

What is claimed is:

1. The method of using a “binary-categorical ”DNA methylation signature of cancer for detecting hepatocellular carcinoma (HCC) Liver cancer (detect) and for differentiating from other tumors (spec) comprising the step of deriving said “binary” DNA methylation signature by using a “binary-categorical differentiation (BCD)” method from genome wide DNA methylation maps to discover regions that are binary and categorically different between cancer and all normal tissues notwithstanding the amount of normal DNA; and measuring DNA methylation levels of one or more of the CG IDs from the following tables deriving a “cancer methylation score” using either a “binary categorical” equation or using a linear regression equation and Receiver operating characteristics (ROC) assays in DNA originating from the tumor in cell-free plasma DNA derived from the patient wherein the tables are the following:

Liver_detect					
cg00370303	cg10900437	cg02012576	cg16460359	cg04035559	cg17419241
cg00931619	cg11223367	cg03768777	cg16977570	cg04085025	cg18607529
cg05040544	cg19289599	cg06233293	cg24804544	cg26523670	cg09992116
cg05739190	cg24599205				

Liver_spec					
cg12137206	cg14126493	cg06105778	cg22076972	cg13341720	cg03705926
cg09363194	cg07036412	cg02702614	cg10181419	cg05876864	cg11068343
cg17167468	cg15375239	cg00026222	cg17283781	cg16147221	cg26386472
cg14570307	cg06207432	cg07610192	cg03422204	cg11684022	cg23693289
cg21107197	cg04920951	cg20385508	cg25296314	cg20707679	cg26703661
cg00456086	cg05009389	cg19388016	cg08460435	cg04739306	cg04221886
cg26797073	cg04109768	cg05337743	cg00483503	cg18668780	cg10604002
cg27650175	cg05684891	cg26026416	cg00177496	cg14221460	cg16551483
cg13438961	cg24432073	cg21059834	cg23305567	cg04809136	cg21105227

2. The method of using a “binary-categorical ”DNA methylation signature of cancer for detecting lung cancer (detect) and for differentiating from other tumors (spec) comprising the step of deriving said “binary” DNA methylation signature by using a “binary-categorical differentiation

(BCD)” method from genome wide DNA methylation maps to discover regions that are binary and categorically different between cancer and all normal tissues notwithstanding the amount of normal DNA; and

measuring DNA methylation levels of one or more of the CG IDs from the following tables and deriving a “cancer methylation score” using either a “binary categorical” equation or using a linear regression equation and Receiver operating characteristics (ROC) assays in DNA originating from the tumor in cell-free plasma DNA derived from the patient wherein the tables are the following:

Lung_detect					
cg04223424	cg06530490	cg08944430	cg09463882	cg11017065	cg12405785
cg16405026	cg21410080	cg23141355	cg25024074		

Lung_spec					
~~cg05917732~~	cg02682457	cg23407396	cg23601095	cg23141355	cg15386964
cg02578368	cg24631970	cg27487839	cg16405026		
cg23141355	cg06530490	cg04223424	~~cg25470077~~	cg07138603	cg23460835
cg20678442	cg15436096				

3. The method of using a “binary-categorical ”DNA methylation signature of cancer for detecting prostate cancer (detect) and for differentiating from other tumors (spec) comprising the step of deriving said “binary” DNA methylation signature by using a “binary-categorical differentiation (BCD)” method from genome wide DNA methylation maps to discover regions that are binary and categorically different between cancer and all normal tissues notwithstanding the amount of normal DNA; and

measuring DNA methylation levels of one or more of the CG IDs from the following tables and deriving a “cancer methylation score” using either a “binary categorical” equation or using a linear regression equation and Receiver operating characteristics (ROC) assays in DNA originating from the tumor in cell-free plasma DNA derived from the patient wherein the tables are the following:

Prostate_detect_spec			
cg14283569	cg18085998	cg13303553	cg17929627

4. The method of using a “binary-categorical” DNA methylation signature of cancer for detecting breast cancer (detect) and for differentiating from other tumors (spec) comprising the step of deriving said “binary” DNA methylation signature by using a “binary-categorical differentiation (BCD)” method from genome wide DNA methylation maps to discover regions that are binary and categorically different between cancer and all normal tissues notwithstanding the amount of normal DNA; and

measuring DNA methylation levels of one or more of the CG IDs from the following tables and deriving a “cancer methylation score” using either a “binary categorical” equation or using a linear regression equation and Receiver operating characteristics (ROC) assays in DNA originating from the tumor in cell free DNA derived from the patient wherein the tables are the following:

