 126 236 294 376 388 415 500	0.036
34 41 90 126 201 294 376 388 415 500	0.036
34 41 90 126 201 294 376 388 415 772	0.036
34 41 64 90 126 294 388 415 490 500	0.036
34 41 64 90 126 294 376 388 415 500	0.036
34 41 90 126 201 294 388 500 742 772	0.037
29 34 415 428 490 645 680 742 766 772	0.038
34 41 90 126 201 236 294 376 388 500	0.038
29 34 36 64 428 490 742 766 772 775	0.038
34 41 64 90 126 201 294 388 742 772	0.038
41 90 126 201 236 294 376 388 415 500	0.038
29 57 64 126 428 454 742 766 772 789	0.038
34 41 90 126 201 236 294 388 490 500	0.039
34 126 135 428 680 742 766 772 787 789	0.039
34 41 90 126 201 294 388 500 772 775	0.039
34 41 90 126 201 236 294 376 388 772	0.039
29 34 80 135 415 428 742 766 772 775	0.039
34 41 90 201 236 294 376 388 500 772	0.039
41 64 90 126 294 376 388 415 490 500	0.039
41 64 90 126 201 294 376 388 415 500	0.039
41 90 126 135 236 294 376 388 415 500	0.039
34 41 90 135 201 236 294 376 388 500	0.039
34 41 64 90 126 201 294 376 415 500	0.039
41 64 90 201 236 294 376 388 415 500	0.039
34 41 90 126 201 294 376 388 500 772	0.040
34 41 64 90 201 236 294 376 388 500	0.040
41 57 90 126 201 236 294 376 388 500	0.040
34 41 90 126 201 294 376 388 490 500	0.040
123 402 415 456 490 645 667 680 742 756	0.040
34 41 242 415 667 680 742 766 772 789	0.040
29 34 135 435 667 680 742 766 772 787	0.040
34 41 64 90 201 294 376 415 500 775	0.040
34 41 90 126 135 201 294 376 388 500	0.040
34 41 80 142 311 415 742 766 772 775	0.040
41 57 64 90 126 201 294 376 388 500	0.040
29 34 123 135 428 680 742 766 772 787	0.040
126 396 415 428 454 667 680 742 766 789	0.040
34 41 64 90 126 201 294 376 388 500	0.040
34 41 64 90 126 201 294 388 500 772	0.041
57 90 126 201 294 376 388 415 456 500	0.041
34 36 126 428 645 680 742 766 772 775	0.041
34 41 64 90 126 201 294 388 490 500	0.041
29 135 415 428 454 680 742 766 772 789	0.041
34 41 57 90 126 294 388 500 742 772	0.041
123 135 142 242 296 402 456 667 680 797	0.041

Feature ID	MAE
29 201 435 454 667 680 742 766 772 787	0.041
34 41 288 490 667 680 742 766 772 787	0.041
29 34 36 64 435 667 680 742 766 772	0.041
29 126 428 454 634 645 680 742 772 787	0.041
34 41 90 126 236 294 376 388 742 772	0.041
57 90 126 201 236 294 388 415 490 500	0.041
41 90 126 201 236 294 376 388 456 500	0.041
34 41 90 126 135 201 294 388 500 772	0.041
34 135 415 645 667 680 742 766 772 775	0.041
34 41 90 126 135 201 294 388 490 500	0.041
29 36 396 415 428 435 454 742 766 789	0.041
29 135 428 454 667 680 766 772 775 789	0.042
34 41 64 90 126 135 201 294 388 500	0.042
34 41 64 90 126 201 294 376 388 772	0.042
34 41 90 126 236 294 376 388 500 772	0.042
41 64 90 126 201 236 294 376 388 500	0.042
19 29 396 415 428 435 454 680 766 789	0.042
29 34 135 311 428 680 742 766 772 775	0.042
41 90 126 201 236 294 376 388 490 500	0.042
64 90 126 135 201 294 376 388 415 500	0.042
41 90 126 135 201 236 294 376 388 500	0.042
29 135 142 201 242 454 742 766 772 775	0.042
34 64 201 242 428 680 742 766 772 787	0.042
34 36 41 135 311 667 680 742 772 775	0.042
123 135 396 415 435 454 500 680 742 766	0.042
29 135 242 428 454 742 766 772 775 789	0.042
288 402 490 547 634 645 667 680 742 787	0.042
29 34 135 428 667 680 742 766 772 775	0.042
34 41 90 126 294 376 388 500 742 772	0.042
135 201 402 428 435 454 742 766 775 789	0.043
34 41 64 90 126 294 376 388 490 772	0.043
34 41 90 126 294 376 388 490 500 772	0.043
29 135 396 402 428 435 454 490 766 775	0.043
29 126 135 388 415 428 435 454 490 789	0.043
135 201 402 428 454 680 742 766 772 787	0.043
29 242 428 454 645 667 680 756 775 789	0.043
29 201 428 454 667 680 742 756 772 789	0.043
34 41 90 126 135 201 294 376 490 500	0.043
34 36 41 242 288 311 742 766 772 775	0.043
29 201 428 435 454 667 680 742 766 789	0.043
57 64 90 126 201 294 376 388 490 500	0.043
8 19 296 338 415 456 680 766 775 789	0.043
29 135 201 428 435 454 742 756 775 789	0.043
34 41 64 90 126 135 201 294 376 500	0.043
29 135 142 454 667 680 742 766 772 775	0.043
34 36 41 80 135 242 766 772 775 787	0.043
29 123 236 428 454 742 766 772 775 789	0.043

Feature ID	MAE
34 41 64 90 126 294 376 388 500 772	0.043
142 288 396 402 435 454 634 645 666 775	0.043
34 41 64 90 126 294 388 500 742 772	0.044
19 126 135 388 396 428 454 667 680 789	0.044
135 242 396 402 415 634 645 667 674 680	0.044
126 135 428 454 645 667 680 766 772 789	0.044
41 64 90 126 135 201 294 376 388 500	0.044
34 41 90 126 201 294 376 456 500 772	0.044
34 41 90 126 135 294 388 490 500 772	0.044
201 415 454 634 645 667 680 742 766 772	0.044
29 34 64 428 667 680 742 766 772 789	0.044
135 142 428 454 680 742 766 772 775 789	0.044
29 135 454 490 667 680 742 766 772 775	0.044
29 123 135 376 396 454 680 742 766 789	0.044
135 242 376 396 402 415 428 435 454 490	0.044
34 41 90 201 294 376 500 645 742 772	0.044
64 90 126 135 201 236 294 376 388 500	0.044
37 278 288 331 338 376 547 634 645 787	0.044
34 41 57 90 201 294 376 500 742 772	0.044
19 29 36 135 142 388 396 435 454 789	0.044
90 126 135 201 236 294 376 388 490 500	0.044
29 123 135 142 396 415 435 454 766 775	0.044
29 396 428 435 454 490 680 742 766 789	0.045
29 64 135 142 428 454 490 766 772 789	0.045
29 428 435 454 634 645 680 742 766 772	0.045
135 396 402 435 454 490 742 766 775 789	0.045
29 135 454 634 645 667 680 742 766 772	0.045
29 135 428 454 645 667 680 742 766 772	0.045
34 41 64 90 126 294 376 388 490 500	0.045
29 142 288 428 454 667 680 742 766 772	0.045
123 205 288 402 435 634 645 667 680 787	0.045
34 36 135 428 490 667 680 742 766 772	0.045
29 428 454 634 645 667 680 742 766 772	0.045
29 388 428 454 634 645 667 680 742 772	0.045
29 135 396 428 454 490 742 766 775 789	0.045
41 64 90 135 201 294 376 388 456 500	0.045
29 142 396 428 435 454 490 766 775 789	0.045
29 135 415 428 435 454 500 766 775 789	0.045
29 135 428 454 490 680 742 766 772 789	0.045
19 135 142 415 428 454 490 766 775 789	0.045
64 205 225 278 296 415 544 634 645 674	0.045
29 135 142 428 454 667 680 742 766 772	0.045
29 34 288 428 435 667 680 742 766 772	0.045
123 278 288 396 415 435 454 456 766 789	0.045
29 388 428 435 454 645 667 680 742 772	0.045
8 142 415 435 645 667 674 680 766 775	0.045
29 135 428 454 490 634 645 680 766 772	0.045
64 90 126 201 236 294 376 388 490 500	0.045
64 90 126 135 201 294 376 388 490 500	0.046
34 428 435 667 680 742 766 772 775 789	0.046
36 135 428 435 454 645 667 680 742 766	0.046

Feature ID	MAE
34 135 402 630 634 645 680 742 766 772	0.046
135 201 428 435 454 674 680 742 766 789	0.046
8 123 288 402 490 667 680 742 766 775	0.046
123 201 396 402 428 435 454 766 775 789	0.046
205 258 338 402 456 490 736 766 787 789	0.046
29 396 402 428 435 456 634 667 680 787	0.046
123 435 454 630 634 645 667 680 787 789	0.046
19 288 331 396 402 415 435 630 634 742	0.046
396 428 435 454 667 680 742 766 775 789	0.046
36 201 428 435 454 490 500 680 766 789	0.046
64 123 135 142 205 278 634 645 674 787	0.047
29 135 142 242 388 428 454 490 787 789	0.047
237 288 296 331 338 435 547 634 775 787	0.047
34 41 135 634 645 667 680 742 766 772	0.047
123 142 242 288 415 634 645 667 680 789	0.047
135 396 402 634 645 667 674 680 787 789	0.047
8 19 64 142 288 296 435 667 674 787	0.047
118 225 236 258 278 286 296 311 456 589	0.047
19 64 415 490 634 645 674 775 776 789	0.047
8 64 123 135 142 278 415 634 645 674	0.047
29 123 201 428 435 454 490 500 766 775	0.047
19 36 201 428 435 454 742 766 775 789	0.047
29 123 454 645 667 680 742 766 772 789	0.047
36 135 142 201 415 454 500 766 775 789	0.047
8 19 142 278 396 415 674 766 775 789	0.047
123 288 435 634 645 680 742 766 772 775	0.048
34 41 311 630 634 645 667 680 742 772	0.048
8 64 278 286 296 338 544 634 645 787	0.048
8 64 205 278 415 544 634 645 674 789	0.048
123 135 242 547 634 645 667 680 742 776	0.048
8 37 142 278 288 296 331 338 415 634	0.048
34 36 41 80 135 242 311 435 490 787	0.048
29 34 36 57 135 242 428 772 775 789	0.048
34 135 428 634 645 667 680 742 766 772	0.048
142 278 288 396 454 630 634 645 666 789	0.048
288 296 402 547 630 634 645 667 674 680	0.048
8 123 135 142 242 396 402 456 490 787	0.048
8 142 237 258 296 402 456 695 776 787	0.048
123 242 288 428 634 645 667 680 766 775	0.048
142 278 288 396 428 454 634 645 775 789	0.049
83 205 225 236 286 402 456 544 589 708	0.049
123 242 288 396 402 634 645 667 680 742	0.049
142 205 278 288 396 415 435 634 645 742	0.049
8 288 296 415 456 634 645 667 680 766	0.049
36 225 288 428 500 667 674 680 787 789	0.049
135 376 402 415 428 435 454 500 775 789	0.049
29 123 135 396 454 667 674 680 787 789	0.049
8 123 242 288 296 415 742 766 775 789	0.049
135 142 428 454 634 645 667 680 742 766	0.049
19 118 278 288 296 338 547 634 653 787	0.049
19 64 123 142 288 396 415 674 742 789	0.049

Feature ID	MAE
8 29 118 135 142 205 242 415 674 680	0.049
64 135 142 242 396 415 456 634 645 667	0.049
142 288 396 435 454 490 630 634 645 666	0.049
142 242 338 416 544 634 645 667 680 787	0.049
9 211 236 258 296 348 376 544 621 666	0.049
258 357 402 415 456 544 621 666 674 695	0.049
142 278 331 396 428 435 454 634 645 787	0.049
29 123 142 205 288 634 645 667 680 787	0.049
8 19 64 205 278 288 296 338 653 787	0.049
29 36 64 135 142 428 435 454 775 787	0.049
123 142 237 296 396 415 645 667 680 776	0.049
286 288 296 490 547 634 645 666 667 787	0.049
19 29 123 135 376 396 634 645 680 766	0.050
123 142 205 396 435 454 456 680 742 766	0.050
236 242 258 306 402 544 621 666 674 695	0.050
29 225 288 296 461 634 645 667 674 680	0.050
19 135 142 396 435 454 674 775 787 789	0.050
8 80 123 205 237 288 396 402 766 775	0.050
118 205 547 634 645 667 674 680 695 787	0.050
8 52 64 278 288 296 338 415 435 490	0.050
15 225 306 311 402 469 589 607 630 695	0.050

Table S21. Information on predictive pan-cancer features using in silico samples generated with random subsets of healthy samples.

Columns
ID: feature index
Transcript: transcript ID
Gene: gene name
Chr: chromosome
Site: coordinate of nucleosome-depleted site (GRCh37)
Region: location of nucleosome-depleted site
Group: gene group based on its expression in blood and tumor
$FPKM_{blood}$: FPKM value in normal blood. Their FPKM values in tumors of 20 cancer types are all <1.

ID	Transcript	Gene	Chr	Site	Region	Group	$FPKM_{blood}$
8	ENST00000221954.6	CEACAM4	19	42133442	promoter	blood	32.81
9	ENST00000225275.3	MPO	17	56358296	promoter	blood	7.23
15	ENST00000262407.5	ITGA2B	17	42466873	promoter	blood	12.34
19	ENST00000264260.6	IL18RAP	2	103035149	promoter	blood	42.11
29	ENST00000299663.7	CLEC4E	12	8693559	promoter	blood	29.27
34	ENST00000307395.4	GP9	3	128779610	promoter	blood	9.72
36	ENST00000310544.8	PHOSPHO1	17	47307890	promoter	blood	30.92
37	ENST00000312156.8	NFE2	12	54689544	promoter	blood	11.15
41	ENST00000324134.10	NLRP12	19	54327597	promoter	blood	9.17
52	ENST00000342063.4	C19orf35	19	2282175	promoter	blood	8.64
57	ENST00000355524.7	FCAR	19	55385736	promoter	blood	53.04
64	ENST00000375448.4	PADI4	1	17634692	promoter	blood	95.04
80	ENST00000391726.7	FCAR	19	55385704	promoter	blood	6

83	ENST00000392847.1	HMBS	11	118958697	promoter	blood	7.28
90	ENST00000398632.3	MX2	21	42774561	promoter	blood	7.28
118	ENST00000452208.1	RGL4	22	24038671	promoter	blood	64.94
123	ENST00000460208.1	LILRB3	19	54721567	promoter	blood	51.15
126	ENST00000462275.5	TBXAS1	7	139529072	promoter	blood	6.07
135	ENST00000465984.5	SLC11A1	2	219246911	promoter	blood	10.54
142	ENST00000467972.5	SLC12A9	7	100454416	promoter	blood	6.8
201	ENST00000487767.5	GPSM3	6	32160645	promoter	blood	14.37
205	ENST00000488970.1	BTK	X	100609209	promoter	blood	7.4
211	ENST00000490872.1	SLC11A1	2	219254688	promoter	blood	26.15
225	ENST00000496915.1	PREX1	20	47259276	promoter	blood	5.23
236	ENST00000509314.5	FBXL5	4	15661487	promoter	blood	10.24
237	ENST00000509339.1	MXD3	5	176735063	promoter	blood	30.07
242	ENST00000517813.1	DENND3	8	142194587	promoter	blood	13.47
258	ENST00000523369.1	LCP2	5	169685502	promoter	blood	9.88
278	ENST00000533815.2	BTNL8	5	180336564	promoter	blood	5.72
286	ENST00000538842.1	ATG16L2	11	72527790	promoter	blood	6.35
288	ENST00000539932.5	SLC11A1	2	219246926	promoter	blood	50.32
294	ENST00000542481.1	ATG16L2	11	72534940	promoter	blood	25.18
296	ENST00000543576.5	DENND1C	19	6481798	promoter	blood	12.06
306	ENST00000554736.5	GNG2	14	52328042	promoter	blood	9.3
311	ENST00000559347.5	MAN2A2	15	91459225	promoter	blood	8.61
331	ENST00000566082.1	USB1	16	58049017	promoter	blood	6.82
338	ENST00000570439.1	ACAP1	17	7248650	promoter	blood	5.27
348	ENST00000574548.1	RNF167	17	4847675	promoter	blood	6.4
357	ENST00000581974.1	DHRS13	17	27226541	promoter	blood	5.97
376	ENST00000590974.1	LYL1	19	13213975	promoter	blood	5.48
388	ENST00000597611.7	FKBP8	19	18654887	promoter	blood	9.25
396	ENST00000599180.2	FFAR2	19	35939203	promoter	blood	24.79
402	ENST00000601502.1	MYO1F	19	8610602	promoter	blood	8.05
415	ENST00000615340.4	RASGRP4	19	38916837	promoter	blood	6.88
416	ENST00000616356.4	FCN1	9	137809723	promoter	blood	16.99
428	ENST00000221954.6	CEACAM4	19	42133268	junction	blood	32.81
435	ENST00000262407.5	ITGA2B	17	42466654	junction	blood	12.34
454	ENST00000307395.4	GP9	3	128779693	junction	blood	9.72
456	ENST00000310544.8	PHOSPHO1	17	47307830	junction	blood	30.92
461	ENST00000324134.10	NLRP12	19	54327140	junction	blood	9.17
469	ENST00000338372.6	VSTM1	19	54566998	junction	blood	10.71
490	ENST00000380299.3	HBD	11	5255572	junction	blood	138.84
500	ENST00000394430.5	RASGRP2	11	64510266	junction	blood	17.61
544	ENST00000465984.5	SLC11A1	2	219247098	junction	blood	10.54
547	ENST00000466612.5	ABTB1	3	127392451	junction	blood	6.18
589	ENST00000484762.1	CSF3R	1	36933423	junction	blood	8.26
607	ENST00000488970.1	BTK	X	100608858	junction	blood	7.4
621	ENST00000496915.1	PREX1	20	47258945	junction	blood	5.23
630	ENST00000509314.5	FBXL5	4	15661350	junction	blood	10.24
634	ENST00000513001.5	ACSL1	4	185678973	junction	blood	17.65
645	ENST00000521442.1	ATP6V1B2	8	20075793	junction	blood	8.33
653	ENST00000526387.5	TBC1D10C	11	67171411	junction	blood	7.1

666	ENST00000532897.5	MKNK1	1	47037735	junction	blood	6.23
667	ENST00000533815.2	BTNL8	5	180336697	junction	blood	5.72
674	ENST00000538842.1	ATG16L2	11	72527872	junction	blood	6.35
680	ENST0000054248[illegible].1	ATG16L2	11	72535167	junction	blood	25.18
695	ENST0000055934[illegible].5	MAN2A2	15	91459486	junction	blood	8.61
708	ENST00000564894.1	RNF166	16	88767670	junction	blood	7.9
736	ENST00000581974.1	DHRS13	17	27226145	junction	blood	5.97
742	ENST00000585852.5	FMNL1	17	43308054	junction	blood	19.81
766	ENST0000059761[illegible].7	FKBP8	19	18654719	junction	blood	9.25
772	ENST00000599180.2	FFAR2	19	35939281	junction	blood	24.79
775	ENST00000599716.5	SHKBP1	19	41082891	junction	blood	10.66
776	ENST00000600463.1	IFI30	19	18286032	junction	blood	6.41
787	ENST00000614135.4	RASGRP4	19	38916709	junction	blood	8.18
789	ENST00000616356.4	FCN1	9	137809615	junction	blood	16.99

Supplementary Data 1

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chr10	121481850	121482177	461_60370_2263(FGFR2)_20a	0	-
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chr10	121517318	121517463	461_60360_2263(FGFR2)_10a	0	-
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chr11	108246963	108247127	427_14218_472(ATM)_12	0	-
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chr12	132642176	132642397	470_129079_5426(POLE)_38	0	-
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chr12	132659294	132659509	470_129067_5426(POLE)_26	0	-
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chr12	132665301	132665450	470_129062_5426(POLE)_21	0	-
chr12	132667502	132667648	470_129061_5426(POLE)_20	0	-
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chr12	132668634	132668737	470_129059_5426(POLE)_18	0	-
chr12	132668810	132668939	470_129058_5426(POLE)_17	0	-
chr12	132672214	132672322	470_129057_5426(POLE)_16	0	-
chr12	132672626	132672839	470_129056_5426(POLE)_15	0	-
chr12	132673163	132673277	470_129055_5426(POLE)_14	0	-
chr12	132673574	132673707	470_129054_5426(POLE)_13	0	-
chr12	132675397	132675517	470_129053_5426(POLE)_12	0	-
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chr12	132676093	132676204	470_129051_5426(POLE)_10	0	-
chr12	132676545	132676653	470_129050_5426(POLE)_9	0	-
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chr12	132679953	132680046	470_129046_5426(POLE)_5	0	-
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chr12	132680606	132680687	470_129044_5426(POLE)_3	0	-
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chr13	28015156	28015256	461_60874_2322(FLT3)_23a	0	-
chr13	28015589	28015701	461_60873_2322(FLT3)_22a	0	-
chr13	28018466	28018589	461_60872_2322(FLT3)_21a	0	-
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chr13	28024860	28024943	461_60870_2322(FLT3)_19a	0	-
chr13	28027087	28027241	461_60869_2322(FLT3)_18a	0	-
chr13	28028177	28028288	461_60868_2322(FLT3)_17a	0	-
chr13	28033886	28033991	461_60867_2322(FLT3)_16a	0	-
chr13	28034081	28034214	461_60866_2322(FLT3)_15a	0	-
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chr13	32357741	32357929	427_15664_675(BRCA2)_16	0	-
chr13	32362522	32362693	427_15665_675(BRCA2)_17	0	-
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chr13	48380164	48380241	472_141458_5925(RB1)_16a	0	-
chr13	48381246	48381443	472_141459_5925(RB1)_17a	0	-
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chr15	90091552	90091644	463_79502_3418(IDH2)_3a	0	-
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chr16	2048586	2048753	476_182339_7249(TSC2)_2	0	-
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chr16	2057104	2057178	476_182346_7249(TSC2)_9	0	-
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chr16	2072848	2072983	476_182358_7249(TSC2)_21	0	-
chr16	2074199	2074389	476_182359_7249(TSC2)_22	0	-
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chr16	2086731	2086871	476_182375_7249(TSC2)_38	0	-
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chr16	68829653	68829797	428_25434_999(CDH1)_15	0	-
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chr17	12113232	12113360	465_99955_6416(MAP2K4)_9	0	-
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chr17	12129138	12129287	465_99957_6416(MAP2K4)_11	0	-
chr17	12139838	12139884	465_99958_6416(MAP2K4)_12	0	-
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chr17	31155982	31156126	469_118575_4763(NF1)_2a	0	-
chr17	31159009	31159093	469_118576_4763(NF1)_3a	0	-
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chr7	55191718	55191874	431_48565_1956(EGFR)_25	0	-
chr7	55192765	55192841	431_48566_1956(EGFR)_26	0	-
chr7	55198716	55198863	431_48567_1956(EGFR)_27	0	-
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chr8	38424508	38424699	461_60323_2260(FGFR1)_10a	0	-
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Supplementary Data 2

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chr17	31338024	31338139	469_118618_4763(NF1)_45a	0	-
chr17	31337818	31337880	469_118617_4763(NF1)_44a	0	-
chr17	31337367	31337582	469_118616_4763(NF1)_43a	0	-

chr17	31336634	31336914	469_118615_4763(NF1)_42a	0	-
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chr17	31334837	31335031	469_118613_4763(NF1)_40a	0	-
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chr17	31227217	31227291	469_118592_4763(NF1)_19a	0	-
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chr17	31155982	31156126	469_118575_4763(NF1)_2a	0	-
chr17	31095309	31095369	469_118574_4763(NF1)_1a	0	-
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chr17	31362287	31362364	469_118631_4763(NF1)_58a	0	-
chr17	31360486	31360703	469_118630_4763(NF1)_57a	0	-
chr17	31358968	31359015	469_118629_4763(NF1)_56a	0	-
chr17	31358479	31358622	469_118628_4763(NF1)_55a	0	-
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chr16	2086192	2086379	476_182374_7249(TSC2)_37	0	-
chr16	2080164	2080377	476_182367_7249(TSC2)_30	0	-
chr16	2075798	2075892	476_182360_7249(TSC2)_23	0	-
chr16	2065518	2065635	476_182353_7249(TSC2)_16	0	-
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chr17	31338703	31338805	469_118619_4763(NF1)_46a	0	-
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chr17	31225094	31225250	469_118590_4763(NF1)_17a	0	-
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chr4	54285370	54285486	470_126854_5156(PDGFRA)_19a	0	-
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chr4	54261094	54261412	470_126839_5156(PDGFRA)_4a	0	-
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chr4	54289008	54289114	470_126858_5156(PDGFRA)_23a	0	-
chr4	54288798	54288898	470_126857_5156(PDGFRA)_22a	0	-
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chr4	54290312	54290554	470_126859_5156(PDGFRA)_24a	0	-
chr4	54281580	54281978	470_126853_5156(PDGFRA)_18a	0	-
chr4	54272393	54272520	470_126845_5156(PDGFRA)_10a	0	-
chr4	54258768	54258817	470_126838_5156(PDGFRA)_3a	0	-
chr7	129210964	129211113	474_160573_6608(SMO)_10a	0	-
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chr3	10146513	10146636	477_191809_7428(VHL)_2	0	-
chr3	10141847	10142187	477_191808_7428(VHL)_1	0	-
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chr7	116740851	116741025	466_106284_4233(MET)_8a	0	-
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chr3	36997155	36997300	466_106459_4292(MLH1)_4	0	-
chr3	36996618	36996709	466_106458_4292(MLH1)_3	0	-
chr3	36993768	36993890	466_106457_4292(MLH1)_2	0	-
chr3	36993547	36993663	466_106456_4292(MLH1)_1	0	-
chr3	37048903	37049017	466_106475_4292(MLH1)_20	0	-
chr3	37017505	37017599	466_106467_4292(MLH1)_12	0	-
chr3	37000954	37001053	466_106460_4292(MLH1)_5	0	-
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chr1	43348842	43349002	466_106806_4352(MPL)_9a	0	-
chr1	43346791	43346934	466_106805_4352(MPL)_8a	0	-
chr1	43346444	43346629	466_106804_4352(MPL)_7a	0	-
chr1	43340386	43340513	466_106803_4352(MPL)_6a	0	-
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chr1	43338098	43338231	466_106799_4352(MPL)_2a	0	-
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chr1	43349262	43349359	466_106807_4352(MPL)_10a	0	-
chr1	43338541	43338720	466_106800_4352(MPL)_3a	0	-
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chr9	5054562	5054884	463_81649_3717(JAK2)_7	0	-
chr9	5073697	5073785	463_81656_3717(JAK2)_14	0	-
chr9	5090738	5090911	463_81664_3717(JAK2)_22	0	-
chr9	5021987	5022213	463_81562_3717(JAK2)_3	0	-
chr9	5044402	5044520	463_81564_3717(JAK2)_5	0	-
chr1	64883276	64883475	463_81625_3716(JAK1)_4a	0	-
chr1	64855508	64855698	463_81633_3716(JAK1)_12a	0	-
chr1	64841450	64841601	463_81640_3716(JAK1)_19a	0	-
chr1	64844063	64844215	463_81639_3716(JAK1)_18a	0	-
chr1	64841244	64841339	463_81641_3716(JAK1)_20a	0	-

