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(54) METHODS AND MATERIALS FOR CLASSIFICATION OF TISSUE OF ORIGIN OF TUMOR SAMPLES

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(52) **U.S. Cl.**
CPC ***C12Q 1/6886*** (2013.01); *C12Q 2600/178* (2013.01); *C12Q 2600/158* (2013.01)

(57) **ABSTRACT**

The present invention provides a process for classification of cancers and tissues of origin through the analysis of the expression patterns of specific microRNAs and nucleic acid molecules relating thereto. Classification according to a microRNA tree-based expression framework allows optimization of treatment, and determination of specific therapy.

Specification includes a Sequence Listing.

FIG. 1A

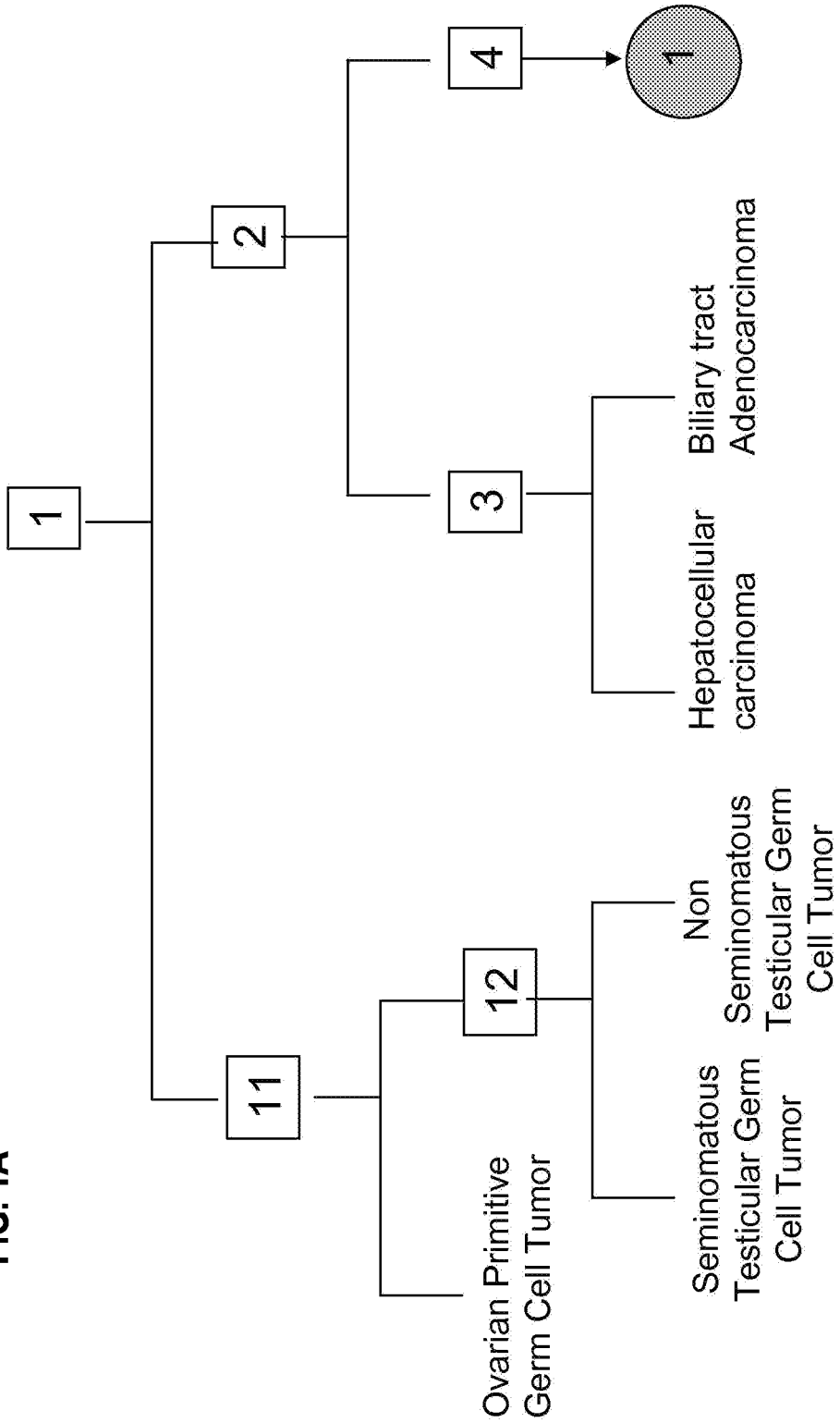

1
2
4
1
3
Biliary tract Adenocarcinoma
Hepatocellular carcinoma
11
12
Non Seminomatous Testicular Germ Cell Tumor
Seminomatous Testicular Germ Cell Tumor
Ovarian Primitive Germ Cell Tumor

FIG. 1B

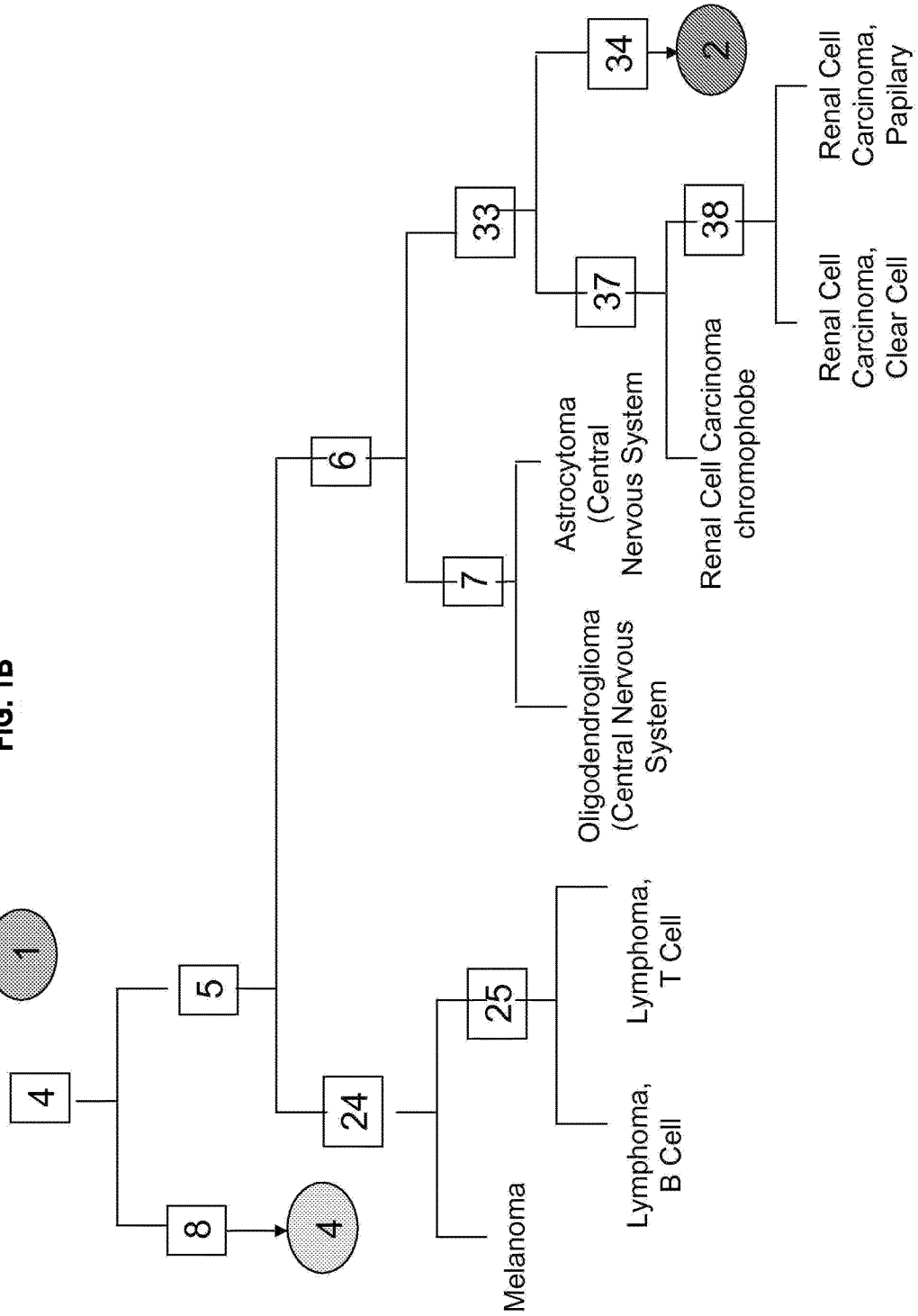
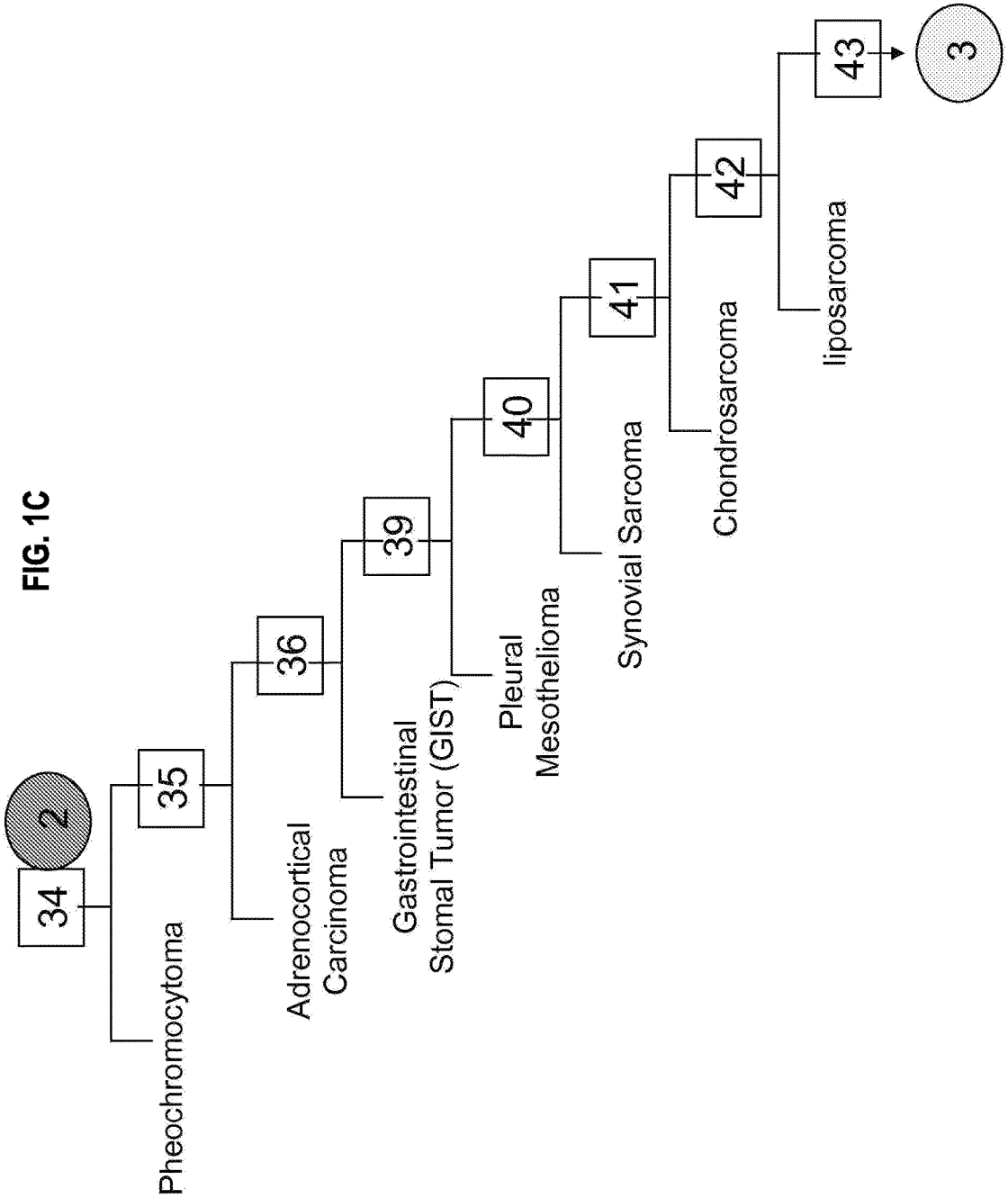

