

Claims

What is claimed is:

1. A method for detecting a predisposition to colorectal cancer or predicting likelihood, treatment response, prognosis or recurrence of colorectal cancer in a subject, comprising (a) providing a biological sample from the subject, and (b) determining the methylation status of a target DNA sequence comprising *TMEM240* or a fragment thereof or *MROH6* or a fragment thereof in the biological sample, wherein the presence of hypermethylation or hypomethylation in the target DNA sequence of the subject is indicative of the predisposition to, likelihood, poor treatment response, poor prognosis or recurrence of, colorectal cancer.
2. The method of claim 1, wherein the biological sample is a tissue, cell, blood, urine, serum, plasma, stool, ascites, sputum, saliva, gastric juice, bile, or oral mucosa.
3. The method of claim 1, wherein the method further comprises a step of defining a score as 1 if the presence of hypermethylation or hypomethylation of each gene or a fragment thereof and, defining a score as 0 if the absence of hypermethylation or hypomethylation of each gene or a fragment thereof, and summing the score.
4. The method of claim 1, wherein the presence of hypermethylation or hypomethylation in the target DNA sequence of the subject is determined by comparing the methylation status of the target DNA sequence to a methylation status of a control DNA sequence.
5. The method of claim 1, wherein the methylation status is determined by a polymerase chain reaction.
6. The method of claim 5, wherein the hypermethylation is indicated when a C_t value of the polymerase chain reaction for determining the methylation status of *TMEM240* or a fragment thereof in the human subject is less than 50; or the hypermethylation is indicated when a C_t value of the polymerase chain reaction for determining the methylation status of *MROH6* or a fragment thereof in the human subject is less than 45.
7. The method of claim 5, wherein the hypermethylation is indicated when a C_t value of the polymerase chain reaction for determining the methylation status of *TMEM240* or a fragment thereof in the human subject is less than 45; or the hypermethylation is indicated when a C_t value of the polymerase chain reaction for determining the methylation status of *MROH6* or a fragment thereof in the human subject is less than 40.

8. The method of claim 1, wherein a target DNA sequence methylation specific primer for *TMEM240* or a fragment thereof or *MROH6* or a fragment thereof is used in the methylation determination, wherein the target DNA sequence methylation specific primer for *TMEM240* or a fragment thereof has an identity of about 85% to a sequence selected from the group consisting of SEQ ID NOs: 1, 2, and 3; and the target DNA sequence methylation specific primer for *MROH6* or a fragment thereof has an identity of about 85% to a sequence selected from the group consisting of SEQ ID NOs: 5, and 6.

9. The method of claim 1, wherein a target DNA sequence methylation specific probe for *TMEM240* or a fragment thereof or *MROH6* or a fragment thereof is used in the methylation determination, wherein the target DNA sequence methylation specific probe for *TMEM240* or a fragment thereof has an identity of about 85% to a sequence of SEQ ID NO: 4; and the target DNA sequence methylation specific probe for *MROH6* or a fragment thereof has an identity of about 85% to a sequence of SEQ ID NO: 7.

10. The method of claim 1, wherein the target DNA sequence further comprises one or more DNA sequences selected from the group consisting of *BEND5* or a fragment thereof and *SMAD3* or a fragment thereof, or any of combinations thereof.

11. The method of claim 10, wherein the target DNA sequence comprises any of the following combinations of the DNA sequences: *TMEM240* or a fragment thereof and *MROH6* or a fragment thereof; *TMEM240* or a fragment thereof, *MROH6* or a fragment thereof and *BEND5* or a fragment thereof; *TMEM240* or a fragment thereof, *MROH6* or a fragment thereof, *BEND5* or a fragment thereof and *SMAD3* or a fragment thereof; *TMEM240* or a fragment thereof, *BEND5* or a fragment thereof and *SMAD3* or a fragment thereof; *TMEM240* or a fragment thereof, *MROH6* or a fragment thereof, and *SMAD3* or a fragment thereof; *MROH6* or a fragment thereof and *BEND5* or a fragment thereof; and *MROH6* or a fragment thereof, *BEND5* or a fragment thereof and *SMAD3* or a fragment thereof.