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chr1	64839602	64839795	463_81642_3716(JAK1)_21a	0	-
chr4	55115280	55115411	464_88699_3791(KDR)_4a	0	-
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chr4	55113303	55113481	464_88702_3791(KDR)_7a	0	-
chr4	55110653	55110768	464_88703_3791(KDR)_8a	0	-
chr4	55107736	55107893	464_88705_3791(KDR)_10a	0	-
chr4	55106686	55106810	464_88706_3791(KDR)_11a	0	-
chr4	55105831	55105940	464_88707_3791(KDR)_12a	0	-
chr4	55104642	55104984	464_88708_3791(KDR)_13a	0	-
chr4	55102361	55102508	464_88709_3791(KDR)_14a	0	-
chr4	55101896	55102028	464_88710_3791(KDR)_15a	0	-
chr4	55098696	55098803	464_88711_3791(KDR)_16a	0	-
chr4	55097661	55097766	464_88713_3791(KDR)_18a	0	-
chr4	55096228	55096342	464_88714_3791(KDR)_19a	0	-
chr4	55095576	55095665	464_88715_3791(KDR)_20a	0	-
chr4	55094801	55094955	464_88716_3791(KDR)_21a	0	-
chr4	55092616	55092714	464_88717_3791(KDR)_22a	0	-
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chr12	120993519	120993706	463_81840_6927(HNF1A)_3	0	-
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chr22	23793558	23793688	474_160330_6598(SMARCB1)_3	0	-
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chr4	55082535	55082635	464_88723_3791(KDR)_28a	0	-
chr4	55081955	55082041	464_88724_3791(KDR)_29a	0	-
chr4	55079940	55080163	464_88725_3791(KDR)_30a	0	-
chr12	120997473	120997665	463_81844_6927(HNF1A)_7	0	-
chr12	121001064	121001192	463_81846_6927(HNF1A)_9	0	-
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chr16	2088047	2088139	476_182377_7249(TSC2)_40	0	-
chr16	2087862	2087941	476_182376_7249(TSC2)_39	0	-
chr16	2086731	2086871	476_182375_7249(TSC2)_38	0	-
chr16	2085229	2085322	476_182373_7249(TSC2)_36	0	-
chr16	2084950	2085026	476_182372_7249(TSC2)_35	0	-
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chr16	2083694	2083816	476_182370_7249(TSC2)_33	0	-
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chr16	2076067	2076257	476_182361_7249(TSC2)_24	0	-
chr16	2074199	2074389	476_182359_7249(TSC2)_22	0	-

chr16	2072848	2072983	476_182358_7249(TSC2)_21	0	-
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chr16	2071509	2071616	476_182355_7249(TSC2)_18	0	-
chr16	2070455	2070578	476_182354_7249(TSC2)_17	0	-
chr16	2064271	2064427	476_182352_7249(TSC2)_15	0	-
chr16	2062971	2063053	476_182351_7249(TSC2)_14	0	-
chr16	2062496	2062600	476_182350_7249(TSC2)_13	0	-
chr16	2061870	2062008	476_182349_7249(TSC2)_12	0	-
chr16	2060669	2060813	476_182348_7249(TSC2)_11	0	-
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chr15	90102275	90102390	463_79500_3418(IDH2)_1a	0	-
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chr11	533765	533944	463_79035_3265(HRAS)_3a	0	-
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chr10	8055655	8055896	462_69261_2625(GATA3)_4a	0	-
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chr19	17844233	17844430	463_81744_3718(JAK3)_2a	0	-
chr19	17843776	17843900	463_81745_3718(JAK3)_3a	0	-
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chr19	17843026	17843172	463_81747_3718(JAK3)_5a	0	-
chr19	17842315	17842610	463_81748_3718(JAK3)_6a	0	-
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chr19	17840229	17840341	463_81751_3718(JAK3)_9a	0	-
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chr19	17832789	17832929	463_81760_3718(JAK3)_18a	0	-
chr19	17832518	17832708	463_81761_3718(JAK3)_19a	0	-
chr19	17831673	17831798	463_81762_3718(JAK3)_20a	0	-
chr19	17831227	17831400	463_81763_3718(JAK3)_21a	0	-
chr19	17830502	17830620	463_81764_3718(JAK3)_22a	0	-
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chr4	152324183	152324394	461_64095_55294(FBXW7)_16	0	-
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chr10	43126574	43127504	473_148937_5979(RET)_19a	0	-
chr10	43123670	43123808	473_148935_5979(RET)_17a	0	-
chr10	43121945	43122016	473_148934_5979(RET)_16a	0	-
chr10	43120080	43120203	473_148933_5979(RET)_15a	0	-
chr10	43119530	43119745	473_148932_5979(RET)_14a	0	-
chr10	43118372	43118480	473_148931_5979(RET)_13a	0	-
chr10	43116583	43116731	473_148930_5979(RET)_12a	0	-
chr10	43113555	43113675	473_148928_5979(RET)_10a	0	-
chr19	17847945	17848061	463_81743_3718(JAK3)_1a	0	-
chr13	48477354	48477404	472_141468_5925(RB1)_26a	0	-
chr13	48476700	48476843	472_141467_5925(RB1)_25a	0	-
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chr13	48465204	48465368	472_141465_5925(RB1)_23a	0	-
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chr13	48452992	48453111	472_141460_5925(RB1)_18a	0	-
chr13	48381246	48381443	472_141459_5925(RB1)_17a	0	-
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chr13	48342598	48342714	472_141445_5925(RB1)_3a	0	-
chr13	48307279	48307406	472_141444_5925(RB1)_2a	0	-
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chr4	152382188	152382512	461_64084_55294(FBXW7)_5	0	-
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chr4	152330731	152330868	461_64091_55294(FBXW7)_12	0	-
chr4	152329671	152329785	461_64092_55294(FBXW7)_13	0	-

chr4	152328207	152328389	461_64093_55294(FBXW7)_14	0	-
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chr4	152323088	152323149	461_64096_55294(FBXW7)_17	0	-
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chr10	43109030	43109230	473_148924_5979(RET)_6a	0	-
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chr13	32326100	32326150	427_15653_675(BRCA2)_5	0	-
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chr17	43097243	43097289	427_15613_672(BRCA1)_8	0	-
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chr17	43045677	43045802	427_15629_672(BRCA1)_24	0	-
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chr18	51049294	51049324	474_158718_4089(SMAD4)_4	0	-
chr19	2164184	2164265	431_55601_84444(DOT1L)_1	0	-
chr22	29043298	29043430	478_203546_84133(ZNRF3)_7	0	-
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chr22	29049196	29050948	478_203550_84133(ZNRF3)_11	0	-
chr22	29053578	29053622	478_203551_84133(ZNRF3)_12	0	-
chr19	2180712	2180756	431_55602_84444(DOT1L)_2	0	-
chr4	1805354	1805476	461_60345_2261(FGFR3)_12a	0	-
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chr4	1807115	1807262	461_60352_2261(FGFR3)_19a	0	-
chr4	1793934	1794043	461_60335_2261(FGFR3)_2a	0	-
chr4	1799253	1799523	461_60336_2261(FGFR3)_3a	0	-
chr4	1799746	1799812	461_60337_2261(FGFR3)_4a	0	-
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chr19	2185854	2185929	431_55603_84444(DOT1L)_3	0	-
chr19	2189731	2189795	431_55604_84444(DOT1L)_4	0	-
chr19	2191011	2191240	431_55605_84444(DOT1L)_5	0	-
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chr19	2210620	2210855	431_55614_84444(DOT1L)_14	0	-
chr19	2211750	2211842	431_55616_84444(DOT1L)_16	0	-
chr19	2213538	2213640	431_55617_84444(DOT1L)_17	0	-
chr19	2213848	2213986	431_55618_84444(DOT1L)_18	0	-

chr19	2214470	2214596	431_55619_84444(DOT1L)_19	0	-
chr19	2216280	2216765	431_55620_84444(DOT1L)_20	0	-
chr15	66444655	66444707	465_99854_5604(MAP2K1)_6a	0	-
chr15	66481754	66481879	465_99855_5604(MAP2K1)_7a	0	-
chr15	66484989	66485191	465_99856_5604(MAP2K1)_8a	0	-
chr15	66487227	66487292	465_99857_5604(MAP2K1)_9a	0	-
chr15	66489214	66489276	465_99858_5604(MAP2K1)_10a	0	-
chr15	66489717	66489763	465_99859_5604(MAP2K1)_11a	0	-
chr19	2216954	2217090	431_55621_84444(DOT1L)_21	0	-
chr19	2217771	2217918	431_55622_84444(DOT1L)_22	0	-
chr19	2221975	2222559	431_55624_84444(DOT1L)_24	0	-
chr19	2223280	2223486	431_55625_84444(DOT1L)_25	0	-
chr19	2225387	2225452	431_55626_84444(DOT1L)_26	0	-
chr19	2226182	2227127	431_55627_84444(DOT1L)_27	0	-
chr19	2227736	2229792	431_55628_84444(DOT1L)_28	0	-
chr9	5050685	5050831	463_81648_3717(JAK2)_6	0	-
chr9	5055668	5055788	463_81650_3717(JAK2)_8	0	-
chr9	5064882	5065040	463_81651_3717(JAK2)_9	0	-
chr9	5066677	5066789	463_81652_3717(JAK2)_10	0	-
chr9	5069021	5069208	463_81653_3717(JAK2)_11	0	-
chr9	5069924	5070052	463_81654_3717(JAK2)_12	0	-
chr9	5072491	5072626	463_81655_3717(JAK2)_13	0	-
chr9	5077452	5077580	463_81657_3717(JAK2)_15	0	-
chr9	5078305	5078444	463_81658_3717(JAK2)_16	0	-
chr9	5080228	5080380	463_81659_3717(JAK2)_17	0	-
chr9	5080532	5080683	463_81660_3717(JAK2)_18	0	-
chr9	5081724	5081861	463_81661_3717(JAK2)_19	0	-
chr9	5089673	5089863	463_81662_3717(JAK2)_20	0	-
chr9	5090445	5090570	463_81663_3717(JAK2)_21	0	-
chr9	5123003	5123121	463_81665_3717(JAK2)_23	0	-
chr9	5126332	5126446	463_81666_3717(JAK2)_24	0	-
chr9	5126683	5126791	463_81667_3717(JAK2)_25	0	-
chr4	1801619	1801743	461_60339_2261(FGFR3)_6a	0	-
chr4	1801834	1802025	461_60340_2261(FGFR3)_7a	0	-
chr10	121518681	121518829	461_60359_2263(FGFR2)_9a	0	-
chr10	121487353	121487424	461_60367_2263(FGFR2)_17a	0	-
chr10	121593708	121593817	461_60353_2263(FGFR2)_3a	0	-
chr10	121565437	121565704	461_60354_2263(FGFR2)_4a	0	-
chr10	121564501	121564579	461_60355_2263(FGFR2)_5a	0	-
chr10	121551289	121551459	461_60356_2263(FGFR2)_6a	0	-
chr10	121538591	121538715	461_60357_2263(FGFR2)_7a	0	-
chr10	121519978	121520169	461_60358_2263(FGFR2)_8a	0	-
chr10	121517318	121517463	461_60360_2263(FGFR2)_10a	0	-
chr10	121515116	121515319	461_60361_2263(FGFR2)_11a	0	-
chr10	121503789	121503941	461_60362_2263(FGFR2)_12a	0	-
chr10	121500825	121500947	461_60363_2263(FGFR2)_13a	0	-
chr10	121498494	121498605	461_60364_2263(FGFR2)_14a	0	-
chr10	121496531	121496722	461_60365_2263(FGFR2)_15a	0	-
chr10	121487990	121488113	461_60366_2263(FGFR2)_16a	0	-
chr10	121485394	121485532	461_60368_2263(FGFR2)_18a	0	-
chr10	121483697	121483803	461_60369_2263(FGFR2)_19a	0	-
chr10	121481850	121482177	461_60370_2263(FGFR2)_20a	0	-

chr10	121479580	121480021	461_60371_2263(FGFR2)_21a	0	-
chr8	38461095	38461106	461_60316_2260(FGFR1)_3a	0	-
chr8	38421796	38421941	461_60324_2260(FGFR1)_11a	0	-
chr8	38413917	38414023	461_60333_2260(FGFR1)_20a	0	-
chr8	38457355	38457534	461_60317_2260(FGFR1)_4a	0	-
chr8	38440305	38440373	461_60318_2260(FGFR1)_5a	0	-
chr8	38429681	38429948	461_60319_2260(FGFR1)_6a	0	-
chr8	38428345	38428435	461_60320_2260(FGFR1)_7a	0	-
chr8	38427920	38428093	461_60321_2260(FGFR1)_8a	0	-
chr8	38426121	38426245	461_60322_2260(FGFR1)_9a	0	-
chr8	38424508	38424699	461_60323_2260(FGFR1)_10a	0	-
chr8	38419532	38419735	461_60325_2260(FGFR1)_12a	0	-
chr8	38418227	38418373	461_60326_2260(FGFR1)_13a	0	-
chr8	38417869	38417991	461_60327_2260(FGFR1)_14a	0	-
chr8	38417305	38417416	461_60328_2260(FGFR1)_15a	0	-
chr8	38415869	38416060	461_60329_2260(FGFR1)_16a	0	-
chr8	38414778	38414901	461_60330_2260(FGFR1)_17a	0	-
chr1	64838464	64838589	463_81643_3716(JAK1)_22a	0	-
chr1	64837931	64838104	463_81644_3716(JAK1)_23a	0	-
chr1	64836097	64836215	463_81645_3716(JAK1)_24a	0	-
chr1	64835395	64835506	463_81646_3716(JAK1)_25a	0	-
chr8	38414558	38414629	461_60331_2260(FGFR1)_18a	0	-
chr8	38414151	38414289	461_60332_2260(FGFR1)_19a	0	-
chr8	38413627	38413804	461_60334_2260(FGFR1)_21a	0	-
chr7	148832633	148832750	461_59349_2146(EZH2)_6	0	-
chr7	148816683	148816778	461_59357_2146(EZH2)_14	0	-
chr1	64834561	64834657	463_81647_3716(JAK1)_26a	0	-
chr1	64886258	64886341	463_81624_3716(JAK1)_3a	0	-
chr1	64879024	64879148	463_81626_3716(JAK1)_5a	0	-
chr1	64873369	64873523	463_81627_3716(JAK1)_6a	0	-
chr22	29031584	29031631	478_203544_84133(ZNRF3)_5	0	-
chr7	148807645	148807706	461_59365_2146(EZH2)_22	0	-
chr7	148850453	148850470	461_59346_2146(EZH2)_3	0	-
chr7	148847181	148847305	461_59347_2146(EZH2)_4	0	-
chr7	148846469	148846598	461_59348_2146(EZH2)_5	0	-
chr7	148829727	148829848	461_59350_2146(EZH2)_7	0	-
chr7	148828739	148828880	461_59351_2146(EZH2)_8	0	-
chr7	148827163	148827266	461_59352_2146(EZH2)_9	0	-
chr7	148826453	148826632	461_59353_2146(EZH2)_10	0	-
chr7	148819595	148819687	461_59354_2146(EZH2)_11	0	-
chr7	148817876	148818117	461_59355_2146(EZH2)_12	0	-
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chr7	148815505	148815546	461_59358_2146(EZH2)_15	0	-
chr7	148814913	148815039	461_59359_2146(EZH2)_16	0	-
chr7	148813958	148814137	461_59360_2146(EZH2)_17	0	-
chr7	148811624	148811720	461_59361_2146(EZH2)_18	0	-
chr7	148810332	148810414	461_59362_2146(EZH2)_19	0	-
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chr1	64869310	64869474	463_81628_3716(JAK1)_7a	0	-
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chr1	64860104	64860262	463_81631_3716(JAK1)_10a	0	-
chr1	64857655	64857779	463_81632_3716(JAK1)_11a	0	-
chr1	64850803	64850910	463_81634_3716(JAK1)_13a	0	-
chr1	64847531	64847675	463_81635_3716(JAK1)_14a	0	-
chr1	64846648	64846736	463_81636_3716(JAK1)_15a	0	-
chr1	64845512	64845640	463_81637_3716(JAK1)_16a	0	-
chr1	64844753	64844889	463_81638_3716(JAK1)_17a	0	-
chr15	90088586	90088747	463_79504_3418(IDH2)_5a	0	-
chr15	90084815	90084908	463_79510_3418(IDH2)_11a	0	-
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chr11	534211	534322	463_79034_3265(HRAS)_2a	0	-
chr13	48479997	48480071	472_141469_5925(RB1)_27a	0	-
chr13	48459687	48459833	472_141462_5925(RB1)_20a	0	-
chr13	48373404	48373492	472_141454_5925(RB1)_12a	0	-
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chr17	58354942	58354986	473_154862_54894(RNF43)_10	0	-
chr17	58357467	58358823	473_154861_54894(RNF43)_9	0	-
chr17	58360148	58360251	473_154860_54894(RNF43)_8	0	-
chr17	58360782	58360944	473_154859_54894(RNF43)_7	0	-
chr17	58362543	58362648	473_154858_54894(RNF43)_6	0	-
chr17	58363274	58363406	473_154857_54894(RNF43)_5	0	-
chr17	58370910	58371033	473_154855_54894(RNF43)_3	0	-
chr17	58415325	58415577	473_154854_54894(RNF43)_2	0	-
chr22	29042494	29042569	478_203545_84133(ZNRF3)_6	0	-
chr22	23834140	23834180	474_160336_6598(SMARCB1)_9	0	-
chr22	23833571	23833703	474_160335_6598(SMARCB1)_8	0	-
chr22	23825224	23825415	474_160334_6598(SMARCB1)_7	0	-
chr22	23816769	23816936	474_160333_6598(SMARCB1)_6	0	-
chr22	23803294	23803422	474_160332_6598(SMARCB1)_5	0	-
chr22	23800943	23801135	474_160331_6598(SMARCB1)_4	0	-
chr22	23791755	23791894	474_160329_6598(SMARCB1)_2	0	-
chr22	23787169	23787262	474_160328_6598(SMARCB1)_1	0	-
chr7	129212023	129212451	474_160575_6608(SMO)_12a	0	-
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chr7	129210362	129210548	474_160572_6608(SMO)_9a	0	-
chr7	129209288	129209397	474_160571_6608(SMO)_8a	0	-
chr7	129208758	129208851	474_160570_6608(SMO)_7a	0	-
chr7	129206463	129206587	474_160569_6608(SMO)_6a	0	-
chr7	129206149	129206369	474_160568_6608(SMO)_5a	0	-
chr7	129205609	129205782	474_160567_6608(SMO)_4a	0	-
chr7	129203383	129203589	474_160565_6608(SMO)_2a	0	-
chr7	129189151	129189482	474_160564_6608(SMO)_1a	0	-
chr22	28917388	28917481	478_203541_84133(ZNRF3)_2	0	-
chr22	29048388	29048491	478_203549_84133(ZNRF3)_10	0	-
chr13	28070490	28070612	461_60854_2322(FLT3)_3a	0	-
chr2	212124751	212124903	461_58773_2066(ERBB4)_2a	0	-
chr2	211704103	211704194	461_58782_2066(ERBB4)_11a	0	-
chr2	211623921	211624044	461_58790_2066(ERBB4)_19a	0	-
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chr13	28037184	28037288	461_60862_2322(FLT3)_11a	0	-
chr13	28024860	28024943	461_60870_2322(FLT3)_19a	0	-
chr22	28883766	28884066	478_203540_84133(ZNRF3)_1	0	-

chr22	28986622	28986639	478_203542_84133(ZNRF3)_3	0	-
chr22	28987075	28987201	478_203543_84133(ZNRF3)_4	0	-
chr4	1802913	1803064	461_60341_2261(FGFR3)_8a	0	-
chr4	1804329	1804520	461_60343_2261(FGFR3)_10a	0	-
chr4	1806828	1806934	461_60351_2261(FGFR3)_18a	0	-
chr4	1803691	1803836	461_60342_2261(FGFR3)_9a	0	-
chr4	1804823	1804969	461_60344_2261(FGFR3)_11a	0	-
chr19	2194514	2194577	431_55607_84444(DOT1L)_7	0	-
chr19	2211098	2211212	431_55615_84444(DOT1L)_15	0	-
chr19	2220107	2220222	431_55623_84444(DOT1L)_23	0	-
chr19	1221948	1222006	475_170593_6794(STK11)_7a	0	-
chr19	1206913	1207203	475_170587_6794(STK11)_1a	0	-
chr19	1218416	1218500	475_170588_6794(STK11)_2a	0	-
chr2	211619176	211619275	461_58791_2066(ERBB4)_20a	0	-
chr2	211561902	211562088	461_58792_2066(ERBB4)_21a	0	-
chr2	211430944	211431100	461_58793_2066(ERBB4)_22a	0	-
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chr2	211422006	211422104	461_58796_2066(ERBB4)_25a	0	-
chr2	211420440	211420611	461_58797_2066(ERBB4)_26a	0	-
chr2	211386852	211387150	461_58799_2066(ERBB4)_28a	0	-
chr2	211383614	211384060	461_58800_2066(ERBB4)_29a	0	-
chr12	56087794	56087913	461_58655_2065(ERBB3)_6a	0	-
chr12	56094098	56094189	461_58757_2065(ERBB3)_14a	0	-
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chr19	1219323	1219413	475_170589_6794(STK11)_3a	0	-
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chr19	1220580	1220717	475_170591_6794(STK11)_5a	0	-
chr19	1221212	1221340	475_170592_6794(STK11)_6a	0	-
chr19	1222984	1223172	475_170594_6794(STK11)_8a	0	-
chr19	1223637	1226446	475_170595_6794(STK11)_9a	0	-
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chr20	37393894	37393993	475_169919_6714(SRC)_7a	0	-
chr12	56099647	56099745	461_58767_2065(ERBB3)_24a	0	-
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chr12	56100173	56100245	461_58769_2065(ERBB3)_26a	0	-
chr12	56101060	56101361	461_58770_2065(ERBB3)_27a	0	-
chr12	56101528	56102055	461_58771_2065(ERBB3)_28a	0	-
chr20	37402748	37402880	475_169926_6714(SRC)_14a	0	-
chr20	37384153	37384403	475_169917_6714(SRC)_5a	0	-
chr20	37386074	37386174	475_169918_6714(SRC)_6a	0	-
chr20	37394173	37394277	475_169920_6714(SRC)_8a	0	-
chr20	37396161	37396311	475_169921_6714(SRC)_9a	0	-
chr20	37397698	37397854	475_169922_6714(SRC)_10a	0	-
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chr20	37403170	37403379	475_169927_6714(SRC)_15a	0	-
chr15	66435026	66435237	465_99851_5604(MAP2K1)_3a	0	-
chr17	39700000	39700311	461_58728_2064(ERBB2)_6a	0	-
chr17	39712321	39712448	461_58736_2064(ERBB2)_14a	0	-

chr17	39723318	39723457	461_58744_2064(ERBB2)_22a	0	-
chr17	39726814	39727003	461_58752_2064(ERBB2)_30a	0	-
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chr17	39711927	39712047	461_58735_2064(ERBB2)_13a	0	-
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chr15	66387347	66387427	465_99849_5604(MAP2K1)_1a	0	-
chr15	66401862	66401947	465_99850_5604(MAP2K1)_2a	0	-
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chr1	113643742	113643774	465_103747_260425(MAGI3)_12	0	-
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chr17	31356459	31356582	469_118625_4763(NF1)_52a	0	-
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chr5	112737858	112737925	426_2904_324(APC)_2a	0	-
chr5	112738331	112738460	426_2905_324(APC)_3a	0	-
chr5	112754872	112755025	426_2906_324(APC)_4a	0	-
chr5	112755074	112755094	426_2907_324(APC)_5a	0	-
chr5	112766325	112766410	426_2908_324(APC)_6a	0	-

chr5	112767188	112767390	426_2909_324(APC)_7a	0	-
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chr5	112792445	112792529	426_2912_324(APC)_10a	0	-
chr5	112815494	112815593	426_2914_324(APC)_12a	0	-
chr5	112818965	112819344	426_2915_324(APC)_13a	0	-
chr5	112821895	112821991	426_2916_324(APC)_14a	0	-
chr5	112827107	112827247	426_2917_324(APC)_15a	0	-
chr5	112827928	112828006	426_2918_324(APC)_16a	0	-
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chr16	68815514	68815759	428_25429_999(CDH1)_10	0	-
chr16	68737415	68737463	428_25420_999(CDH1)_1	0	-
chr16	68738296	68738411	428_25421_999(CDH1)_2	0	-
chr16	68808423	68808567	428_25423_999(CDH1)_4	0	-
chr1	113614600	113614658	465_103742_260425(MAGI3)_7	0	-
chr1	113618531	113618606	465_103743_260425(MAGI3)_8	0	-
chr1	113619735	113619830	465_103744_260425(MAGI3)_9	0	-
chr1	113622805	113622994	465_103745_260425(MAGI3)_10	0	-
chr1	113641910	113642516	465_103746_260425(MAGI3)_11	0	-
chr1	113646485	113646642	465_103748_260425(MAGI3)_13	0	-
chr1	113649236	113649328	465_103749_260425(MAGI3)_14	0	-
chr1	113651013	113651206	465_103750_260425(MAGI3)_15	0	-
chr1	113653829	113654018	465_103751_260425(MAGI3)_16	0	-
chr1	113659079	113659265	465_103752_260425(MAGI3)_17	0	-
chr1	113671733	113671836	465_103753_260425(MAGI3)_18	0	-
chr1	113672614	113672741	465_103754_260425(MAGI3)_19	0	-
chr1	113681197	113681336	465_103756_260425(MAGI3)_21	0	-
chr1	113682211	113684014	465_103757_260425(MAGI3)_22	0	-
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chr16	68810196	68810341	428_25425_999(CDH1)_6	0	-
chr16	68811683	68811859	428_25426_999(CDH1)_7	0	-
chr16	68812134	68812263	428_25427_999(CDH1)_8	0	-
chr16	68813312	68813495	428_25428_999(CDH1)_9	0	-
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chr7	152249875	152249953	464_94976_58508(KMT2C)_13	0	-
chr7	152222572	152222682	464_94984_58508(KMT2C)_21	0	-
chr7	152194439	152194568	464_94993_58508(KMT2C)_30	0	-
chr7	152171263	152171342	464_95004_58508(KMT2C)_41	0	-
chr7	152154009	152154146	464_95013_58508(KMT2C)_50	0	-
chr7	152139674	152139791	464_95021_58508(KMT2C)_58	0	-
chr16	68819279	68819425	428_25430_999(CDH1)_11	0	-
chr7	152180710	152182594	464_95000_58508(KMT2C)_37	0	-
chr7	152179833	152180126	464_95001_58508(KMT2C)_38	0	-
chr7	152176190	152178010	464_95002_58508(KMT2C)_39	0	-
chr7	152174130	152174242	464_95003_58508(KMT2C)_40	0	-
chr7	152169185	152169249	464_95005_58508(KMT2C)_42	0	-
chr7	152167145	152167378	464_95006_58508(KMT2C)_43	0	-
chr7	152162116	152163826	464_95007_58508(KMT2C)_44	0	-
chr7	152158856	152159072	464_95008_58508(KMT2C)_45	0	-
chr7	152157760	152157925	464_95009_58508(KMT2C)_46	0	-
chr7	152156204	152156346	464_95010_58508(KMT2C)_47	0	-

chr7	152155909	152156057	464_95011_58508(KMT2C)_48	0	-
chr7	152154266	152154445	464_95012_58508(KMT2C)_49	0	-
chr7	152152704	152152954	464_95014_58508(KMT2C)_51	0	-
chr7	152151441	152151581	464_95015_58508(KMT2C)_52	0	-
chr7	152150899	152151007	464_95016_58508(KMT2C)_53	0	-
chr7	152148032	152149152	464_95017_58508(KMT2C)_54	0	-
chr7	152146598	152146735	464_95018_58508(KMT2C)_55	0	-
chr7	152145152	152145295	464_95019_58508(KMT2C)_56	0	-
chr7	152144712	152144881	464_95020_58508(KMT2C)_57	0	-
chr7	152435625	152435786	464_94964_58508(KMT2C)_1	0	-
chr7	152358586	152358675	464_94965_58508(KMT2C)_2	0	-
chr7	152330600	152330742	464_94966_58508(KMT2C)_3	0	-
chr7	152311797	152311946	464_94968_58508(KMT2C)_5	0	-
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chr7	152273704	152273867	464_94970_58508(KMT2C)_7	0	-
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chr7	152263015	152263130	464_94972_58508(KMT2C)_9	0	-
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chr16	68822000	68822225	428_25431_999(CDH1)_12	0	-
chr7	152251938	152252090	464_94974_58508(KMT2C)_11	0	-
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chr7	152247901	152248620	464_94977_58508(KMT2C)_14	0	-
chr7	152238706	152238826	464_94978_58508(KMT2C)_15	0	-
chr7	152235816	152235933	464_94979_58508(KMT2C)_16	0	-
chr7	152230219	152230321	464_94980_58508(KMT2C)_17	0	-
chr7	152229922	152230027	464_94981_58508(KMT2C)_18	0	-
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chr5	112834950	112835165	426_2920_324(APC)_18a	0	-
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chr14	104776658	104776770	426_1773_207(AKT1)_7a	0	-
chr14	104775075	104775207	426_1775_207(AKT1)_9a	0	-
chr14	104774937	104775003	426_1776_207(AKT1)_10a	0	-
chr14	104773911	104773980	426_1777_207(AKT1)_11a	0	-
chr14	104773454	104773580	426_1778_207(AKT1)_12a	0	-
chr14	104773250	104773379	426_1779_207(AKT1)_13a	0	-
chr14	104772877	104773092	426_1780_207(AKT1)_14a	0	-
chr14	104772364	104772452	426_1781_207(AKT1)_15a	0	-
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chr9	130714319	130714455	426_351_25(ABL1)_1	0	-
chr9	130835443	130835525	426_352_25(ABL1)_2	0	-
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chr1	11209311	11209458	466_105905_2475(MTOR)_26a	0	-
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chr1	11129737	11129838	466_105920_2475(MTOR)_41a	0	-
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chr7	152139185	152139259	464_95022_58508(KMT2C)_59	0	-
chr7	140801411	140801560	427_15635_673(BRAF)_6	0	-
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chr9	130883968	130885683	426_362_25(ABL1)_12	0	-
chr9	130862762	130863035	426_355_25(ABL1)_5	0	-
chr13	32316460	32316527	427_15650_675(BRCA2)_2	0	-
chr13	32319076	32319325	427_15651_675(BRCA2)_3	0	-
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chr13	32329442	32329492	427_15656_675(BRCA2)_8	0	-
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chr13	32344557	32344653	427_15660_675(BRCA2)_12	0	-
chr13	32354897	32355325	427_15662_675(BRCA2)_14	0	-
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chr4	54658014	54658081	464_88966_3815(KIT)_1	0	-
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chr4	54699629	54699766	464_88969_3815(KIT)_4	0	-
chr6	152098731	152098966	461_58886_2099(ESR1)_12	0	-
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chr6	151944172	151944508	461_58882_2099(ESR1)_8	0	-
chr6	152011655	152011794	461_58883_2099(ESR1)_9	0	-
chr4	54703720	54703892	464_88970_3815(KIT)_5	0	-
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chr4	54733069	54733192	464_88982_3815(KIT)_17	0	-
chr7	140787547	140787584	427_15638_673(BRAF)_9	0	-
chr7	140783020	140783157	427_15639_673(BRAF)_10	0	-
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chr7	140777990	140778075	427_15641_673(BRAF)_12	0	-
chr7	140776911	140777088	427_15642_673(BRAF)_13	0	-
chr7	140754186	140754233	427_15643_673(BRAF)_14	0	-
chr7	140753274	140753393	427_15644_673(BRAF)_15	0	-
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chr7	140739811	140739946	427_15647_673(BRAF)_18	0	-
chr7	140734011	140734770	427_15648_673(BRAF)_19	0	-
chr4	54736720	54736820	464_88984_3815(KIT)_19	0	-
chr7	140719333	140726516	427_15649_673(BRAF)_20	0	-
chr9	130854063	130854237	426_353_25(ABL1)_3	0	-
chr9	130854800	130855096	426_354_25(ABL1)_4	0	-
chr1	26696403	26697540	426_4218_8289(ARID1A)_1a	0	-
chr1	26729650	26729863	426_4219_8289(ARID1A)_2a	0	-
chr1	26731151	26731604	426_4220_8289(ARID1A)_3a	0	-
chr1	26732675	26732792	426_4221_8289(ARID1A)_4a	0	-
chr4	54737174	54737280	464_88985_3815(KIT)_20	0	-
chr1	26760855	26761096	426_4222_8289(ARID1A)_5a	0	-
chr1	26761383	26761473	426_4223_8289(ARID1A)_6a	0	-
chr5	56884663	56884826	465_99634_4214(MAP3K1)_18a	0	-
chr5	56887377	56887520	465_99636_4214(MAP3K1)_20a	0	-
chr5	56888225	56888357	465_99637_4214(MAP3K1)_21a	0	-
chr5	56893530	56893680	465_99638_4214(MAP3K1)_22a	0	-
chr17	12110374	12110426	465_99954_6416(MAP2K4)_8	0	-
chr1	26762972	26763285	426_4225_8289(ARID1A)_8a	0	-
chr1	26766220	26766366	426_4226_8289(ARID1A)_9a	0	-
chr13	32357741	32357929	427_15664_675(BRCA2)_16	0	-
chr2	29296887	29297057	426_1978_238(ALK)_9	0	-
chr2	29275401	29275496	426_1979_238(ALK)_10	0	-
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chr2	29239679	29239830	426_1982_238(ALK)_13	0	-
chr2	29232303	29232448	426_1984_238(ALK)_15	0	-
chr2	29228883	29229066	426_1985_238(ALK)_16	0	-
chr2	29227573	29227672	426_1986_238(ALK)_17	0	-
chr2	29226921	29227074	426_1987_238(ALK)_18	0	-
chr2	29225460	29225565	426_1988_238(ALK)_19	0	-
chr2	29223341	29223528	426_1989_238(ALK)_20	0	-
chr2	29222516	29222607	426_1990_238(ALK)_21	0	-
chr2	29222343	29222408	426_1991_238(ALK)_22	0	-
chr2	29213983	29214081	426_1993_238(ALK)_24	0	-
chr2	29209785	29209878	426_1994_238(ALK)_25	0	-
chr2	29207170	29207272	426_1995_238(ALK)_26	0	-
chr2	29197541	29197676	426_1996_238(ALK)_27	0	-
chr3	142559250	142559441	427_14859_545(ATR)_7	0	-
chr3	142550131	142550302	427_14866_545(ATR)_14	0	-
chr3	142538481	142538625	427_14871_545(ATR)_19	0	-
chr3	142513500	142513638	427_14878_545(ATR)_26	0	-
chr3	142496360	142496520	427_14886_545(ATR)_34	0	-
chr3	142461939	142462090	427_14894_545(ATR)_42	0	-
chr2	29196769	29196860	426_1997_238(ALK)_28	0	-
chr2	29193223	29193922	426_1998_238(ALK)_29	0	-
chr14	104775651	104775799	426_1774_207(AKT1)_8a	0	-
chr14	104770744	104770847	426_1782_207(AKT1)_16a	0	-
chr14	104792597	104792643	426_1770_207(AKT1)_4a	0	-
chr14	104780087	104780216	426_1771_207(AKT1)_5a	0	-
chr4	54738428	54738557	464_88986_3815(KIT)_21	0	-
chr2	29328349	29328481	426_1975_238(ALK)_6	0	-