1
4
5
8
4
24
6
25
7
33
34
2
37
38
Melanoma
Lymphoma, B Cell
Lymphoma, T Cell
Oligodendroglioma (Central Nervous System
Astrocytoma (Central Nervous System
Renal Cell Carcinoma chromophobe
Renal Cell Carcinoma, Clear Cell
Renal Cell Carcinoma, Papilary

FIG. 1C


2
34
35
36
39
40
41
42
43
3
Pheochromocytoma
Adrenocortical Carcinoma
Gastrointestinal Stomal Tumor (GIST)
Pleural Mesothelioma
Synovial Sarcoma
Chondrosarcoma
liposarcoma

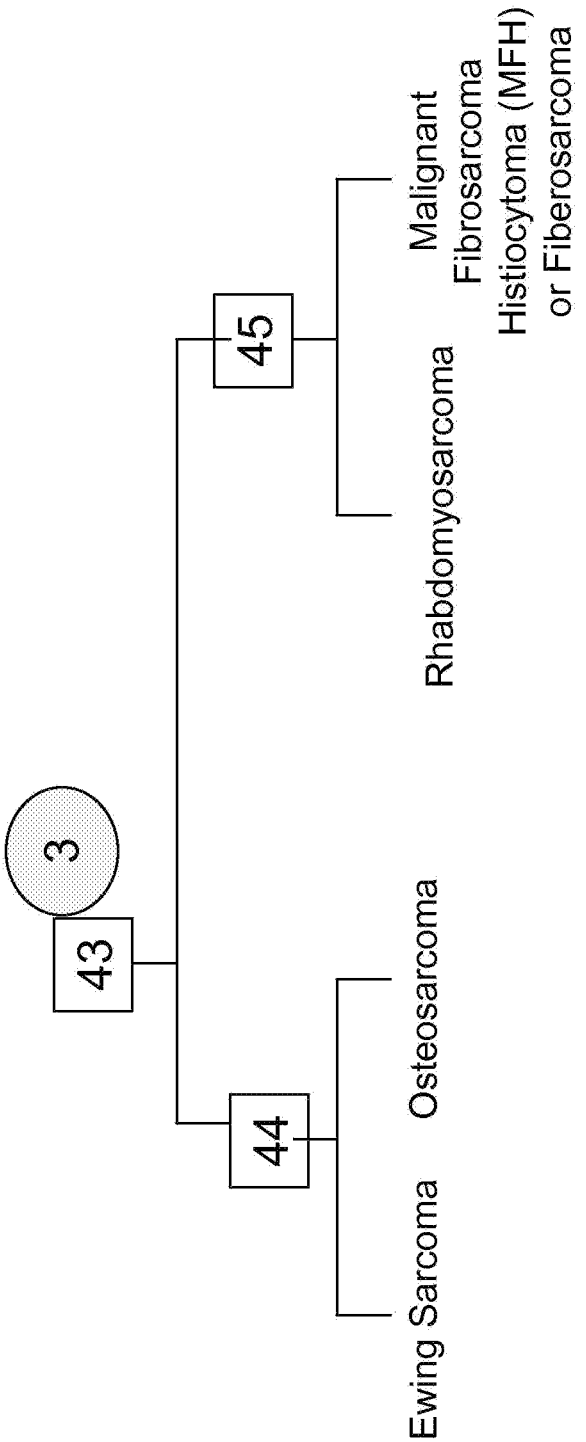

3
43
44
45
Ewing Sarcoma
Osteosarcoma
Rhabdomyosarcoma
Malignant Fibrosarcoma Histiocytoma (MFH) or Fiberosarcoma

FIG.1D

FIG. 1E

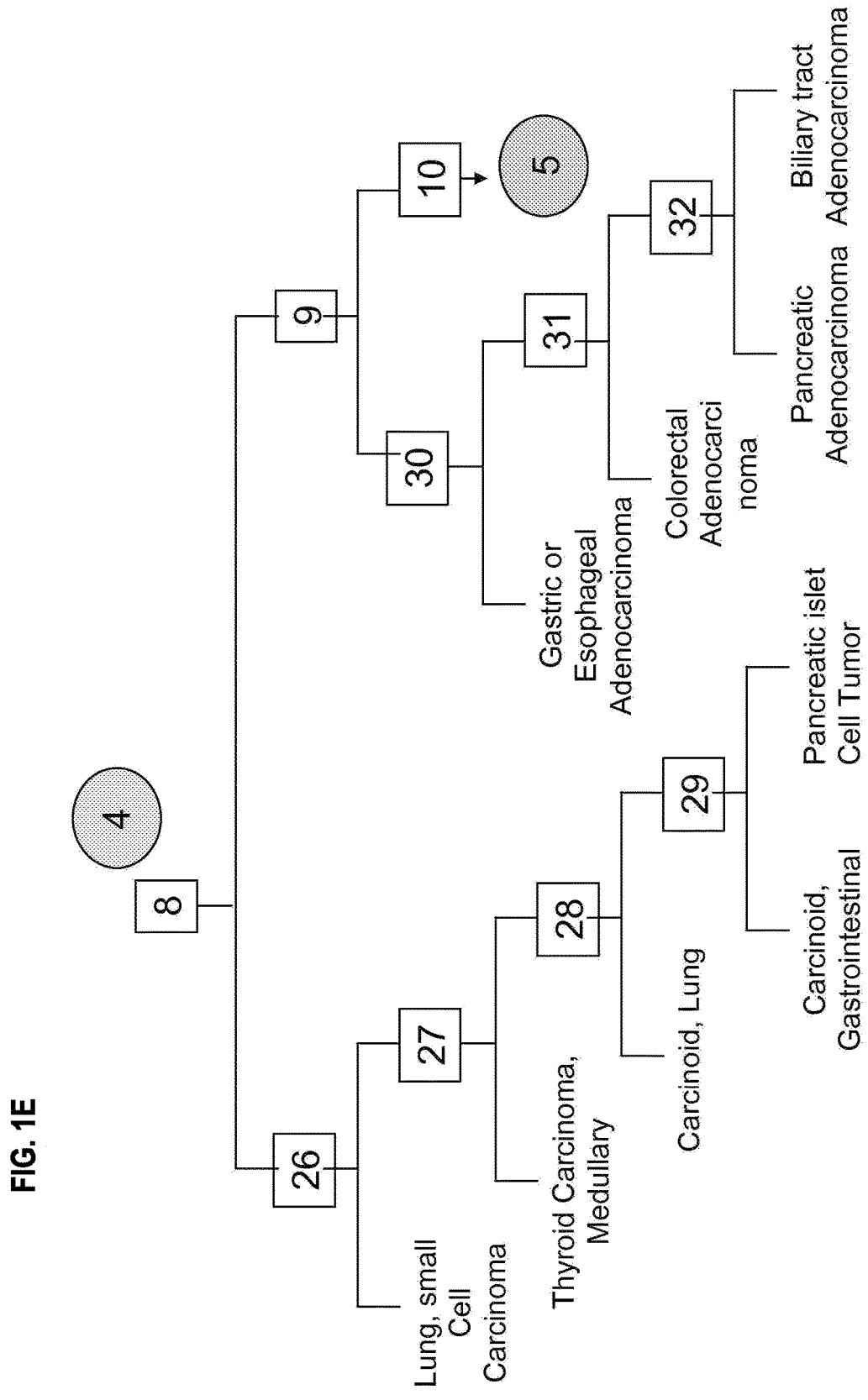

4
8
9
10
5
26
27
28
29
30
31
32
Lung, small Cell Carcinoma
Thyroid Carcinoma, Medullary
Carcinoid, Lung
Carcinoid, Gastrointestinal
Pancreatic islet Cell Tumor
Gastric or Esophageal Adenocarcinoma
Colorectal Adenocarcinoma
Pancreatic Adenocarcinoma
Biliary tract Adenocarcinoma

