

WHAT IS CLAIMED IS:

1. A method for detecting the presence of one or more nucleic acids indicative of a health condition, tissue of origin, germ layer of origin or organ of origin in a mixture of nucleic acids comprising:

performing methylation analysis on a sample comprising a plurality of nucleic acids; and

determining whether said sample includes a plurality of methylation haplotype blocks indicative of the presence of one or more nucleic acids indicative of a health condition, tissue of origin, germ layer of origin, organ of origin or any combination thereof, wherein said methylation haplotype blocks comprise a plurality of methylation sites for which the methylation status is coordinated.

2. The method of Claim 1, wherein said methylation analysis is performed on cell-free DNA.

3. The method of any one of Claims 1 and 2, wherein said methylation analysis is performed on cell-free DNA in a blood sample.

4. The method of any one of Claims 1-3, wherein said plurality of methylation haplotype blocks comprises at least 2, at least 3, at least 4, at least 5, at least 10, at least 20, at least 40, at least 50, at least 100, at least 200, at least 300, at least 400, at least 500 or more than 500 methylation haplotype blocks.

5. The method of any one of Claims 1-4, wherein said health condition is a tumor.

6. The method of Claim 5, further comprising determining whether said sample includes a plurality of methylation haplotype blocks indicative of the presence of one or more nucleic acids indicative of a normal tissue or normal organ corresponding to the tissue or organ of origin of said tumor.

7. The method of any one of Claims 1-6, wherein said health condition is fetal aneuploidy.

8. The method of any one of Claims 1-7, wherein said sample is a blood sample.

9. The method of any one of Claims 1-8, further comprising quantitating the level of said one or more nucleic acids indicative of a health condition, tissue of origin, organ of origin or any combination thereof in said sample.

10. The method of any one of Claims 1-9, wherein said methylation analysis is performed using a technique selected from the group consisting of bisulfite methylation analysis, reduced representation bisulfite sequencing, WGBS, BSPP, micro-droplet PCR, selector probe based methods, and MeDiP.

11. The method of any one of Claims 1-10, further comprising determining a methylation haplotype load for each methylation haplotype block, wherein said methylation haplotype load comprises the normalized fraction of methylated haplotypes at different lengths.

12. The method of any one of Claims 1-10, further comprising determining a unmethylated haplotype load for each methylation haplotype block, wherein said unmethylated haplotype load comprises the normalized fraction of unmethylated haplotypes at different lengths.

13. The method of any one of Claims 1-11, wherein said methylation haplotype blocks have an average size of 95bp.

14. The method of any one of Claims 1-12, wherein said methylation haplotype blocks have a minimum of 3 CpGs per block.

15. The method of any one of Claims 1-13, further comprising quantifying the level of said plurality of methylation haplotype blocks indicative of the presence one or more nucleic acids indicative of a health condition, tissue of origin, germ layer of origin, organ of origin or any combination thereof in said sample.

16. The method of Claim 6, further comprising quantifying the level of said plurality of methylation haplotype blocks indicative of the presence of a tumor in said sample and quantifying the level of said plurality of methylation haplotype blocks indicative of the presence of one or more nucleic acids indicative of a normal tissue or normal organ corresponding to the tissue or organ of origin of said tumor in said sample

17. A method of identifying methylation haplotype blocks comprising:
determining methylation haplotypes in a plurality of nucleic acid segments;
combining the methylation haplotypes and calculating methylation linkage disequilibrium on the combined methylation haplotypes; and
partitioning each segment into a plurality of methylation haplotype blocks, wherein said methylation haplotype blocks comprise a plurality of methylation sites for which the methylation status is coordinated.

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18. The method of Claim 16, wherein said methylation haplotypes are determined for a portion of a genome.

19. The method of any one of Claims 16 and 17, wherein said methylation haplotypes are determined across a whole genome.

20. The method of any one of Claims 16-18, wherein said methylation haplotype blocks are defined as the genomic region in which the r^2 value of two adjacent CpG sites is no less than 0.5.

21. The method of any one of Claims 16-19, wherein said methylation haplotype blocks are identified in nucleic acids from a tumor tissue.

22. The method of any one of Claims 16-20, wherein said methylation haplotype blocks are identified in nucleic acids from a known type of tissue.

23. The method of any one of Claims 16-21, wherein said methylation haplotype blocks are identified in nucleic acids from a fetus.

24. The method of any one of Claims 16-22, wherein said methylation haplotype blocks are identified in nucleic acids from an embryonic stem cell.

25. The method of any one of Claims 16-23, wherein said methylation haplotype blocks are identified in nucleic acids from a known germ layer.

26. The method of any one of Claims 16-24, wherein said methylation haplotype blocks have an average size of 95bp.

27. The method of any one of Claims 16-25, wherein said methylation haplotype blocks have a minimum of 3 CpGs per block.

28. The method of any one of Claims 16-26, wherein said methylation haplotype blocks are identified in nucleic acid regions from a Whole Genome Bisulfite Sequencing analysis.

29. The method of any one of Claims 16-27, wherein said methylation haplotype blocks are identified in data sets from methylation analysis of ENCODE cell lines or tissue samples.

30. The method of any one of Claims 16-28, wherein said methylation haplotype blocks are identified in data sets from methylation analysis of Infinium HumanMethylation450 BeadChip (HM450K).

31. The method of any one of Claims 16-29, further comprising calculating the pairwise correlation coefficient of adjacent CpG methylation levels across different sample sets for block partitioning.

32. The method of any one of Claims 16-30, further comprising determining methylation haplotype load for each methylation haplotype block, wherein said methylation haplotype load comprises the normalized fraction of methylated haplotypes at different lengths.

33. The method of any one of Claims 16-30, further comprising determining unmethylated haplotype load for each methylation haplotype block, wherein said unmethylated haplotype load comprises the normalized fraction of unmethylated haplotypes at different lengths.