chr2	29233564	29233696	426_1983_238(ALK)_14	0	-
chr2	29220705	29220835	426_1992_238(ALK)_23	0	-
chr2	29919992	29920659	426_1970_238(ALK)_1	0	-
chr2	29717577	29717697	426_1971_238(ALK)_2	0	-
chr2	29694849	29695014	426_1972_238(ALK)_3	0	-
chr2	29531914	29532116	426_1973_238(ALK)_4	0	-
chr2	29383731	29383859	426_1974_238(ALK)_5	0	-
chr2	29320750	29320882	426_1976_238(ALK)_7	0	-
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chr13	32362522	32362693	427_15665_675(BRCA2)_17	0	-
chr13	32363178	32363533	427_15666_675(BRCA2)_18	0	-
chr13	32370401	32370557	427_15667_675(BRCA2)_19	0	-
chr13	32370955	32371100	427_15668_675(BRCA2)_20	0	-
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chr18	51077306	51077419	474_158726_4089(SMAD4)_12	0	-
chr18	51067018	51067187	474_158724_4089(SMAD4)_10	0	-
chr18	51065422	51065606	474_158723_4089(SMAD4)_9	0	-
chr18	51059865	51059916	474_158722_4089(SMAD4)_8	0	-
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chr18	51054780	51054993	474_158719_4089(SMAD4)_5	0	-
chr18	51048685	51048860	474_158717_4089(SMAD4)_3	0	-
chr18	51047046	51047295	474_158716_4089(SMAD4)_2	0	-
chr18	51076637	51076776	474_158725_4089(SMAD4)_11	0	-
chr9	77922160	77922345	462_70176_2776(GNAQ)_2	0	-
chr13	32379316	32379515	427_15670_675(BRCA2)_22	0	-
chr11	108235669	108235834	427_14214_472(ATM)_8	0	-
chr6	152060990	152061124	461_58884_2099(ESR1)_10	0	-
chr6	152094384	152094568	461_58885_2099(ESR1)_11	0	-
chr13	32379749	32379913	427_15671_675(BRCA2)_23	0	-
chr13	32380006	32380145	427_15672_675(BRCA2)_24	0	-
chr13	32394688	32394933	427_15673_675(BRCA2)_25	0	-
chr13	32396897	32397044	427_15674_675(BRCA2)_26	0	-
chr13	32398161	32398770	427_15675_675(BRCA2)_27	0	-
chr2	29318303	29318404	426_1977_238(ALK)_8	0	-
chr1	26771118	26771326	426_4229_8289(ARID1A)_12a	0	-
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chr1	26772811	26772987	426_4231_8289(ARID1A)_14a	0	-
chr1	26773579	26773717	426_4233_8289(ARID1A)_16a	0	-
chr1	26773801	26773898	426_4234_8289(ARID1A)_17a	0	-
chr13	28100467	28100510	461_60853_2322(FLT3)_2a	0	-
chr13	28061866	28062069	461_60855_2322(FLT3)_4a	0	-
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chr13	28034081	28034214	461_60866_2322(FLT3)_15a	0	-
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chr17	43067607	43067695	427_15622_672(BRCA1)_17	0	-
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chr2	211657753	211657828	461_58788_2066(ERBB4)_17a	0	-
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chr2	211630461	211630594	461_58789_2066(ERBB4)_18a	0	-
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chr12	56083750	56083902	461_58651_2065(ERBB3)_2a	0	-
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chr7	55146605	55146740	431_48545_1956(EGFR)_5	0	-
chr7	55151293	55151362	431_48546_1956(EGFR)_6	0	-
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chr7	55154010	55154152	431_48548_1956(EGFR)_8	0	-
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chr1	162770301	162770512	431_48994_4921(DDR2)_16a	0	-
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chr1	162773468	162773596	431_48996_4921(DDR2)_18a	0	-
chr1	162775651	162775843	431_48997_4921(DDR2)_19a	0	-
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chr10	87894024	87894109	472_139787_5728(PTEN)_2	0	-
chr10	87925512	87925557	472_139788_5728(PTEN)_3	0	-
chr10	87931045	87931089	472_139789_5728(PTEN)_4	0	-
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chr1	11237842	11238048	466_105893_2475(MTOR)_14a	0	-
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chr1	11233397	11233487	466_105895_2475(MTOR)_16a	0	-
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chr1	11230924	11231054	466_105898_2475(MTOR)_19a	0	-
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chr1	11216147	11216234	466_105900_2475(MTOR)_21a	0	-
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chr7	152207299	152207428	464_94987_58508(KMT2C)_24	0	-
chr1	11210813	11210906	466_105904_2475(MTOR)_25a	0	-
chr1	11204560	11204703	466_105906_2475(MTOR)_27a	0	-
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chr7	152205105	152205225	464_94988_58508(KMT2C)_25	0	-
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chr7	152194228	152194261	464_94994_58508(KMT2C)_31	0	-
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chr1	11157151	11157291	466_105910_2475(MTOR)_31a	0	-
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chr1	11144967	11145045	466_105913_2475(MTOR)_34a	0	-
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chr1	11139528	11139658	466_105915_2475(MTOR)_36a	0	-
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chr1	11134350	11134466	466_105917_2475(MTOR)_38a	0	-
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chr1	11130528	11130777	466_105919_2475(MTOR)_40a	0	-
chr1	11128854	11128951	466_105921_2475(MTOR)_42a	0	-
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chr17	12020886	12021001	465_99947_6416(MAP2K4)_1	0	-
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chr3	142519668	142519784	427_14876_545(ATR)_24	0	-
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chr3	142512259	142512470	427_14879_545(ATR)_27	0	-
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chr3	142498596	142498774	427_14884_545(ATR)_32	0	-
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chr20	58891370	58891865	462_70273_2778(GNAS)_5	0	-
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chr20	58898940	58898985	462_70276_2778(GNAS)_8	0	-
chr20	58903527	58903585	462_70277_2778(GNAS)_9	0	-
chr20	58903671	58903791	462_70278_2778(GNAS)_10	0	-
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chr3	142459226	142459383	427_14895_545(ATR)_43	0	-
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chr9	77797519	77797648	462_70178_2776(GNAQ)_4	0	-
chr9	77794462	77794592	462_70179_2776(GNAQ)_5	0	-
chr9	77728513	77728667	462_70180_2776(GNAQ)_6	0	-
chr9	77721322	77721513	462_70181_2776(GNAQ)_7	0	-
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chr19	17834851	17835003	463_81758_3718(JAK3)_16a	0	-

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chr12	56097784	56097940	461_58764_2065(ERBB3)_21a	0	-
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chr7	55181292	55181478	431_48564_1956(EGFR)_24	0	-
chr7	55192765	55192841	431_48566_1956(EGFR)_26	0	-
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chr12	112482073	112482205	472_140058_5781(PTPN11)_10a	0	-
chr10	87952117	87952259	472_139791_5728(PTEN)_6	0	-
chr1	11115395	11115468	466_105931_2475(MTOR)_52a	0	-
chr1	11114812	11114887	466_105932_2475(MTOR)_53a	0	-
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chr1	11112851	11112917	466_105934_2475(MTOR)_55a	0	-
chr1	11109289	11109370	466_105936_2475(MTOR)_57a	0	-
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chr1	11106604	11107500	466_105938_2475(MTOR)_59a	0	-
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chr19	3110148	3110333	462_70068_2767(GNA11)_2	0	-
chr19	3113329	3113484	462_70069_2767(GNA11)_3	0	-

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chr11	108253813	108254039	427_14223_472(ATM)_17	0	-
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chr11	108334968	108335109	427_14265_472(ATM)_59	0	-
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chr5	150055236	150055336	429_36471_1436(CSF1R)_20a	0	-
chr5	150054321	150054430	429_36472_1436(CSF1R)_21a	0	-
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Supplementary Data 3

SEQ ID NO	Sequence Name	Sequence
1	632327_26682354_Target2.1_1	TGGCATTAGGGACCCCAAATCCAGGTCTGCTCCCAGTGCCATAGGAAGCAACCAGCCCCCAACCCCCACCTGCTCTTGGGAGCTGGCCCACACCAGAAATGGACTGAGTAGACATGAGAA
2	632327_26682354_Target2.1_2	CTGACCCCAGCTTCCACCAATGCCGTTAAGATGCCGCCACTTGGGTGAGGGGCTCCTCCAGGTACTGCACCAAAGCCTGGGCCTGCAGAGGGAGAACAGAGATCAGTCCCGCACACAGCC
3	632327_26682354_Target2.1_3	CCAAGACACATGACAGGAGTTGAAGTTTATTCTTGGAAAAAACAAAGTCCCATCCTCCCCCCATTGTCTAAGAAGGTTCTTCTAGGAGGCCCCGCCCCTCCAAATGGTCATTTCTCTTTT
4	632327_26682354_Target2.1_4	CTACTTTCTTGGATGGGAGGAATCAGAGAAGATAGGAAGAAGCAGGCATCGCTTCTAGGATTCCTCATGTTCTGCAAGGATGGACTTCTACCCACCCCTTCACCATGACCTTCTGCGAAC
5	632327_26682354_Target2.1_5	AATGGTTCTTGGCAGTTACGCCAAATAGTCCTTGTCCTCACCAATGGCATGACCTCACCTAGACCCTGCTGCTCAGAACAGAGTCTTACCCACCTCATAGGCAAAACTGGGAGTGAGCTC
6	632327_26682354_Target2.1_6	AGACCCTCTCAAAAAAATAAAAGGCACGCACGCCCCCAAACCTGAAATGATAGACACTAACCTCTCAGGGCCTTTATATTCTCTGTGCAACACAACCCCCCACCAGACCCTTGCACCTCT

7	632327_26682355_Target2.2_1	TGTGTAAGCACATAAACACCTGGAAGAAGAAGAAAGGGATAGCTTGT TCTAGGCTGTTAGGGGCACCCTCCCAACCCCAAGAATAGAAAAGGCA CTCACTGGCCAGTCGAAGTGGTTCAT
8	632327_26682355_Target2.2_2	GTGTTTATGTGCTTACACAGACCCTCCCCAGATCTTGAAGCCCTTTGT AGACAAGAGGCCTTTGCTGTGAGGCCTCAGGTCCTGTACAGGGAGT AGAAGTAACCCAGACCTCCCAAAGGC
9	632327_26682355_Target2.2_3	ACCCAGACCTCCCAAAGGCCTTCATCTCCAGACCCTGCTCCTACACT CAGACCACTCACCCCAGCTGTCTGTTTCTGCCCCAGGTCTCTGCCTA CCCAATATCCTTAAAGCAGGTCTGTA
10	632327_26682355_Target2.2_4	TCCTTAAAGCAGGTCTGTATAGGGAGCTACCAGCCCCCTTCCCCAGT GCCATATAAAGGAACCCATCCCAGAGAAGTGGGTAGGTTTCGAGTCC CAGCTCCACCCAAGATGAGAAACACT
11	632327_26682355_Target2.2_5	ACCCAAGATGAGAAACACTGCCCATCCCAGGCCCTGGGCTGTCAAG GAAGGGCAGAAGTTACTGTGGCCATGATACTCCCACAGCTCTGCATT GCAGCAGGGTGACTGGTGTTCTATCAG
12	632327_26682355_Target2.2_6	GTGACTGGTGTTCTATCAGCCCCTGGTCTAATATCCCTTACTCTGGTT CCCCCAGTGTACCCCCCTACCAGCTCTGAAGGAAAAGCAGGCCAAG TGGGTTTCTTCCTTTTTTTTTTTTT
13	632327_26682356_Target2.3_1	CACTGAGGGCTGAGTGTGCATTGCTGGGCTTCTGGAATCTGTGGTGA GGGCCGGTCCCCCAACTAATGAGCAAGAAATAGCCCCTCAGAAACC CACTTGAGGCCAGGCGCGGTGGCTCAC
14	632327_26682356_Target2.3_2	GTGGGCTGTCTCTGAAGGTCCTGTCCCTTTTTCGCTTCCCCCCCGCT GGAGCTGCTTCTCCCGCTTGCGGGAGCCCAGGCTGAGAGCAGACAC CCAACCTGTCGAACCTGTCTGACGTCA
15	632327_26682356_Target2.3_3	TCATCATCTCTCCACCCACCTGGGCCCCAGGTCTCCAGCCACCCCG CTCTTCCTGTTCTCAGCTTCCGTCCTCTCTGCTTCCTTACAGCACCCC CACCTGCCAGAGCTGATCCTCCCTAG
16	632327_26682356_Target2.3_4	GCTCAATGCCCTCAACCCTCAGCTCTCAAAAGATCTGGTCCTGCCCC TCCTCTCATTGGGGGTAAGGGGACTTCTGCAGCCAGAGGGATTGGG GGCCAACTCAAGGTTAGGCAGGGCCTA
17	632327_26682356_Target2.3_5	GAACCCAACTCACCCTTGAAGACAAAGTTATAATCTTCCTCAGTTCCA TTCCCCATCTTGGCTCCGCATGGAGGGTGCAGGTGTCTTCGGGGAC AGAGGCGACAAATCTGTGTGTTGGCT
18	632327_26682356_Target2.3_6	TTCTGAAGGAATGAGGAGCCCCAGGAGGTCTTGGTAAGAGATAAAAA AACAGGAGGGGGCCCTCTCTGGCTCTATTCAATCTCTTTCTGGGTCT CTCAGGCTTCCTCTTGCTTCAGGGAA
19	632327_26682356_Target2.3_7	TAACTCAGCACTCTTAAGGAGGAATCAACATCATTATTTACCACAGTA GAGCATACTCAGAAGCTCCCTGACTTTTGCCCCTGCAACCAGACCCT CCCCCACTCCCTGCAGCTTTCTTTC
20	632327_26682356_Target2.3_8	TTAGGCTCCTCTGCCCCGTTCCTAATAGAAACCCAAATCCCTGGTGT CAGCCAGTGCAGCACAAGAGATGGAGGTCAGACTTCAGAAAGGACT TCCCTCTTTTATTTTTTTTTCTGAGA
21	632327_26682357_Target2.4_1	ATGAGCCACCACACCCGGCCAGGACTTCTCTCTTGAGAAGAAAGGG AAACCAGCAAACAAGAGGAAGAAAGTCATCTTTTCTGGGCAGGTGTA CAGGGAACGAGAGAAAGGAGAGACACA
22	632327_26682357_Target2.4_2	CAGACGAGGCTACAACCCTAGGAGTCCTCTGGATTCTATCAGACTCT GCAGCAAATTCATGATATTTTCTGTCTTCCCTATGTATTTATTGCCCCA CCCTATAATGGGATGTGTCTCTCC
23	632327_26682357_Target2.4_3	AGCCTCGTCTGCCTGGCCCTTGGCTGACTCACTGGACCTGCATACCA GGCACTGGGCTCAACTTTGCTGTCCCTGGAAGCATGCATGTATCTTT CTAGCCCCTGTGTTTGGTGCCTTTGC

24	632327_26682357_Target2.4_4	GGTGCCTTTGCTGTTTTCCAACCCCACCTTCATACTTCCTTTAGGGCAGGGTGGACTCTCCAGCCACCCTACCCCAATGCCTCTCCCAACCTCAGCCCGGCCCCTCCCTTGAGCTGGGAC
25	632327_26682357_Target2.4_5	AATGGTAGTTCCTCATATTATTGCCCCAGACTATTGCTAACCCTTTCCTTCCTGGAAAAGATGCCAGTAGTACAGGTTCCCCAGCTCAAGGGCGGGTTCTGGAGTGAGAGTCCCAGCTCA
26	632327_26682358_Target2.5_1	TCCCCTACTGGGCACATCTCCCTCATCCCTCTCAGTGGGTGGGCTCTCAGCCCTAGCGTCATACCACAAAGGTGCTTAGGGCAAGGGAATTGAAGTCAGACTTTGTGGCCTTTTGTAAAC
27	632327_26682358_Target2.5_2	GTGTGTATATGTGTGTGTGTTCCTGCCTCTCCCCTACTGGGCACATCTCCCTCATCCCTCTCAGTGGGTGGGCTCTCAGCCCTAGCGTCATACCACAAAGGTGCTTAGGGCAAGGGAA
28	632327_26682359_Target2.6_1	CACACACGCATACACACACATCCTCTTACCCACACATATCCATATTATTTCCAGCTTTTCCATACTGTCCTATGCAAATAAGGAATGTTTAAATATATATTTTTTATTTTTATTTTTTGA
29	632327_26682360_Target4.1_1	CCAGGACCAAGTGGGGTGATCAGGACCCCTCCAGGTGGGTCCCGGGTGCGGATGGCCAGTTGGGCGCATGCTTATTGGGCCTGCATCCGTTGGCCACGGAGGCTCTTTGGGACAAGCAAA
30	632327_26682360_Target4.1_2	GGCCACCCTGTTGTTGTGGGAGTATTAGGGGAAGTTGCCACTAAGGCTGGCAGGTCCTGGAGTTCCACCCAGGATGGGGACATGGGGGAGGGAAGAGGAGGTGCCCCTCAGAGCCTGAGG
31	632327_26682360_Target4.1_3	GGATAGGAGCCATGCTCCCCTGGGGTGGCTCTGGAACGTGGGCCCCGTGCACAGGCTATGTAGTCTGCTCACACCCTTGCTGCCTGCCACCCGGGCACCCAGGACTTGAGCCCAGACCCT
32	632327_26682360_Target4.1_4	GCCACCCCACAGGTGGCTTTTTATTCCCTCCTGCTGCTGAGTGTCACGCGTGGGGCTGAGGGCCTGCACGCCTTCCCGGCCTCATCCTCTCCGACGATTCACGCCCTCCTAAGGCTGGCA
33	632327_26682360_Target4.1_5	CACTGCCAAGGGCTCCCCGACACAAGCACAGAGCACAGCCTGGCCTTGGCTGCAGCACCACAGCAGATGCCTTTATGCCCAGGGCCAGCTATGGGCTGAAAGCACACCCCAGTCCTCACT
34	632327_26682360_Target4.1_6	TCCGCACTGTCTGTGGGGTGTTTTGGGTTGCAGGTTCCATGTCCTGAAGCAGGAGAGCCCTCCCCATGCCACCTCCTCTGCCCAGCCTCTTAGGGACAGTGCCTGGGATGCCCTGGCTGG
35	632327_26682360_Target4.1_7	CAGCCTCACACCGAGCTCTCTGCCAAAACCCCGGATCACAAGCATGAGCTCCAGCAGGTCCGCTTGAGTGAACACCGCTGATCCTGCCTGCAGGGGTATAGGCCTGGGGCCTGCCAGCCG
36	632327_26682360_Target4.1_8	TTCTAGCCTGGGGCAGAAGTAGGGTGGAGGGGTGGGTCTAGCCTCCTTGATGACACAGTTGGGGTTGGAGGTGGGGGCTACCCCTATTCTGGGCCTGGTGCTGTCCCTGAAGTCAGGGGT
37	632327_26682360_Target4.1_9	TGTAGAGGTGGGAGGAAGTCAGGGAAGCAAGACACAGGTGGAGCCAGGGCCTCTCCTGTGCTCGGAGGGCCAGGAAGGGCCTGACAGAGGGCAGAGCCCCACCCTCTTACACGGAGACCA
38	632327_26682360_Target4.1_10	AGGAGGCAGTTTTGGAGTCAGAGGTGAAGTGTGGGGAGTGGGATTGGGTGATAGGGAAGTTTCTCCAGCAAAGACACTGGGCAAGCCTCTTCCTTGGCCCCCAGATAAAGGGCTGCAGGG
39	632327_26682360_Target4.1_11	CCCTTTTCTTCTGAGCCTGGACAACTCCTTCCCTTGCCCCCAGGAGCCCACAGCCGGCTAAACCAACTGGTCAGCTAGAACCAACCAGCAGGGGAGGTGCGCTCCAGGGGGGCTTCTAAG
40	632327_26682360_Target4.1_12	TGGTAGGACCTCCTAAAGGGACAGCAGATGCCAGGAGAGGGCCGCAAAGGCACAGCGTTGGAACCAGAGGGTTCCTACCAAGTTGACAACTCCAAAAGAGCATGGTGGTCCCCCAAGGAC

41	632327_26682360_Target4.1_13	ACAGAGAGACAGTCAGTTGTCCTCAGAATTGGATCCAGAACCTCGTCTTCTGGCATGGCCCCCCAGTGCAGCACCACATGTGGCCTCCGAATTCCCAGTCTGGGATTGGGGGAGCTCTG
42	632327_26682361_Target4.2_1	TGGCCCCAGGTCTAGGCGAGGGATGGAAATAAGGACAGTGCCACTAGGGCCTCCTGTCTGTACAGGAGGGGCCCTGAGACAGCTCCTCAAACCCCTTTCCCATTATACGGATGGTGCAGA
43	632327_26682361_Target4.2_2	GGCCATGGTACCAGTACACAGTGCTCACCCTCCTGCTCAGACAAACAGTAACGGCCAGAAGCTCCAAGCCTCCTGCCCCAGCCCAAGGTGACTTTCCTGGCAGAACCTGGGACTGCCCTG
44	632327_26682361_Target4.2_3	CCCTGCCCTGCCCTGCCTCCACCCAGCTCCCGGGCAAGCAGTGCCAGGAGGAAGTGTCAGCAGCTCCTCCCCAAAGCTCTTTTCCCCACAGCCCCGCCACCCCCGTACCTGGGCCCCGAT
45	632327_26682361_Target4.2_4	CCCATCGCCCTGGGCCGGGACACGCCCCCTCTTGTGCCCATTCCTTTCCCTCGGTGGAGAGTTGGGTGGTGGGGGCTGGCCGGCCTGTGAGAGCAGGTGTCGGGGTGCCTGGAGAATCGG
46	632327_26682361_Target4.2_5	TCCCTCCTGAGAGTCCCTGGTTTCCTTTCCCACACCCCTCCCGGGGCCCGCCGCAGCTTTGGTCACCTTCTCAGAATGACCATGGGTTGATCTCTTTCTTTGCTAGTGAGATGTTTCCCAT
47	632327_26682361_Target4.2_6	AGGGAACGGGAGCCTTGTGGTAGAAAAGGAGCTGCTGTCCCCGATCTGGAACTCGAAACCCCAACATCTTCCAGGCCGTAAGCCCCTCACCCCGCACCCCTAGGCAAATCTCCGCTTTCC
48	632327_26682361_Target4.2_7	TTTCCCAACTCCCTCACCTCGGTCCAGCGATCAGCCTCTCGGACCCTCGAGAGGGAGCTCCGACCCTGCTCTAGCTCTTGCGGGTCCCCCAACCATGGACTCCAAAGCCTTCATGTCCAC
49	632327_26682361_Target4.2_8	CGCCGCGGGCTTTGCAGCCCCGCACGCCGAGCGCCGGTGGAAGCCGGGTCCTGGCCACAGGAGTCCTAGCCGCACGCGAGTGTCGCGGGAGGGGGCCAGGGCCGGGTTCTGCAGTGTGGA
50	632327_26682361_Target4.2_9	CGGCGCGCCCGCCCCCACTCCCGCTCCGCTCCCGGAACCCCGCGCCGGCGGCCGGAGTGAATCATTAACTGGAGCCGGGTGCTCCGGCTGCGCAGCCTTCCCCGCTGGCGCCACGCACTT
51	632327_26682361_Target4.2_10	CACTTGCCCGCCCGGCCTCGGTCCCCCGGAGCTCCTCCCTCTCCGGGAGCCGGTGGGCAGTCCCCACGCCACACCAGCCGGACCACCCGCCAGAGGCTCAACGGCCCCTCCTCGCAG
52	632327_26682362_Target4.3_1	GCGTTGGCGGGGCCGGGCGCGGGGGCCGCCAGCCGGTAGGAGGGTTCCTGTGTCGGGAAAGTGGCTGGCGGGGCCCGCGCTCCCCGGCCGACGGCCGCCTGCTGTGTCACCTTGGGCCTC
53	632327_26682362_Target4.3_2	GGCCCCGCCAACGCACCCGAGGCGCACAGGCTCCGGAGCCCCCGCGGTTCCTGCCTCCCCGCTTCCCGGCCAGGGCAGAAGGAGATCCCAGGGCCGCGGACCCCGGCCGGCGGTTCCCAG
54	632327_26682362_Target4.3_3	CCGGCGGTTCCCAGGCCCCGCAGGTCCGGCAGGAAATGCCGCTCGCTTAACCCCTTCCAGCCCGCTGCCGCCTCCAAGCCCGTACGCGGCCCGGCCCCACCTGGCGCCCTCACCAGGTGG
55	632327_26682362_Target4.3_4	ACCGGGGCGGCTGCGGCGCGCTCGGAGCCCCGAGGGCACGCGGCCCGGGCAGCTCGGTGTGCGCCCCCGCGAGAGCCGGGGCCCCAGGCCCGCCGGACACCATGAACCACCTGGTGAGGG
56	632327_26682362_Target4.3_5	GCAGCCGCCCCGGTGCCGCCGCGCAGCTGCCGCCTCGGCCACCCAGAGCCGGTCCAGCCGCTCTCCGCCTGCCGCCACGGCCCAGCCGGCCCAGCCCGATCCCAGCATGCCCGGCCGCGC
57	632327_26682362_Target4.3_6	GGGGGCGGGGCGGGGGGCGGCCCCTACTGGGCGGGCTTCTGTCTGCGCGCCCGCGCCCCCGACAGGCGGCTTATTTGCATGGAGAGCGGCGGCGGCCAATGGGCGCGCGCGGCCGGGCAT

58	632327_26682363_Target4.4_1	GAGGCTCCAGGCCCCTGCCCGAGGCCAGGCTTCCAGCCTAGGGCG CAGGACACCGCTCTCCAACAAATGCACGTCCCCGCCTTCCACCCAG GCGAGAACGCACCGAAGGCCTACGCAAAC
59	632327_26682363_Target4.4_2	ACGCAAACTCCTCCACTTCTGGGAAGGCTGCCCGGTTTGCCTTCTTC CTCCAGAGCCGAGACATGGCCTCAAGTCGACTTGTCTTTCCCGCTAA CCAACCCCAGGGCATTCATCGCGTGT
60	632327_26682363_Target4.4_3	GGTGGGACCGTCTACAGTCGGAGCTGTGGTGGTGATGATTCGTCTC CTACAGGCTGGGGCACGCCCCCTCCCCTTTCCCTCTAGATTCAGATT TGAGTCCCACGGCCCATGGACACGCGA
61	632327_26682363_Target4.4_4	TCCCCAGATGTCGGCACAATGCAGGGGAAGGTAGGTGCTGCCCGTG AAAAGCGCTGGGTCGAGAGCTCGCCAGCCTCCCTGCTTGAGGCTTC ATTTCCTGGGGTCCTTACACGGTGGGAC
62	632327_26682363_Target4.4_5	GCTGAAGCAGATGAGTTGGAGCAGGACTCAGGAGGGTACTAGGCCC AGGTTTTAGGCTGAACCTAGGAATGAGTAATGAGAGGAGGCAGATCA GCTGGAGGACCAGCCCGAGTCCCCAGA
63	632327_26682363_Target4.4_6	ACCGAGCAAGGGGCAACTCAGGAGAGCCAAGGTTGTCTCCACTCGG TTTCCCCCGAGTGATTCTTCCTTCTATCTCCCTCATTCCCCCAGTGCC GCTCTCCTACCCCATGTCGCTGAAGC
64	632327_26682363_Target4.4_7	TGCTCGGTTGCAGGTCAGTGACTGTCACCCCATGCAGCAGAACCAG GGTGCCAGAGCCCCTGGGCCAGGCCAGGGAGGCACAATCTGCAGG GAGATGATAGGACCGAGCCTGGTCCAGAC
65	632327_26682363_Target4.4_8	CTCTGCTGCGTGAAGCCGGGTCTACCCCGCTGCTTCCCTGCCACCA GGGCTGCCTCGTGGCATCCCATTGCTCAGCCAGTGGCCCAGGATTG TTGACTGAGGGTCCTGTCTGGTCTGGAC
66	632327_26682363_Target4.4_9	CAGCAGAGAATTCTCAAGCATGGCCTATGGAAGACACAAGCCCAGGT GGGCCTGCAGCTGCCCCTCTGTCTGACCCCCAGGGCTCAGCCTACG CAGCGCCTGGCCAGATGTGCCACCTTG
67	632327_26682364_Target4.5_1	AGACTCCTGTGTCCCACCCCTCCCAAAAAACTGGACGTCTGCATTTC TTCAATATTTGGCTTGGGAAGCATTGGCCAGAACTCACAGCACAGCG GGTGAGGAAGGAGCAGTGGGATGAGA
68	632327_26682364_Target4.5_2	GACAGAGCATGACCCAGAGTCCTCAGGAGGAACAGAACAGCTAGCC AACACCCTGTGCCTCCCCGACACAGCCCGCCTCGCCTCAGAAGAGG AGCCAGCCTTCAGGGAAGCTGCCTGGAG
69	632327_26682364_Target4.5_3	AGCATCTCCTCCTGCTTGTTCCCAAGAGCTGTGCCGGGCCCCTCCTG CACCCTGACCCTGTCCAGCCACCCACTCCTCAGCCTGGCTGGCACA CCAGCTTCCCAGAGAGCAGGTCTGAAC
70	632327_26682364_Target4.5_4	GCAGAGACTGCTGCCTGGGGCCCTGCCAGCAGGGCACTGCCTGCC CATGAGGCCTGGTCTCCCCTCCCCACAGAAGTGGAGGCCCAGGGAT GACCTCAGGCTCCTGAGGGTCCCGCTGGT
71	632327_26682364_Target4.5_5	TCATCCCCCAAGGTTCCAGCCATCCACCTCCTCTCTGCACCGCCCTC CTTGGCCAACTAGGATGGAGCAGGGGCCAGCTCCCTTGAGGGCCAG GCCTTTTGTGTCCTTGCCCGTCCCTGC
72	632327_26682364_Target4.5_6	AAAAGGAGCAAATTTTTGAAATGCCTGTGTCGGAGCCTGTTTCCCTTG CTGCCTCCTGCTCACACCAGCAGCCCCACCCCCAGTGCTGTTCTAAT GCAGCTACTGGGGGAGGAGGGTCTC
73	632327_26682364_Target4.5_7	CCCCACCCCCCAGCTACATCCCCATCAACACTGTGGGGCTTAACTTC TGGGGCCTTGTTTCCAAAGCGGAAATGCCATTCTGGGAGGCACAGG CTTTTGGGGGAGGGAATTTAAGTGGAA
74	632327_26682364_Target4.5_8	GGGTATGTGGGGCTGCATCCCTGTCCTTGACAGCGGAGGTCCGGGA GGCTGGACTGGGGGTGGGGTGAGGTTCTGCCCCCATATACCCCGGC CAGAGCCTGGCCAGTGGGTGCTCCTCCC