FIG. 1F

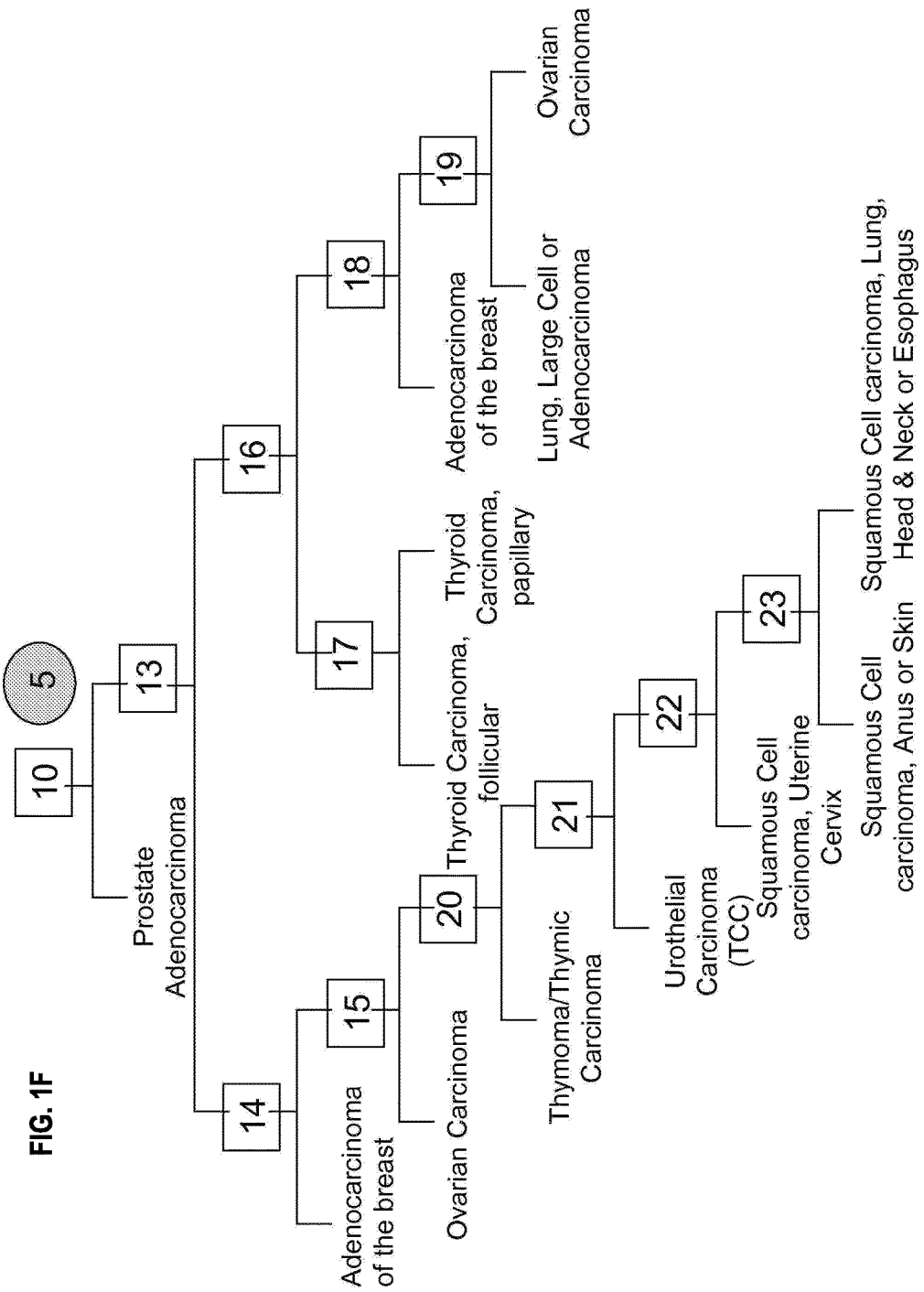

5
10
13
Prostate Adenocarcinoma
16
14
Adenocarcinoma of the breast
15
20
Ovarian Carcinoma
Thymoma/Thymic Carcinoma
21
17
Thyroid Carcinoma, follicular
Thyroid Carcinoma, papillary
18
19
Adenocarcinoma of the breast
Lung, Large Cell or Adenocarcinoma
Ovarian Carcinoma
22
Urothelial Carcinoma (TCC)
Squamous Cell carcinoma, Uterine Cervix
23
Squamous Cell carcinoma, Anus or Skin
Squamous Cell carcinoma, Lung, Head & Neck or Esophagus

FIG. 2A

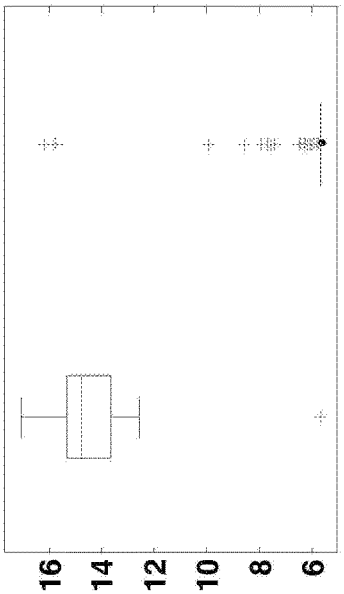


FIG. 2B

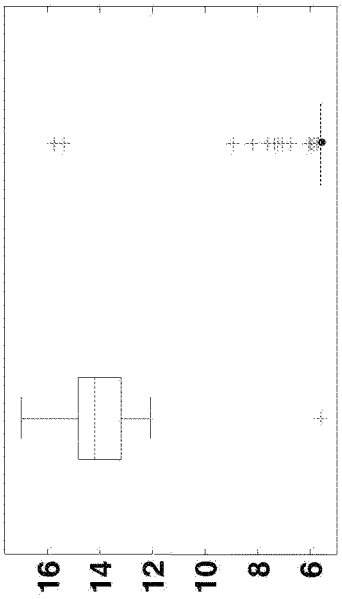


FIG. 2C

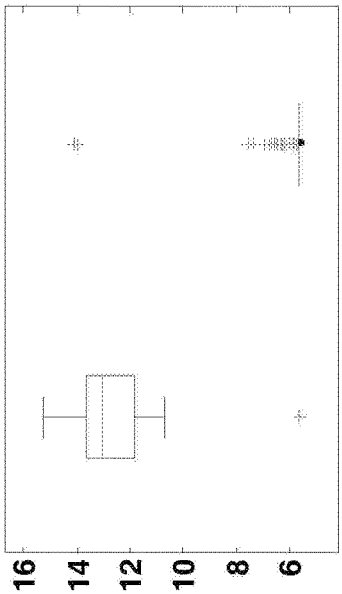
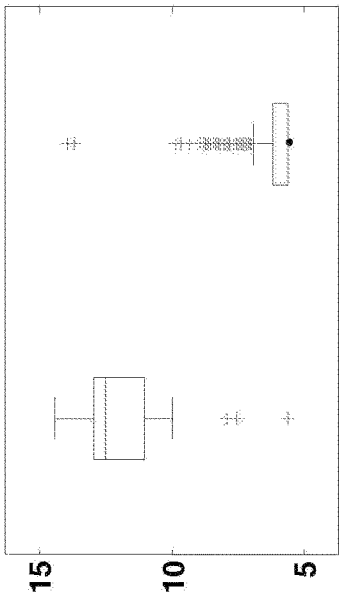