12. The method of claim 10 or 11, wherein the methylation status is determined by a polymerase chain reaction, and the hypermethylation is indicated when a C_t value of the polymerase chain reaction for determining the methylation status of *BEND5* or a fragment thereof in the human subject is less than 50; or the hypomethylation is indicated when a C_t value of the polymerase chain reaction for determining the methylation status of *SMAD3* or a fragment thereof in the human subject is higher than 40.

13. The method of claim 10 or 11, wherein the methylation status is determined by a polymerase chain reaction, and the hypermethylation is indicated when a C_t value of the polymerase chain reaction for determining the methylation status of *BEND5* or a fragment thereof in the human subject is less than 45; or the hypomethylation is indicated when a C_t value of the polymerase chain reaction for determining the methylation status of *SMAD3* or a fragment thereof in the human subject is higher than 45.

14. The method of claim 10 or 11, wherein a target DNA sequence methylation specific primer *BEND5* or a fragment thereof, or *SMAD3* or a fragment thereof or a combination thereof is used in the methylation determination, wherein the target DNA sequence methylation specific primer for *BEND5* or a fragment thereof has an identity of about 85% to a sequence selected from the group consisting of SEQ ID NOs: 8 to 11; and the target DNA sequence methylation specific primer for *SMAD3* or a fragment thereof has an identity of about 85% to a sequence selected from the group consisting of SEQ ID NOs: 14 to 15.

15. The method of claim 10 or 11, wherein a target DNA sequence methylation specific probe for *BEND5* or a fragment thereof, or *SMAD3* or a fragment thereof or a combination thereof is used in the methylation determination, wherein the target DNA sequence methylation specific probe for *BEND5* or a fragment thereof has an identity of about 85% to a sequence selected from the group consisting of SEQ ID NOs: 12 to 13; and the target DNA sequence methylation specific probe for *SMAD3* or a fragment thereof has an identity of about 85% to a sequence of SEQ ID NO: 16.

16. The method of any one of claims 1 to 11, wherein determining the methylation status further comprises a step of measuring the specificity and sensitivity by a weighted sum score analysis.

17. An isolated nucleic acid molecule having a sequence selected from the group consisting of: SEQ ID Nos: 1 to 16.

18. A kit for detecting a predisposition to colorectal cancer or predicting likelihood, treatment response, prognosis or recurrence of colorectal cancer in a subject, which comprises an target DNA sequence methylation specific primer pair for detection of a methylation status of a target DNA sequence comprising *TMEM240* or a fragment thereof or *MROH6* or a fragment thereof.

19. The kit of claim 18, further comprising a target DNA sequence methylation specific probe for detection of a methylation status of a target DNA sequence comprising *TMEM240* or a fragment thereof or *MROH6* or a fragment thereof.

5 20. The kit of claim 18, wherein the target DNA sequence methylation specific primer pair for *TMEM240* or a fragment thereof comprises SEQ ID NOs: 1 and 2 or 1 and 3; and the target DNA sequence methylation specific primer pair for *MROH6* or a fragment thereof comprises SEQ ID NOs: 5 and 6.

21. The kit of claim 19, wherein the target DNA sequence methylation specific probe for *TMEM240* or a fragment thereof comprises SEQ ID NO: 4; and the target DNA sequence
10 methylation specific probe for *MROH6* or a fragment thereof comprises SEQ ID NO: 7

22. The kit of any of claims 18 to 21, wherein the target DNA sequence further comprises *BEND5* or a fragment thereof or *SMAD3* or a fragment thereof, and the kit further comprises one or more target DNA sequence methylation specific primer pairs for detection of a methylation status of *BEND5* or a fragment thereof or *SMAD3* or a fragment thereof, or any combination
15 thereof.

23. The kit of claim 22, wherein the target DNA sequence methylation specific primer pair for *BEND5* or a fragment thereof comprises SEQ ID Nos. 8 and 9 or 10 and 11; the target DNA sequence methylation specific primer pair for *SMAD3* or a fragment thereof comprises SEQ ID Nos. 14 and 15.

20 24. The kit of claim 22, wherein the kit further comprises one or more target DNA sequence methylation specific probe for detection of a methylation status of *BEND5* or a fragment thereof or *SMAD3* or a fragment thereof, or any combination thereof, wherein the target DNA sequence methylation specific probe for *BEND5* or a fragment thereof comprises SEQ ID NO: 12 or 13; and the target DNA sequence methylation specific probe for *SMAD6* or a fragment thereof comprises
25 SEQ ID NO: 16.