75	632327_26682364_Target4.5_9	TCTCAAAAAAAAAAAAAATTGGGGCTAACGGTGAGCCTGTTTTGCAG GATTGCTGTGTGCACAAAATAAATGCATGGGCATAGGGCCCCTGGCA CTGGCTGGGCGCAGAGGCTGTGCTGG
76	632327_26682365_Target4.6_1	TTTCTTCCCTGGCCCTGTCCCTTCTGTGCCCCGAAATGTGTGGGATG GGGCAGTGGTTGGTAAACTGGGTCTCGGTCTCTTCATGTGAAAAATG GGGCTAGGCTGGGTGCAGTGGCTCAC
77	632327_26682365_Target4.6_2	GCCTGTCCTTTTGCAGTCTGAGTGTGACAGGGGTGTTTGGCTTTCTG AGCCTGGAGTGCTGCTGTCCCTGTCCCTAGATTCCCTTCCTGCTGCA GGGTGGGCTGAGGTCTAGCAGCCCCA
78	632327_26682365_Target4.6_3	TCAACAAATGTTTACTGCACCCCTTCTCACCAATGGGGCTAAACTTAG TGGGGTGGGGGTGGTGCTGGCCCCAGTGCTGAGCTCAGTTTTACTG GGGAGGAAGGTGCTTAGGTCTCAGTT
79	632327_26682365_Target4.6_4	GTGTGTGCCTCTGCACTTAGGCGTGACTTAACCACCCCCATCCTCCA GACTGGGGCAGCCTCAGATTTCTTCACCCAGGCCAGCCTATCCCATG AGGGCCACCTCTGAGGTCCCACCCAG
80	632327_26682366_Target1.1_1	GACCATTGAGGAGAGCTGGTGGTCACTCTGCAGAGCGTCCCTCCGT GGGGATGGTCCTGGGTGGCCTCAGGACTCAATGGAGGGAGTCCCG GGCGTGGCGTGTGTCTGTCTCAGGCCCCC
81	632327_26682366_Target1.1_2	GCCCCCTGAGTATCACCAGCCACCCTTTGCTGGGTCCTGGGTACACA AGCCACCCATCTTCAGATGTCAGGGTCTCCTCCAGCGGGCGCAGTC CCTCTGCCCTCCCTCAGCCCTTGGGAC
82	632327_26682366_Target1.1_3	TCCCTCCCCCGGCCTCCCTCCCCCAGCTTCCCTAAATTCTGTCCTCT TGCTCAACCCTCCAGGCTGTGATCGAAGCCAGGGCGCGAAAGTTGA TTCCAAATGGCCCCCTCTGCCCCAGCC
83	632327_26682367_Target1.2_1	AGAGAAGCACTGAATGAACTTGGAGGCCAAAAAGAAAAAAAGCTTTT TAACGTTTCATTTGGAAAGGATTTCACGCTTACAGAAGTCCAAAGGGT CCAAACTCCCTCCCCGCTCCCCAAA
84	632327_26682367_Target1.2_2	TTTTCTTTTTGGCCTCCAAGTTCATTCAGTGCTTCTCTCCATTTCACTG TAGGTTTAAACCGTTCAGTTATAAATAAATAATTTTATCCTCTGTCCTC GGCTTTCCCCCGTTTCCGGCAC
85	632327_26682367_Target1.2_3	GACTTGGAGGGAGCTCCTGGCAGGGCCCTGCAGTGCCCAGGATGG CCCCGCCGCAGAGACAAATCCAGCCCCCATGTCTGCAGTGCCGGAA ACGGGGGAAAGCCGAGGACAGAGGATAAA
86	632327_26682368_Target1.3_1	AGAATCACCCCAGGGTTAGAGGATTCCACAGACCCCAAGAGACTCTG AGTCCCATGATCCTCTGCCCTGCTGAGGTCCCAGGAGGCTGCACAC ATTGAAATCCACACCCTGAGTGGGAGG
87	632327_26682368_Target1.3_2	TCCCGATGGGGCGTACGGCATAAACCCGGGGGACCCCAGCTCCCG GGACTCGCCTCCTCTCTCCCTCCCACTCAGGGTGTGGATTTCAATGT GTGCAGCCTCCTGGGACCTCAGCAGGGC
88	632327_26682368_Target1.3_3	AAATAAAAATAAAAAATAAAAAATCCAGTCTGCCCCCTGCTCACACCG GACACCAGAATAAACTCCCGATGGGGCGTACGGCATAAACCCGGGG GACCCCAGCTCCCGGGACTCGCCTCC
89	632327_26682369_Target1.4_1	CAGGGCCCCACCACGAGTGCCCTCAGTGCCTCACCTGAGGCCCCAG CGAACATCCTCCTGCCAGTTTTGTCTGGGGGTTTTCTTCCCCCTTTAA GGCCAGGATTCTCAATCAAGAGGTGA
90	632327_26682369_Target1.4_2	GAGGTCCCTGTGGCCCCAGCAAAGCCGGCCGTGGCAGGTGTGTCC CGTGGGTGGGTGAGCTGGAAACGGACAGACAGCAGGACGTAGCAG GGGACAGGATGCAGAGCTCGGGAAGGCAGG
91	632327_26682369_Target1.4_3	CCTCGTCAGGGAGGCGTCTCCTTGTGGGTGGCACGTGGGCATGTGT TGCTCTGAGGGCTGTGGCCATGTTGCCCACCTGGCCAGGGACCCCC GACTTGGGTGGGTGACAGCCAGCCTCCC

92	632327_26682369_Target1.4_4	CAATGCCCAGGCTGGGTCCCCACTTCCTCCTTTTGCCTTGGGAGCCTGGGAGTCAGAACGGACTCCGGGGAGGAGGTGGGGGCTTTGGGCTCAAGGTCCCAACCTTTGTGGGGGCGGGGA
93	632327_26682369_Target1.4_5	ATTGGGCAACTCAACGGCCTCTGGCATTGGGCTATAAGAGGAGCTTGACCGTGGGTGCACCCTGGACCCCACCATGGCTCACCGGCCCCCCAGCCCTGCCCTGGCGTCCGTGCTGCTGGC
94	632327_26682369_Target1.4_6	CCCAGCTGTGCCAGAAGGGCTTTGGATGGACCTCGTGGTGGATATTTCCCCACAATCCACCGGGGCCTGGAGGCTGGATGGATGGGCACGTGGCTCACTCACCGCTCAGCAGCAAGGCCA
95	632327_26682369_Target1.4_7	ACAGATAGGCAACTGAGTCAAATGGCCAGGGCTCCCCCTTGCCCTTGTCCTCCCCACCCCTGCAAGCGTTGGTCCCGAGCAGTGAGTGGAGTCTCCCCTGACCCTGCCTCAGTTTCCCCA
96	632327_26682370_Target1.5_1	GCAAATGCTCAGTGAATATGCATGAATGAATGAATGAGTGAATGAATGAGTGAGTGAGTGAATGAGTGAACAAATGAATGAGTGAATGAATCAATGAGTGAGTGAATGAATGAGTGAATG
97	632327_26682370_Target1.5_2	AGTGAATGAGTGAACGAATGAATGAGTGAATGAATCAATGAGTGAGTGAATGAATGAGTGAATGAGTGAATGAATGAGTGAATGAGTGAATGAGTGAACGAATGAATGAGTGAATGAATG
98	632327_26682370_Target1.5_3	AAAAAAGAAAAAGAAAAAGAAAATCACCCTCAGGATAGGGACCTGAGGGGGCCCATGCTCTCTTCTTCCCCTGATTCCAGCATCACTAACTCCTCGACCCTTTCACTCACTCACTCATT
99	632327_26682371_Target1.6_1	GTGAGCCACTGCACCCAGCCACCTGGTCTGCGTCTTAAAAGCCTTCCTGACTCTCAGGACTGAAAGCTGCCACCAGGGCGCCTTTGGAAATCGTCGTAATTATAACCCCCCCGGCCTGGG
100	632327_26682371_Target1.6_2	GGGAGCCCCCAGGCTGCAGGGAAAGGGGGGATGGCAGAGCAGCCCCTGGGCCTCTCCGAGCCTCCGTCTCCCGATCTGCAACCCGGTCAGTGCCTGCTGGCTGGTGGGAAGGACTCAGCG
101	632327_26682371_Target1.6_3	GCCCGGGTTCCCCCGCATCTGCAGGGAGGCCATGTAGGGCCGGGAGTGTGGCTGCGCCTCGTGCCCGCCCACGATCTCCGCAGCTCGGGCAGCACCTGCAGGGGGGGAGTCCAGGCGTCA
102	632327_26682371_Target1.6_4	AGCCACTTCTGCGGAGGCACCTTGATCCACCCCAGCTTCGTGCTGACGGCCGCGCACTGCCTGCGGGACATGTGAGCGGCCGCCTCCACACCCCTGTCCGCCCGCCCCGCCCTCTTCCTC
103	632327_26682371_Target1.6_5	CTCGGCGACCCTGCCCCGGGCCTCCCCCCAGAACTGCCCACGCGCGCGGGGCCTGGGGTCTGCAGACGGGGCTTAGCTGGGTCCTCCCCGGGCAGAGGGACAGTGGCCGGGCCAGGGCTG
104	632327_26682371_Target1.6_6	CCACGTTCACCAGGCGCTGGGGTCTGCGGGGGTGGGGTGGTCACTCCTCGGCGCCCTGGACACTCGCCGCCGCCCACAGCCGGCCCTTCCCGAGGCCGCGGTGCAGCCCCAGACCCCTCC
105	632327_26682371_Target1.6_7	TGCTCGGAGCCCACAACGTGCGGACGCAGGAGCCCACCCAGCAGCACTTCTCGGTGGCTCAGGTGTTTCTGAACAACTACGACGCGGAGAACAAACTGAACGACGTTCTCCTCATCCAGG
106	632327_26682372_Target7.1_1	CCATTTCTGTCTCCATAGAGTGGGGACAGCCCCCCATTTCCCCATGACACACATGAGATACTAAAGAGGTGCCCTACAAAGTCCCATCACCACTAGATGATTTTTTTTTTTTTTTTTTG
107	632327_26682372_Target7.1_2	GAGTTGGGGCTCCGCGGTGGCGGTCAGCAGCATAGGCCCAGGTCCCATGTGACCCAAGGCTGTCTCTGAACCTCCATTTCTGTCTCCATAGAGTGGGGACAGCCCCCCATTTCCCCATGA
108	632327_26682372_Target7.1_3	TCCCCCCCTTATGACCTGTAAACCCAGTTTCTGGCGGCCAAGGATGGGGAGACAGGAGGCAACTGCTTGAGCGGAGTTGGGGCTCCGCGGTGGCGGTCAGCAGCATAGGCCCAGGTCCCA

109	632327_26682373_Target7.2_1	CTGCCCCTCCACTCCCGACTATGAGAACATGTTTGTGGGCCAGCCAG CAGCCGAGCACCAGTGGGATGAACAAGGGTAAGTAAGCCACTGAGA CACCTGCCAAAGTGGTGAATAATAAGG
110	632327_26682373_Target7.2_2	CCGGGAGCTGAACAAACCCTGGGCTGCTCAGGATGGGCCCAAGCCC GGTTTAGGCTTGCAGCCACGGTACGGCAGCCGGAGCGCCCCCAAGC CCCAAGTGGCCGTGCCATCCTGCCCCTC
111	632327_26682373_Target7.2_3	AGCTCCCGGCTTCTGGCCACTCGGCATCGCCAGAGTCTCCAGGCCA GCACAGGGCCAGCGATGGCAAGTCCAAGAAGCAGGCACCCGCTGAC CACCACTGCCCCGATAGTTGCAGAGGCC
112	632327_26682373_Target7.2_4	CGACATCCGCCGAGACAACTGCTCTGGCCAGAAGCCTCTGCTCTGC TGGGACACAACCAGCTCCCAGCACAACCTCTCTGCCTTCCTGGAGGT CAGCTGCGCCCCTGGCCTGGCCTCTGC
113	632327_26682373_Target7.2_5	TGAGGTCCTGAACGTGCTACGCAACCCCTTGTCTCGTGTGGATGGG GCGCTGGCCGCCCGCTGTGACCTTGACCTGCAGGCCGACTGCAACT GTGCCCTGGAGTCCTGGCACGACATCCG
114	632327_26682373_Target7.2_6	AGGACCTCAAGCTTCTGCAGGTGGGCAAAGAAGGTCACTGGAAGCT CTCGCAGGCCGTTCCCAGACAGGTCAAGGAGAATCACGTTGCTGGC CCGCAGAGACTGGTTGTGAGGCAGGCTC
115	632327_26682373_Target7.2_7	GGCAGGCTCAGGCTGAGGCCACTGAAATTCAGGCACGTGGCACTGA ACTCCGCGTTCCAGTCCACATCCGCGGAGGACACGGTGCACGACGG TTCTAGGCTGTCTGACTCCCGCAGCAGC
116	632327_26682373_Target7.2_8	CGCAGCAGCAGCGGCAACAGCAGCGTCCATGCCAGGGTGCCCCCC ATTCAAGCAACCTACGTAGAGACACCGGAATCCTAGCCCTGACCTCA GCCCTGTGGTCGCCCTCGCCTCCACCGC
117	632327_26682373_Target7.2_9	CTCCACCGCCAGTGTTTATTATTATAGCTCAGACCAGCTCAAGCCGC TTCTGAAATGGTAAAACGCAGCCCCAGTCTGGTCGCCTCCTTTGGCT GGTGGGCTGCCTCAGTCTCCCCTTCT
118	632327_26682374_Target7.3_1	GCATAGGGTCCCGTCCTGGCCAACGAGGGCGCCCCAAATGTTCAGG ACATAGAAGAAGCGGTTAACTGGCCCGGATCTCCTCCTCGCCTTCCA AGCCCGCTAAGCACTGGGGTTATCTAC
119	632327_26682374_Target7.3_2	GCCCCCACTCCACCCTATCCCAGGACTTCCCAGCGACCCGCCGTTC TGGGAGATACCGGGAGCGTGATCAGGGGGCGGGGCCGTTTCCAAG GCAACCGCTTATTTGCATAGGGTCCCGTC
120	632327_26682374_Target7.3_3	GCAGAGGCAAAAGCGTGGCAGTGGGACCCAAAAGGTAGGACTGAGG CTCTAGAACTTGCACCTGTGCAGGGACTGCAAACCAGACCTGGGAG GACCCTTTCAGCAGCCCCCACTCCACCC
121	632327_26682374_Target7.3_4	AGCGACCCCAGCAGCGCTGCGGACGGTGCTGGCCGTGGCCGCTGC GGCCCCCGTGTCCAGGTGGGCCAGGACGCAGCCTCTGGGCGCCGT CGCTTTTCCAGCATCGCAGAGGCAAAAGCG
122	632327_26682374_Target7.3_5	CCTGCAAGGGGGCGGATCTCTGTCTTCATTCTTCCCCTCTGCACTCC ACCCAGACACCAGTTCCTCTTCCCCCTGAGTCGCTGGGTGCAGAGC CAGAGGAACGCCAGCGACCCCAGCAGC
123	632327_26682374_Target7.3_6	GCTAATAGAGGACATGAAGTCACTGGGTTCTAGCAAGAGGGAAGCG GGACTCTGGTCCACCCCTCCCTCTTGCCCTCCATCCACCTCTGGTGA GAACCTTGAGGCCCTGCAAGGGGGCGG
124	632327_26682374_Target7.3_7	ATGTCCTCTATTAGCACCCCAACCGACTGCCACCTCATCAACTCGCTT CTTGATCTCAGCTTGGCTGGTTCCCAGCTCATGCAGTCATTTATTCAT TCAACAAGCATCACCCACGCTGGG
125	632327_26682375_Target7.4_1	CCCTCCTCACTGTCCCCTCCAGCATAGAGGTGCCACTGTGCAAGAAC TCAGTGGGAGAGGCTTGGAGGAGCTTGGAGAGCCAATGATAGGTTT GGGGAATCTTAGTGAACTCCTACTCAT

126	632327_26682375_Target7.4_2	GGCTCCACATGGACCTCTTCCCCCACCACCAATTCCTTCTATCCTCTC CACTCCTAACCATGCTATCCCAGCCAGCTACATTTTCCCAAGCTGCT GGGAGCCCTCCTCACTGTCCCCTCC
127	632327_26682375_Target7.4_3	CTGGGACCTCAGCCTCCTCCCCAAGTTGCCCACCCCAGACACCAGG CTCACTCCAGAGGGACTTCTTGAGCCAGTGCCCCTCTGCCCACGCA CCTGCCTTGGCTCCACATGGACCTCTTC
128	632327_26682375_Target7.4_4	TGACACCAGGTTCAGGTGAGGCCTTCTCCCAGCCCACCCCTCCTCA GTATCATTTTTGTCACTACTACCCCTCCAGTCTGCCTCAGGCCCCCAT CTGCTTCTGGGACCTCAGCCTCCTCC
129	632327_26682375_Target7.4_5	CTCACCTGAACCTGGTGTCAGGTGGACCAGGTACAACCTATGCCAGC CCGACTCACTGTGCCACCTTAACTGCGTGTGACACCATGTCCACAGC TGTCAAATGCACAGAGGCTTCTCCGG
130	632327_26682375_Target7.4_6	ATGCACAGAGGCTTCTCCGGGATCTGGGAGGCTGGGAGTCCACTCC CCCACGTTTTCCCCTCTTTTCGGCCTCTGTCCTTCACATCGCCAAACT CCAAGAAATGGTCAAAGGCTTTGAA
131	632327_26682376_Target3.1_1	CGTGCTTTGTTCTACTGGCCCTGTTAAAACTCAAGCCAGATCACGTC CACCTGCTCACAGCCCTCCTGTGGCTCCTCCTCACTCTCAGCAGAAA CTGACCTTCCCCCTCTTATCTCACCT
132	632327_26682376_Target3.1_2	TCTGCTGTCTCCAGGTGGCGGCGAGGGAAAGCGCATCCTGGGGGAA CCCTGGGCGCTTCCTCGCGTTAGACTCCCCCAGGTTGCCAACTGGC CAGTGGCTGGTTTCGGTACCCAGGCGTG
133	632327_26682376_Target3.1_3	CAGAGTCACGCCCAGCGCTGCGCAGGCTGATCGCCGCGCCGCGCC CCCGCCCTCGGTCGCAGGTGGCTCGTTCCGGGAATTCCTAAGCGGA AACCGGTCCCAAGCCCCGCGCCTTCGCTC
134	632327_26682376_Target3.1_4	ATTCCACTTCGGAAGTTTTCGCCACCTCCCCCACCCGTTCCCAACTT GTGGTTCGGCCCCTGGGCATCCCTAGCCCCCGGGTCAGCCCTCCGG AAATTCTGGCTCTTAAAGGGGCCGAGC
135	632327_26682376_Target3.1_5	TTCGGGCCTCCTGTGTCTCCCAGTTAGATGACCTGAGGAACCCTCTA AAGTCCCCGGAAGGGAAGCTCTGCCCCCTCAGGGATGCCCAAGGGG AATCAGGGCCAGGAAAAGTTGGAATTC
136	632327_26682376_Target3.1_6	CGAAGCGCCCCCCCTCCACCCGGTCCGGAGGAACCCCAGTGGAAGT GGAGAAGTCAGGCGCCACCAACAAGCCTCTCCCAGCCAGGACTTTG CTTAGACTCGCTCCTCCCGGCAGGGCGC
137	632327_26682376_Target3.1_7	TGCAACCGAGACCCACTTGGAGCGATTCACCTGTTGAGATAGGGCG GGTCCCGCCGCGCACCTGTTCCCTCCCTGCCCAAACCCCTCTCCCC GGCTGGCGATGGACCCGCCTAGGTGCGC
138	632327_26682376_Target3.1_8	GCGCTCCGTCCCCCAGGGCCCGAACCAAGTGACTGGCCCGCTGGG AGGGCGCCTGCGGACCACAGGTCCCTTCCGGCCCCCATCTGCTCCG GCCAAACCAAGCGCACCGAGATCCATGCA
139	632327_26682376_Target3.1_9	CTCCGGTGAATGGTTCGGCCCAGGTACACAAGGGTGGGAGCCGAGG GCTGGGCTTAGGGGTGAGCGGCGGGGAGGGGTTCCTCTGCCTCCC TCCCCGGAAGTGGGCTGACCCAGGTGCGC
140	632327_26682376_Target3.1_10	GGAGCGCGCAGCGGGTGGAGTGTGGCTCGGAGGACCGCGGCGGG TCAAGCACCTTTCTCCCCCATATCTGAAAGCATGCCCTTTGTCCACGT CGTTTACGCTCATTAAAACTTCCAGAAT
141	632327_26682376_Target3.1_11	GCGCGTCCCTTCCAAAGTACCTTAGGGGGCGCGGCGCGCACCAAGG CCAGGAGGGGTGCACGCTCCTCCCCTTCCCACTTCCGTTCCTTGTCC CTACTCCAAGTCCGTCCTGTTGCATTC
142	632327_26682376_Target3.1_12	GCGCGGGCCAGACGCGCCCAGACGGCCGCGATGGCGCTGTTGGCC GGCGGGCTCTCCAGAGGGCTGGGCTCCCACCCGGCCGCCGCAGGC CGGGACGCGGTCGTCTTCGTGTGGCTTCTG

143	632327_26682376_Target3.1_13	ACCCCCGCTTCCCGCTTCCCGCCGCCTCCAACTCCATCCATCCCCCT CTACAGTTCCCTCCGGCGTTCCGCAGCGTCAGAGGCCCCGTGCCCC GTACCTGTGCACCAGGTGCTAAGCAGA
144	632327_26682376_Target3.1_14	TATCTTCCAGATAAGGGCGCGGGGAGCGCTCCCCGGCACAAATGGG GAATTCCTCTCACTCCCGCGCGCAACAGATCGCCCAAGACCCAGGG GATCGGAAGGTCCCAGCCTCTGAGACCC
145	632327_26682376_Target3.1_15	TCCCATCCCGGCTTTTCTTTTCCCAGAGATCGGGCGGTCTTCCACTC CCTCCCCACAAAGAGTTCCATTCTCCCTGCCGCTCCGGGTCTCACCG TCCAGGGAGTTTCACTTCCTGCTATC
146	632327_26682376_Target3.1_16	ACCCGAGGCCTAGGCATTGTTCCTTCGTCTCTGTCCCTCTAGGAAGC GTCTGATCCAGCCCTCCCGTGCCCTCTCCCCGTTACTCCAAAACTTA GAAATCCCCGGGTGCGCCCAAGTCCC
147	632327_26682376_Target3.1_17	CAGAAGTCGGTTTCAAGTCCGTAAATCCATCCCACCAGACTCTTACG CACGTATAATCCGGAGCCCGCGGGAGGTGGGTGGGGTGCGGGGGA TGGGGAGTCCCCAGTCCCACACCCACCC
148	632327_26682376_Target3.1_18	TCTGCTGGCAGGCTTTCACCTGGATGGCATATTTGGGTGGTGATGAG GTCTTTCCCGAGACACTTTTGGTTCAGTCATTTGAAATGACTTTAGAG TAGGGTGAGGTGGTGGGAGGCTGAT
149	632327_26682376_Target3.1_19	ACCGACTACGAAGGATTCCAGGTTACCCGGGGCCTTTTGAATTTGGA GGGAAAACCATGGAGTTGTTTGCCTGAACTGCTTTGCCATGGAGGGA CTAAAGCCCCCACAATATCTCCATCA
150	632327_26682376_Target3.1_20	CACCAGTCCCCTCTTCCCTTTGCCATTCACCCACAACAAGGGGCCTC TGTGTGGCCTGGGCAGGCAAGCCCAGATGGCCATGTTGATGCCCCC AGCGCCCAAGGCCCCACTTCAAAACCG
151	632327_26682376_Target3.1_21	GGTGTGGTTCAGAGGCCACAGGCTGGGAAGAGGGATGGCGGGCGA GTCCAAGGAAACTGGCCGTGTCACCGTGCACCTGCCACTTCAGCCC CACGGGTCTATAAAATGGGCATGATTAT
152	632327_26682377_Target3.2_1	GTGCCAGGCACTCTGTAAACCACATACTTGCGAGTGTCAAGCTGGTG ACAGGTGGCGTTCCTGTTGAAGCACCTCCCTGAGCTCACAGCAACCC TTGCTGTCTCTCCTCTTGCCCTCAGC
153	632327_26682377_Target3.2_2	TCTCTCCTCTTGCCCTCAGCTCCTGCCAGGGCCATCCAGGTGACCGT GTCCAACCCCTACCACGTGGTGATCCTCTTCCAGCCTGTGACCCTGC CCTGTACCTACCAGATGACCTCGACC
154	632327_26682377_Target3.2_3	CCTACCAGATGACCTCGACCCCCACGCAACCCATCGTCATCTGGAAG TACAAGTCTTTCTGCCGGGACCGCATCGCCGATGCCTTCTCCCCGGC CAGCGTCGACAACCAGCTCAATGCCC
155	632327_26682377_Target3.2_4	CGACAACCAGCTCAATGCCCAGCTGGCAGCCGGGAACCCAGGCTAC AACCCCTACGTTGAGTGCCAGGACAGCGTGCGCACCGTCAGGGTCG TGGCCACCAAGCAGGGCAACGCTGTGAC
156	632327_26682377_Target3.2_5	GCCAGTCCCACCACCCGGGCAAGCCCAGCCTCATCCCCCTGCCCTG CCCAACATACTTCCGGTGATGGTAATCCTCCGGCCCTGGTAGTAATC TCCCAGGGTCACAGCGTTGCCCTGCTT
157	632327_26682377_Target3.2_6	GCCCGGGTGGTGGGACTGGCGTCCTTGTGCGGGACCTGGAGTCCC CATCTGAAAGCTCTTGAGTGCCAGTGTCTGAAAGGACCATTGAAGGG AGCAATTCTTTTTTTTTTTTTTTTTGA
158	632327_26682378_Target3.3_1	GTGTGCAGTTCCTGGCATGTCACAGGCTTTCTCCATTAAGCTCTCTTG CCCCTGCAGTTCACTCCTGCCATCTCCTCTGTGAGTCCTCTGCGGAC CACCCTAGGCAAGCAAAGGGATTAG
159	632327_26682378_Target3.3_2	GTAACCTCTCTGTGCCTCAGCTGTCAGGAGGGTAGAGGAGAGGACT CAATGGGAGAATATGTGTGCAGTTCCTGGCATGTCACAGGCTTTCTC CATTAAGCTCTCTTGCCCCTGCAGTTC

160	632327_26682379_Target6.1_1	CCTCCCAAAGTGCTGGGATTTGTTTCCGGTTTTTTTCCTACTATGCTA TACTTTTGACTTTGTTTCCCTGACTAGGATGTCAATTCCGTGAGGCTG GATTTTTGCTGATTTTTTTTTTTA
161	632327_26682379_Target6.1_2	ACTATGCTATACTTTTGACTTTGTTTCCCTGACTAGGATGTCAATTCC GTGAGGCTGGATTTTTGCTGATTTTTTTTTTTAACCTCTGTACCCCTAG CTTTTTTTTTTTTTTTTTTTTTT
162	632327_26682380_Target6.2_1	GCTTCCTCCGCGGCGCTTTAACACGCAGGGCGCTGCTGCCAGGGGC GTCCCGTGTTCTAACTCGCTCCCACAGCCCCTCCGGCTTGGTGAGCA GCGTCTGAGGGGTGAGGGGCATAGACT
163	632327_26682380_Target6.2_2	GGGGGCTCTGTGGATGGCATTCGGGGAGCTACAGGTTTCCCCCAAA AGCTCAGATGCTCGTTCTTGAAGAGGGAGGTGCTGCCCCTGCCTTCC TGCGTACCGCGACAATACAGCTTCCTC
164	632327_26682380_Target6.2_3	GAGCCCCCCTCAGTCGGCCTCCCCTGAGGCACCAAGGCTGGCGGAA GCAGTCACCTGTCCATCTCCCCCACTTCTCACAGAGGAAATCCTGGG TGGTGCCGGGCAATGAGTCAGGGCTGA
165	632327_26682380_Target6.2_4	CCTAAGGCCAAGGGCGCCTGGGCCCTGCAGAGGAGCGGAGCAGGG GGAGGAGCGCTGAGACCTGCCCGTTGGAGGAATGCTGAGACGCCC CACCCAACCTCTGTCCTGGTCCTCAGCCCT
166	632327_26682380_Target6.2_5	TTGGTGCAGGCAGCTTCTGGGCTTGAGTCCGGCCCCCTGCACCTCC AGTCCACACTCCCCAGGAGCTCACCTGCTCCCAGGTCGAACTCCATG GCGGTAAGAGAAGTTGGGTCCTAAGGC
167	632327_26682380_Target6.2_6	TCCGACCGGCCCTGAACTTTGTGGGGACTGAGCTTGGGATCTCCCC CGTGGCCCGCCCCCACACCGGGCTTCTGGGAGGTGGGCTCCAGGG CTGTGGAGAGAAGTTGGGTGGTTGGTGCA
168	632327_26682380_Target6.2_7	TGAAGTTGGAGGCCTAAGGCAGGACCCTGGGGTCAGGGGCAACCCC AGCCTTCCCGCCCCTCCGCAGCCGGTGATGAGGCGACTTACCTTTG GACCCGGACCTGCCCCTGCCTCCGACCG
169	632327_26682380_Target6.2_8	TACCTTCACATCCGTGTCCGAATCGCTGGAGCTGCTGCTGGAGTCGG AAGAGCTGTGGTGTCCTTGCTGGATGGAGGTGCGGCAGTGAGGCGG CGCCCCTTACCCAGCCCCCTGAAGTTG
170	632327_26682380_Target6.2_9	GGCTGGAAGCGAGACAGGGGGACCACTCCCCGCACCCTCCCCGCC AGCCCCAGTGCGGGGACGCCTCTCTGGGGTGCAGGGCACGTGCTT GGGGACGCTGGCGAGAGCCCCTTACCTTCA
171	632327_26682380_Target6.2_10	TTCCAGCCCAGAACCATCTCTTCTCTCCCATCCCTGCCCTCGGCCCC ACAGTCCCACGCTGCTGGCTCCAAGCAGCACGAGAGCATCCCGGGC AAGGCCAAGAAGCCCAAAGTGAAGAAG
172	632327_26682381_Target6.3_1	AGAAGGGCAAGAAGAAGGAGGCTCCCCACTGAAGGGCCCTGGACAG GGCTCATTAAACCTTCCTCTCTGCCTTCTGCGACTGGTCAGCGTGGT GCCTACTCTGGCCCGTCCCCAGCTCCC
173	632327_26682381_Target6.3_2	CCAGCTCCCTGCCCCCTGCCCAGCGCTGGGCCCGCCCATTCGTGCG CGAGGCCAAGGAGAGGCTGTCCACGCCATGCCCATCAGGGTTTATT GTTTCTGTAACAGCGGCCACGCCCTGGG
174	632327_26682381_Target6.3_3	GGCCCCAAGGTCCACCCTGTCTGGCCACAGGCACCGCCTCCATCCC ATGTCCCGCCCAGCCCCGCCCCCAACCCAAGGTGCTGAGAGATCTC CAGCTGCACAGGCCACCGCCCCAGGGCG
175	632327_26682381_Target6.3_4	CATGTACTGGCTCACCTTCCACCTGGTGCGGTGAGCGCGCCCGCTG AACCTCCCGCTGCTGCTGCTGCTGCTGGGGGCCACTGTGGCCGCCG AACTCATCTCCTGCCTGCAGGCCCCAAG
176	632327_26682381_Target6.3_5	CAGTACATGAGCATAGGCTGCGCCGCCGCCACCGCCATGGTCAGGT ACATGCGCAGCTGGTTCCGGGCCCCACGCACCGGGACCCCCTCAGC TGCTGCGTCTGCCAAGATCTTCAGCCGC