Breast_detect					
cg13031251	cg19595750	cg16842053	cg18565473	cg09734791	cg25694349
cg09695735	cg03637878	cg26261793	cg18800085	cg16132520	cg05617413
cg17228900	cg06945936	cg08406370	cg24427504	cg26937500	cg11297107
cg02215070	cg14140647	cg05377226	cg07070305	cg24899571	cg07844931

Breast_Spec				
cg00467244	cg04194674	cg06879394	cg10720997	cg19966212
cg00722320	cg04751811	cg06998282	cg11498607	cg24525457
cg01308827	cg06282270	cg08066035	cg14862207	cg26228266
cg03113878	cg06405186	cg08296680	cg17945153	cg20180843

5. The method of using a “binary-categorical” DNA methylation signature of cancer for detecting colorectal cancer (CRC) (detect) and for differentiating from other tumors (spec) comprising the step of deriving said “binary” DNA methylation signature by using a “binary-categorical

differentiation (BCD)” method from genome wide DNA methylation maps to discover regions that are binary and categorically different between cancer and all normal tissues notwithstanding the amount of normal DNA; and measuring DNA methylation levels of one or more of the CG IDs from the following tables and deriving a “cancer methylation score” using either a “binary categorical” equation or using a linear regression equation and Receiver operating characteristics (ROC) assays in DNA originating from the tumor in cell free DNA derived wherein the tables are the following:

CRC_detect_spec					
cg08808128	cg03788131	cg09854653	cg21627760	cg08169901	cg07494047
cg01566242	cg13788592	cg24102266	cg17716617	cg16733654	

6. The method of using a “binary-categorical ”DNA methylation signature of cancer for detecting pancreatic cancer (detect) and for differentiating from other tumors (spec) comprising the step of deriving said “binary” DNA methylation signature by using a “binary-categorical differentiation (BCD)” method from genome wide DNA methylation maps to discover regions that are binary and categorically different between cancer and all normal tissues notwithstanding the amount of normal DNA; and measuring DNA methylation levels of one or more of the CG IDs from the following tables and deriving a “cancer methylation score” using either a “binary categorical” equation or using a linear regression equation and Receiver operating characteristics (ROC) assays in DNA originating from the tumor cell free DNA derived from the patient wherein the tables are:

Pancreas_detect					
cg11017065	cg23833588	cg25024074	cg21277995	cg22286978	cg06241792
cg11591516	cg10096177	cg12035092	cg03611007	cg17996329	cg13807970
cg16678602	cg15386964	cg01423964	cg07900968	cg19118812	cg06728579
cg16232979	cg08406370				
Pancreas_spec					
cg01237565	cg08182975	cg15323936	cg19102272	cg01311909	cg26927232
cg22290704	cg15832577	cg20983577	cg26466027	cg09796911	cg15850155
cg15510118	cg25591377	cg16165258	cg25595541	cg18151519	cg19749445
cg14870128	cg13441142				

7. The method of using a “binary-categorical ”DNA methylation signature of cancer for detecting brain cancer (glioblastoma) (detect) and for differentiating from other tumors (spec) comprising the step of deriving said “binary” DNA methylation signature by using a “binary-categorical differentiation (BCD)” method from genome wide DNA methylation maps to discover regions that are binary and categorically different between cancer and all normal tissues notwithstanding the amount of normal DNA; and measuring DNA methylation levels of one or more of the CG IDs from the following tables and deriving a “cancer methylation score” using either a “binary categorical” equation or using a linear regression equation and Receiver operating characteristics (ROC) assays in DNA originating from the tumor in cell free DNA derived from the patient wherein the tables are the following:

Brain_detect-spec					
cg06887260	cg19116006	cg10938374	cg03663746	cg25568243	cg27449131
cg24917627	cg04134305	cg09797645	cg02892595	cg13231951	cg26269703
cg09183941	cg16842053	cg26551897	cg26988692	cg07849581	cg25026703
cg06798642	cg22963915	cg04245373	cg25533556	cg27659841	cg24917627
cg04692993	cg06045408	cg06887260	cg11345323	cg17167076	cg17526812
cg19929355	cg22513169	cg22865720			

