

What is claimed is:

1. An *in-vitro* method for obtaining early predictors of cervical cancer, the method comprising the steps of: (a) measuring DNA methylation from a cervical specimen sample, (b) performing statistical analysis on the DNA methylation measurement
5 obtained in step a, (c) determining DNA methylation status of a multitude of independent genomic CG positions called CG identifiers (CGIDs) by performing analysis of progressive DNA methylation alterations (APDMA) of genome wide DNA methylation profiles obtained in step b, (d) classifying CGIDs based on frequency of their DNA methylation correlating with cervical cancer premalignant stage progression,
10 (e) obtaining candidate CGIDs from classification in step d to obtain early predictors of cervical cancer as DNA methylation biomarkers, characterized in that said candidate CGIDs as the early predictors of cervical cancer as DNA methylation biomarkers, wherein the CGIDs are selected from a group as set forth in SEQ NO: 4, SEQ ID NO: 7, SEQ ID NO: 17, SEQ ID NO: 19, SEQ ID NO: 34, SEQ ID NO: 39, SEQ ID NO: 42, SEQ ID NO: 43, SEQ ID NO: 49, SEQ ID NO: 56, SEQ ID NO: 57, SEQ ID NO: 58, SEQ ID NO: 65, and SEQ ID NO: 70, and wherein the CGIDs are at least as set forth in SEQ ID: 3 and SEQ ID: 31.
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2. The method according to claim 1, said measuring DNA methylation is performed using
20 methods comprising, Illumina 27K, 450K or 850K arrays, genome wide bisulfite sequencing on platforms including, HiSeq, MiniSeq, MiSeq or NextSeq sequencers, torrent sequencing, methylated DNA Immunoprecipitation (MeDIP) sequencing, hybridization with oligonucleotide arrays, DNA pyrosequencing, mass spectrometry based (Epityper™) or PCR based methylation assays; and
25 said statistical analysis on the DNA methylation measurement includes Pearson correlation, Receiver operating characteristics (ROC) assays, and hierarchical clustering analysis.
3. The method according to claim 1, said cervical cancer premalignant stage progression
30 comprises cervical intraepithelial neoplasia lesions at stages CIN1, CIN2 and CIN3.

- 5 4. A kit for predicting cervical cancer, comprising reagents and primers for DNA
methylation measurements of CGIDs as set forth in SEQ ID NO:3, SEQ ID NO:31, and
a combination thereof, wherein the reagents and primers are selected from:
- 10 a) a forward, biotinylated primer consisting of the nucleotide sequence SEQ ID NO:80,
a reverse primer consisting of the nucleotide sequence SEQ ID NO:81, and a
pyrosequencing primer consisting of the nucleotide sequence SEQ ID NO:82, for
DNA methylation measurements of the CGIDs as set forth in SEQ ID NO: 31;
- b) a forward primer consisting of the nucleotide sequence SEQ ID NO:90, and a reverse
primer consisting of the nucleotide sequence SEQ ID NO:91, for DNA methylation
measurements of the CGIDs as set forth in SEQ ID NO: 31;
- 15 c) a forward, biotinylated primer consisting of the nucleotide sequence SEQ ID NO:83,
a reverse primer consisting of the nucleotide sequence SEQ ID NO:84, and a
pyrosequencing primer consisting of the nucleotide sequence SEQ ID NO:85, for
DNA methylation measurements of the CGIDs as set forth in SEQ ID NO: 3;
- 20 d) a forward primer consisting of the nucleotide sequence SEQ ID NO:88 and a reverse
primer consisting of the nucleotide sequence SEQ ID NO:89, for DNA methylation
measurements of the CGIDs as set forth in SEQ ID NO: 3; or
a combination of any one of a) – d).
- 25 5. The kit of claim 4, wherein the kit is for a DNA pyrosequencing methylation assay for
predicting cervical cancer.
6. The kit of claim 4, wherein the kit is for a multiplexed targeted-amplification bisulfite
sequencing methylation assay for detecting cervical cancer.
- 30 7. The kit according to claim 4, wherein the kit is for a mass spectrometry based or PCR
based methylation assay of DNA extracted from a sample for detecting cancer.

8. The kit of claim 4, further comprising reagents and primers for DNA methylation measurements of CGIDs as set forth in SEQ NO:4, SEQ ID NO:7, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:34, SEQ ID NO:39, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:49, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:65, SEQ ID NO:70 and combinations thereof.

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