177	632327_26682381_Target6.3_6	TTCAGCCGCAGCGTCCGGATCTGGGTGGGAAAGAGAGAGAGGAACC AAGGGATTTACCCTTGAGCCCTCTGGGCCAGAGTGAGAGCCCGGAC ATACTTCCAGCCTCTGCCTAGAAGCCCC
178	632327_26682381_Target6.3_7	AGGGCCCGGGGAGAAGCAAATCCTCACCATGTTAGGAGGTTTGGGG AAACTGAGGCCCCGGGAGCAGAAACCTGAGGCTGCAGAGGGCCAG GGACTTGTCCCCAGCTGCCTGGGGCTTCT
179	632327_26682381_Target6.3_8	GGGCCACGTCTCCCACCCCCTCAGGCCGGGTGTCCACCGGGAAGTC CCCCTTCACCCGCTCCAAGACCTTGCCTGGCATTTGAGTATGGAACC TTCTCAGATTTTGCCCACAGGGCCCGG
180	632327_26682381_Target6.3_9	ACGTGGCCCAGGATGCTGCCCCCCCTTATGCTGGCCACACGGCAAT TTCTGAAGACACGCCAGAAATGCTATCTTTATTTTTATTAAAGGACAG GGTCTCTGGCCTGGTGCGTTGGCTCA
181	632327_26682382_Target6.4_1	TGTGAGTCACGTGCTTGGCCTAAACTTTTAAATGATGAGACTTAAGTC AAAGTTTATCCAAGGCTCTGCCCTGGCCCACCAGCCACCACAGTCTG CCCTCTGCTTCTCACATGC
182	632327_26682383_Target6.5_1	CAGAATTTCCCTGGAAGGAGATTCTCTAGAGCCCTTCCCACTGGAGT CAGGGGTGCTGGTGAAGAGCACTGGGGTCTGCAGGCTGGGTGGAC CCCAAGCTTAGTTGGATCCTGGGCAAAT
183	632327_26682383_Target6.5_2	CCAGGCTGCTAGAGGCTGGGGATCCCCAGCACACAGGCTCCAGGCT GGGCTCTCACTCTCATTCCACTCTCCTTACATGGGAGCCTTCCTGCC AGAATTTCCCTGGAAGGAGATTCTCTA
184	632327_26682384_Target8.1_1	CTCCTCTCCCCACAGGCCTGTGTGGCCCAGCCATGCGCTCTCCCAC TTGGGTCCCTGCCCTGGCCGCGGCCTGGGCTACCCACCCAGGTAGC CAAAGGAATCTTTTTTTGTTTTGTTTTG
185	632327_26682384_Target8.1_2	GTGTTAGTTATTACTCTCAACATCTCTTCAAACCACCTTTATGCTTGCC TCTCTCAGACTCCTCTTCCTCCTCTCCCCACAGGCCTGTGTGGCCCA GCCATGCGCTCTCCCACTTGGGTC
186	632327_26682384_Target8.1_3	GAGAGGCAAGCATAAAGGTGGTTTGAAGAGATGTTGAGAGTAATAAC TAACACTTGTTATCTCATTCAATCTTCACAAGATGCAATGAAGAAGTG GGCTTTTTTTTTTTTTGAGACAGAG
187	632327_26682385_Target8.2_1	AAATTCACCTATTATTCCAGCTTCTCTCTTCCAAATACGGCCTCTGTG CCCTGTTTCTTCCCCCAGGAGGAGATGAACGGCTGGCTGGAGGCTG TAGCTTCCTCGGTGGCGGAACACGCA
188	632327_26682385_Target8.2_2	GGGGTGGGAAGTCACTTCCTGCGCCCGCTGGCCCTGCGATCTCCGC CTTCCCTCTTAGGGTTGCCCTCATCTGTGGATGAAGTAGTGGGTAGT GTCTGGCCCCAGCGGGCGATCTCTGCG
189	632327_26682385_Target8.2_3	CCCACCATGTCACGCGTCCTCAGTGTTGGAACTAGGGGCTCCCGCC CCTGCGGAAGAAAAAGTGTCTTTGTGCCCACAGTGCGGAAAAGAGG GGAGACGAGATGTGTCAGGTCCTGGGGGG
190	632327_26682385_Target8.2_4	GACCCCCAGCACCTGGGGTGGGGGTGGTGAGTGGGAAGGGGCCGA GATATGGCTATAGGGGCAGCAATCTCCCCACCACTTCTTGGGGTGCA GGAGAAGTCCCCTCCTTTCCGGTGCCCA
191	632327_26682385_Target8.2_5	TACTGCCCCCACCACCCCAGCTTCTTGGGGCAGGATCTGCAGATCG GGGCTGGGGGCTTGGCTCAACTGGCCCCCTGCCCACCCCCATCAAG CTCAGTTATTGCATAAAAATAAGGGACC
192	632327_26682385_Target8.2_6	GTGAGGTAAAGGCGGGGAGGGGGTGTCCCCTCCCTGCCCCCTAGC ACCCTGGATGGTCCAGGGGACCTCACCAGCGCCCCCGTGCCCATCC CTAGGGCAGAGAGGGGGGCAGGAATTACT
193	632327_26682385_Target8.2_7	TTTTGCAAAAATAAACTAAGTCAGGAATTAACCGCATGGCTCTGAGGC GGCGGAGTGCAGGGGGCTAGGGCCCCTTCACTCCCCCCTCCCAGA CAGAGATCAAGGCAGCATTGGAAGTGA

194	632327_26682385_Target8.2_8	CATGAAGTGGCATTTACAACTGGAGGGGGGAGGAGAGAGGAAAACAGTTTTGAGCTTTGACGCCCCTCCCATTAAAAGCCTTCGCGGATGCGGGGCGGGGGAGGAGGAGATCGACGTTTT
195	632327_26682385_Target8.2_9	CCCCAGCGGCTTCTCCAGGCGGCCATGGGGACTGCCCACAACCCAATCCCCCGACTCCCCAGGGAGGTGCTCCAGCCAGAAGCATGCAGGGGTGGGCTTCCCCTCGCCCCTCCCCTCATG
196	632327_26682385_Target8.2_10	AATCCTCCCGGGCGCAGCCCAGAAAACCCAAACAAAGGACCATAGACCGTCAAAGCCAAAGGGTTTATTATAGGTACATACAGTGTGCGCCCGCCACACCGCCCCACACCCCCGGGCCCC
197	632327_26682385_Target8.2_11	CCCCGAAATTAAGTCCACATAAAAGGGTACATCTGGATGTTCTCCGCAGCCACGGTACCCCCGTGCCCCTCTCCCCACCCCGCACCCACCCCTACAGCCACCACAGCCCTCCTTTCAATC
198	632327_26682385_Target8.2_12	CGCCTTTCCTGAACTTGACGGGGCGGACCCGGAGTCTCCTTTGGGGAAGTTTATTACGAAGCATAACGAAATATTCTCCATCCCTCTAGGTTCTCGTCAAGGGGCGTGTGTTTAGACCCC
199	632327_26682385_Target8.2_13	GCACCCGGACCCCGCCTCCATAGGCTGCTCATTGGGCCAGAGACTCCAGGAGTCACTAGCGATTGGACAGAGCGCCTGCCCATCGCGGTTAACTTTTCCGCCTCCTTAAAGGGGTCCGCC
200	632327_26682385_Target8.2_14	CATTCAGATGAATGACTTCCCCGGGAGGCCCCCGACTGGGGACCCCCTCGGCTGCAGTAGCCGCTGCTGCCATGGCCCCCGGGCGAGCCGGCTGGCCCGCACCCACTTCCGGGTGTGCAC
201	632327_26682385_Target8.2_15	GCGGAGCAACCCTTGATGGACAGGGATTCCCCCAGGAGAGGCGGATACTCCCACCCCGCTTCCCGCCCCCGAGGATGGGACCTCAGGAGTCTCCCACACTCACCTCTTGCCTCCCACATT
202	632327_26682385_Target8.2_16	AGAGATGAAGAGGAGCGGGTGAGGAATGCGTCCCCCTCCCGCAGGATCCAGGGTTCCCTCCCCTTCCCCCTCCCCCGGCGTTTTTCCAGAATCTCGCGCCTCCAAAGGGGGGGGGGGCGG
203	632327_26682385_Target8.2_17	CTCCTACCCTCGCCCCAAACTCGCTCTCCCGATCACCTGGAGAAGAAGGAGTCTGGGATCCAGGTGAGAGTCTGGCGAGAGGTACTGAATCTGGGCGGGGAAGGTAAACGGACGCAAGAG
204	632327_26682385_Target8.2_18	GGAGGGATGGAGAGGGCGTGGGAGACCTAATATCCACTCCCCCGGCCCGTGACGCCTGCTCGGTGTCCCTTCCCTGCAGTCTTCTGAGCGGACCGCATCTCGACGCTGAAAGATGAGACCG
205	632327_26682385_Target8.2_19	GGGAAAGGGGGGCAGAGGATGGATGGGGTAAAAGGCAGGACTGAGTGGGGTCCTGCCCCTCTTCCTACCAACCCCTCCCCCCCATCCCATTTCAGTTCTTGTCCGACTCACTGCTCCGGT
206	632327_26682385_Target8.2_20	AGACAGTGAGGGACTCCCTCCCCTTTTTCCATGCCAACCTGGGATCCAACTCTTTGGTGCGCAGGAAGTTGAGGATGGGGGCGAAGACTGTAGGGTCCCTGTCGATGAAGATCTGCGGGA
207	632327_26682385_Target8.2_21	GTCTTCAGTCCCTGAGGAGTTCTTTCACCTCCTCTGAATGTCCACGTGAGCTCCATTCTATTAGAATTCTCATTCAGAACCTTGATCACAGGCCGGGCGCGCCGGGATTGCT
208	632327_26682386_Target8.3_1	ACACACACACACACACACACTCAACATTTCCTCCACCCATATCATCACTCCTTAGCATCTTTATTCCATCAAAACTTTCTACCCCTTGACATTCTCTGTGCAGTTTTGAAAATTACCCTC
209	632327_26682386_Target8.3_2	GAGTGAGCCCATAGAACTGGGCTTCATGGAGGAGGCTGGAACCGTGGACACCCCTGGGTAGTAGAATTGACTAGAGGTCAGGGTCTAGGTGTGGGGGTGAACAGAGAATGCTGAGAGGGT
210	632327_26682386_Target8.3_3	CCACCTCTACCCCAGCCCTCTTTCAGGAGAGAAGGGGAAGAGGGGCAGGTAGCATCACAGAGTTGGTTTTCTATACAATGAGGATGATAGCTGGGGGCTCCCACTTACCCAGAGGAGTGA

211	632327_26682386_Target8.3_4	ACTTAGGGAGATGCTGAGGCCACCCCATTTCCCCCTCCCCATTTCTTTCTACACAGAGTACCAATACTCCTCCCAGTACGAATACAGACCCGGCCAGGGCCATAACCAGTCCTCCCACCT
212	632327_26682386_Target8.3_5	CTAAGTCCCAGCCTTTAAGTCCTCCTGTTGCAGTTCGTCGCCTGCAGCTTCGAGAGGAGTTGGATCGATCTTCTTGTGGAAACGTCCTCTTCAATGGTTACCTGCCGCCACCAGGTAGGC
213	632327_26682386_Target8.3_6	GAACTACACCTCCCACTGTATCTCAGGACGCACAGCACAGGCACCCGAGAGCTGCAGCCTTATGGGAAATGTAGTCTTTGGCCCACCTCCGCGCCCCTCCATTCCATTGGGAGTGCCTAC
214	632327_26682386_Target8.3_7	TAGTTCCCTATCAGATGCTTGGGCTGATGCTTGGAAAGGAAGTTGGACACAGCATTTCCCATGAGACAATGGGCCAGCTAACTCTTGAGGCTCAGAAGGATGTCCTGGAGCCCCATGGGA
215	632327_26682386_Target8.3_8	GGCTATCATGGGCATTACTGTCAATAACTTCCTATTAATATTTCTCCCCTCCATACGAAGAATCCCAGGTCTTCCAAAGCCCCCCCTACAAAGAAACCAAACCCGGACTACAACTCCCAT
216	632327_26682386_Target8.3_9	ATAGCCAGCCCACTGGCCATGGAAGGTATGCCCCAGTGGTTATTGGAACTAGGCTTTTCTGATTGGTAGAAGTAACAGAGTAGGGAAATTTCATCTACAGCTTTATTTCCCTAACTGCAG
217	632327_26682386_Target8.3_10	CTGCAGTCAGCACCTGCTACCTTCATGAAAGTTGCCAGATATAAAGATCTGTAGTAGTACTTTTCCAACTTAGTTTTATCCTGTTTTCCGAAAAACAATCATTTATTTATTTATTTATTT
218	632327_26682387_Target5.1_1	CATTATATACAACCCAAGGCTTGCCACAAACTGAAATTTCTTATGCATTGACATTCAGCATTTGATGTAAAATGACAATCTTAGAGTCGCTGCCACAAACCCTGGTAAAACTGCCCCTGC
219	632327_26682387_Target5.1_2	CTTCTCCAGTTCACTAAGTTCAGCTACTCCTTCAGGGCTTGTGCTCCTTTAAAACTTTTCAGAAGCCCCTTGAAGTACCAACATGTTGAAACTCAAACTCAACTGCCTGCAGCTTCAGAT
220	632327_26682387_Target5.1_3	CAGCTCTGGCCACTGAGAATTCTTCTCCAGGCCCCAGTGTCAAAGGCACTTTTGACCATCATGTGTTTGTCTGACTACCAAGTTGGACTGCCAACCTTCACTAAAAACTCCGGCACCTTT
221	632327_26682387_Target5.1_4	ATCTACCTCCTGTCAGATCACCGCCTGTCAGAGAGGGAGGCCTAAAAAGGCTTCAGGATATCAACAGCTTTGAGCTGCCTTAGAGGAACTTCTTTTCTATTTTGTAGTACAGGAGCCTCA
222	632327_26682387_Target5.1_5	TGCACTGCATCATCCAAACAAGACTCTCCACAAAACATTACTAATGGATTCTAATTGAACAGAGTTTGGTTACAAGAGACAGTAAACACAAATGGGCACCTGTTTTAAATGGCAAACTTA
223	632327_26682387_Target5.1_6	CACAATAAATTCAATTGATCTTAAAAACTAAACATTCCTCTAAGGTTACTGACTATAAATATCTAGAAATTACTACTCCTATAGTCTTGCTATTTCCAGACAAGTGAAACTGGAAGGGAG
224	632327_26682387_Target5.1_7	AGAGGAGAAATACCCAGTTATAATGACAAGACAACCTTATCTTTTCTCAAAAGCCTCCCCAAACACACAACCATTTTCCACAAAACAGTTACATCAAAAAAGATGTAGCAAGACCTAGAC
225	632327_26682387_Target5.1_8	ATTAAGCATGCTAGAAAGTAGGGACAGTTTTACCAGTGTTTGTGGCAGCAACTCTGAGATAGTCATTTTACATCAAATGCTAAATGTCAATGCATAAGAAATTTCAGTTTGTGGTAAGCC
226	632327_26682387_Target5.1_9	CTGGGTTATATATAATGGCAACAAGAGAAAACTATCACATAATCTGAATTACGTTCATTTTTCTGCATACACCATGCATGCTGGTACACTTTCAGTTAGCCTAAACTTCACCCAAAAGTA
227	632327_26682387_Target5.1_10	GAGGTGGCTATGAAAACTCTACCTGCATGGTATAAATAGATACCTAACCCTACATGCATGGGTCACTTGTATCTACCTCCTAAATACCAAAAACTTAGAAGCCCAGATTTCTTTTCAGTC

228	632327_26682387_Target5.1_11	AAAAACAAAACAAAACAAAAAATTACCCTTCCCCACAATTATAAGCATTTTGGCATATTTCCTTCCTGTCTCTGTTGTTCCTATTTTGGCAGTATTTTTATTGTTATCGCAGGCAGCCT
229	632327_26682388_Target5.2_1	GCCGCACACCTTATACCTCTCCCCTTTAAAACAGACATATTAAAGACTTCTGTTTTCTGAATTTACTGTAAACAGAATACTTAAAAAAAAATTACCCAGACAGGCGTGGTGGCTCACTGT
230	632327_26682388_Target5.2_2	TGAACAAACTGCATTAGACTAAAATCTTTCACGAGTCCAAATTCTGCGACTAGAAAAATAAACTTGTTAGCCGCACACCTTATACCTCTCCCCTTTAAAACAGACATATTAAAGACTTCT
231	632327_26682388_Target5.2_3	ACTTACTTTCTTGTTCTGACTCAACTCGGAAAACACCTCCCTAGTCTGAGGCCCCCCTCCTTATATTTGTGAACAAACTGCATTAGACTAAAATCTTTCACGAGTCCAAATTCTGCGACT
232	632327_26682389_Target5.3_1	TTTCCACTATATCACACTGCACTGTCTGGCTCCAATCTGATGGCGAGCAATGGTTCCTTAAAAAGCTCCATCTTCTCAAGCCTACCCAGCACAGACCTACAACTCAAACTTTAAGTTTTA
233	632327_26682389_Target5.3_2	AGCCAGCCTAACCTTCCACGTCCACTTGAAAAAAGAAAAAAAAGAAAGAAACAATCAACCGGAAGCCTTTGATTTTTTTGCTAGCAAGAAGCCAATAATTGTTTTCTTTGGGACAATCAC
234	632327_26682389_Target5.3_3	CAGGTTAAGTTGTGAAATGGGTGGCAGAAACTGCAAGATTTAACCAGTTTCTCTCAACGCTAATCAAAGGTCAAGAAAATAAAAGACAGGGCAGTGAGAGTCGCGGGACTTTAGACACTC
235	632327_26682389_Target5.3_4	AGTGTGGAAACCCCTTCCCCACTCAGTCCAATTTCAAGGTTATGGAGCATAATTAAGAGTGACCATTCTAAAAGCGTTCTCTAGTGCCCTGGCTAAGACTTTTAAGCTTCTTGGTGCAGG
236	632327_26682389_Target5.3_5	AGAAGCAAAGATGATGTCTGTCACCTGGCAGCGTAGACGGAGAGTGGCGGTAGATGACTTGAATGGACACGTGGATTCGAGTCTGGGGACAGGCGTTCCCCCAGTCGGTGCGTTGTGAGA
237	632327_26682389_Target5.3_6	TCAATTTCAAAAAATGCCAGCACTCCTTAGATCAATGACTCCACGGCCAAGTGCAAGGGCCACGGGCACTCCTCTGGAGTCACCGAGAGAATGTCTGCCTCTGGCAGCGGCCTCTGAGCT
238	632327_26682389_Target5.3_7	GGCCCCCGCCTGCCCAGAGGCCGGGCTCGCGGGCGTTCGGACCGCGCGTGGGGCGAGACTGCACTCGCGCCCGCTGAGATGCCGGCCCCACCGCAGCGCGGCGGCACGAGGCCCACAGGCA
239	632327_26682389_Target5.3_8	CGCGGACGAGGGCAACGTCAGCGGCCCAGCTGGGCCACCTCCTCCCAGCCGAAGCGCGGCCTCCGGCTGCTTCGCCGGGCCGGTCCCCGCCGCCGCACACACAAGGGTCGGTCCCGCGCG
240	632327_26682389_Target5.3_9	CTGCCCGCGGCCCCGCTTCCCTCGGCAGCCGGAGGCCTCCGGGGTGCCCGTGCTGCCGCAGCTTCCTGTGTCTGAGTCGCGGGCGGCGCGGGCGCGGGGCTGGTGCGCGGCCGGGGATGC
241	632327_26682389_Target5.3_10	GGGCCCCGGCCGAGGCGCCGGCTGACGTTGCCCTTCAGGGCCGAGCCCGGAGCAGCGCCCGCCGCGGAGGCGCGTGAGCCACCCCAGGCTCGTGGGGCCGCGCCGCCTTTCCGGCCTCC
242	632327_26682390_Target5.4_1	GCCGCGGGAGCAGGCGCGGCTCCGCACGGCGGGCGCACTCACCTCCTCCGTGGACCGGCCGCTCCGCCGCCGGCTGTCACTGCAGCCCACTCCCTGCCCCGCGCCGGCTCTGGATGCTAT
243	632327_26682390_Target5.4_2	TCTGGATGCTATTTAAGGCGCCGCTGGCGCCGCCGCCTCGGCCCGCTGGTTGCGCCCCCGCCACCGCCGCGGCTGAGCCAGGATGCTGCTGGTGCGCTCGCCGCGCCGGCCCCGCCCTCC
244	632327_26682391_Target5.5_1	CGCCGAGCGCCCGGCCGCCCTCCTGTCTGGGCGCGCGTGGCTGGCGGGTGGCCGGCGGTCGAGAGGCTGCGGCGGGCGAACGCCGCTGGAGTCGCCCAGACTGCCTCGGATTTCATAATG

245	632327_26682391_Target5.5_2	CAGGATCCGGAGGGCGCCGCCCGCCCCTCGGGCATCGCGGGGCCCAGGGTCCGCGGGGCCTCTGAGCTGAGGCGGTCCAATGTACCCTTTGTCCTTCCTCAGATTCATTATGAAATCCGA
246	632327_26682391_Target5.5_3	GCCCTCCGGATCCTGCACCCTCAGCCCGTGCCCCGCTGGCCTCCTGGCAGGCCGGGCAGAATTCTGCTGCGAGGGCCCTGGAGGCAAGGGCCTTCCTCTCCGTTTTTCCTTGACACTGAC
247	632327_26682391_Target5.5_4	TTCCTTGACACTGACGGGCGCGGCCCCACAGGGTTTCCCCCACGCTCCCTGGCCGGAAGACCTTTTCTGTCTGGTGTCTGCAGAGCCTGACGTGGGCAGCGCCCGCAGCTCGCGCCGGTG
248	632327_26682391_Target5.5_5	TGGGCATGGCAGGGACGCGGAAGCCCTCAGAACCGCGGAAGCCCTCAGAACCGCACAGCAGGTGGCCGCCGTGGTGCAGCGCGCAGTCGGCCCTCAGCTCCCCTGCACCGGCGCGAGCTG
249	632327_26682391_Target5.5_6	GTTGTTAGAGGTTGAGGTTCCTGGTAGGTCCCAGGTGCTAAAAGGAAGAGCAGCCTTTGGGATGTGAGCCCGAAAACCATCGTGTTGGCTTCTGAAGCCCCAAGATGGGCATGGCAGGGA
250	632327_26682391_Target5.5_7	TCAACCTCTAACAACATTGGTCCCCGTTACCGTGGAGTTTGCGCCCAGCGTTCGCTGGAGGGCCGTTTGAAGAATGATTGTTGTCGTAAAGGCCTTTGATAATAATAGATACTGTTTACC
251	632327_26682392_Target5.6_1	GTCAGTTTCCCCTGCCTGCAGCCCAGGCATAGCCCTGCGTTGGTTGTGCCCACACTCTGGGGGCAGCCTGAGTGCCAAGTGTGGTACTGCTCTCACTAGCATTTAACCTCTGTGCCCCAG
252	632327_26682392_Target5.6_2	TGCGCCCAGCACACTGTGGGAGACACCCAGGGAAAGTCCTTCAGTTATTTGTGGGAGTGAACTGCAGTGTGGCTGAGGCCTGGAGCGAACCACGGTCAGTTTCCCCTGCCTGCAGCCCAG
253	632327_26682392_Target5.6_3	CCATTTTTTCTAGATCTGGAAGATGGAGATCTAAAAGGACTGAGCTGCTAGAGAGGTTGCTGGTGTGTGCGTTGTCCTCACCCCACTGCACCACTGCGCCCAGCACACTGTGGGAGACAC
254	632327_26682392_Target5.6_4	CCATCTTCCAGATCTAGAAAAAATGGACTCCACGTTCGTTTTCACTGGTTCCCGCTTGGCTAATCCCTGGTTTTTCTGTCCAGATCTCGCCTCCCCATCCGTGATTTTGTCATCTTTGCC
255	632327_26682392_Target5.6_5	CCATCCGTGATTTTGTCATCTTTGCCTCTCCTTTTTCCTCTTCTCCAACCGGTCCCTCAGCCCCAGAACCTCTGCAGGCACCTCCCAAGTTCTGTGGTCTATTGTTTTCAAGGGCTGCTG
256	632327_26682393_Target5.7_1	TGACAATTCAACCCGTAACATGTGGATGGTCGTCACTGGCTGTCTCACCTTACGTCTTCTCCTCAAGACACTTTTCTTTTAAACTGGGTGCCTCTCCCTGGGCTCTAGCCCTTAATGAGG
257	632327_26682393_Target5.7_2	AAGACACTTTTCTTTTAAACTGGGTGCCTCTCCCTGGGCTCTAGCCCTTAATGAGGTGATTTCCAACTCAAGGCTGGGAAAGGCACACAACCCAGTATCAGACCTGAGTTCACACTCCTT
258	632327_26682394_Target5.8_1	CCCATACATTGTAAAACTTTTTGGAGTGATTAGATAAAAACTTTTTTGTTTTTTTTAAGTGTGTGTGCTGAAAGAGACCTAAGAGATTATTTAGCCAAGCCCCCTTATAGCCTGAGGAG
259	632327_26682394_Target5.8_2	TCTTAACCACTATGCAATACTGCCTCCCATCAAAGTCTCTATCTCAAGTCCACAAGACAACCCCATACATTGTAAAACTTTTTGGAGTGATTAGATAAAAACTTTTTTGTTTTTTTTTAA
260	632327_26682395_Target5.9_1	GACAGGTGTCATAGGATTGACAGCCACGCCCTTGGCGTTCTCATTAAATGAAGATTCCAGACTCTATAGTTGGGAGTTTGTGACTTAGGTAAGAAACCAGTCTCTTTTTTTGAGACGGAG
261	632327_26682395_Target5.9_2	TGTCATAGGATTGACAGCCACGCCCTTGGCGTTCTCATTAAATGAAGATTCCAGACTCTATAGTTGGGAGTTTGTGACTTAGGTAAGAAACCAGTCTCTTTTTTTTGAGACGGAGTCTCAC

262	patch	CTCTGTCGCCCAGGCTGGAGTGCAGTGGCACAATCTCTGCTCACTG CAAGCTCCGCCTCCCGGGTTCACGCCATTCTCCTGCCTCAGCCTCCC GAGTAGCTGGGACTACAGGCGCCCGCT
263	patch	GCCCGCCTCGGCCTCCCAAAGTGCTGGGATTACAGGCGTGAGCCAC CGCGCCCGGCCCACAGCTCTAGTTCTTTAATACACATCAGGTCGGTC ATGGTGGCTCATGCCTGTGATCCCAGC
264	patch	TTGCTATGTTGCCCTGGCTGGTCTTGAACTGCCAGCCTTCAGGGACG CTCCTGCCTTGACCTCCCCAAATGCTGGGATCACAGGCATGAGCCAC CATGACCGACCTGATGTGTATTAAAG
265	patch	GAGCGTCCCTGAAGGCTGGCAGTTCAAGACCAGCCAGGGCAACATA GCAAGACCCCATTTCTACAAAAAATTAAACAGCCAACCAAAAAAAAAA AAAAAAAGAAAGAAAAACTTTAGCTG
266	patch	CCTGGGCTCAAGCAATTCTCCTGCCTCAACCCCCCAAGTAGCTGGGA CCACAGGCATGCTCCACCATGTCCAGCTAAAGTTTTTCTTTCTTTTTTT TTTTTTTTTTGGTTGGCTGTTTAA
267	patch	GACAGGGTCTGGCTGTGTCACCCAGGCTGGAGTGCAGTGGTGTAAT CATGGCTCACTGCAGCCTCGACCTCCTGGGCTCAAGCAATTCTCCTG CCTCAACCCCCCAAGTAGCTGGGACCA
268	patch	CATGATTACACCACTGCACTCCAGCCTGGGTGACACAGCCAGACCCT GTCTCAAAAAATATATATGTATATTTTAAAATATTATATATTATATAATG TAAATAATATACATGCTACATAT
269	patch	TTTTAAAATATTATATATTATATAATGTAAATAATATACATGCTACATAT TTTATGTATACATCTATGTTATATACATTAATATAGCCAGGTGCAGTGG CTCACACCTGTGTTCCCAGCA
270	patch	ATATACATTAATATAGCCAGGTGCAGTGGCTCACACCTGTGTTCCCA GCACTTTGGCGGGATTACGGGCGGGTCACCTGAGGTCAGGAGTTCG AGACCAGCCTGGCCAATATAGTGAAAC
271	patch	GGTCACCTGAGGTCAGGAGTTCGAGACCAGCCTGGCCAATATAGTG AAACCCCGTCTTTACTAAAAATACAAAAAAAAAAAAAAATTAGCCAGG CGTGGTGGTGGGCGTCTATAATCCCA
272	patch	AAAAAAAAAAAAAAATTAGCCAGGCGTGGTGGTGGGCGTCTATAATC CCAGCTATACAGGAGGCTGAGGCAGGAGAATTGTTTGAACCCGGGA GGCGGAGATTGCAGTGAGCTGAGATCG
273	patch	TTCCCCTTTGGATTTTTTTTTTTTTTTTGAGACAGAGTCTCGCTCTGTCA CCAGGCTGGAGAGCAGTGGTGCGATCTCAGCTCACTGCAATCTCCG CCTCCCGGGTTCAAACAATTCTCCT
274	patch	GTGCTGATGGTAATAACCTTGACCACGTGGTCAGGGCATCTGCCGGT TCCTGCACTGTCCAGTTACTGTTTTCCCCTTTGGATTTTTTTTTTTTTTT GAGACAGAGTCTCGCTCTGTCAC
275	patch	GGGAGTCCCGGGCGTGGCGTGTGTCTGTCTCAGGCCCCCCACGTC GAAGCCCATGGCTTCGGCCTGTCTCGTGCTGATGGTAATAACCTTGA CCACGTGGTCAGGGCATCTGCCGGTTCC
276	patch	ACTCAATGGAGGGAGTCCCGGGCGTGGCGTGTGTCTGTCTCAGGCC CCCCACGTCGAAGCCCATGGCTTCGGCCTGTCTCGTGCTGATGGTA ATAACCTTGACCACGTGGTCAGGGCATC
277	patch	CCTCTAACCCTGGGGTGATTCTGCCCCCAGGGGTCCCTGTGTGAGG CCTGGAGACATCCGTGGTTGTCACGACTTGGAGGGAGCTCCTGGCA GGGCCCTGCAGTGCCCAGGATGGCCCCG
278	patch	CTCAGAGTCTCTTGGGGTCTGTGGAATCCTCTAACCCTGGGGTGATT CTGCCCCCAGGGGTCCCTGTGTGAGGCCTGGAGACATCCGTGGTTG TCACGACTTGGAGGGAGCTCCTGGCAG