FIG. 2D



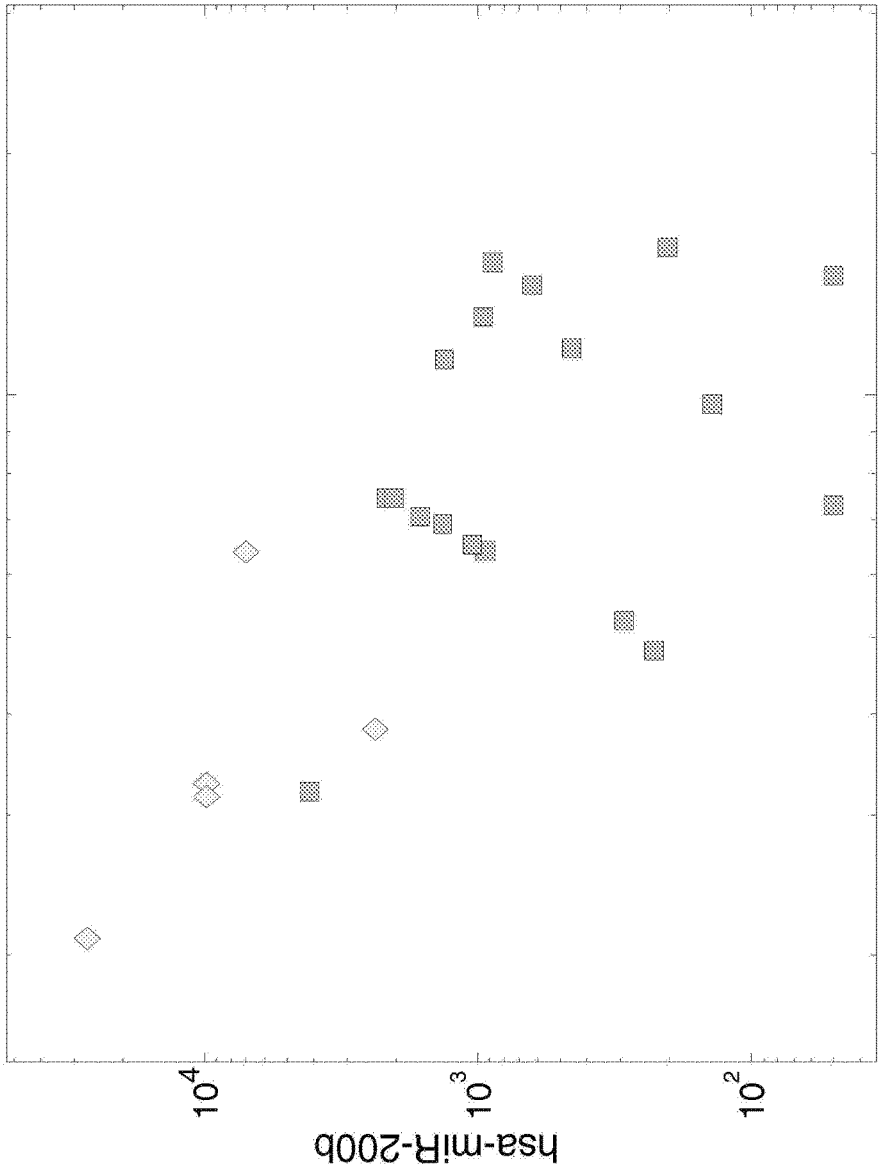


FIG. 3

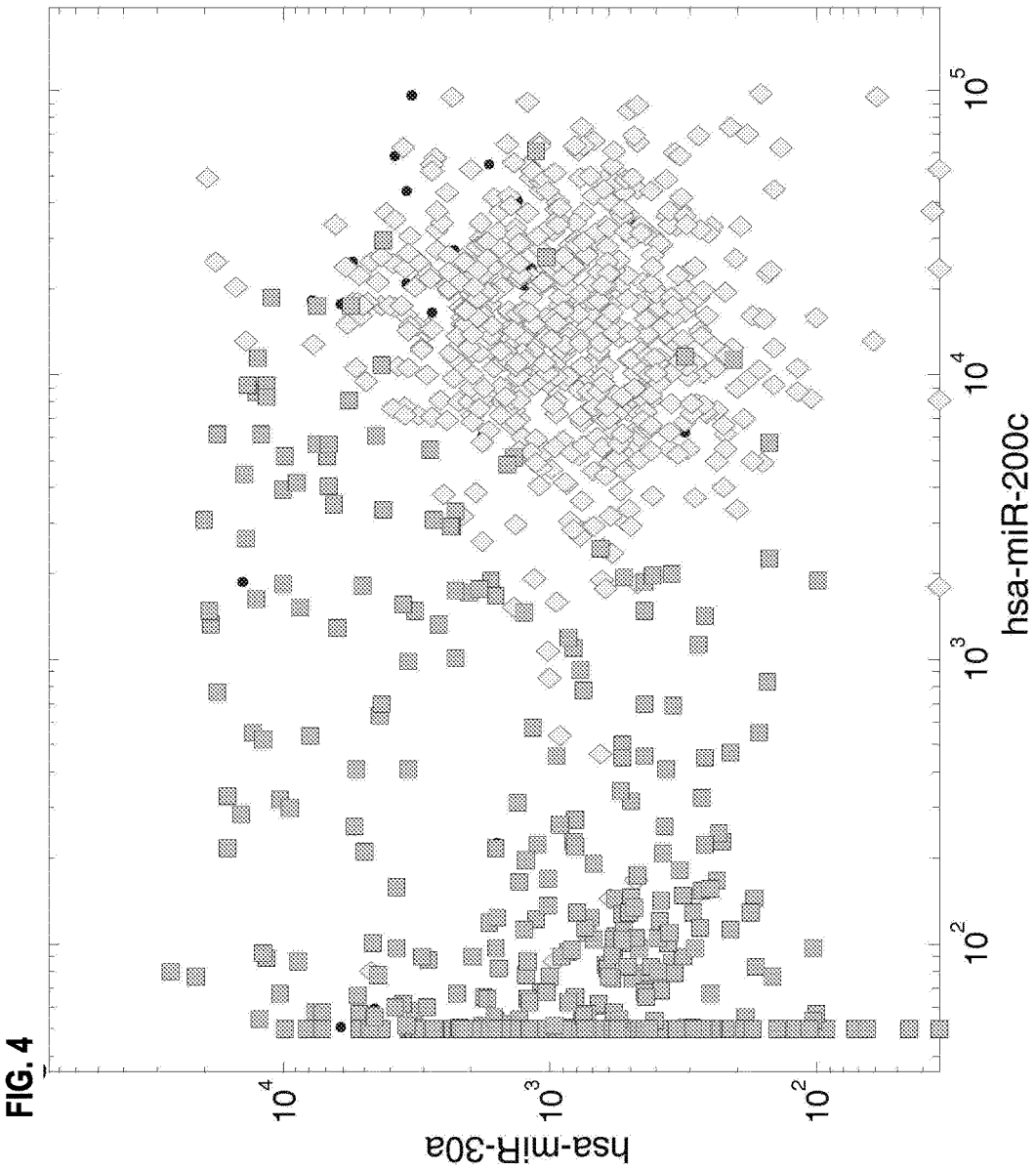
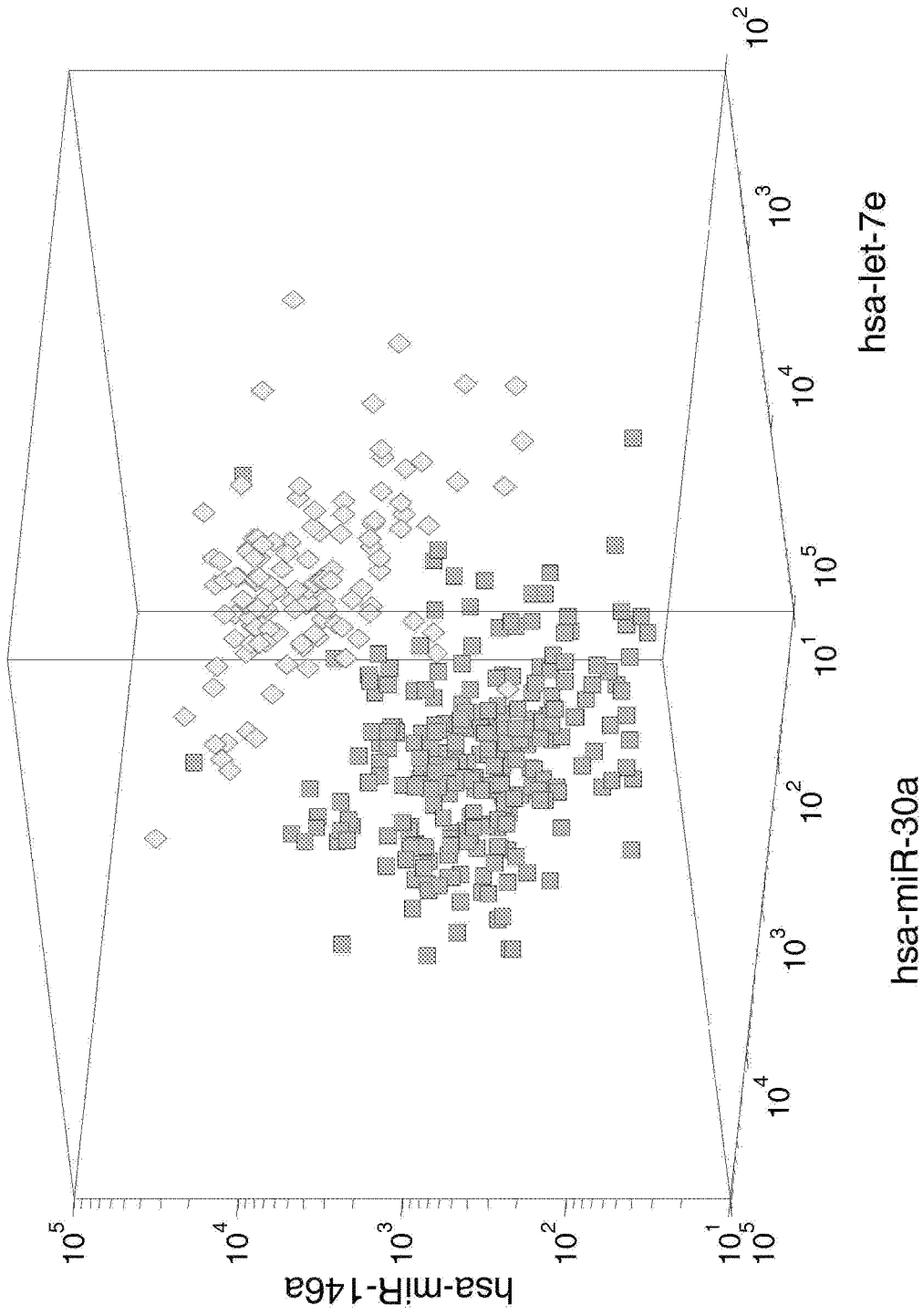


FIG. 4

FIG. 5


hsa-miR-146a
hsa-let-7e
hsa-miR-30a
10^5
10^4
10^3
10^2
10^1
10^5
10^4
10^3
10^2
10^1
10^5
10^4
10^3
10^2

