Claims:

1. A method for identifying 5-methylcytosine (5mC) in a target nucleic acid comprising the steps of:

    a. providing a nucleic acid sample comprising the target nucleic acid;

    b. modifying the nucleic acid comprising the steps of:

        i. adding a blocking group to the 5-hydroxymethylcytosine (5hmC) in the nucleic acid sample;

        ii. converting the 5mC in the nucleic acid sample to 5-carboxylcytosine (5caC) and/or 5-formylcytosine (5fC); and

        iii. converting the 5caC and/or 5fC to dihydrouracil (DHU) to provide a modified nucleic acid sample comprising a modified target nucleic acid; and

    c. detecting the sequence of the modified target nucleic acid comprising detecting the presence of DHU in the sequence, or converting the DHU to thymine (T) and detecting the presence of the thymine (T) in the sequence;

    wherein a cytosine (C) to DHU transition or a cytosine (C) to thymine (T) transition in the sequence of the modified target nucleic acid compared to the target nucleic acid provides the location of a 5mC in the target nucleic acid.

2. The method of claim 1, wherein the percentages of a DHU or T at each transition location provide a quantitative level of 5mC at each location in the target nucleic acid.

3. A method for identifying 5mC or 5hmC in a target nucleic acid comprising the steps of:

    a. providing a nucleic acid sample comprising the target nucleic acid;

    b. modifying the nucleic acid comprising the steps of:

        i. converting the 5mC and 5hmC in the nucleic acid sample to 5-carboxylcytosine (5caC) and/or 5fC; and

ii. converting the 5caC and/or 5fC to dihydrouracil (DHU) to provide a modified nucleic acid sample comprising a modified target nucleic acid; and

c. detecting the sequence of the modified target nucleic acid comprising detecting the presence of DHU in the sequence, or converting the DHU to thymine (T) and detecting the presence of the thymine (T) in the sequence;

wherein a cytosine (C) to DHU transition or a cytosine (C) to thymine (T) transition in the sequence of the modified target nucleic acid compared to the target nucleic acid provides the location of either a 5mC or 5hmC in the target nucleic acid.

4. The method of claim 3, wherein the percentages of a DHU or T at each transition location provide a quantitative level of 5mC or 5hmC at each location in the target nucleic acid.

5. A method for identifying 5mC and identifying 5hmC in a target nucleic acid comprising:

a. identifying 5-methylcytosine (5mC) in the target nucleic acid comprising the steps of:

i. providing a first nucleic acid sample comprising the target nucleic acid;

ii. modifying the nucleic acid in the first sample comprising the steps of:

(1). adding a blocking group to the 5-hydroxymethylcytosine (5hmC) in the first nucleic acid sample;

(2). converting the 5mC in the first nucleic acid sample to 5caC and/or 5fC; and

(3). converting the 5caC and/or 5fC to dihydrouracil (DHU) to provide a modified first nucleic acid sample comprising a modified target nucleic acid;

iii. detecting the sequence of the modified target nucleic acid comprising detecting the presence of DHU in the sequence, or converting the DHU to thymine (T) and detecting the presence of the thymine (T) in the sequence; wherein a cytosine (C) to DHU transition or a cytosine (C) to thymine (T)

transition in the sequence of the modified target nucleic acid compared to the target nucleic acid provides the location of a 5mC in the target nucleic acid.

b. identifying 5mC or 5hmC in the target nucleic acid comprising the steps of:

i. providing a second nucleic acid sample comprising the target nucleic acid;

ii. modifying the nucleic acid in the second sample comprising the steps of:

(1). converting the 5mC and 5hmC in the second nucleic acid sample to 5caC and/or 5fC; and

(2). converting the 5caC and/or 5fC to dihydrouracil (DHU) to provide a modified second nucleic acid sample comprising a modified target nucleic acid; and

iii. detecting the sequence of the modified target nucleic acid from the second sample comprising detecting the presence of DHU in the sequence, or converting the DHU to thymine (T) and detecting the presence of the thymine (T) in the sequence; wherein a cytosine (C) to DHU transition or a cytosine (C) to thymine (T) transition in the sequence of the modified target nucleic acid compared to the target nucleic acid provides the location of either a 5mC or 5hmC in the target nucleic acid; and

c. comparing the results of steps (a) and (b), wherein a C to DHU or C to T transition present in step (b) but not in step (a) provides the location of 5hmC in the target nucleic acid.