279	patch	AGGGAGCCAAGATCGTGCCACTGCACTCCAGCCTGGGCAACAGAGC AAGACTCCATCTCAAAACATAAATAAATAAAAATAAAAAATAAAAAATC CAGTCTGCCCCCTGCTCACACCGGA
280	patch	TCTTGCTCTGTTGCCCAGGCTGGAGTGCAGTGGCACGATCTTGGCTC CCTGCAACCTTCGCCTCCCAGGCTCAAGTGATTCTCCTGCCTCAGCC TCCTGAGTAGCTGGGACTACAGGCGC
281	patch	ACCAGCCTGGCCAACATAGTGAAACCCCATCTCTACTAAAAATACAAA AATTAGCTGCGCGTGTTGGCGGGCGCCTGTAGTCCCAGCTACTCAG GAGGCTGAGGCAGGAGAATCACTTGA
282	patch	GCCTCACACCTGTAATCCCAGCACTTTGGGAGGCCGAGGCGGGTGG ATCGCCTGAGGTCAGGAGTTCAAGACCAGCCTGGCCAACATAGTGAA ACCCCATCTCTACTAAAAATACAAAAA
283	patch	CGATCCACCCGCCTCGGCCTCCCAAAGTGCTGGGATTACAGGTGTG AGGCACCGCACCTGGCCATTTTTTTCCCCAAATAATGAACACTGGTCT CTCCCCTGGGCCCTGTGGACATCGGG
284	patch	GTGGAGGCCAAGGATGATGCCTAGCACCCTGCAGTGCCCAGGACGG GCCTGCCCCAGAGAAGGATCCAGCCCCGATGTCCACAGGGCCCAGG GGAGAGACCAGTGTTCATTATTTGGGGA
285	patch	AGGCCCGTCCTGGGCACTGCAGGGTGCTAGGCATCATCCTTGGCCT CCACCCACTCCATGCCAGGAGCTCCCCTTTCGTGACAGCCACAGGT GTCCTCAGACCTCGCCCAGGGTCCCCTG
286	patch	TGGGGGTTTTCTTCCCCCTTTAAGGCCAGGATTCTCAATCAAGAGGT GATTCTGCCCCCAGCGGACCCTGGGCGAGGTCTGAGGACACCTGTG GCTGTCACGAAAGGGGAGCTCCTGGCA
287	patch	GAATTCGCCTGTTACTAGCTAATTCCCAAAACAGCTCCTCAGGAGGG AAGGGCTGGGTTTTGCCCGTTTTACAGATAGGCAACTGAGTCAAATG GCCAGGGCTCCCCCTTGCCCTTGTCC
288	patch	CTTCCCTCCTGAGGAGCTGTTTTGGGAATTAGCTAGTAACAGGCGAA TTCCTGGACAGCACCCAGCCTTCAGCAAATGCTCAGTGAATATGCAT GAATGAATGAATGAGTGAATGAATGA
289	patch	CCCCTCAGGTCCCTATCCTGAGGGTGATTTTCTTTTTCTTTTTCTTTTT TTTTTTTTTGAGACGGAGTCTCGCCCTGTCGCCCAGGCTGGAGTGCA GTGGCGCGATCTCGGCTCACTGCA
290	patch	CGCCCTGTCGCCCAGGCTGGAGTGCAGTGGCGCGATCTCGGCTCAC TGCAAGCTCAGCCTCCCGGGTTCACGCCTTTCTCCTGCCTCAGCCTC CCGAGTAGCTGGGACTACAGGCGCCCA
291	patch	AGACCATCCTGGCTAACACCTTGAAACCCCGTCTCTACAAAAATTACA AAAAATTATCCAGGCATGGTGGTGGGCGCCTGTAGTCCCAGCTACTC GGGAGGCTGAGGCAGGAGAAAGGCG
292	patch	CGGTGGCTCACGCCTGTAATCCCAGCACTTTGGGAGGCTGAGGCAG GCGGATCACGAAGTCAGGAGATCGAGACCATCCTGGCTAACACCTT GAAACCCCGTCTCTACAAAAATTACAAA
293	patch	CCGCCTGCCTCAGCCTCCCAAAGTGCTGGGATTACAGGCGTGAGCC ACCGCGCCTGGCCCTTTTTTTTTCTTTTTTGAAACGGAATCTTGCTCT GTCGCCCAGGCTGGAGTGCAGTGGTG
294	patch	GCTACTCAAGAGGCGGAGGCAGGAGAATCATTTGACCCCAGGAGGC TGAGGCTGCAGTAAACTGAGATTGCACCACTGCACTCCAGCCTGGG CGACAGAGCAAGATTCCGTTTCAAAAAA
295	patch	GTGGTGAAACCCCATCTCTACTAAAAATACAAAAACTAGCCAGGTGT GGTGGTGTGTGCTTGTAATCCCAGCTACTCAAGAGGCGGAGGCAGG AGAATCATTTGACCCCAGGAGGCTGAG

296	patch	TTTGCAGATGAACAAACTGAGGCATTGAAAATCCCCCTCAGGTCAGG AGTTCGAGACCAGCCTGACCAACGTGGTGAAACCCCATCTCTACTAA AAATACAAAAACTAGCCAGGTGTGGT
297	patch	AACAAAACAAAACAAAATAAAAAAAAAGAAGCAAAAAAAAAAAAAAAA ATCAGCCAACAAAGAGACCCATTTTGCAGATGAACAAACTGAGGCAT TGAAAATCCCCCTCAGGTCAGGAGT
298	patch	AAAAAAAAAAAAAAAAAAAAAAAATCCTGGGCGCAGTGGCTCATGCCT GAGTGAGACCCCATCTCAAAAAAACAAAACAAAACAAAATAAAAAAAA AGAAGCAAAAAAAAAAAAAAAAAT
299	patch	TCAGGCATGAGCCACTGCGCCCAGGATTTTTTTTTTTTTTTTTTTTT TGAGACAGAATCTCACTCTGTTGCCCAGGCTGGAGTGCAGTGGTGTG ATCTCGGCTCACTGCAACCTGTGC
300	patch	TGCCCAGGCTGGAGTGCAGTGGTGTGATCTCGGCTCACTGCAACCT GTGCCTCCTGGGTTCAAGCGATTCTCCTGCCTCAGCCTCCCAGGCA GCTGAGATTACAGGTGCGAACCACCACA
301	patch	TCCTGCCTCAGCCTCCCAGGCAGCTGAGATTACAGGTGCGAACCAC CACACCTGGCTAATTTTTTTTTTTTTTTTTTTGAGACGGAGTGTCATT CTGTTGCCAGGCTGGAGTGCAGTGG
302	patch	TACTCCGGAGGTTGACGCAGGAGAATCGCTTGAACCCAGGAAGCGG AGGTTGTGGTGAGCCAAGATCGCCCCACTGCACTCCAGCCTGGCAA CAGAATGACACTCCGTCTCAAAAAAAAA
303	patch	ACCTCCGCTTCCTGGGTTCAAGCGATTCTCCTGCGTCAACCTCCGGA GTAGCTGGGACTACAGGCACGTGCCACCACGCCCAGCTAATGTTTGT ATTTTTAGTAGAGACAGGGTTTCACC
304	patch	CCACCACGCCCAGCTAATGTTTGTATTTTTAGTAGAGACAGGGTTTCA CCATGTTGGCCAGGATGGTCTCCATCTCTTGACCTCAGGTGATCCAC CCACCTCGGCCTCCCAAAGTATTGG
305	patch	CATCTCTTGACCTCAGGTGATCCACCCACCTCGGCCTCCCAAAGTAT TGGGATTACAGGCGTGGGCCAACCGCACCCGACCAATTTTTCTGCTT CTTTAAAAACATTTTTTTAAATTTTG
306	patch	CGCACCCGACCAATTTTTCTGCTTCTTTAAAAACATTTTTTTAAATTTT GTTTTAGAGACAGGGTCTTGCTCTGTTGCCCAGGCTGGAGTGCAGTG GTGTGATCTCAGTTCACTGCAGCC
307	patch	TCTGTTGCCCAGGCTGGAGTGCAGTGGTGTGATCTCAGTTCACTGCA GCCTTGACCTCCTGGGCTCAAGCGATCCTCCCTCCTCAGCCTCCCAA GTAGCTGGGACGACAGGTGCACACCA
308	patch	TCAAGACCAGCCTGGGCAAAATTGTGAGGACCCCATCTCTACAAAAA ATTTTAAAATTAGCCAGGCATGGTGGTGTGCACCTGTCGTCCCAGCT ACTTGGGAGGCTGAGGAGGGAGGATC
309	patch	GCAGTGGCTCACGCCTGTAATCCCAACACTTTGGGAGGCCGAGGCA GGAGGCTCCCTTGAGCTCAGGAGTTCAAGACCAGCCTGGGCAAAAT TGTGAGGACCCCATCTCTACAAAAAATT
310	patch	AGGCTGGTCTTGAACTCCTGAGCTCAAGGGAGCCTCCTGCCTCGGC CTCCCAAAGTGTTGGGATTACAGGCGTGAGCCACTGCACCCAGCCA CCTGGTCTGCGTCTTAAAAGCCTTCCTG
311	patch	GAGGTGGAATCACTTGAGCCTGCAGTGAGCTGAGATTGTGTCACTGC ATTACAGCCTGGGCAACAGAGGGAGACCCTCTCAAAAAAATAAAAGG CACGCACGCCCCCAAACCTGAAATGA
312	patch	AATGCAGTGACACAATCTCAGCTCACTGCAGGCTCAAGTGATTCCAC CTCAGCCTCCCGAGTTGCCTGGATTATAGGCACACACCATCATGCCT GGCTAATTTTTGGGTTTTTGTTTTTT

313	patch	TGAGCAACATATTGAGACCTCATCTCTACCAAAAACAACAAAAACAAC AAAAAAAACCCCTAAAAAACACAAAAAACAAAAACCCAAAAATTAGCC AGGCATGATGGTGTGTGCCTATAA
314	patch	TTGTTGTTTTTGTTGTTTTTGGTAGAGATGAGGTCTCAATATGTTGCTC AGGCTGTTCTCCAACTTCTGGGCTCAAGCCATCCTCCTGCCTCCCAA AGTGCTGGGATTACAGATATGAAC
315	patch	CAACCCCAAGAATAGAAAAGGCACTCACTGGCCAGTCGAAGTGGTTC ATATCTGTAATCCCAGCACTTTGGGAGGCAGGAGGATGGCTTGAGCC CAGAAGTTGGAGAACAGCCTGAGCAA
316	patch	GCTCTGAAGGAAAAGCAGGCCAAGTGGGTTTCTTCCTTTTTTTTTTTT TTTGAGATAGAATCTCTTGCTCTGTCACCCGGGCTGGAGTGCAATGG CACAATCTTGGCTCACTGCAATCTC
317	patch	TGTCACCCGGGCTGGAGTGCAATGGCACAATCTTGGCTCACTGCAAT CTCCGCCTCCCGAGTTCAAGCAATTCTCCTGCCTCAGCCTCCTGAGT AGCTGGGATTACAGGCGCGTGACACC
318	patch	TTCTCCTGCCTCAGCCTCCTGAGTAGCTGGGATTACAGGCGCGTGAC ACCATGCCTAGCTAATTTTTGTATATTTTTAGTAGAGACAGGGTTTCA CCATGTTGGTAAGGCTGGTCTTGAA
319	patch	TATTTTTAGTAGAGACAGGGTTTCACCATGTTGGTAAGGCTGGTCTTG AACTCCTGACCTCGTGATCCGCTGGCCTCGGCCTCCTAAAGTGCTGG GATTACAGGTGGGAGCCACCGCACC
320	patch	TGGCCTCGGCCTCCTAAAGTGCTGGGATTACAGGTGGGAGCCACCG CACCAGGCCTCTTTTTTTTTTTGAGACGGAGTCTTGCTCTGTCGCCCA GGCTGGAGTGCAGTGGCGCGATCTCG
321	patch	GACGGAGTCTTGCTCTGTCGCCCAGGCTGGAGTGCAGTGGCGCGAT CTCGGCTCACTGCAAGCTCTGCCTCCTGGGTTCACGCCATTCTCCTG CCTCAGTCTCCCGAGTAGCTGGGACTA
322	patch	CCTGGGTTCACGCCATTCTCCTGCCTCAGTCTCCCGAGTAGCTGGGA CTACAGGCACCTGCCACTACGCCTGGCTAATTTTTTGTATTTTTAGTA GAGACACAGTTTCACCGTTTCTACC
323	patch	AAGGAATGAGGAGCCCCAGGAGGTCTTGGTAAGAGATAAAAAAACAG GAGGGGGCCCTCTCTGGCTCTATGGTAGAAACGGTGAAACTGTGTCT CTACTAAAAATACAAAAAATTAGCCA
324	patch	ACCTGTAATTCCAGCACTTTGGGAGGCCGAGGCGGGCGGATCACAA GGTCAGGAGATCGAGACCATCCTGAAGGAATGAGGAGCCCCAGGAG GTCTTGGTAAGAGATAAAAAAACAGGAG
325	patch	GACCTTGTGATCCGCCCGCCTCGGCCTCCCAAAGTGCTGGAATTACA GGTATGAGCCACCGCACCCGGCCTTTTTTTTTTTTTTTTGAGAAGCAG TCTCTGTTGCCCAGACTGGAGTGCA
326	patch	TTTTTTTTTTTTTTTTGAGAAGCAGTCTCTGTTGCCCAGACTGGAGTG CAGTGGCACGATCTCAGCCCACTGGAACCTCTGCCTCCCGGCTTCAA GCAATTCTCCTACCTTGGCCGCCCA
327	patch	TGGAACCTCTGCCTCCCGGCTTCAAGCAATTCTCCTACCTTGGCCGC CCAAGTAGCTGGGATTGCAGGCGCCCACCACCATGCCCAGCTAATTT TTTTTTTTTTTTTTTTTAGACGGAGT
328	patch	CCCACCACCATGCCCAGCTAATTTTTTTTTTTTTTTTTTTAGACGGAG TTTCGCTCTTGTTACCCAGGCTGGAGTGCAAGGGCGCGATCTCGACT CACCACAACCTCCGCCTCCTGGGT
329	patch	TGGAGTGCAAGGGCGCGATCTCGACTCACCACAACCTCCGCCTCCT GGGTTCAAGCGATTCTCCTGTCTCAGCCTCCCAAGTAGCTGGGTTTA CAGCCATGTGCCACCACGCCCAGCTAA

330	patch	CTGAGGTCGGGAGTTTGAGACCAGCCTGACCAACATGGAGAAACCC CGTTTCTACTAAAAAAATACAAAATTAGCTGGGCGTGGTGGCACATG GCTGTAAACCCAGCTACTTGGGAGGCT
331	patch	ACTTGAGGCCAGGCGCGGTGGCTCACGCCTGTAATCCCAGCACTTT GGGAGGCTGAGGTGGGCGGATCACCTGAGGTCGGGAGTTTGAGAC CAGCCTGACCAACATGGAGAAACCCCGTT
332	patch	AAGAAATAGCCCCTCAGAAACCCACTTGAGGCCAGGCGCGGTGGCT CACGCCTGTAATCCCAGCACTTTGGGAGGCTGAGGTGGGCGGATCA CCTGAGGTCGGGAGTTTGAGACCAGCCT
333	patch	GGAGGTCAGACTTCAGAAAGGACTTCCCTCTTTTATTTTTTTTTCTGA GACGGAGTCTTGCTCTGTCGCCCAGGCTGGAGTGCAGTGGTACAAT CTCAGCTCACTGCAACCTCCACCTCC
334	patch	CAGGCTGGAGTGCAGTGGTACAATCTCAGCTCACTGCAACCTCCACC TCCTGGGTTCAAGCGATTCTTCTGCCTCGGCCTCCCAAGTAGCTGGG ACTACAAGCACCTGCCACCACGCCCG
335	patch	TGAGGTCAGTTCCAGACCATCCTGGCCAATATGGTGAAACCCCGTCT CTATTAAAAATACAAAAATAAGCCGGGCGTGGTGGCAGGTGCTTGTA GTCCCAGCTACTTGGGAGGCCGAGGC
336	patch	AAGTCCTGGCCGGGTGTGGTGGCTCATGCCTGTAATCCCAGCACTTT GGGAGGCCGAGGTAGGCGGATCATGAGGTCAGTTCCAGACCATCCT GGCCAATATGGTGAAACCCCGTCTCTA
337	patch	TGGCCAGGATGGTCTGGAACTGACCTCATGATCCGCCTACCTCGGC CTCCCAAAGTGCTGGGATTACAGGCATGAGCCACCACACCCGGCCA GGACTTCTCTCTTGAGAAGAAAGGGAAA
338	patch	TAAAATATGACTTTCGGGGATTGTTATGGTATTAATGAGGTAGTGGCA GGTACATAGTAAGTGCTCAATAAATGGTAGTTCCTCATATTATTGCCC CAGACTATTGCTAACCCTTTCCTT
339	patch	TTGTAAGTGGCAGGGCTGAGATCTGAACCCAGTCTGGCTCCTGACCA CAATGTTACACTGCCCCTCAAAATAAAATATGACTTTCGGGGATTGTT ATGGTATTAATGAGGTAGTGGCAGG
340	patch	TTGTGGTCAGGAGCCAGACTGGGTTCAGATCTCAGCCCTGCCACTTA CAAGTATTGCGGGTTGGTCAGCCGGGTGCAGTGGCTCACGCCTGTA ATCCTAGCACTTTGGGAGGCCGAGGCG
341	patch	TTTTAGTAGAGACAGGGTTTCCCCATGTTGGCCAGGCTGGTCTGGAA CTCCAGACCTTAAGTGATCCCGCCGCCTCGGCCTCCCAAAGTGCTAG GATTACAGGCGTGAGCCACTGCACCC
342	patch	TCTCCTGTCTCAGCCTCCCGAGTAGCTGGGATTACAGGCACGTGCCA CCACACCCAGATAATTTTTGAATTTTTAGTAGAGACAGGGTTTCCCCA TGTTGGCCAGGCTGGTCTGGAACTC
343	patch	TGGTGGCACGTGCCTGTAATCCCAGCTACTCGGGAGGCTGAGACAG GAGAATCACTTGAACCCAGGAAGCAGAGGTTGCAGTAAGCCGAGAC TGTGCCACTGCACTCCAGCCTGGGCAAC
344	patch	TCTAGGGACCCCAACCCAACCCTCAATACTTTTTTTTTTTTTTTTTTTT TTTAGACAGAGTCTTGCTCTGTTGCCCAGGCTGGAGTGCAGTGGCAC AGTCTCGGCTTACTGCAACCTCT
345	patch	CAACAGAGCGAGACTCCGTCTCAAAAAACAAACAAACATTGAACACC CCAACTTCTTCTCAGCGTCTGCTTCTAGGGACCCCAACCCAACCCTC AATACTTTTTTTTTTTTTTTTTTT
346	patch	AGGAGGCGGAGGTTGTAGGAAGGCGGAGATTGCAGTGAGCCAAGAT CGCTCCACTGCACTCCAGCCTGGGCAACAGAGCGAGACTCCGTCTC AAAAAACAAACAAACATTGAACACCCCA

347	patch	AGCGATCTTGGCTCACTGCAATCTCCGCCTTCCTACAACCTCCGCCT CCTGGGTTCAAGCGATTCTCCTGCCTCAGCCTCCTGAGTAGCTGGGA CTACAGGTGTGCACCACCACACCCAG
348	patch	CCTCAGCCTCCTGAGTAGCTGGGACTACAGGTGTGCACCACCACAC CCAGCTAATTTTTGTATTTTTAGTAGAGACAGGGTTTCATCATGTTGG CTAGGATGGTCTCGATCTCTTGACCT
349	patch	AGAGACAGGGTTTCATCATGTTGGCTAGGATGGTCTCGATCTCTTGA CCTTGTGATCCGCCCTCCTAGGCCTCCCAAAGTGCTGGTATTACAGG CGTGAGCCACCGCGCCCAGCTCAATG
350	patch	CTCCCAAAGTGCTGGTATTACAGGCGTGAGCCACCGCGCCCAGCTC AATGTTTTTTTACAAATCAGCACCTGTGAAAGGAAGGGAGAGGAAAC ATAATTGGGCAGAGGGAGAAGTCAAAC
351	patch	GTGCTCAAGCAAGGTGAGGCAATCACAGAGCTCCCCGCCCTTGACC CAGGTTTGTCCAGCCTGTGTTGCTGTTTGACTTCTCCCTCTGCCCAAT TATGTTTCCTCTCCCTTCCTTTCACA
352	patch	TCAGCGTCTGCCTCTGGTGCAGACAGCGGCCTCACTGGAAGTCATG CCTTTTCTGGGCAGCCTACACCCAGTGCTCAAGCAAGGTGAGGCAAT CACAGAGCTCCCCGCCCTTGACCCAGG
353	patch	CCTTCAAGGAAGGACTTGCCCCAAGCTGCAGGGAGTGCAGGCTGCA GACAGGCTCCAGCTGTCAGCTCCTTCAGCGTCTGCCTCTGGTGCAG ACAGCGGCCTCACTGGAAGTCATGCCTT
354	patch	GGAGGTCAAATGACTTGCCCAAGATAACAGGGCTAGTGTTGTAAACA CAGAGATGTGCTGGCCAGATCAGCCTTCAAGGAAGGACTTGCCCCA AGCTGCAGGGAGTGCAGGCTGCAGACA
355	patch	CTGTGTTTACAACACTAGCCCTGTTATCTTGGGCAAGTCATTTGACCT CCAAAGCGCCTTGTCTGTAAAAACAGGTAAAATAGTAATGGGATTCAT GGCATTCTTATGAGGATTAAATGA
356	patch	ACAGGTAAAATAGTAATGGGATTCATGGCATTCTTATGAGGATTAAAT GAGGTAATATGTGTAAAGCTTTTAACGACACTGCCTGGCACATAGTAA GCATTCAGTACACTGTAAACATGA
357	patch	TAACGACACTGCCTGGCACATAGTAAGCATTCAGTACACTGTAAACAT GAACCATTAGTATCTCCACTTTACAACTGAGGCTTAGAGGCAAAGTAG TTTACAAAAGGCCACAAAGTCTGA
358	patch	AAGCATTCAGTACACTGTAAACATGAACCATTAGTATCTCCACTTTAC AACTGAGGCTTAGAGGCAAAGTAGTTTACAAAAGGCCACAAAGTCTG ACTTCAATTCCCTTGCCCTAAGCAC
359	patch	GGACCCTTCTACCACATACTAAAATTAAAATGGCCCAGGCCGGGTGC AGTGGCTCACACCTATGTGAGCACTTTGGGAAGCCAAGGCAGGTAG ATTACTTGAGGTCAGGAGTTCGAGACC
360	patch	CTTTGGGAAGCCAAGGCAGGTAGATTACTTGAGGTCAGGAGTTCGAG ACCAGCCTGGCCAACATGGTGAAACCCCATCTCTTCTAAAAATACAAA AATTAACCCAGTGTGGTGGCATGCA
361	patch	ACCCCATCTCTTCTAAAAATACAAAAATTAACCCAGTGTGGTGGCATG CACCTGTAATCCCAAATACTCGGGAGGCTGAGGCATGAGAATCGGTT GAACCCGGCAGGTGGAGGTTGCAGT
362	patch	GGAGGCTGAGGCATGAGAATCGGTTGAACCCGGCAGGTGGAGGTTG CAGTAAGCGGAGATCACACCACTGCACTCCAACCTGGGCGACAAAG TGAGACTCAGTCTCAAAAAATAAAATGA
363	patch	CACTCCAACCTGGGCGACAAAGTGAGACTCAGTCTCAAAAAATAAAA TGAAATAAAATAAAGTGGCTCAAAGACTCAATTTAAGAGTTAAAACTAT AAAACTCTTAGAAGAAAATATTGT

364	patch	AGACTCAATTTAAGAGTTAAAACTATAAAACTCTTAGAAGAAAATATTG TTGAAAATCTTCATCACATTGGACTTGGCAACAACTGCATAAATAGGA TACCAAAAGTACAAGGAAGAAAA
365	patch	GACTTGGCAACAACTGCATAAATAGGATACCAAAAGTACAAGGAAGA AAAAATAGTAGGTAAATTGAACTTCATCAAATTAAGAACTTTTGTGCAC CAAAGGACACTATCAAGAAAGTGA
366	patch	TCATCAAATTAAGAACTTTTGTGCACCAAAGGACACTATCAAGAAAGT GAAAAAACCTGGAGAATGGAAGAAAATATTTGCAGATCATATATCTAA CAAGGGATTAATATTCAAAATATA
367	patch	AAAATATTTGCAGATCATATATCTAACAAGGGATTAATATTCAAAATAT ATATAGAACTCCTACAACTTGACAACAAAAAAACAAACAACCCAATTC AAAAATGGGCAAAGTACTTGAAT
368	patch	ACAACAAAAAAACAAACAACCCAATTCAAAAATGGGCAAAGTACTTGA ATAGACACTTCTCCAAAGAAGATATACTAATGGACAATAAATTCGTGG AAATATGCTCAACATCGTTAGTCA
369	patch	TTCTTGATTATGGCCATCCTGGTTAGTGTGAAGTGGCATCTCATTGTG GTTGTAATCTGCATTTCCCCAATGACTAACGATGTTGAGCATATTTCC ACGAATTTATTGTCCATTAGTATA
370	patch	GTACATTCCCACCAGCAATGCACGGAGGATTCCAATTTCTCCACATC CCCACCAAAACTTATTATCCATTTTCTTGATTATGGCCATCCTGGTTA GTGTGAAGTGGCATCTCATTGTGGT
371	patch	GTGACTTGGTAGTTCTATTTTTAACCTTTTGAGGAACTGCCAAACTGT TTTCCCCAATGACTGCACTATTGTACATTCCCACCAGCAATGCACGGA GGATTCCAATTTCTCCACATCCCC
372	patch	AAACAGTTTGGCAGTTCCTCAAAAGGTTAAAAATAGAACTACCAAGTC ACCCAGCAATTCCATTCTTAGGCATATATTCAAAAGAAATGAAAGCAG ATATTTGTACACCAGTGTTCACAG
373	patch	CATATATTCAAAAGAAATGAAAGCAGATATTTGTACACCAGTGTTCAC AGCTGCACTATTTACAATAGTCAAAAGGTAGAAACAACCTAGGTCCAT CCACAAATGAATGGATAAATAAAA
374	patch	AAAAGGTAGAAACAACCTAGGTCCATCCACAAATGAATGGATAAATAA AACGTAGCATATACATACAATGGTACACTAGTCCGCTGTAAAAAGAAA TTTTGATCTTACTGCATGCTACAT
375	patch	GTACACTAGTCCGCTGTAAAAAGAAATTTTGATCTTACTGCATGCTAC ATGGCTTCGACATACTACAACATGGATGGACCTTGAAAACATTATTCT TTGTGAAATAAACTAGACACAGGA
376	patch	TGGATGGACCTTGAAAACATTATTCTTTGTGAAATAAACTAGACACAG GACAAATGTTAGACGATTCCACTTATATGAGGCACCTAGAATGGGCA ATTTGGTAAGCAAAGTAGAATAGAA
377	patch	ATCCCCAACATAAACTCTGTGACCATTAAACAGTAACTCCCCATTCCC TGCTACCTGTGCCCCTAGTAATTTCTATTCTACTTTGCTTACCAAATTG CCCATTCTAGGTGCCTCATATAA
378	patch	TCAGTGGCATTAAGTATATTCACAATGTCGTGTACCAATCACCACTCT TTATCCCCGAAACTGTTTCATCATCCCCAACATAAACTCTGTGACCAT TAAACAGTAACTCCCCATTCCCTG
379	patch	AAAGAGTGGTGATTGGTACACGACATTGTGAATATACTTAATGCCACT GAATTTTACACTTGAAGTGGTTAAAGCGATAAATATTATAGTTTGCATA TTTTATCATAAAAATATTTTTTT
380	patch	AAAGCGATAAATATTATAGTTTGCATATTTTATCATAAAAATATTTTTTT AAACGATGAAGGGACGTGAACGGGTTGAAATTTTATAAAAAGTGGCC AGGGAAGGTGTCACTGCAATGGT