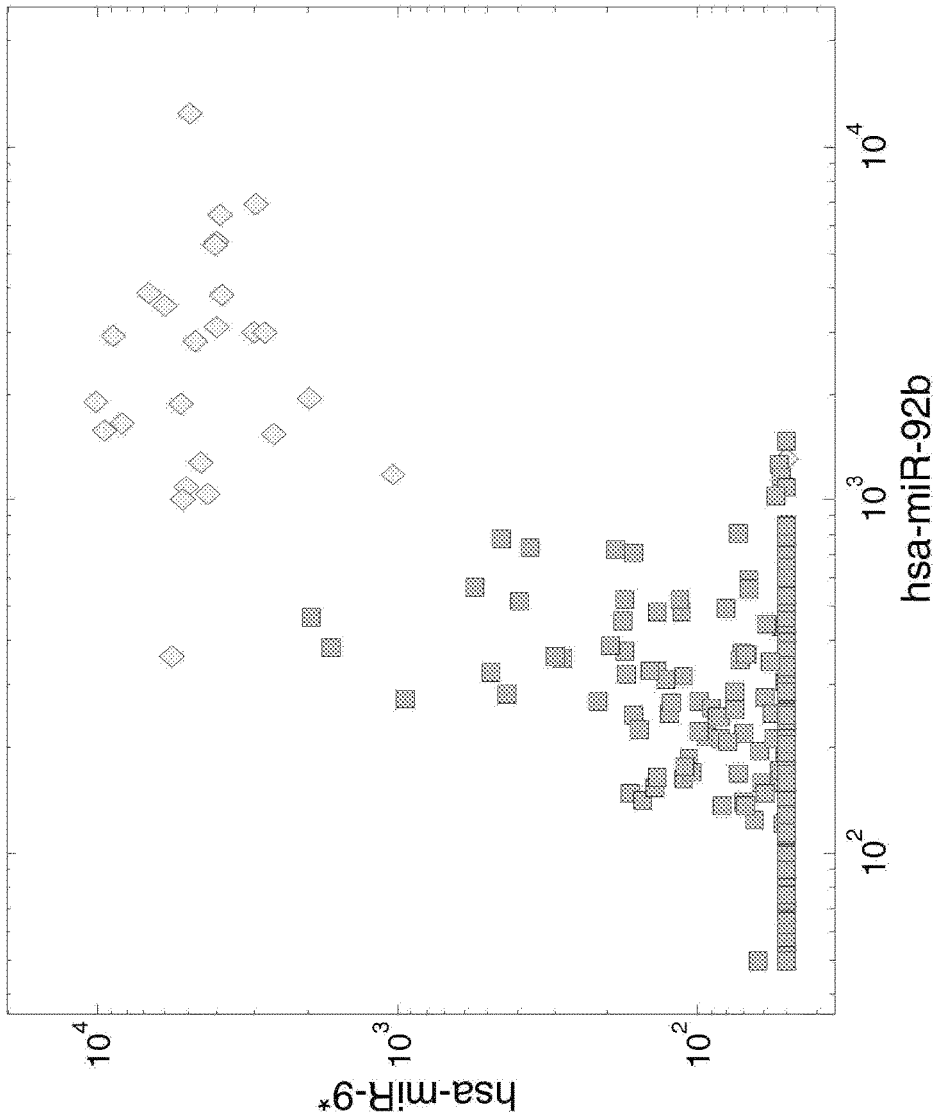


FIG. 6

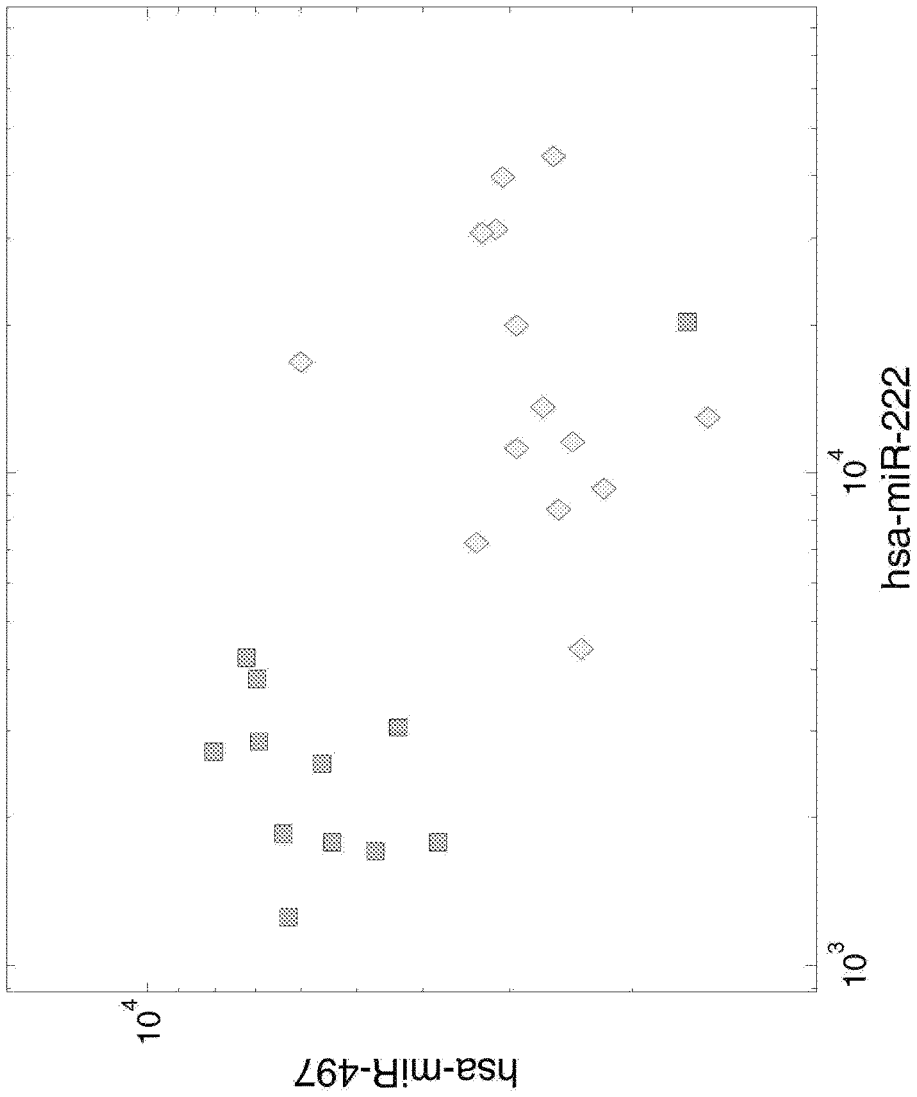


FIG. 7

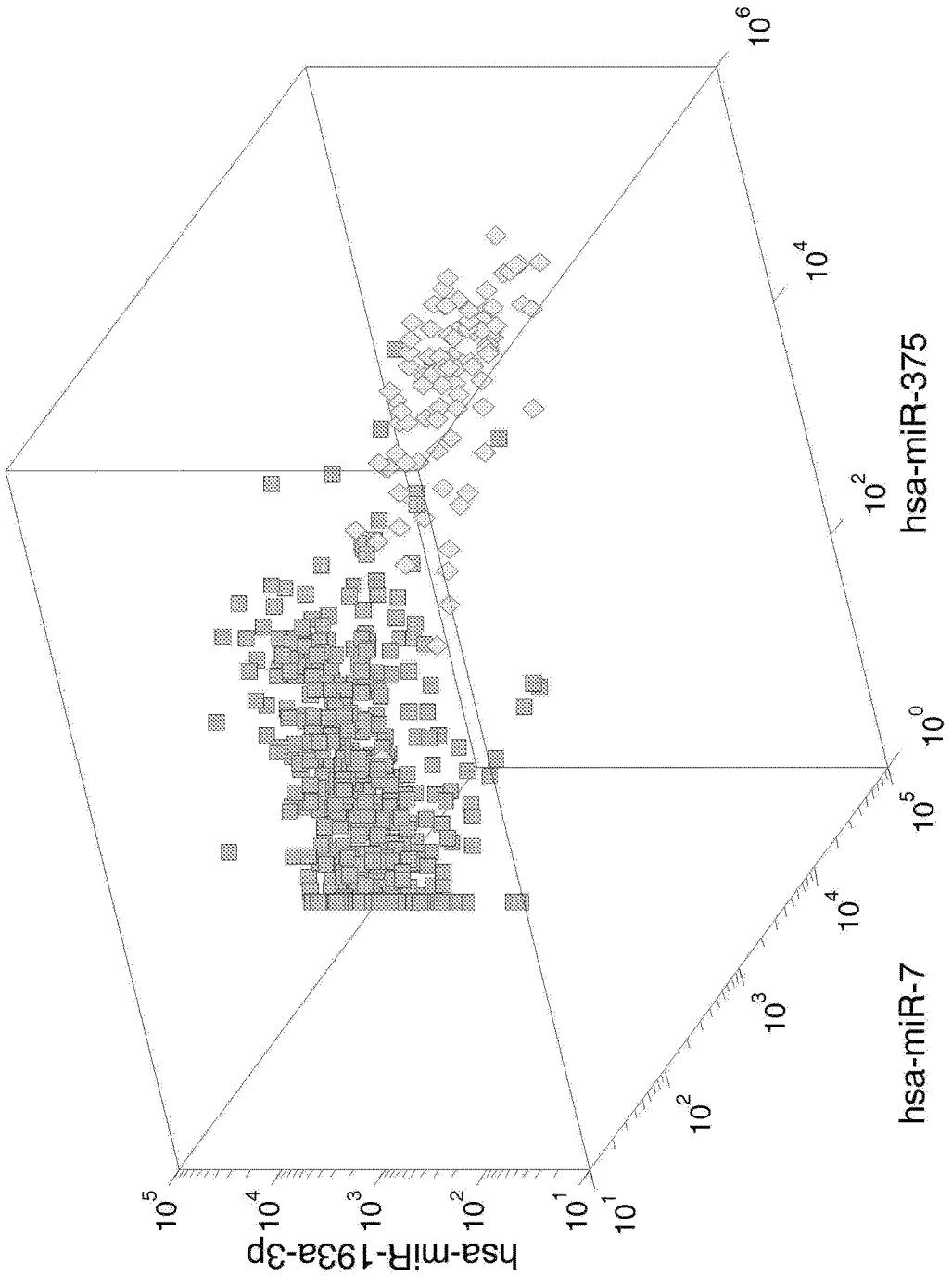


