

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 ID NO: 3, SEQ NO: 4, SEQ ID NO: 7, SEQ ID NO: 17, SEQ ID NO: 19, SEQ ID NO: 31, SEQ ID NO: 34,
15 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.
2. The method according to claim 1, said measuring DNA methylation is performed using methods comprising, Illumina 27K, 450K or 850K arrays, genome wide bisulfite
20 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.

4. A panel of DNA methylation biomarkers for screening and early detection of cervical cancer, wherein the panel comprises of CGIDs derived by the APDMA method having sequences selected from the group as set forth in SEQ ID NO: 3, SEQ NO: 4, SEQ ID NO: 7, SEQ ID NO: 17, SEQ ID NO: 19, SEQ ID NO: 31, 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 optionally said panel is used in combination with other biomarkers as early predictors of cervical cancer.
5. A combination of DNA methylation biomarkers for screening and early detection of cervical cancer, said combination comprises of CGIDs derived using the APDMA method of claim 4, for detecting cervical cancer by measuring DNA methylation levels of said CGIDs in DNA originating from cervical specimens and deriving a “cervical cancer methylation predictor” using linear regression equations and Receiver operating characteristics (ROC) assays, wherein the CGIDs are selected from a group as set forth in SEQ ID NO: 3, SEQ NO: 4, SEQ ID NO: 7, SEQ ID NO: 17, SEQ ID NO: 19, SEQ ID NO: 31, 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 combinations thereof.
6. A kit for detecting cervical cancer, comprising one of
- a) means and reagents for DNA methylation measurements of CGIDs and deriving a DNA methylation predictor of cervical cancer and an instruction manual, wherein the CGIDs are as set forth in SEQ ID NO: 3, SEQ NO: 4, SEQ ID NO: 7, SEQ ID NO: 17, SEQ ID NO: 19, SEQ ID NO: 31, 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;
- b) a panel of CGIDs in the form of a chip for detecting cervical cancer, wherein the panel of CGIDs are as set forth in SEQ ID NO: 3, SEQ NO: 4, SEQ ID NO: 7, SEQ ID NO: 17, SEQ ID NO: 19, SEQ ID NO: 31, 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;

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;

5 c) means and reagents for DNA pyrosequencing methylation assays for predicting cervical cancer by measuring DNA methylation of CGIDs combinations of claim 5, wherein the forward, biotinylated primer is as set forth in SEQ ID NO: 83, the reverse primer is as set forth in SEQ ID NO: 84, and the pyrosequencing primer is as set forth in SEQ ID NO: 85;

10 d) means and reagents for multiplexed targeted-amplification bisulfite sequencing methylation assays on a next generation sequencer for detecting cervical cancer by measuring the DNA methylation levels of CGIDs combinations of claim 5, wherein the CGIDs are as set forth in SEQ ID NO: 3, SEQ NO: 4, SEQ ID NO: 7, SEQ ID NO: 17, SEQ ID NO: 19, SEQ ID NO: 31, SEQ ID NO: 34, SEQ ID NO: 39, SEQ ID NO: 42, 15 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

20 e) means and reagents for mass spectrometry based (Epityper™) or PCR based methylation assays of DNA extracted from sample for detecting cancer by measuring the DNA methylation levels of CGIDs combinations according to claim 5.

7. A use of multivariable linear regression equation or neural network analysis for 25 calculating a methylation score predicting cervical cancer by using measurements of DNA methylation CGIDs combinations according to claim 5.

8. A use of Receiver operating characteristics (ROC) assays to define a “methylation 30 score” threshold differentiating cervical cancer from noncancer cervical tissue by using measurements of DNA methylation combinations according to claim 5.