381	patch	CGGGTTGAAATTTTATAAAAAGTGGCCAGGGAAGGTGTCACTGCAAT GGTGTCCTACAGGAGGAGGAAGATCATGTGGACATCTGCGGGAAGG GTGTTCTGGCAGAGGGAGTAGCACGGG
382	patch	TCATGTGGACATCTGCGGGAAGGGTGTTCTGGCAGAGGGAGTAGCA CGGGCGATGGCTCTGAGGACTGTGAGAAGTATAGTTGGAAACAGCG AGGAGGCCAGGGTGTCCGAAGCTGAGTA
383	patch	CTCCTCCTCACTCTCAGCAGAAACTGACCTTCCCCCTCTTATCTCACC TCCTCCCACTCTCTCTGGCTTACTCAGCTTCGGACACCCTGGCCTCC TCGCTGTTTCCAACTATACTTCTCA
384	patch	CGTGCACCTGCCACTTCAGCCCCACGGGTCTATAAAATGGGCATGAT TATCGTGGCTACCTCACTGGTCCTGGCAATTAAGGAACAATGTGTGC CAGGCACTCTGTAAACCACATACTTG
385	patch	CCCCACGGGTCTATAAAATGGGCATGATTATCGTGGCTACCTCACTG GTCCTGGCAATTAAGGAACAATGTGTGCCAGGCACTCTGTAAACCAC ATACTTGCGAGTGTCAAGCTGGTGAC
386	patch	TGTCTGAAAGGACCATTGAAGGGAGCAATTCTTTTTTTTTTTTTTTTG AAGATGGAGTCTTGCTCTGGACTCCAGGCTGGAGTGCAGTGGTGCG ATCTCAGCTCACTGCAACCTCCACC
387	patch	CTCCAGGCTGGAGTGCAGTGGTGCGATCTCAGCTCACTGCAACCTC CACCTCCCAGGTTCAAGCAATTCTCTTGCCTCAGCCTCCCGAGTAGC TGGGACTCCAGGTGCGTGCCACCACGC
388	patch	CAGGAGTTTGAGACCAGCCTGGCCAACATGGTGAAACCCCATCTCTA CTAAAAATACAAAAATTAACTGGGCGTGGTGGCACGCACCTGGAGTC CCAGCTACTCGGGAGGCTGAGGCAAG
389	patch	CGCTCCCTTTAGGCTGGGTATGGTGTCTCTCAGCACTTTGCGAGGCC AAGGCGGGCAGATCATTTGAGGTCAGGAGTTTGAGACCAGCCTGGC CAACATGGTGAAACCCCATCTCTACTA
390	patch	CTTGGCCTCGCAAAGTGCTGAGAGACACCATACCCAGCCTAAAGGG AGCGATTCTATTCTACTATTCTTCCTTCTGCTAATCCTTCCATTCTTTA ATTTAATAACGAAGATTTTTTGAGT
391	patch	CTTCTGCTAATCCTTCCATTCTTTAATTTAATAACGAAGATTTTTTGAG TACCTGTCATATACCAGGTGCTGTTCTGGGCCCTGGGAATACAGCTG TTAACAAAATCATCAAACCACTTC
392	patch	TGTTCTGGGCCCTGGGAATACAGCTGTTAACAAAATCATCAAACCACT TCCCTCGTGGAGCCCACATTGCAGTGAGAGAGACAAACACGACACA CACTCTCAAGTCCTTGAAGATAAAGA
393	patch	AGTGAGAGAGACAAACACGACACACACTCTCAAGTCCTTGAAGATAA AGAAAACTGGGTAACGGAGAGAAGAGGCCAGGGTTTGTTCTATAATC ATTAATAACACGAGCAGTAAGAAGTA
394	patch	GAGGCCAGGGTTTGTTCTATAATCATTAATAACACGAGCAGTAAGAA GTAAAATTTATCTAACTAACAACTTATAAAGGGTCTACTGTGTGCTAA GCTCTCATCCAGGTTCCCAAGGATT
395	patch	TTATAAAGGGTCTACTGTGTGCTAAGCTCTCATCCAGGTTCCCAAGG ATTAACTCAGACCACACAGTAATTGAATAGATTCTATCATTGTCATCTT ACAGAGGCCCAGAGAGAGAAAGTG
396	patch	CTTGGCCACTAGACCCAAAGTGGCTGAGTTAGAATCCCAGCCCCGTT ACCAGCTATGACACTAGGCAAGTCACTTTCTCTCTCTGGGCCTCTGT AAGATGACAATGATAGAATCTATTCA
397	patch	CTCCTCTGTGAGTCCTCTGCGGACCACCCTAGGCAAGCAAAGGGATT AGGAGCTTGGCCACTAGACCCAAAGTGGCTGAGTTAGAATCCCAGC CCCGTTACCAGCTATGACACTAGGCAA

398	patch	GGTTCTCAGGGCTGCCTGGGTTCAAACCCCAGCTCCAGACTTTGACT TCCTATGCACCCATTTGAACAAGGTAACCTCTCTGTGCCTCAGCTGTC AGGAGGGTAGAGGAGAGGACTCAAT
399	patch	AGCCGAGATCCCGCCACTGCACTCCAGCCTGGGCGACAGAGCGAGA CTCCGTCTCAAAAAAAAAGAACAAGGTTCTCAGGGCTGCCTGGGTTC AAACCCCAGCTCCAGACTTTGACTTCC
400	patch	GCCACACCAGCCGGACCACCCGCCAGAGGCTCAACGGCCCCTCCTC GCAGCCGAGGAAACTGAGGCTCGGAGGCAGGGCGCAGAGGCCCAA GGTGACACAGCAGGCGGCCGTCGGCCGGG
401	patch	GGCCCGCGCTCCCCGGCCGACGGCCGCCTGCTGTGTCACCTTGGG CCTCTGCGCCCTGCCTCCGAGCCTCAGTTTCCTCGGCTGCGAGGAG GGGCCGTTGAGCCTCTGGCGGGTGGTCCG
402	patch	GCAGCAAATCATGGGCTGTCCTAGCCCCTTTTCAGATGAGAAAGGAG CCCAGAGAGGGGAGAGGGCCTGCCAAGGTGGCACATCTGGCCAGG CGCTGCGTAGGCTGAGCCCTGGGGGTCA
403	patch	AGACGTCCAGTTTTTTGGGAGGGGTGGGACACAGGAGTCTGTTTTTT AACTAGCTCCCCAGAGCACCTGAGCAGCAAATCATGGGCTGTCCTAG CCCCTTTTCAGATGAGAAAGGAGCCC
404	patch	AAGAAATGCAGACGTCCAGTTTTTTGGGAGGGGTGGGACACAGGAG TCTGTTTTTTAACTAGCTCCCCAGAGCACCTGAGCAGCAAATCATGG GCTGTCCTAGCCCCTTTTCAGATGAGA
405	patch	GAGGCTGAGGTGGGTGAATCACTTGAGGTCAGGAGTTCGAGACCAG CCTGACCAATATGGTGAAACCCCATCTCAAAAAAAAAAAAAATTGGGG CTAACGGTGAGCCTGTTTTGCAGGAT
406	patch	CAGGCTGGTCTCGAACTCCTGACCTCAAGTGATTCACCCACCTCAGC CTCCCAAAGTGCTGGGATTATAGGCGTGAGCCACTGCACCCAGCCTA GCCCCATTTTTCACATGAAGAGACCG
407	patch	AGGCTGGTCTCGAACTCCTGACCTCAAGTGATTCACCCACCTCAGCC TCCCAAAGTGCTGGGATTATAGGCGTGAGCCACTGCACCCAGCCTA GCCCCATTTTTCACATGAAGAGACCGA
408	patch	AGGCAGAAGTTGTGATGAGCTGAGATCCCGCCACTGCACTCCAGACT GGGCAACAGAGCAGGACTCTGTAAAAAACAAAACAAAACAAAAAATT ACCCTTCCCCACAATTATAAGCATTT
409	patch	CCCAGTCTGGAGTGCAGTGGCGGGATCTCAGCTCATCACAACTTCTG CCTCCTGAGTTCAAGCGATTCTCCTGGCTCAGCCTCTCGAGTAGCTG GGACTAGAGATGCATGCCACCACGCC
410	patch	CTGGCTCAGCCTCTCGAGTAGCTGGGACTAGAGATGCATGCCACCA CGCCTGGCTAATTATTTGTATTTTTAGTAGAGATAGGGTTTCTCCATG TTGGTCAGGCTGGTCTCGAACTCCTG
411	patch	TAGTAGAGATAGGGTTTCTCCATGTTGGTCAGGCTGGTCTCGAACTC CTGACCTCAAATGATCTGCCCGCCTCGGTCTCCCAAAGTGCTGGGAT TACAGTGAGCCACCACGCCTGTCTGG
412	patch	TTGGTCAGGCTGGTCTCGAACTCCTGACCTCAAATGATCTGCCCGCC TCGGTCTCCCAAAGTGCTGGGATTACAGTGAGCCACCACGCCTGTCT GGGTAATTTTTTTTTAAGTATTCTGT
413	patch	GGCTGAGCCAGGATGCTGCTGGTGCGCTCGCCGCGCCGGCCCCGC CCTCCCGCGGCCCCGCCCCGCCCGCAGGCCCCGCCCCCGGCAGGC CCCGCCCCGCCGAGCGCCCGGCCGCCCTCC
414	patch	CTCGCCGCGCCGGCCCCGCCCTCCCGCGGCCCCGCCCCGCCCGCA GGCCCCGCCCCCCGGCAGGCCCCGCCCCGCCGAGCGCCCGGCCGC CCTCCTGTCTGGGCGCGCGTGGCTGGCGGGT

415	patch	AGAATGATTGTTGTCGTAAAGGCCTTTGATAATAATAGATACTGTTTA CCCAGTGCTTGATGCCAGGCATTGCTACAAACACTGCGTACACATTA TTCTATTTAATCTTCATAACCCAGT
416	patch	TCACTAGCATTTAACCTCTGTGCCCCAGCTTCCTCTTCTGTGAAAGGA CAGTAATGACAGTACCTACCTCACTGGGTTATGAAGATTAAATAGAAT AATGTGTACGCAGTGTTTGTAGCA
417	patch	GTGCCAAGTGTGGTACTGCTCTCACTAGCATTTAACCTCTGTGCCCC AGCTTCCTCTTCTGTGAAAGGACAGTAATGACAGTACCTACCTCACTG GGTTATGAAGATTAAATAGAATAAT
418	patch	TCTGCAGGCACCTCCCAAGTTCTGTGGTCTATTGTTTTCAAGGGCTG CTGGAACGAAGTACCACACACTAAGTGGCTTCAACAACCGAAATGTA TGGTCTGTCCTGGTTCTGGAGACTAG
419	patch	AGTGGCTTCAACAACCGAAATGTATGGTCTGTCCTGGTTCTGGAGAC TAGAAGTACAAAATCACGGCGTGGGAGGGCTGGCTGCTTCCGAGGC CCATGAAAGAGCATGTGTGCCCGGCCA
420	patch	GGAGGGCTGGCTGCTTCCGAGGCCCATGAAAGAGCATGTGTGCCCG GCCACTCTGACTTGCAGATGCCCATCTTCTCCCTATGTCTCCTCACAC CATCTTCCCTGTGGTGTGTGTGTGCA
421	patch	TCTTCTCCCTATGTCTCCTCACACCATCTTCCCTGTGGTGTGTGTGTG CAAATCCCTTCTTTCTATAAGGACACCAGTCATACTGGACTAGGGCC CACCCGAATTGCCTCATTTTAACTT
422	patch	ACACCAGTCATACTGGACTAGGGCCCACCCGAATTGCCTCATTTTAA CTTGATGACCTCTCTAATCATGAGGTAATGTCCAAGTAAGGTCCCATT CTAAGATACCTGAATGCCCAGGCAC
423	patch	GGTAATGTCCAAGTAAGGTCCCATTCTAAGATACCTGAATGCCCAGG CACGGTGGTTCATGCCTGTAATCCCAGCACTTTGGGAGGCCGAGGC AGGCAGATCAACTGAGGTCAGGAGTTC
424	patch	CCACCATGCCCCGCTAATTTTTTTATTTTTAGTAGAGACAGGGTTTCA CCATGTTGGCCAGGCTGGTCTTGAACTCCTGACCTCAGTTGATCTGC CTGCCTCGGCCTCCCAAAGTGCTGG
425	patch	CCTCCACCTCCCTGGGTTCAAACAATTCTTCTGCCTCAGCCTCCCGA GTAGCTGGGACTACAGGTACGCACCACCATGCCCCGCTAATTTTTTT ATTTTTAGTAGAGACAGGGTTTCACC
426	patch	TACTCGGGAGGCTGAGGCAGAAGAATTGTTTGAACCCAGGGAGGTG GAGGTTGCAATGAGCCAAGATCACGCCACTGCATTCCAGCCTGGGA GACAGAGCAAGACTCTGTCTCAAAACAA
427	patch	TTACGGGTTGAATTGTCACCCCCACATTCCCCAAGTTCATATGTTCAG GGGTTTGTTGTTGTTGTTGTTGTTTTGAGACAGAGTCTTGCTCTG TCTCCCAGGCTGGAATGCAGTGGC
428	patch	GGTGAGACAGCCAGTGACGACCATCCACATGTTACGGGTTGAATTGT CACCCCCACATTCCCCAAGTTCATATGTTCAGGGGTTTGTTGTTGTTG TTGTTGTTGTTTTGAGACAGAGTCT
429	patch	AGGCTGGGAAAGGCACACAACCCAGTATCAGACCTGAGTTCACACTC CTTCTGGCAGGAACTTCTAGGTGACATTGGGAAGCAACTTCATTCCTT AGAACCTAGATTTCTCCTCAGGCTA
430	patch	AAAGAGACCTAAGAGATTATTTAGCCAAGCCCCCTTATAGCCTGAGG AGAAATCTAGGTTCTAAGGAATGAAGTTGCTTCCCAATGTCACCTAGA AGTTCCTGCCAGAAGGAGTGTGAAC
431	patch	AGGTATTATTCCTGATTTAAGGAGGATGCAATGAGGCTTGATGTGGAT TCACCCACCCCAAAGCCTGTGTTCTTAACCACTATGCAATACTGCCTC CCATCAAAGTCTCTATCTCAAGTC

432	patch	ATTTAATGAGAACGCCAAGGGCGTGGCTGTCAATCCTATGACACCTG TCTGAGGTAGGTATTATTCCTGATTTAAGGAGGATGCAATGAGGCTT GATGTGGATTCACCCACCCCAAAGCC
433	patch	GCATGAACCCAGGAGGTAGAGATTGCAGTGAGCCGAGATCGCACCA CTGCACCCCAGCCTGGGCAACAGAGTGAGACTCCGTCTCAAAAAAA GAGACTGGTTTCTTACCTAAGTCACAAA
434	patch	GCAGTGGTGCGATCTCGGCTCACTGCAATCTCTACCTCCTGGGTTCA TGCCATTTTCCTGCCTCAGCCTCCCAAGTAGCTGGGACCACAGGCAC CCACCACCACACCCGGCTAGTTTTTT
435	patch	CTCGGCTCACTGCAATCTCTACCTCCTGGGTTCATGCCATTTTCCTGC CTCAGCCTCCCAAGTAGCTGGGACCACAGGCACCCACCACCACACC CGGCTAGTTTTTTGTATTTTTAGTAG
436	patch	AGCCTGGCCAACATGGTGAAACCCCCTCTCTACTAAAAATACAAAAAT TAGCTGGGCATGGTGGTGGGTGCCTATAATCCCAGCTACTCGGGAA GCTGAGGCAGGACAATCATTTGAACC
437	patch	GGTGCAGTGGCTCATGCCTGTAATCTCAGCACTTTGGGAGGCCGAG GCAGGCGGTCAAGAGTTCGAGACCAGCCTGGCCAACATGGTGAAAC CCCCTCTCTACTAAAAATACAAAAATTA
438	patch	CTGCCTCGGCCTCCCAAAGTGCTGAGATTACAGGCATGAGCCACTG CACCAGGCCTGTCTTCAGGTCTTTTTTATTTTATTATTTATTTATTTATT TATTTATTTATTTATTTATTTTGA
439	patch	TTTATTTTATTATTTATTTATTTATTTATTTATTTATTTATTTTGAGA CAGAGTCTCGCTCTGTCGCCCAGGCTGGAGTGCCGTGGTGCGATCT CGGCTCACTGCAAGCTCCACCT
440	patch	CCCAGGCTGGAGTGCCGTGGTGCGATCTCGGCTCACTGCAAGCTCC ACCTCCCGGGTTCACGCCATTCTCCTGTCTCAGCCTCCCGAGTAGCT GGGATTACAGGCGCCTGCCACCATGCC
441	patch	AGGAAATCGAGACCATCCTGGCCAACTTAGTGAAACCCCATCTCTAC TAAAAATACAAAAAAATTAGCTGGGCATGGTGGCAGGCGCCTGTAAT CCCAGCTACTCGGGAGGCTGAGACAG
442	patch	GGCCGGGTGCAGTGGCTCATGCCTGTAATCCCAGCACTTTGGGAGG CCGAGGCAGGCAGATCACGAGGTCAGGAAATCGAGACCATCCTGGC CAACTTAGTGAAACCCCATCTCTACTAA
443	patch	TCGGCCTCCCAAAGTGCTGGGATTACAGGCATGAGCCACTGCACCC GGCCCACATACTACATTTTCTATCCACTCACCAGTTGATGAAGACTTA ATTTGTTTCCAGTTTTCTTTTTTCTT
444	patch	CACTCACCAGTTGATGAAGACTTAATTTGTTTCCAGTTTTCTTTTTTCT TTTTTTTGAGATGGGATCTCCCTGTATTGCCCAGGTTGGTCTTGAACT CCTGGGCTCAAGTGATCCTCCCA
445	patch	TGAGATGGGATCTCCCTGTATTGCCCAGGTTGGTCTTGAACTCCTGG GCTCAAGTGATCCTCCCACCTAAGCCTCCCAAAGTGCTGGGATTTGT TTCCGGTTTTTTTCCTACTATGCTAT
446	patch	TTTTTTTTTTAACCTCTGTACCCCTAGCTTTTTTTTTTTTTTTTTTTTTT TTGAGATGGATTCTTGCTCTGTCGCCCAGGCTGGAGTGCAGCAGTGT GATCTTGGCTCACTGCAACCTC
447	patch	TGTCGCCCAGGCTGGAGTGCAGCAGTGTGATCTTGGCTCACTGCAA CCTCCACCCCCCGGGTTCAAGCAATTCTCCTGCCTCAGCCTCCCAAG TAGCTGGGATTACAGGCGTACGCCACC
448	patch	TTGAGACCAGCCTAGCCAACATGGTCAAACCCCGTCTCTACTAAAAA AAATACAAAAATTAGCCAGGCATGGTGGCGTACGCCTGTAATCCCAG CTACTTGGGAGGCTGAGGCAGGAGAA

449	patch	CAGTGGCTCACACCTGTAATTCCCAGCACTTTGGGAGGCTGAGGCA GGCGGATCACCTGAGGTTAGGAGTTTGAGACCAGCCTAGCCAACAT GGTCAAACCCCGTCTCTACTAAAAAAAA
450	patch	CGCCTGCCTCAGCCTCCCAAAGTGCTGGGAATTACAGGTGTGAGCC ACTGTGCTCAGCCTGTGTGTTTTGAGACAGGGTCTTGCTTCGTCACC CAGGCTGGAGTGCAGTGGCTCAATCAC
451	patch	AGACAGGGTCTTGCTTCGTCACCCAGGCTGGAGTGCAGTGGCTCAA TCACAGCTTACTGCAGCCTGGACTTCCCAGGCTCAAGTGATCCTCCC GCCTCAGCCTCTCAAGTAGCTGGAACT
452	patch	TCCCAGGCTCAAGTGATCCTCCCGCCTCAGCCTCTCAAGTAGCTGGA ACTACAGGCGAGTGCCACCATGCCTGGCTAAGTTTTAATTTTATGTAG AGATGGTCTCAGTATGTTGCCCAGG
453	patch	CTGGCTAAGTTTTAATTTTATGTAGAGATGGTCTCAGTATGTTGCCCA GGCTGATTTCAAACTCTTGGGCCCAAGTGATCCTCCTGCCTTGCTTC CCTCCCAAAGTGCTAGGATTACAGG
454	patch	CCAAGTGATCCTCCTGCCTTGCTTCCCTCCCAAAGTGCTAGGATTAC AGGCATGAACCACTTCACCTGGCCCATGCTATATGTTTGCCCCTCGT CTTCTTACCTACTCCCTCAGTTTTCT
455	patch	CTTCAGCACAGGAGTTTGGGGAAGACACAAACATTCAACCCCTACTG TTCCAACCCCTGCTTCACAGATGAGAAAACTGAGGGAGTAGGTAAGA AGACGAGGGGCAAACATATAGCATGG
456	patch	ATTAATAAGGGCTCCACCCACATCACCTGATGACCTCCCAGAGGTCC TACCTCCAAATACCATCACTCAGCTTCAGCACAGGAGTTTGGGGAAG ACACAAACATTCAACCCCTACTGTTC
457	patch	GTAGGACCTCTGGGAGGTCATCAGGTGATGTGGGTGGAGCCCTTAT TAATGGGATTTGTGCCCTTATAGAAAGGGACACAACATGAGATGATCT TGCTCTGGGCCATGCCGGGAGGAAGG
458	patch	AAGGGACACAACATGAGATGATCTTGCTCTGGGCCATGCCGGGAGG AAGGGAGAAGGTGGCTGTCAACGAGCCAGGAAGCGGCACTCCTGAC ACTGGATCTACCAACACCCCTATCTCAG
459	patch	GCCAGGAAGCGGCACTCCTGACACTGGATCTACCAACACCCCTATCT CAGACTTCCAGCCTCCAGGACCGTGAGAACTGTTTCCTGTTGAAGCC ACCCTCTCTATATTTGTTACAGCAGC
460	patch	TGAGAACTGTTTCCTGTTGAAGCCACCCTCTCTATATTTGTTACAGCA GCCCACACTGATTAAGACACTTTTTTTTTTTTTTTTTTTTTTTTTTTT GAGATGGAGCCTCGCTCCATC
461	patch	TTTTTTTTTTTTTTTTTTTTTTTTTTTTTTGAGATGGAGCCTCGCTCCATC ACCCAGGCTGGAGTGCAATGGCGCAATCTCGGCTCACTGCAACCTC TGCCTCCCGGGTTCAAGTGATTAT
462	patch	GCGCAATCTCGGCTCACTGCAACCTCTGCCTCCCGGGTTCAAGTGAT TATCCTGGGTCAGCCTCCCAAGTAGCTGGGATTGCAGGCACCTGCC ACCATGGCTGGCTAAATTTTGTATTTT
463	patch	AGCTGGGATTGCAGGCACCTGCCACCATGGCTGGCTAAATTTTGTAT TTTTAGTAGAGACAGGGTTTCACCATGTTGGCCAGGCTGGTCTCCAA CTCCTGACCTCAGGTGATCCACCTGC
464	patch	CATGTTGGCCAGGCTGGTCTCCAACTCCTGACCTCAGGTGATCCACC TGCCTCGGCCTCCCAAAGTGCTGGGCGTGAGCCACCATGCCCGGCC TGACACTTATCTTTTATATCTATATAT
465	patch	GGCGTGAGCCACCATGCCCGGCCTGACACTTATCTTTTATATCTATAT ATTTTTTTCTTTGTTGAGACGGAGTCTCACTGTGTCGCCCAGGCTGGA GTGCAGTGGTGTGATCTTGGCTCA

466	patch	AGTCTCACTGTGTCGCCCAGGCTGGAGTGCAGTGGTGTGATCTTGG CTCACCGAAACCTCTGCCTCCCAGGTTCAAGTGATTCTCGTGCCTCA GCCTCCGGAGCAGCTGGGATTACAGGC
467	patch	GTTCAAGTGATTCTCGTGCCTCAGCCTCCGGAGCAGCTGGGATTACA GGCGTGAGCCACCATGACTGGCCTAAAACACCTACCTTTTATTTTTTA AAAAACCAACACATTATCAGTACTT
468	patch	TAAAACACCTACCTTTTATTTTTTAAAAAACCAACACATTATCAGTACT TCATGCCAGACACCATTCTAGGAAATTAACTCCTCTGACTTTCACATC AATCCCATGGGTAGCTGTTATTT
469	patch	GAAATTAACTCCTCTGACTTTCACATCAATCCCATGGGTAGCTGTTAT TTACAGATGAGGAAACTGAGGCACAGAGGTAAAACAACTTTGCTGAG GTCACCTTGCTGCTAAGTGACACAG
470	patch	ACAGAGGTAAAACAACTTTGCTGAGGTCACCTTGCTGCTAAGTGACA CAGCTGGCATCTAGTGCAGCAGGCTGGCTCCAAGTCTATGCCCCTCA CCCCTCAGACGCTGCTCACCAAGCCG
471	patch	AGCCCCTCCGGCTTGGTGAGCAGCGTCTGAGGGGTGAGGGGCATA GACTTGGAGCCAGCCTGCTGCACTAGATGCCAGCTGTGTCACTTAGC AGCAAGGTGACCTCAGCAAAGTTGTTTT
472	patch	ATCTTTATTTTTATTAAAGGACAGGGTCTCTGGCCTGGTGCGTTGGCT CACGCCTGTAATCCCAGCACTTTGGGAAGCCAAGGCGGGCGGATCA CGAGGTCAGGAGATTGAGACCATCCT
473	patch	TGGGAAGCCAAGGCGGGCGGATCACGAGGTCAGGAGATTGAGACCA TCCTGGCCAACACGATGAAACCCCGTCTCTACTAAAAATACAAAAATT AGCTGGGCGTGGTGGTGAGTGCCTGT
474	patch	GTCTCTACTAAAAATACAAAAATTAGCTGGGCGTGGTGGTGAGTGCC TGTAGTCCCTGCTACTCAGGAGGCTGAGGCAGGAGACTTGCTCCTG AACCCAAGAGGCGGAGGTTGCAGTGAG
475	patch	CTGAGGCAGGAGACTTGCTCCTGAACCCAAGAGGCGGAGGTTGCAG TGAGCCAAGATCCCGCCACTGCACTCCAGCTTCCCGACAGAGCGAG ACTCTGTCTCACAAAAAAAAAAAAAAA
476	patch	TCCAGCTTCCCGACAGAGCGAGACTCTGTCTCACAAAAAAAAAAAAA AAAAAAAAAAAAAAGTCAGGGTCTCACCCTGTCCGCCAGGCTTGACT GCAGTGGCGTGACCTCAGCTTACTGC
477	patch	TCACCCTGTCCGCCAGGCTTGACTGCAGTGGCGTGACCTCAGCTTAC TGCAGCCTCAACCTCCCAGACTCAAGTGATCCTCCCACCTCAGCCTC CTGAGTAGCTGGGACTACAGGTGCAC
478	patch	GATACCAGCCTGGACAACATAGCAAGACCCCATCTCTAAAAAAATATA AAAATTAGCCAGGCATAGCAGTGTGCACCTGTAGTCCCAGCTACTCA GGAGGCTGAGGTGGGAGGATCACTT
479	patch	CGTGACTCACATCTGTGATCCCAGCACTTTGGCAGGCTGAGGCAGG AGGATCACTGGAGGCCAGGAGCTTGATACCAGCCTGGACAACATAG CAAGACCCCATCTCTAAAAAAATATAAA
480	patch	CAGGCTGGTATCAAGCTCCTGGCCTCCAGTGATCCTCCTGCCTCAGC CTGCCAAAGTGCTGGGATCACAGATGTGAGTCACGTGCTTGGCCTAA ACTTTTAAATGATGAGACTTAAGTCA
481	patch	CTCAGTTTCCCCTTTTGTAAAATAGGATGATGATACTTGCACCTCAAG GTGCTGGGAGGATTCACTGTGAGCATGTGAGAAGCAGAGGGCAGAC TGTGGTGGCTGGTGGGCCAGGGCAGA
482	patch	CACACCTGCGCTCCAGCCTGGGTGACAGAGCGAGACTCCGTCTCAA AAAAAAATAAAAATAAAAAATAAACTCAGTTTCCCCTTTTGTAAAATAG GATGATGATACTTGCACCTCAAGGT

483	patch	TTTTTTGAGACGGAGTCTCGCTCTGTCACCCAGGCTGGAGCGCAGGT GTGCGATCTCGGCTCACTGCAACCTCCACCTCCTGGGTTCAAGCGAT TCTCCTGCCTCAGCCTCCTGAGTAGC
484	patch	CGGTGAAACCCCATCTCTACTAAAAATACAAAAAATTAGCTGGGTGTG GTGGTGTGTGCCTGTAGTCCCAGCTACTCAGGAGGCTGAGGCAGGA GAATCGCTTGAACCCAGGAGGTGGAG
485	patch	ATCCCAGCACTTTGGGAGGCCGAGGCGGTCGGATCACGAGGTCAGG AGATCAAGACCATCCTGGCTAACACGGTGAAACCCCATCTCTACTAA AAATACAAAAAATTAGCTGGGTGTGGT
486	patch	CCTGGGCAAATCACTTCCTTTCTTTAAATTCAGTTTCCCCTTTTGCCG GGCGCGGTGGCTCATGCTTGTAATCCCAGCACTTTGGGAGGCCGAG GCGGTCGGATCACGAGGTCAGGAGAT
487	patch	GGGTCTGCAGGCTGGGTGGACCCCAAGCTTAGTTGGATCCTGGGCA AATCACTTCCTTTCTTTAAATTCAGTTTCCCCTTTTGCCGGGCGCGGT GGCTCATGCTTGTAATCCCAGCACTT
488	patch	CCCGGCCTGGGGGGTCAGGAGGGCTTCCTGGAAGAGGGGGTATCC TGAGCCCTGGAAGAGGAGACACCAGCCAGGCTGCTAGAGGCTGGG GATCCCCAGCACACAGGCTCCAGGCTGGGC
489	patch	TAGCAGCCTGGCTGGTGTCTCCTCTTCCAGGGCTCAGGATACCCCCT CTTCCAGGAAGCCCTCCTGACCCCCCAGGCCGGGCAGCCACTCCAG GGCTCCTCAGTTCAGCAATGTGTCTCT
490	patch	TTCAAGTGATTCTTCTTGCCTCAGCCTCCCAAGTAGCTGGGATTACAG GCACCCACGACCATGCCCGGCTAATTTTTGTATTTTTAGTAGAGACAG GGTTTCACCATATTGGCCAGGCTG
491	patch	AATTTTTGTATTTTTAGTAGAGACAGGGTTTCACCATATTGGCCAGGC TGGTCTCGAACTCCTGACCTCGTGATCCTCCTGCCTTGGCCTCCCAA AGTGTTGGGATTACAGGCATGAGCC
492	patch	TGATCCTCCTGCCTTGGCCTCCCAAAGTGTTGGGATTACAGGCATGA GCCACCGTGCCCGGCCTAATTTTTGTATTTTTTAGTAGAAACAGGGTT CCACCATGTTGGTCAGGCTGGTCTT
493	patch	TGTATTTTTTAGTAGAAACAGGGTTCCACCATGTTGGTCAGGCTGGTC TTGAGGTCCTGACCACAGGTGATCTGACCTCGCCTTGGCCTCGAAAA GTGCTGGGATTATAGGCATGAGCCA
494	patch	TCTGACCTCGCCTTGGCCTCGAAAAGTGCTGGGATTATAGGCATGAG CCACCGCACCCCACACCAACCTAGAAAAGTTCAACTCATTTGTCTAA GCCCAGCAAAATCATCCAGAAGCCGG
495	patch	GAAAAGTTCAACTCATTTGTCTAAGCCCAGCAAAATCATCCAGAAGCC GGTGGCGGTGGCTCACACCCATAATGCCAGCACTTTGGGAGGCTAA GACATGAGGATCACTTGAGGCCAAGA
496	patch	AATGCCAGCACTTTGGGAGGCTAAGACATGAGGATCACTTGAGGCCA AGAGTTTGAGACCAGCCTGAGAAATATAGCAAGACCCCCGTCTCTAT GAAAAATACAAAAATTAGTTGGGTGC
497	patch	ATATAGCAAGACCCCCGTCTCTATGAAAAATACAAAAATTAGTTGGGT GCGGCGGCATGTGCCTGTGGTCCCAACTACTCTGGAGACTGAGGCA GGAGGATCACTTGAGGCCAGGAGCTT
498	patch	CCAACTACTCTGGAGACTGAGGCAGGAGGATCACTTGAGGCCAGGA GCTTGAGGCTGCAGTGATCTGTGATGGTGCCACTGCACTCCAGCCA GGGCGACAGAATGACACTGTCTCAAAAA
499	patch	TGGTGCCACTGCACTCCAGCCAGGGCGACAGAATGACACTGTCTCA AAAAAAAATGTCGGCTGGGCGCGGTGGCTCACACCTGTAATCCCAG CACTTAAGGAGGCTGAGGTGGGCGGATC