6. The method of claim 5, wherein in step (a) the percentages of a DHU or T at each transition location provide a quantitative level of 5mC at each location in the target nucleic acid; in step (b), the percentages of a DHU or T at each transition location provide a quantitative level of 5mC or 5hmC at each location in the target nucleic acid; and in step (c) the differences in percentages for a C to DHU or T transition identified in step (b), but not in step (a) provide the quantitative level of a 5hmC at each location in the target nucleic acid.

7. The method according to any one of claims 1-2 or claims 5-6, wherein the blocking group added to the 5hmC is a sugar.

8. The method of claim 7, wherein the sugar is glucose or a modified glucose.

9. The method of claim 7, wherein the blocking group is added to the 5hmC by contacting the nucleic acid sample with uridine diphosphate (UDP) linked to a sugar in the presence of a glucosyltransferase enzyme.

10. The method of claim 9, wherein the glucosyltransferase enzyme is selected from the group consisting of T4 bacteriophage β-glucosyltransferase (βGT), T4 bacteriophage α-glucosyltransferase (αGT), and derivatives and analogs thereof.

11. The method according to any one of claims 1 to 6, wherein the step of converting the 5mC in the nucleic acid sample to 5caC and/or 5fC and the step of converting the 5mC and 5hmC in the nucleic acid sample to 5caC and/or 5fC comprises contacting the nucleic acid sample with a ten eleven translocation (TET) enzyme.

12. The method of claim 11, wherein the TET enzyme is selected from the group consisting of human TET1, TET2, and TET3; murine Tet1, Tet2, and Tet3; *Naegleria* TET (NgTET); Coprinopsis cinerea (CcTET) and derivatives or analogues thereof.

13. The method of claim 12, wherein the TET enzyme is NgTET or murine TET.

14. A method for identifying 5caC or 5fC in a target nucleic acid comprising the steps of:

    a. providing a nucleic acid sample comprising the target nucleic acid;

    b. converting the 5caC and 5fC to dihydrouracil (DHU) to provide a modified nucleic acid sample comprising a modified target nucleic acid;

    c. amplifying the copy number of the modified target nucleic acid; and

    d. detecting the sequence of the modified target nucleic acid;

    wherein a cytosine (C) to thymine (T) transition in the sequence of the modified target nucleic acid compared to the target nucleic acid provides the location of either a 5caC or 5fC in the target nucleic acid.

15. The method of claim 14, wherein the percentages of a T at each transition location provide a quantitative level of 5caC or 5fC at each location in the target nucleic acid.

16. A method for identifying 5caC in a target nucleic acid comprising the steps of:

    a. providing a nucleic acid sample comprising the target nucleic acid;

    b. adding a blocking group to the 5fC in the nucleic acid sample

    c. converting the 5caC to dihydrouracil (DHU) to provide a modified nucleic acid sample comprising a modified target nucleic acid; and

    d. detecting the sequence of the modified target nucleic acid comprising detecting the presence of DHU in the sequence, or converting the DHU to thymine (T) and detecting the presence of the thymine (T) in the sequence;

    wherein a cytosine (C) to DHU transition or a cytosine (C) to thymine (T) transition in the sequence of the modified target nucleic acid compared to the target nucleic acid provides the location of a 5caC in the target nucleic acid.

17. The method of claim 16, wherein the percentages of a DHU or T at each transition location provide a quantitative level of 5caC at each location in the target nucleic acid.