FIG. 8

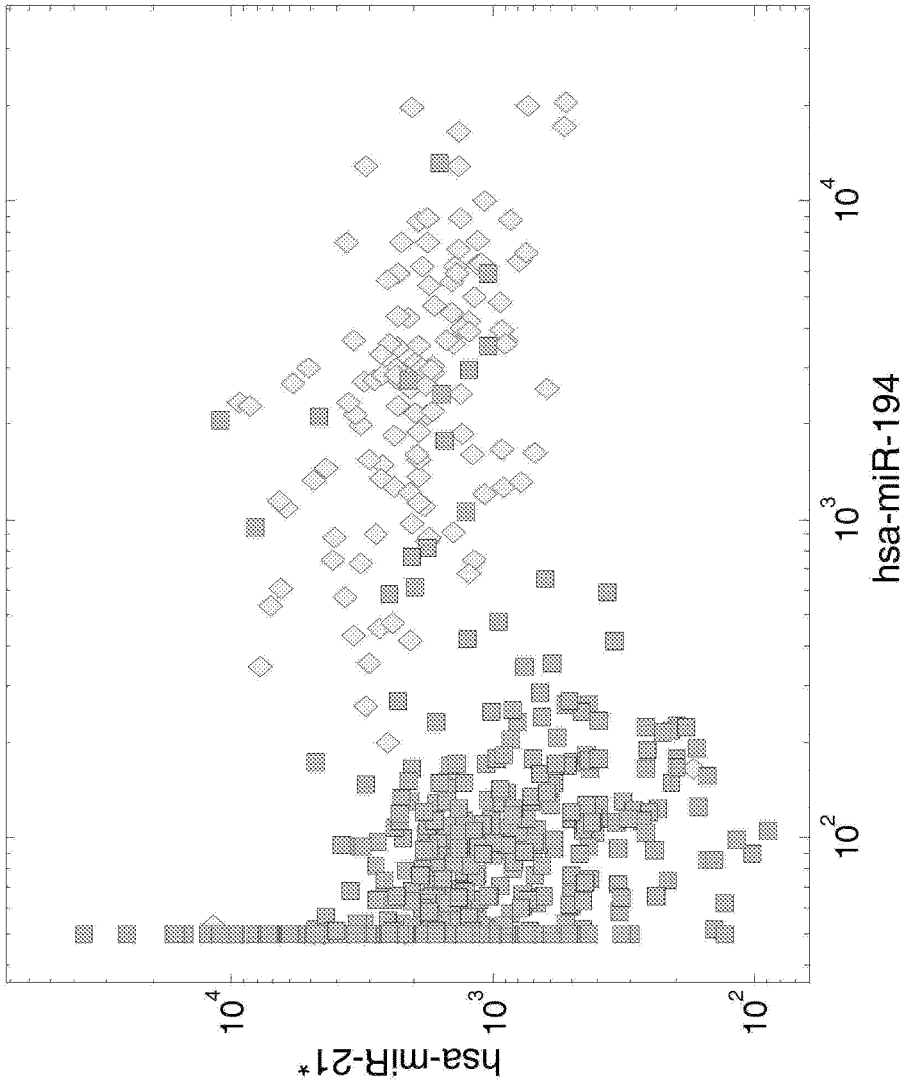


FIG. 9

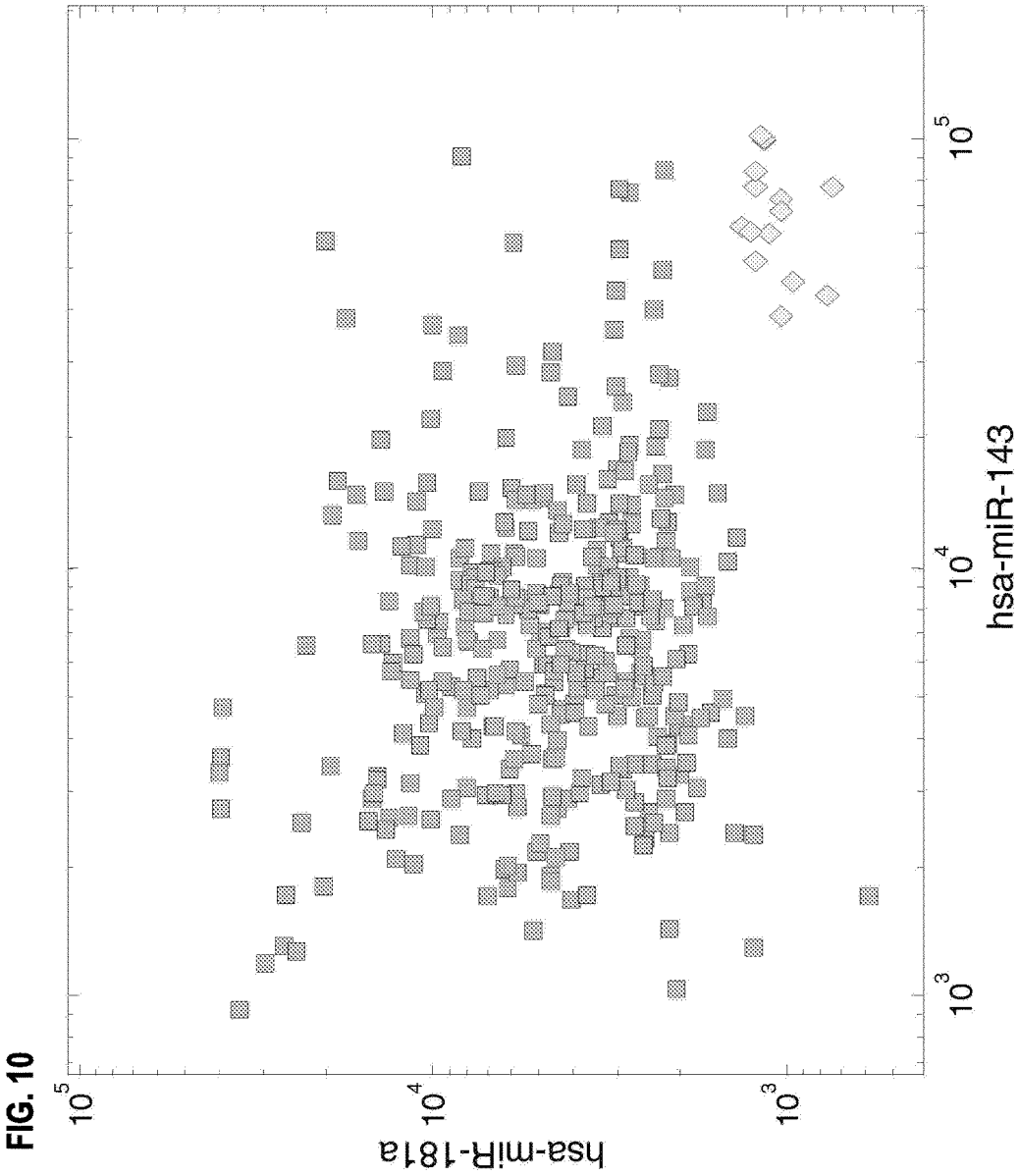


FIG. 10

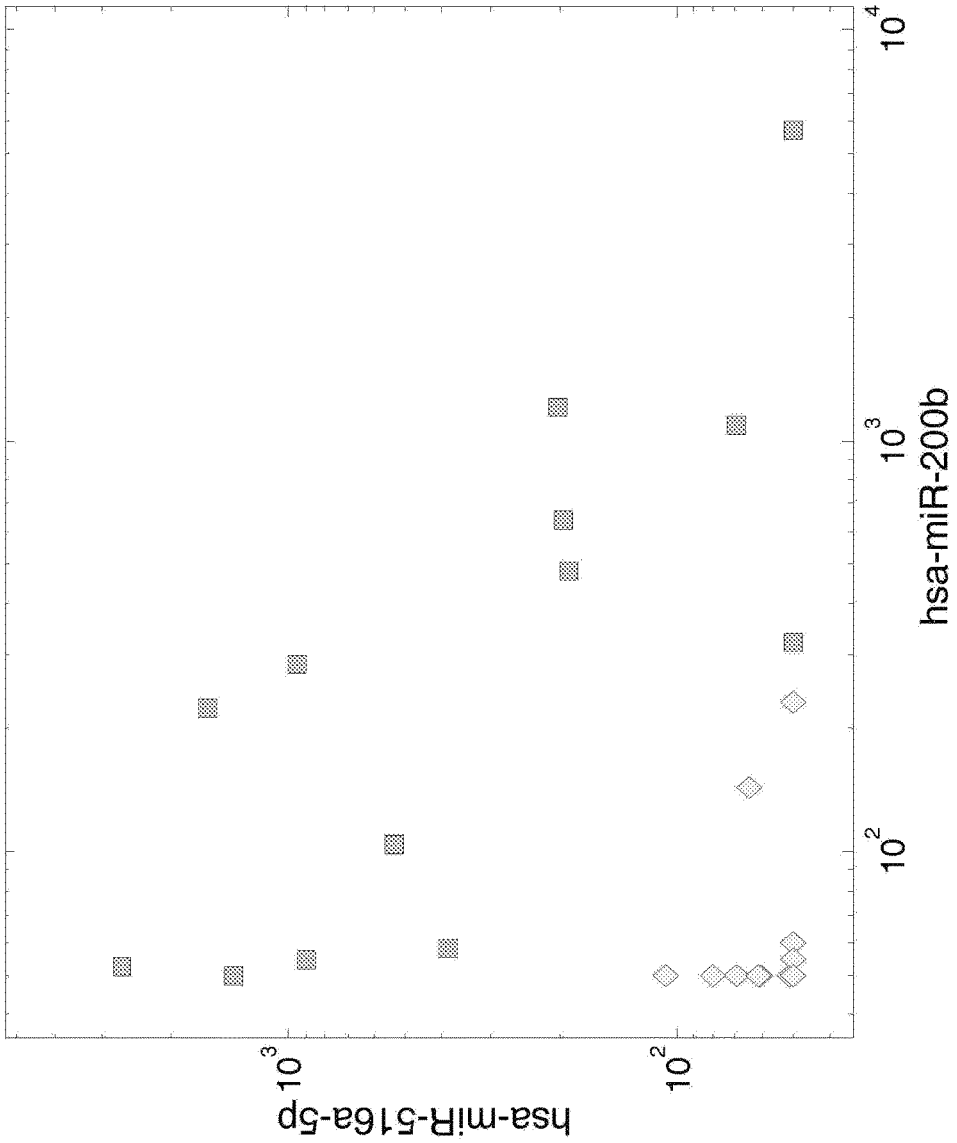