500	patch	TGGCTCACACCTGTAATCCCAGCACTTAAGGAGGCTGAGGTGGGCG GATCACGAGGTCAGGAGATCGAGACCATCCTGGCTAACACGGTGAA ACCCCGTCTCTACTAAAAATACAAAAAA
501	patch	CCATCCTGGCTAACACGGTGAAACCCCGTCTCTACTAAAAATACAAAA AATTAGCCTGGCGTGGTGGCGGGCGCCTGTAGTCCCAGCTACTCGG GAGGCTGAGGCAGGAGAATGGCATGA
502	patch	GCGCCTGTAGTCCCAGCTACTCGGGAGGCTGAGGCAGGAGAATGGC ATGAACCCGGGAGGCGGAGCTGGCAGTGAGCCGAGATCGTGTCACT ACACTCTAGCCTGGATGACAGGGCCAGA
503	patch	AGGCGGAGCTGGCAGTGAGCCGAGATCGTGTCACTACACTCTAGCC TGGATGACAGGGCCAGACTCCATCTCAAAAAAAAAAAAAAAAAATCA TCTAGTGGTGATGGGACTTTGTAGGG
504	patch	GGAGAATTACAGCCCCCATCATAGTGTGTTGGGGTAAGAATTAAGTG AGTTCCCATATATGGGACAAACTTCCCCCCCTTATGACCTGTAAACCC AGTTTCTGGCGGCCAAGGATGGGGA
505	patch	GCACTCCAGCCTGGGTGACAGAGTGAGACTCCATCTCAAAAATAAAA TCAATAAAATAAAGTAAAATGAGGGAGAATTACAGCCCCCATCATAGT GTGTTGGGGTAAGAATTAAGTGAGT
506	patch	TGATTTTATTTTTGAGATGGAGTCTCACTCTGTCACCCAGGCTGGAGT GCAATGGCATGAACTTGGCTCACTGCAACCTCTGACTCCCAGGTTCA AGAGATTCTCTTGCCTCAGCCTCCT
507	patch	CTGCAACCTCTGACTCCCAGGTTCAAGAGATTCTCTTGCCTCAGCCT CCTCAGTAGCTGGAACCACAGGCGCCCGCCACCACACCTGGCTAAT TTTTGTATTTTTAGTACAGACTGGGTT
508	patch	GCCCGCCACCACACCTGGCTAATTTTTGTATTTTTAGTACAGACTGGG TTTCACCGTGTTGGCCAGGCTGGTCTCAAACTCCTGACTTCAAGTGA TCCGCCTGCCTTGGCCTCCCAAAGT
509	patch	GTCTCAAACTCCTGACTTCAAGTGATCCGCCTGCCTTGGCCTCCCAA AGTGCTAGGATTACAGGTGTGAGCCACCATGTCCAGTCCTCTCCCCA TTTTATAGGTGAGGAGACTGAGGCTC
510	patch	CCACCATGTCCAGTCCTCTCCCCATTTTATAGGTGAGGAGACTGAGG CTCAGAGAAGTAAAGCTACTCACCTAAGATCCCACAGCCTTCAAGCG GCAGAGCTGGGATTTGAACCTCGGCC
511	patch	TACTCACCTAAGATCCCACAGCCTTCAAGCGGCAGAGCTGGGATTTG AACCTCGGCCATCTGGGTGTGGAGCCTTATTATTCACCACTTTGGCA GGTGTCTCAGTGGCTTACTTACCCTT
512	patch	CCCAGCTCATGCAGTCATTTATTCATTCAACAAGCATCACCCACGCTG GGCCCCCAAGAGGCCTCAGCCCTGACCAGGTCCTCAAGGAGCTATC TTAAGAGAGGACAGAGCTGGACATAG
513	patch	TGACCAGGTCCTCAAGGAGCTATCTTAAGAGAGGACAGAGCTGGACA TAGACACTCCTAGTCCCATGCAGTTAAGGAAGGTCCAGAGGGAAAGA CAGGGTCCTGGAAGGCTTCCTGGAGG
514	patch	CCAATGATAGGTTTGGGGAATCTTAGTGAACTCCTACTCATGCGTTGA AGCCCCAACTGTAATGCCTCCTCCTCCAGGAAGCCTTCCAGGACCCT GTCTTTCCCTCTGGACCTTCCTTAA
515	patch	TTGGAGAGCCAATGATAGGTTTGGGGAATCTTAGTGAACTCCTACTC ATGCGTTGAAGCCCCAACTGTAATGCCTCCTCCTCCAGGAAGCCTTC CAGGACCCTGTCTTTCCCTCTGGACC
516	patch	CCTCTGTCCTTCACATCGCCAAACTCCAAGAAATGGTCAAAGGCTTT GAACGGAGACCTTGAAGAAAAAGCGGGAAACTGCTTTTCAACATGTC CAGAGATGCTCATTCTTGCCAGGTGC

517	patch	CGGGAAACTGCTTTTCAACATGTCCAGAGATGCTCATTCTTGCCAGG TGCAGTGGCTTACACCTGTAATCCCAACACTTTGGGAGGCTGAAGTG AGCAGATCGCTTGAGCCCAGGAGTTC
518	patch	CCAACACTTTGGGAGGCTGAAGTGAGCAGATCGCTTGAGCCCAGGA GTTCGAGACCAGCCTGGCCATCATGGTGAAACCCCGTCTCTACTTTA AAAAATACAAAAATTAGCCAGGTGTGG
519	patch	GGTGAAACCCCGTCTCTACTTTAAAAAATACAAAAATTAGCCAGGTGT GGTGGTATGTGCCTGTAGTCCCAGCTACTCAGGAGGCTGAGGCAGG AGAATTGTTTGAACCCAGGAGGTGGA
520	patch	AGCTACTCAGGAGGCTGAGGCAGGAGAATTGTTTGAACCCAGGAGG TGGAGGCTGCAGTGAGCCAAGATCACTCCACTGCATTCCAGCCTGG GCAACAGAGTGAGACCTGTCTCAAAAAA
521	patch	ACTCCACTGCATTCCAGCCTGGGCAACAGAGTGAGACCTGTCTCAAA AAAAAAAAAAGTTCACACTTAATAAGAAAACTGCAAATCACAAACTG TTTGTCTTCACCAATCAAATTGGCA
522	patch	CACCAGTGCTACACCATGGACGCACCCCACAGCCTGGCTGGCACAG AATGTCATTGCATTGTTGGATTTTTGCCAATTTGATTGGTGAAGACAA ACAGTTTGTGATTTGCAGTTTTCTTA
523	patch	CAGAAGTGGACTTGCTGTGTCAGCAGGCACATGAGTTTATCATTCCG GTGGCCTGTGCCAGGGTGCCCTCCACCAGTGCTACACCATGGACGC ACCCCACAGCCTGGCTGGCACAGAATG
524	patch	CACCGGAATGATAAACTCATGTGCCTGCTGACACAGCAAGTCCACTT CTGGGAATCCCTGCCTGAATATTTGCATGTTTACAGTGTGAACTGACT AACGAATAAAAAAATGTGGCTCAGC
525	patch	CTGACCTCGTGATCCGCCCACCTTGGTCCCCCAAAGTGCTGGGATTA CAGGCATGAGCCACCACGTCCAGGCTGAGCCACATTTTTTTATTCGT TAGTCAGTTCACACTGTAAACATGCA
526	patch	TGCCCAGCTAATTTTTGTATTTTTAGTGGAGACGGGGTTTCACCATGT TGGCCAGGCTGGTCTGGTACTCCTGACCTCGTGATCCGCCCACCTT GGTCCCCCAAAGTGCTGGGATTACAG
527	patch	CAACATGGTGAAACCCCGTCTCCACTAAAAATACAAAAATTAGCTGG GCATGGTGGCACGTGCCTGTAATCCCAGCTACTAGGGAGGCTGAGG CAGGAGAATCGCTTGAACCCAGGAGGC
528	patch	CCCAGCTACTAGGGAGGCTGAGGCAGGAGAATCGCTTGAACCCAGG AGGCAGAGGTTGCAGTGAGCTGAGATCATGCCACTGCACTCCAGTTT GGGCGTTAGAGCGAGACTCCATCTCAA
529	patch	ATCATGCCACTGCACTCCAGTTTGGGCGTTAGAGCGAGACTCCATCT CAATAATAATAATAATAATAATAATAATAATAATTTAAAAATTAGCTGGG CATGGTGGCTTCAGCCTGTAGTC
530	patch	ATAATAATAATTTAAAAATTAGCTGGGCATGGTGGCTTCAGCCTGTAG TCCCAGCTACTTCAGAGGCTGAGGTGGGAGGATCCCTTGAGCCCAG AAGGTTGTGACTGCAGTGAGCCGTGA
531	patch	GGTGGGAGGATCCCTTGAGCCCAGAAGGTTGTGACTGCAGTGAGCC GTGATTGTGCCACTCCACTCCAGCCTATGCAGCAGAGCAAGACCCTA TCTCTAAAAAATAATTTAAAATAAATG
532	patch	CTATGCAGCAGAGCAAGACCCTATCTCTAAAAAATAATTTAAAATAAA TGGCTGGGCCGGCCGCGGTGGCTCATGCCTGTAATCCCAGCACTTT GGGAGGCTGAGGTGGGCGGATCACCT
533	patch	TCATGCCTGTAATCCCAGCACTTTGGGAGGCTGAGGTGGGCGGATC ACCTGAGGTCCAGAGTTTGAGACTAGCCTGACCAACGTGGAGAAACT CCATCTCTACTAAATACACAAAATTAG

534	patch	AGCCTGACCAACGTGGAGAAACTCCATCTCTACTAAATACACAAAATT AGCCGGGTGTGGTGGCGCATGCCTGTAATCCCAGCTACTTGGGAGG CTGAGGCAGGAGAATCACTTGAGCCT
535	patch	CTGTAATCCCAGCTACTTGGGAGGCTGAGGCAGGAGAATCACTTGAG CCTGGGAGGTAGAGTTTGCAGTTGAGCCGAGATCACGGCACTGCAC TCCAGCCTGGGCAACAAGAGCAAAACT
536	patch	GAGCCGAGATCACGGCACTGCACTCCAGCCTGGGCAACAAGAGCAA AACTCCATCTCAAAATAATAATAATAAATAAATAAATTGGCTAAAATGT TCAATTTTATGTTGTGTGTATGTTG
537	patch	TAAATAAATAAATTGGCTAAAATGTTCAATTTTATGTTGTGTGTATGTT GCAGGTTTGTTTTTTTGAGAAGGCAAAGTCAGGCGTGGTGGCTCACA CCTGTAATCCCAGCACTTTGGGAG
538	patch	GGCAAAGTCAGGCGTGGTGGCTCACACCTGTAATCCCAGCACTTTG GGAGGCTGAGGTGGGCGGATCACAAGGTCAGGAGACTGAGACAATC CTGGCCAACGCTGTGAAACCCTGTCTCT
539	patch	AGGTCAGGAGACTGAGACAATCCTGGCCAACGCTGTGAAACCCTGT CTCTACCAAAAATACAAAAAATTAGCTGGGCGTGGTGGCATGTACCT GTAATCCCAGCTACTCGGGAGGCTGAG
540	patch	GCTGGGCGTGGTGGCATGTACCTGTAATCCCAGCTACTCGGGAGGC TGAGGCAGGAAAATCACTTGAACCAGGGAGTTGGAGGTTGCAGTAA GCCTAGATCGCGCCACAGCACTCCAGCC
541	patch	TCACTTGAACCAGGGAGTTGGAGGTTGCAGTAAGCCTAGATCGCGC CACAGCACTCCAGCCTGGTGACAGAGCGAGACTTCATATAAAAAAAA AAAAGAGAGAGAGAGAGAAGGCAAAAA
542	patch	TACTAAAAATACAAAAAAATTAGCTGGGCATGGTGGCGGGCGCCTGT AGTCCCAGCTACTTGGGAGGCTGAGGCAGAAGAATGGCTTGAACCC GGGAGGTGGAGCTTGCAGTGAGCTGAG
543	patch	AGGCAGAAGAATGGCTTGAACCCGGGAGGTGGAGCTTGCAGTGAGC TGAGATTGCGCCACTGCACTCCAGCCTGAGCGACAGAGCGAGACTC CATCTCAAAACAAAACAAACAAACAAAA
544	patch	CTGCACTCCAGCCTGAGCGACAGAGCGAGACTCCATCTCAAAACAAA ACAAACAAACAAAACAAAACAAAACAAAACAAAACAAAAAAAGATTCC TTTGGCTACCTGGGTGGGTAGCCCA
545	patch	CTTCACAAGATGCAATGAAGAAGTGGGCTTTTTTTTTTTTTGAGACAG AGTTTCTCTCTTGTCACCCAGGCTGGAGTGCCATGGCGCAATCTCAG CTCACTGCAACCTCCACTTCCCGGG
546	patch	CTGGAGTGCCATGGCGCAATCTCAGCTCACTGCAACCTCCACTTCCC GGGTTCAAGCGACTCTCCTGCCTCAGCTACCTGGGTGACTGGGATTA CAGGCTTGCGCCACCATGCCCGGCTA
547	patch	CTGAGGTCAGGAGTTTGAGACCAGCCTGACCAACATGGAGAAACCC CGTCTCTACTAAAAATACATAAATTAGCCGGGCATGGTGGCGCAAGC CTGTAATCCCAGTCACCCAGGTAGCTG
548	patch	ACTTCTGGCCGGGTGTGGTGGCTCATGCCTGTAATCCCAGCACTTTG GGAGGCTGAGGCGGGTGGATCACCTGAGGTCAGGAGTTTGAGACCA GCCTGACCAACATGGAGAAACCCCGTC
549	patch	TCCCAAAGTGCTGGGATTACAGGCATGAGCCACCACACCCGGCCAG AAGTAGGCCTTTACCCACTACATGCCTTCTTTTACTTATCTGCACAAT GAAGATTAAAAATAGTTTCTTGGCCT
550	patch	CCTTCTTTTACTTATCTGCACAATGAAGATTAAAAATAGTTTCTTGGCC TGGCATGGTGCCTCACACCTGTAATTCCAGCACTTTGGGAGGCTGAG GTGGGCAGATCATTTGAGGTCAGA

551	patch	TAATTCCAGCACTTTGGGAGGCTGAGGTGGGCAGATCATTTGAGGTC AGAAGTTCAAGACCAGTGTGGCCAACGTGGCGAAACCCCATCTCTAC TAAAAATACAAAAAGTAGCCAGGCAT
552	patch	AACGTGGCGAAACCCCATCTCTACTAAAAATACAAAAAGTAGCCAGG CATGGTGGCACGTGCCTGTAGTCCCAGACACTCAGGAGACTGAGGC ACAAGAATCTCTTGAACCTGGGAGATG
553	patch	TTTGAGACAGAGTCTTGCTCTGTCCCCCAGGCTGGAGTGCAATGGCT CGATGTCAGCTCACTGCAACCTCCATCTCCCAGGTTCAAGAGATTCT TGTGCCTCAGTCTCCTGAGTGTCTGG
554	patch	GTATCAATTAAACATGGAGCAATTTAATTCTCACAGTAACCCTATGATA AGAGACTTTTTTTTTTTTTTTTTGAGACAGAGTCTTGCTCTGTCCCCC AGGCTGGAGTGCAATGGCTCGA
555	patch	TTATCATAGGGTTACTGTGAGAATTAAATTGCTCCATGTTTAATTGATA CATGATAAACTGATACTTAGCACAGGGCCTAGTAAATATCAGTGCTCT AGTAGTGCCTGCCCATATTATTA
556	patch	ACAGGGCCTAGTAAATATCAGTGCTCTAGTAGTGCCTGCCCATATTAT TATCATTGTTTGTGTCATTTATCTCTGTAGTAGGAAGTATATACAATCC TATTGCATAGGTTTAAGGGAATT
557	patch	CTCTGTAGTAGGAAGTATATACAATCCTATTGCATAGGTTTAAGGGAA TTAATCCACTAAAGTGTTTGGAACAGAGCCTGGCACATATTGCTATGT AACTGCATCATCATCATCATCCCT
558	patch	ACAGAGCCTGGCACATATTGCTATGTAACTGCATCATCATCATCATCC CTTTTTAATAGATGAGAAAACTGAATTTCAGAGAGGGTAGTCTGATCT GAAATTCACCTATTATTCCAGCTT
559	patch	AACTGCATCATCATCATCATCCCTTTTTAATAGATGAGAAAACTGAATT TCAGAGAGGGTAGTCTGATCTGAAATTCACCTATTATTCCAGCTTCTC TCTTCCAAATACGGCCTCTGTGC
560	patch	AGAATTCTCATTCAGAACCTTGATCACAGGCCGGGCGCGCCGGGATT GCTCACGCCTGTAATCCCAACACTTTGGGAGGCCGAGGTGGGAGGA TCACTTGAGCCCAGGATTTGGAGACTA
561	patch	TTTGGGAGGCCGAGGTGGGAGGATCACTTGAGCCCAGGATTTGGAG ACTAGCCTGGGCAACATAGCGAGACCCCTTCTCTAAAAAAGCAAACA GGCAAAACTTCATGAGAATCTTGATCA
562	patch	CCCCTTCTCTAAAAAAGCAAACAGGCAAAACTTCATGAGAATCTTGAT CATGTTAAAATTTTATGTCCTTCGATTTCTCCCTACACACACACACACA CACACACACACACACACACACAC
563	patch	TGAGAATCTTGATCATGTTAAAATTTTATGTCCTTCGATTTCTCCCTAC ACACACACACACACACACACACACACACACACACACACACACACTCAAC ATTTCCTCCACCCATATCATCACT
564	patch	TAGTTTTATCCTGTTTTCCGAAAAACAATCATTTATTTATTTATTTATTT ATTTAATTTTATGAGACAGGGTCTGGCTTTGTCACCCAGGCTGGAGT GCAGTGGTGCGATCTTGGCTCAC
565	patch	GTCTGGCTTTGTCACCCAGGCTGGAGTGCAGTGGTGCGATCTTGGC TCACTGCAACCTCTGCCTCTCAGATTCAAGCCATCCTTCCACCTCAG CTCTGCCACTGAGTAGCTGAGACTACA
566	patch	TTCAAGCCATCCTTCCACCTCAGCTCTGCCACTGAGTAGCTGAGACT ACAAGCACTCGCCACCATGCCCGGCTAATTAAAAAAATAATAATCATT TTAAATGCAAGCTTTATATTATAAA
567	patch	GCTAATTAAAAAAATAATAATCATTTTAAATGCAAGCTTTATATTATAAA TACAAAGTAAACATGAAAATAAAACCCAAACATAGCAGTGTTATTAAA CTCTGGCCTGTAGCAGTGGCTC

568	patch	AAAACCCAAACATAGCAGTGTTATTAAACTCTGGCCTGTAGCAGTGG CTCACACCTGTAATCCTAGCAGTTTGGAGGCCGAGACAGGTGGATTA CTTGAGACCTGGAGTTTGAGACCAGC
569	patch	TTGGAGGCCGAGACAGGTGGATTACTTGAGACCTGGAGTTTGAGAC CAGCCCAGGTGACACAGCAAGACCTCATCTCTACTAAAAATAAAAAAA AATTAGCCAGGTGTGGTGGTATGCAC
570	patch	TCATCTCTACTAAAAATAAAAAAAAATTAGCCAGGTGTGGTGGTATGC ACCTGTGGTCCCAGCTACTTAGGATGCTGGAGTGCGAGGATCGCTT GAGCCCAGGAGGTCAAGGCTGCAGTG
571	patch	GATGCTGGAGTGCGAGGATCGCTTGAGCCCAGGAGGTCAAGGCTGC AGTGAACTATGATCACTCATTACACCCCAGCCTGGGTGACAGAGCGA GATGCTGTCTCAAAACAAAACAAAACG
572	patch	CCCCAGCCTGGGTGACAGAGCGAGATGCTGTCTCAAAACAAAACAAA ACGAAAAACAACTCTGGCTAGATGCTATTGCTTGCCAAGGGTGCAGT CTTCCATTTATTAAAAGTGAAAATTA
573	patch	GCTATTGCTTGCCAAGGGTGCAGTCTTCCATTTATTAAAAGTGAAAAT TAGGGCCAGGCACATTGGCTCATGCCTGTAATCCCAGCACTTTGGGA GGCTGAGGTGGGTGGATCACCTGAG
574	patch	TGCCTGTAATCCCAGCACTTTGGGAGGCTGAGGTGGGTGGATCACC TGAGGTCAGGAGTTCGAGACCAGCCTGGCCAACATGGTGAAACCTTA TCTCTGCCAAAAATATAAAAGATTAGC
575	patch	CTGGCCAACATGGTGAAACCTTATCTCTGCCAAAAATATAAAAGATTA GCCATGTGTCGTGGTGGGTGCTTGTAATCTCAGCTACTTGGGAGGCT GAGGCAGGAGAATCACTTGAACCCA
576	patch	TGTAATCTCAGCTACTTGGGAGGCTGAGGCAGGAGAATCACTTGAAC CCAGGAGGCAGAGGTTGCAGTGAGCCAAGATTGTGCCATTGCACTC CAGCCTGTGCAACGAGCGAAACTCCAA
577	patch	TCAGCTACTTGGGAGGCTGAGGCAGGAGAATCACTTGAACCCAGGA GGCAGAGGTTGCAGTGAGCCAAGATTGTGCCATTGCACTCCAGCCT GTGCAACGAGCGAAACTCCAACTCAAAA

APPLICATION

Profiling of ctDNA may offer a non-invasive approach to estimate disease burden and monitor disease progression. Embodiments of the method described herein provide a quantitative method, which exploits local tissue-specific and gene-specific cfDNA degradation patterns, that can accurately estimate ctDNA burden independent of genomic aberrations.

Nucleosome-dependent cfDNA degradation at selected NDRs (e.g. promoters and first exon-intron junctions) is shown herein to be strongly associated with differential transcriptional activity in tumors and blood. A machine learning model that was developed based on expression-specific DNA degradation patterns was found to be capable of accurately predicting ctDNA fractions (see examples). Leveraging on these findings, embodiments of the methods enable for the first time the detection of tumor DNA burden (even of very low frequency) in blood by only sequencing selected NDRs in cfDNA assays. From only less than 50kb DNA sequence in total (4kb × 6 features or 4kb × 10 features), embodiments of the methods can accurately predict ctDNA levels, and thereby monitor the dynamics of the systemic tumor burden over time from blood/liquid samples. Indeed, using compact targeted sequencing (<25 kb) of predictive regions, the disclosure demonstrates how embodiments of the method enable quantitative low-cost tracking of ctDNA dynamics and disease progression.

Embodiments of the method enjoy several advantages including cost efficiency, flexibility, high accuracy and high sensitivity.

Embodiments of the method requires less sequencing and are therefore cost-efficient. In embodiments of the method, 100x less DNA sequencing (e.g. ~30kb at 100x coverage) is needed than low-pass WGS-based methods requiring whole genome sequencing at ~0.1x. The sequencing cost is also comparable to sequencing a panel at 10,000x (usual target for coding mutation panels). Embodiments of the method also require less sequencing than standard targeted sequencing assays, which usually require more than 1000kb DNA sequence.

Further, embodiments of the method can be implemented as an extension/add-on to a standard targeted panel assay, providing flexibility and further allowing for an extremely cost-effective approach to generic ctDNA profiling. For example, the NDRs identified herein can be easily added to existing cfDNA capture panels, eliminating the

need to perform two separate assays. Notably, WGS or methylation-based assays do not enjoy this flexibility.

Last but not least, embodiments of the method are capable of accurately estimating cancer cell-free DNA burden with a mean deviation of about 3.4%. As compared to conventional coding panel that usually fail (no mutations) in more than 20-30% of patients, embodiments of the method are shown to be able to accurately predict cancer cfDNA in most cancer patients. As demonstrated in the examples, both colorectal cancer and pan-cancer models have high prediction accuracy, with the pan-cancer model generalizing well to most/all solid tumor types.

Overall, embodiments of the method enable quantitative low-cost tracking of ctDNA dynamics and disease progression, and would be invaluable in the clinical setting.

It will be appreciated by a person skilled in the art that other variations and/or modifications may be made to the embodiments disclosed herein without departing from the spirit or scope of the disclosure as broadly described. For example, in the description herein, features of different exemplary embodiments may be mixed, combined, interchanged, incorporated, adopted, modified, included etc. or the like across different exemplary embodiments. The present embodiments are, therefore, to be considered in all respects to be illustrative and not restrictive.

CLAIMS

1. A method of estimating a circulating tumor DNA (ctDNA) burden in a subject, the method comprising:

determining in a blood sample obtained from the subject, a level of cell free DNA (cfDNA) that maps to six or more nucleosome-depleted regions (NDR); and

estimating the ctDNA burden based on said level of cfDNA,

wherein said NDRs

(i) comprises the NDRs of genes which transcripts are differentially expressed between healthy blood tissue and tumor tissue and/or

(ii) are degraded to different extents between healthy blood tissue and blood tissue of a tumor-bearing subject.

2. The method according to claim 1, wherein determining in a blood sample obtained from the subject, a level of cfDNA that maps to six or more NDRs comprises:

sequencing cfDNA fragments in the blood sample to obtain sequencing reads; and

determining the number of sequencing reads that align with the six or more NDRs to obtain said level of cfDNA that maps to six or more NDRs.

3. The method according to claim 2, further comprising

contacting the blood sample with six or more probes capable of binding to the six or more NDRs to capture cfDNA fragments comprising the six or more NDRs prior to the sequencing step.

4. The method according to any one of the preceding claims, wherein the NDRs are selected from the group consisting of: a promoter region, a first exon-intron junction and combinations thereof.

5. The method according to any one of the preceding claims, wherein the estimated ctDNA burden is positively associated with a tumor burden in the subject.

6. The method according to any one of the preceding claims, wherein said transcript that is differentially expressed between healthy blood tissue and tumor tissue comprises a

transcript which FPKM (Fragments Per Kilobase of transcript per Million) value differs by at least 10 times between healthy blood tissue and tumor tissue.

7. The method according to any one of the preceding claims, wherein said NDRs that are degraded to different extents between healthy blood tissue and blood tissue of a tumor-bearing subject comprises NDRs having different sequencing coverage in healthy blood tissue and in tumor tissue.

8. The method according to any one of the preceding claims, wherein said transcript that is differentially expressed in healthy blood tissue and tumor tissue is selected from the group consisting of: a transcript that is more highly expressed in healthy blood tissue than in tumor tissue, a transcript that is more highly expressed in tumor tissue than in healthy blood tissue and combinations thereof.

9. The method according to any one of the preceding claims, wherein said transcript which is differentially expressed between blood tissue and tumor tissue consists of transcript(s) that is more highly expressed in blood tissue than in tumor tissue.

10. The method according to any one of the preceding claims, wherein the six or more NDRs comprise six NDRs, further optionally ten NDRs.

11. The method according to any one of the preceding claims, wherein the total length of the six or more NDRs is no more than 30 kb.

12. The method according to any one of the preceding claims, wherein the NDRs comprise NDRs of genes comprising SLC11A1, NLRP12, PRTN3, HMBS, LILRB3, ACSL1, GP9, MX2, RASGRP4 and ATG16L2.

13. The method according to any one of the preceding claims, wherein the method is a method of determining disease progression in a subject and the method further comprises:

determining in a subsequent blood sample obtained from the subject, a level of cfDNA that maps to six or more NDRs;

estimating the ctDNA burden based on said level of cfDNA;

comparing the ctDNA burden estimated from said subsequent blood sample with

the ctDNA burden estimated from said blood sample; and

identifying the subject as having disease progression if the ctDNA burden estimated from said subsequent blood sample is higher than the ctDNA burden estimated from said blood sample and identifying otherwise if the ctDNA burden estimated from said subsequent blood sample is not higher than the ctDNA burden estimated from said blood sample.

14. The method according to claim 13, the method further comprising changing the treatment regimen received by the subject if the subject is identified as having disease progression.

15. The method according to any one of the preceding claims, wherein the tumor comprises colorectal tumor.

16. The method according to claim 15, wherein the NDRs comprise NDRs of genes comprising SHKBP1, ACSL1, BCAR1, RAB25, PRTN3 and LSR.

17. A kit for estimating a ctDNA burden in a subject, the kit comprising probes that are capable of binding to NDRs, wherein said NDRs

(i) comprise the NDRs of genes which transcripts are differentially expressed between healthy blood tissue and tumor tissue and/or

(ii) are degraded to different extents between healthy blood tissue and blood tissue of a tumor-bearing subject,

wherein said NDRs comprise NDRs of genes comprising SLC11A1, NLRP12, PRTN3, HMBS, LILRB3, ACSL1, GP9, MX2, RASGRP4 and ATG16L2.

18. A kit for estimating ctDNA burden in a subject, the kit comprising probes that are capable of binding to NDRs, wherein said NDRs

(i) comprise the NDRs of genes which transcripts are differentially expressed between healthy blood tissue and tumor tissue and/or

(ii) are degraded to different extents between healthy blood tissue and blood tissue of a tumor-bearing subject,

wherein said tumor comprises colorectal tumor and wherein said NDRs comprise NDRs of genes comprising SHKBP1, ACSL1, BCAR1, RAB25, PRTN3 and LSR.

19. The kit according to claim 17 or 18, wherein the probes comprise the sequence of SEQ ID NO: 1 to SEQ ID NO: 577, or a sequence sharing at least 75% sequence identity thereto.