18. The method of claim 16, wherein the step of adding a blocking group to the 5fC comprises contacting the nucleic acid sample with an aldehyde reactive compound selected from hydroxylamine derivatives, hydrazine derivatives, and hydrazide derivatives.

19. The method of claim 18, wherein the hydroxylamine derivative is O-ethylhydroxylamine.

20. A method for identifying 5fC in a target nucleic acid comprising the steps of:

    a. providing a nucleic acid sample comprising the target nucleic acid;

    b. adding a blocking group to the 5caC in the nucleic acid sample;

    c. converting the 5fC to dihydrouracil (DHU) to provide a modified nucleic acid sample comprising a modified target nucleic acid; and

d. detecting the sequence of the modified target nucleic acid comprising detecting the presence of DHU in the sequence, or converting the DHU to thymine (T) and detecting the presence of the thymine (T) in the sequence;

wherein a cytosine (C) to DHU transition or a cytosine (C) to thymine (T) transition in the sequence of the modified target nucleic acid compared to the target nucleic acid provides the location of a 5fC in the target nucleic acid.

21. The method of claim 20, wherein the percentages of a DHU or T at each transition location provide a quantitative level of 5fC at each location in the target nucleic acid.

22. The method of claim 20, wherein the step of adding a blocking group to 5caC comprises contacting the nucleic acid sample with a carboxylic acid derivatization reagent, and an amine, hydrazine or hydroxylamine compound.

23. The method of claim 22, wherein the step of adding a blocking group to 5caC comprises contacting the nucleic acid sample with 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (EDC) and with ethylamine.

24. A method for identifying 5hmC in a target nucleic acid comprising:

a. providing a nucleic acid sample comprising the target nucleic acid;

b. modifying the nucleic acid in the sample comprising the steps of:

i. converting the 5hmC in the nucleic acid sample to 5caC and/or 5fC; and

ii. converting the 5caC and/or 5fC to dihydrouracil (DHU) to provide a modified nucleic acid sample comprising a modified target nucleic acid; and

c. detecting the sequence of the modified target nucleic acid comprising detecting the presence of DHU in the sequence, or converting the DHU to thymine (T) and detecting the presence of the thymine (T) in the sequence; wherein a cytosine (C) to DHU transition or a cytosine (C) to thymine (T) transition in the sequence of the modified target nucleic acid compared to the target nucleic acid provides the location of 5hmC in the target nucleic acid.

25. The method of claim 24, wherein the percentages of a DHU or T at each transition location provide a quantitative level of 5hmC at each location in the target nucleic acid.

26. The method of claim 24, wherein the step of converting the 5hmC to 5caC and/or 5fC comprises contacting the nucleic acid sample with an oxidizing agent.

27. The method of claim 26, wherein the oxidizing agent is potassium perruthenate or Cu(II)/TEMPO.

28. The method according to any one of claims 1 to 6 and 14 to 27, wherein the method further comprises the step of amplifying the copy number of the modified target nucleic acid.

29. The method of claim 28, wherein the step of amplifying the copy number of the modified target nucleic acid comprises performing the polymerase chain reaction (PCR) or primer extension.

30. The method according to any one of claims 1 to 6 and 14 to 29, wherein the step of converting the 5caC and/or 5fC to DHU comprises contacting the nucleic acid sample with a reducing agent.

31. The method of claim 30, wherein the reducing agent is selected from the group consisting of pyridine borane, 2-picoline borane (pic-BH_3), borane, sodium borohydride, sodium cyanoborohydride, and sodium triacetoxyborohydride.

32. The method of claim 31, wherein the reducing agent is pyridine borane or 2-picoline borane.

33. The method according to any one of claims 1 to 6 and 14 to 27, wherein the step of detecting the sequence of the modified target nucleic acid comprises one or more of chain termination sequencing, microarray, high-throughput sequencing, and restriction enzyme analysis.

34. The method of any one of claims 1-33, wherein the nucleic acid is DNA.

35. The method of any one of claims 1-33, wherein the nucleic acid is RNA.