8. The method of using a “binary-categorical ”DNA methylation signature of cancer for detecting gastric (stomach) cancer (detect) and for differentiating from other tumors (spec) comprising the step of deriving said “binary” DNA methylation signature by using a “binary-categorical differentiation (BCD)” method from genome wide DNA methylation maps to discover regions that are binary and categorically different between cancer and all normal tissues notwithstanding the amount of normal DNA; and measuring DNA methylation levels of one or more of the CG IDs from the following tables and deriving a “cancer methylation score” using either a “binary categorical” equation or using a linear regression equation and Receiver operating characteristics (ROC) assays in DNA originating from the tumor in cell free DNA derived from the patient wherein the tables are the following:

Stomach_detect					
cg04125371	cg05377226	cg05611779	cg06241792	cg07900968	cg09734791
cg11017065	cg12510981	cg13807970	cg15760257	cg18323466	cg19118812
cg19419279	cg19769760	cg20334243	cg26261793		
Stomach_spec					
cg17187167	cg07350470	cg05000488	cg25612145	cg09851120	cg00904726
cg04911739	cg18192294	cg11861709	cg19452853	cg02706110	cg03768513
cg05611779	cg06981182	cg06118999	cg04812509	cg10131095	cg05339066
cg19235339					

9. The method of using a “binary-categorical” DNA methylation signature of cancer for detecting ovarian cancer (detect) and for differentiating from other tumors (spec) comprising the step of deriving said “binary” DNA methylation signature by using a “binary-categorical differentiation (BCD)” method from genome wide DNA methylation maps to discover regions that are binary and categorically different between cancer and all normal tissues notwithstanding the amount of normal DNA; and

measuring DNA methylation levels of one or more of the CG IDs from the following tables and deriving a “cancer methylation score” using either a “binary categorical” equation or using a linear regression equation and Receiver operating characteristics (ROC) assays in DNA

originating from the tumor in cell free DNA derived from the patient wherein the tables are the following:

Ovarian_detect					
cg24339193	cg04008429	cg06849719	cg22694153	cg11252337	cg15804105
cg12479674	cg06961071	cg21210985	cg01556502	cg02537149	cg23983315
cg03597143	cg27209395				
Ovarian_spec					
cg00895834	cg01159194	cg01961086	cg02649698	cg03345116	cg03456771
cg09392827	cg10178270	cg10581012	cg13459217	cg15701612	cg17130982
cg05901462	cg07068768	cg08389588	cg09173621	cg19276014	cg19846609
cg18476766	cg19129687				

10. The method of using a “binary-categorical ”DNA methylation signature of cancer for detecting cervical cancer (detect) and for differentiating from other tumors (spec) comprising the step of deriving said “binary” DNA methylation signature by using a “binary-categorical differentiation (BCD)” method from genome wide DNA methylation maps to discover regions that are binary and categorically different between cancer and all normal tissues notwithstanding the amount of normal DNA; and measuring DNA methylation levels of one or more of the CG IDs from the following tables and deriving a “cancer methylation score” using either a “binary categorical” equation or using a linear regression equation and Receiver operating characteristics (ROC) assays in DNA originating from the tumor in cell free DNA derived from the patient wherein the tables are the following:

Cervix_detect					
cg00578154	cg13644629	cg01423964	cg15745619	cg04522671	cg21621906
cg00757182	cg14962363	cg01601746	cg17228900	cg07126167	cg22806837
cg08134106	cg22922289	cg09260640	cg24625128	cg11259628	cg27420520
cg08535260	cg23141355	cg09734791	cg25024074		
Cervix_spec					
cg00829990	cg02401399	cg04996219	cg07066594	cg07195011	cg07576142
cg09260640	cg12961842	cg13668618	cg18543270		

11. The method of using a “binary-categorical ”DNA methylation signature of cancer for detecting head and neck squamous cell carcinoma (detect) and for differentiating from other tumors (spec) comprising the step of deriving said “binary” DNA methylation signature by using a “binary-categorical differentiation (BCD)” method from genome wide DNA methylation maps to discover regions that are binary and categorically different between cancer and all normal tissues notwithstanding the amount of normal DNA; and measuring DNA methylation levels of one or more of the CG IDs from the following tables and deriving a “cancer methylation score” using either a “binary categorical” equation or using a linear regression equation and Receiver operating characteristics (ROC) assays in DNA originating from the tumor in cell free DNA derived from the patient wherein the tables are the following:

HNSC_detect					
cg01613638	cg02776314	cg03280624	cg04524120	cg05151803	cg07746323
cg07900968	cg08406370	cg11108676	cg12083965	cg15397448	cg17428324
cg18403606	cg20334243	cg26770917	cg27009208	cg27420520	
HNSC_spec					
cg01217080	cg03522799	cg06672120	cg09136346	cg10155875	cg18006328
cg18443253	cg19287220				