FIG. 11

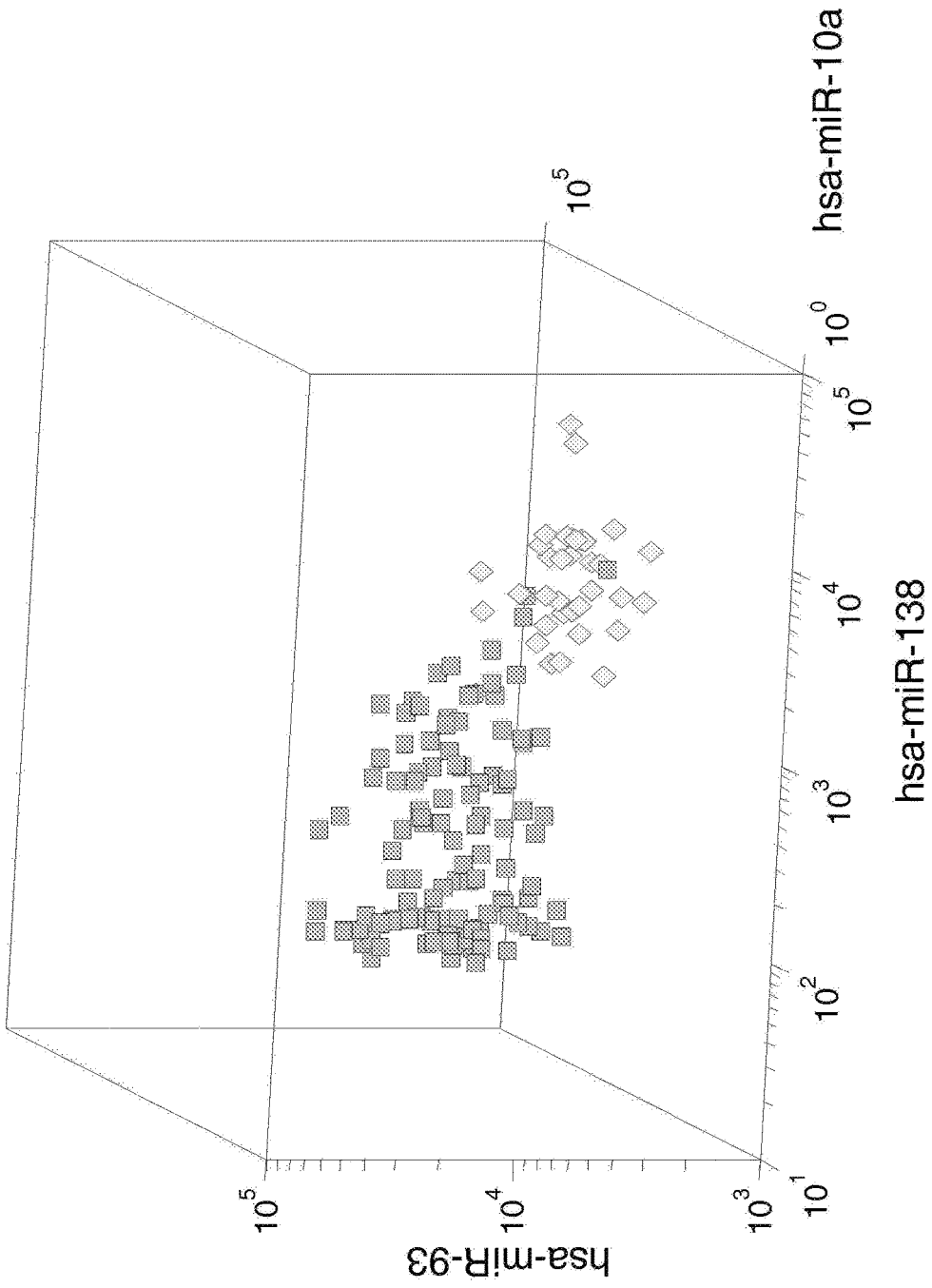

hsa-miR-93
10^5
10^4
10^3
10^1
10^2
10^3
10^4
10^5
hsa-miR-138
10^0
10^5
hsa-miR-10a