12. The method of using a “binary-categorical ”DNA methylation signature of cancer for detecting esophageal carcinoma (detect) and for differentiating from other tumors (spec) comprising the step of deriving said “binary” DNA methylation signature by using a “binary-categorical differentiation (BCD)” method from genome wide DNA methylation maps to discover regions that are binary and categorically different between cancer and all normal tissues notwithstanding the amount of normal DNA; and measuring DNA methylation levels of one or more of the CG IDs from the following tables and deriving a “cancer methylation score” using either a “binary categorical” equation or using a linear regression equation and Receiver operating characteristics (ROC) assays in DNA originating from the tumor in cell free DNA derived from the wherein the tables are the following:

Esophagus_detect					
cg03280624	cg03735888	cg06530490	cg06963053	cg08944430	cg09734791
cg11017065	cg12035092	cg18344922	cg19118812	cg20334243	cg22128431
cg23141355	cg24740531	cg27009208	cg27420520		
Esophagus_spec					
cg00532449	cg02763101	cg04743654	cg08055087	cg08932440	cg09556952
cg10608333	cg12473285	cg12966367	cg17579667	cg17949440	cg18723937
cg21554552	cg22647407	cg23286646	cg23730575	cg27569446	

13. The method of using a “binary-categorical ”DNA methylation signature of cancer for detecting bladder cancer (detect) and for differentiating from other tumors (spec) comprising the step of deriving said “binary” DNA methylation signature by using a “binary-categorical differentiation (BCD)” method from genome wide DNA methylation maps to discover regions

that are binary and categorically different between cancer and all normal tissues notwithstanding the amount of normal DNA; and measuring DNA methylation levels of one or more of the CG IDs from the following tables and deriving a “cancer methylation score” using either a “binary categorical” equation or using a linear regression equation and Receiver operating characteristics (ROC) assays in DNA originating from the tumor in cell free DNA derived from the patient wherein the tables are the following:

Bladder_detect					
cg01423964	cg04223424	cg01556502	cg23141355	cg10723962	cg09734791
cg25024074	cg21039778	cg19113641	cg04342821	cg09008417	cg05873285
Bladder_spec					
cg14773260	cg08827322	cg05085809	cg13544006	cg02293936	cg10153335
cg05039004	cg14718568	cg07790170	cg12995090	cg16495265	cg01508045
cg04933208	cg03231163	cg06708937	cg00675569	cg06312813	cg14126688
cg12984729	cg02384661	cg08307030	cg26884027	cg20540209	cg04355159
cg08857479	cg23395715	cg22006640	cg26279336	cg19898108	cg17446010
cg12911122					

14. The method of using a “binary-categorical ”DNA methylation signature of cancer for detecting renal (kidney) cancer (detect) and for differentiating from other tumors (spec) comprising the step of deriving said “binary” DNA methylation signature by using a “binary-categorical differentiation (BCD)” method from genome wide DNA methylation maps to discover regions that are binary and categorically different between cancer and all normal tissues notwithstanding the amount of normal DNA; and measuring DNA methylation levels of one or more of the CG IDs from the following tables and deriving a “cancer methylation score” using either a “binary categorical” equation or using a linear regression equation and Receiver operating characteristics (ROC) assays in DNA originating from the tumor in cell free DNA derived from the patient wherein the tables are the following:

Renal cancer_detect_spec					
cg08884571	cg00011225	cg14535274	cg05507490	cg10367244	cg07190763
cg02971546	cg19990785	cg03084949	cg08765317	cg02820958	cg23946709
cg26642667					

15. The method of using a “binary-categorical ”DNA methylation signature of cancer for detecting testicular cancer (detect) and for differentiating from other tumors (spec) comprising the step of deriving said “binary” DNA methylation signature by using a “binary-categorical differentiation (BCD)” method from genome wide DNA methylation maps to discover regions that are binary and categorically different between cancer and all normal tissues notwithstanding the amount of normal DNA; and measuring DNA methylation levels of one or more of the CG IDs from the following tables and deriving a “cancer methylation score” using either a “binary categorical” equation or using a linear regression equation and Receiver operating characteristics (ROC) assays in DNA originating from the tumor in cell free DNA derived from the patient wherein the tables are the following:

Testicular_detect_spec					
cg14531093	cg11777290	cg13283877	cg03966099	cg26939375	cg26297530
cg16157016	cg14002772	cg09890687	cg05134918	cg09719850	cg06456125
cg17978367	cg20100671	cg26627956	cg19789755	cg14393609	cg21634331
cg02039634	cg25159927	cg01895439			

16. The method of using a “binary-categorical ”DNA methylation signature of cancer for detecting 13 common solid tumors (Pan cancer) (bladder cancer, brain cancer, breast cancer, cervical cancer, colorectal cancer CRC, esophageal cancer, liver cancer, lung cancer, ovarian cancer, pancreatic cancer, prostate cancer, and stomach cancer) comprising the step of deriving said “binary” DNA methylation signature by using a “binary-categorical differentiation (BCD)”

method from genome wide DNA methylation maps to discover regions that are binary and categorically different between cancer and all normal tissues notwithstanding the amount of normal DNA; and

measuring DNA methylation levels of one or more of the CG IDs from the following tables and deriving a “cancer methylation score” using either a “binary categorical” equation or using a linear regression equation and Receiver operating characteristics (ROC) assays in DNA originating from the tumor in cell free DNA derived from the patient wherein the tables are the following:

Pan-cancer_detect					
cg01423964	cg04223424	cg06530490	cg06543087	cg07900968	cg08406370
cg08848774	cg09734791	cg10723962	cg11017065	cg15759056	cg15760257
cg16405026	cg17228900	cg21277995	cg22286978	cg23141355	cg24427504
cg25024074	cg27420520				

17. The method of using a “binary-categorical ”DNA methylation signature of cancer for detecting acute myeloid leukemia (AML) comprising the step of deriving said “binary” DNA methylation signature by using a “binary-categorical differentiation (BCD)” method from genome wide DNA methylation maps to discover regions that are binary and categorically different between cancer and all normal tissues notwithstanding the amount of normal DNA; and

measuring DNA methylation levels of one or more of the CG IDs from the following tables and deriving a “AML methylation score” using either a “binary categorical” equation or using a linear regression equation and Receiver operating characteristic (ROC) assay in DNA originating from the tumor in cell free DNA derived from the patient wherein the tables are the following:

AML_detect-spec					
cg00594866	cg05608159	cg18658397	cg18780412	cg20439288	cg22828045
cg25375340					

18. The method of using a “binary-categorical” DNA methylation signature of cancer for detecting melanoma comprising the step of deriving said “binary” DNA methylation signature by using a “binary-categorical differentiation (BCD)” method from genome wide DNA methylation maps to discover regions that are binary and categorically different between cancer and all normal tissues notwithstanding the amount of normal DNA; and measuring DNA methylation levels of one or more of the CG IDs from the following tables and deriving a "melanoma methylation score" using either a "binary categorical" equation or using a linear regression equation and Receiver operating characteristic (ROC) assay in DNA originating from the tumor in cell free DNA derived from the patient wherein the tables are the following:

Melanoma_detect-spec					
cg00325866	cg01228636	cg04616691	cg04824711	cg05569109	cg06019853
cg08611163	cg10830649	cg12593303	cg15307891	cg18866529	cg19530886
cg19634213	cg20146030	cg21755725	cg22280705	cg24217704	cg24678095
cg26127345	cg27084903				

19. The methods of claims 1-18 wherein said genome wide DNA methylation maps derived from one or more of cancer cells, normal tissues and blood DNA.

20. The methods of claims 1-18 wherein said “binary-categorical differentiation (BCD)” method includes use of one or more of the following: Illumina 27K, 450K or EPIC arrays, genome wide bisulfite sequencing, methylated DNA Immunoprecipitation (MeDIP) sequencing and hybridization with oligonucleotide arrays.

21. The methods of claims 1-18 further comprising the step of using DNA pyrosequencing methylation assays for predicting cancer by using DNA methylation combination of two or more CG IDs.

22. The methods of claims 1 -18 further comprising the step of using multiplexed amplification targeted bisulfite sequencing on a next generation sequencer such as the Illumina MiSeq for detecting cancer.

23. The methods of claims 1-18 further comprising the step of using a “binary categorical assay” for calculating a methylation score for predicting cancer.

24. The methods of claims 1 -18 further comprising the step of using a multivariate linear regression equation for calculating a methylation score to predict cancer.

25. The methods of claims 1-18 further comprising the step of using a Receiver operating characteristics (ROC) assay to define a “methylation score” threshold differentiating cancer from noncancer and tissue of origin by using measurements of DNA methylation combinations of two or more CG IDs.