FIG. 12

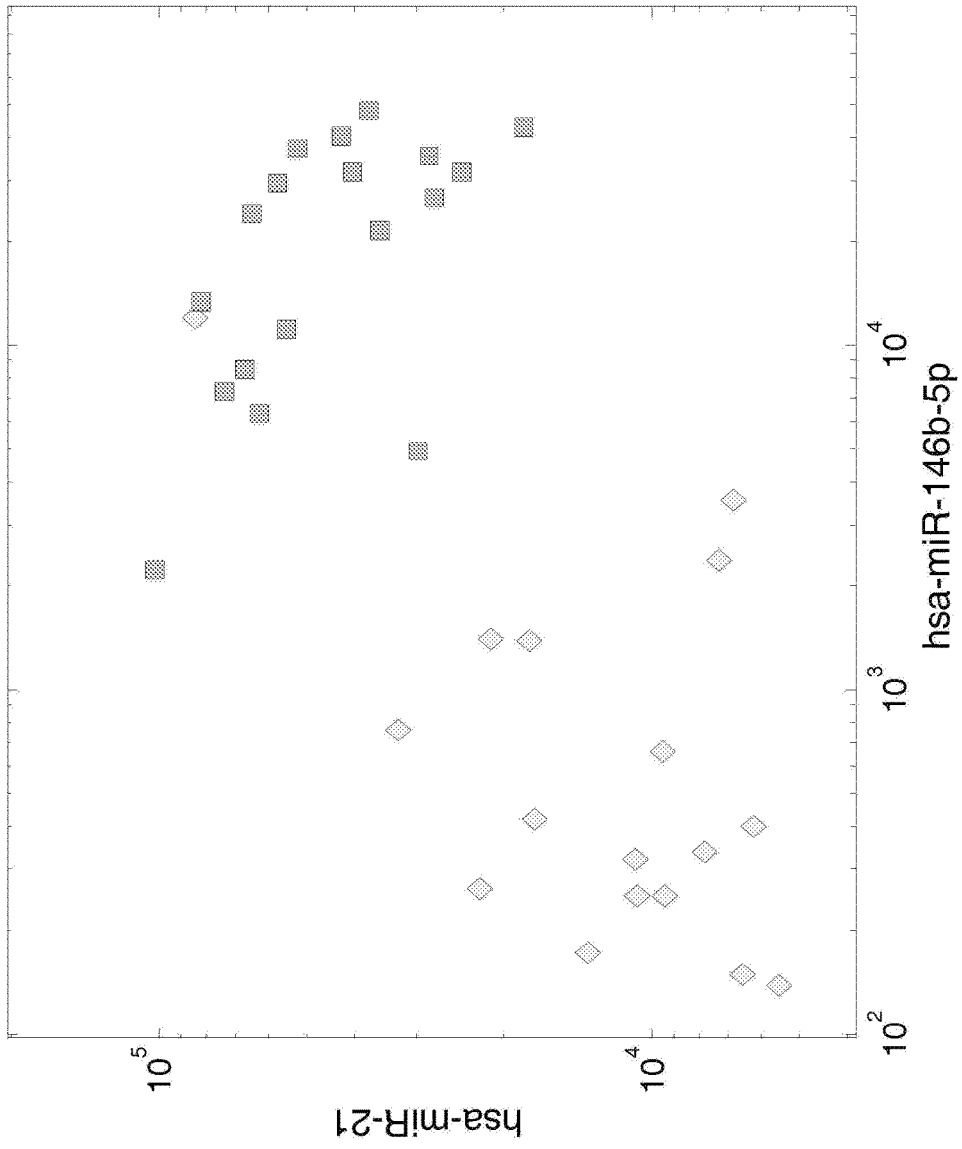


FIG. 13

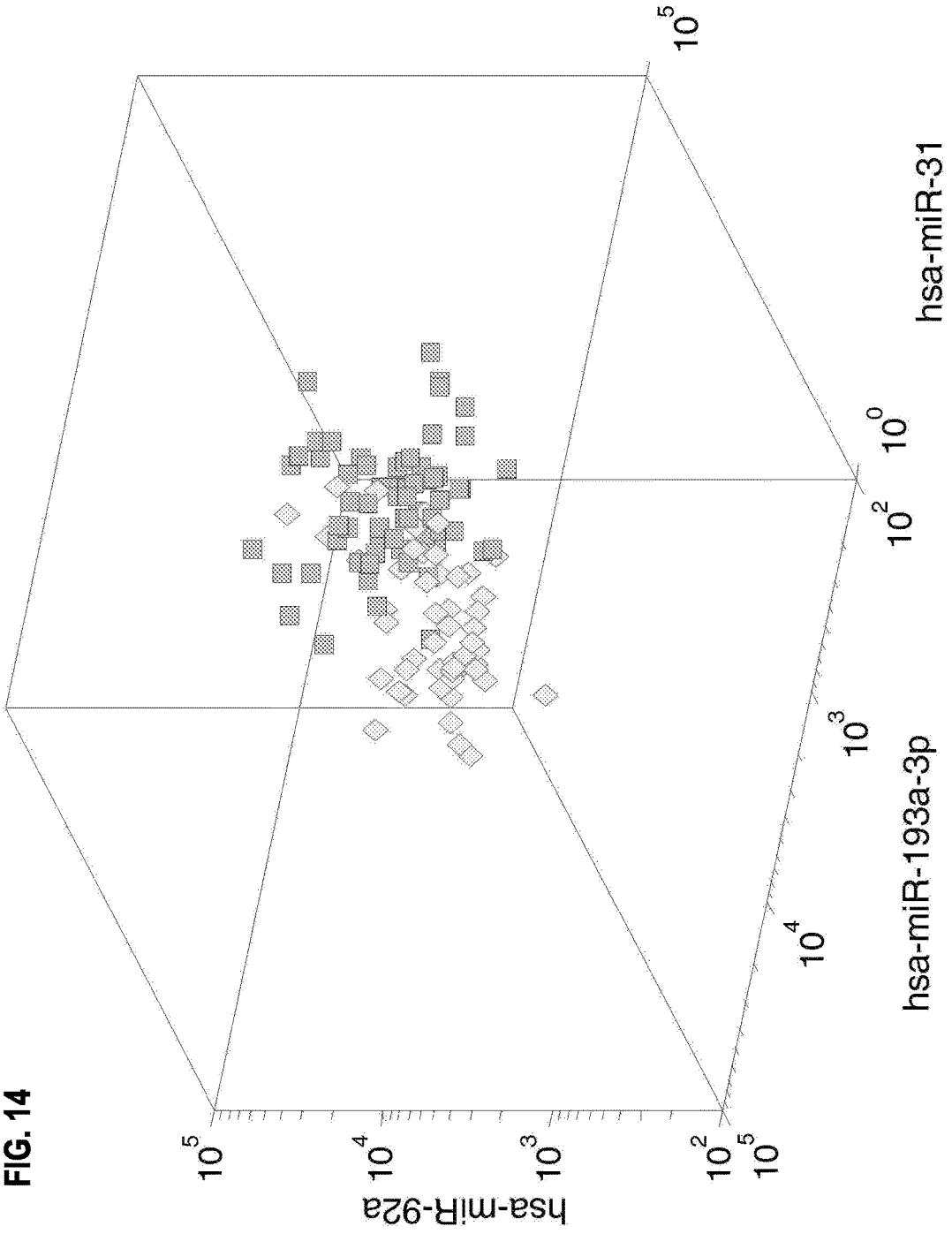

hsa-miR-92a
hsa-miR-193a-3p
hsa-miR-31
10^5
10^4
10^3
10^2
10^5
10^2
10^0

FIG. 14

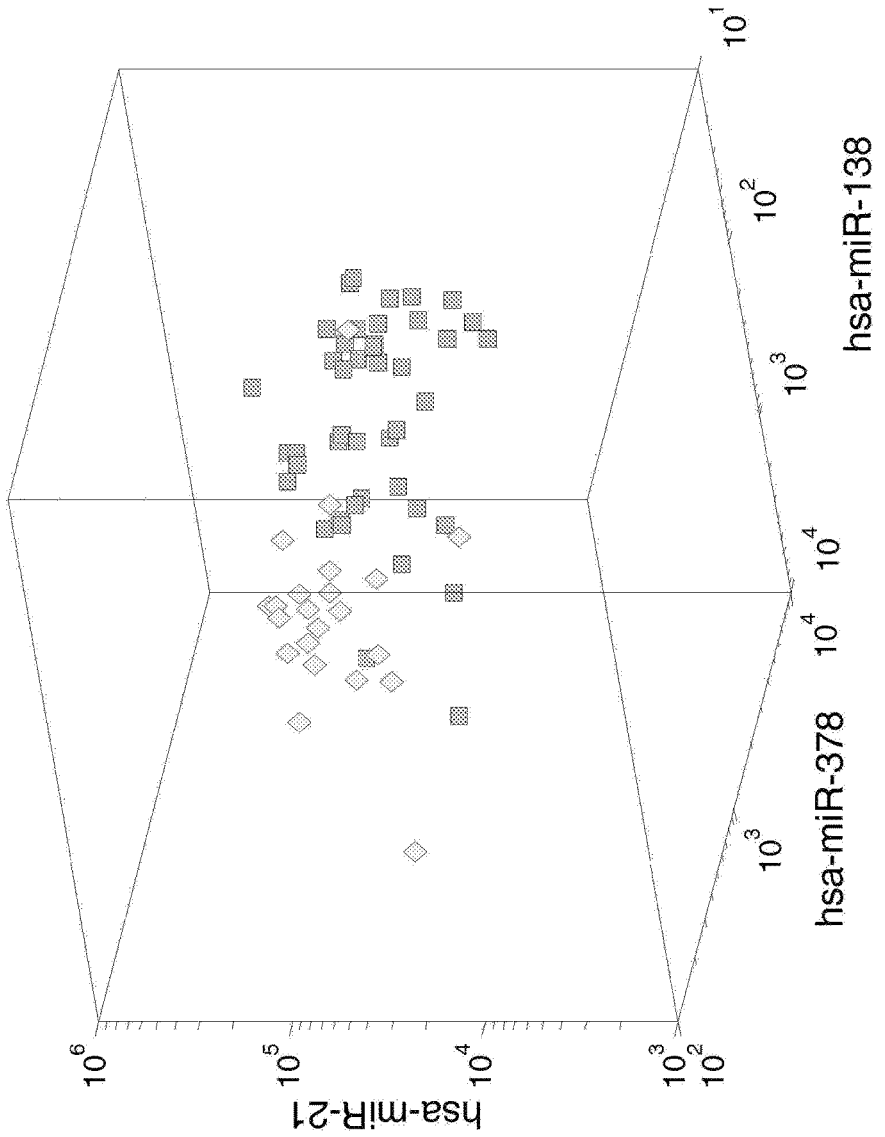

hsa-miR-21
10^6
10^5
10^4
10^3
10^2
hsa-miR-378
10^3
10^4
10^4
hsa-miR-138
10^3
10^2
10^1

FIG. 15

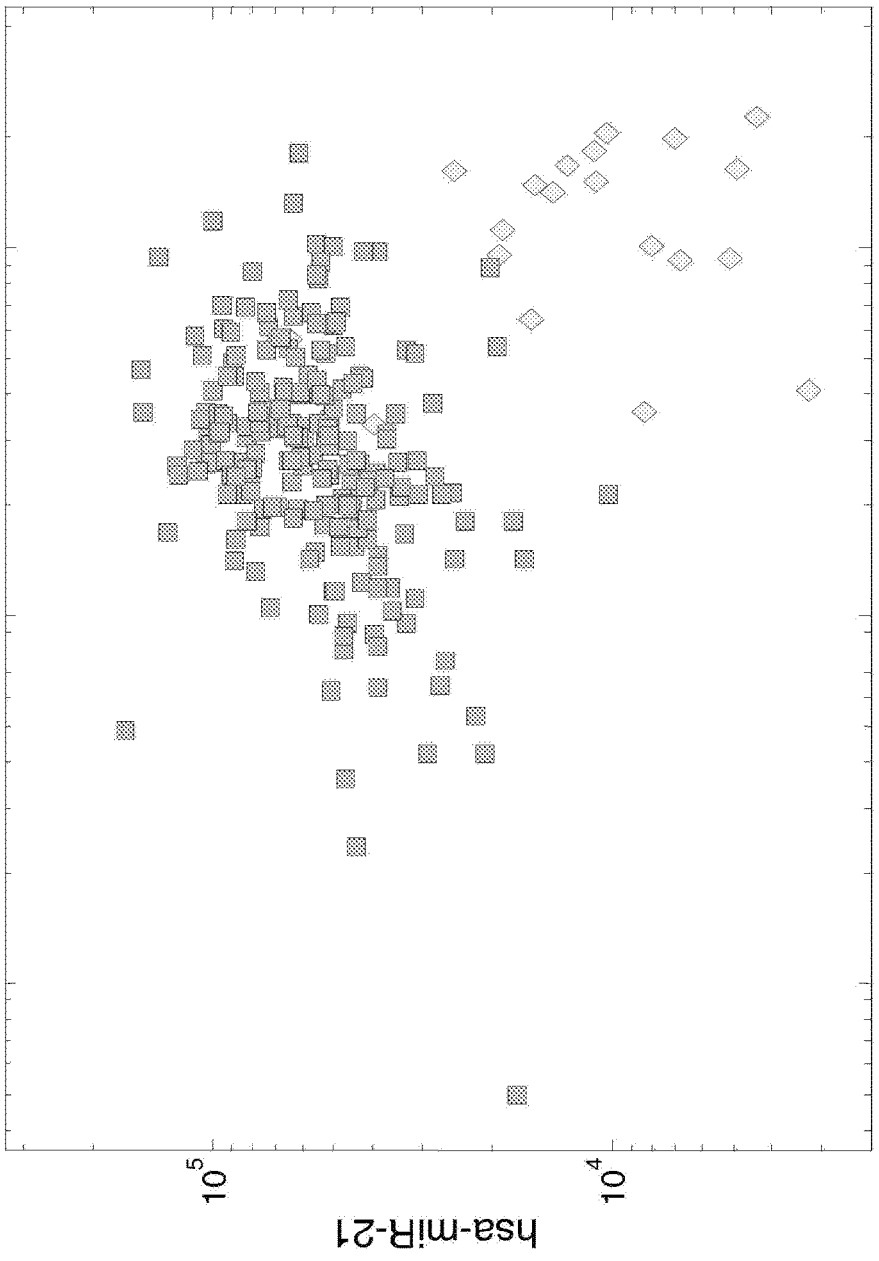


FIG. 16

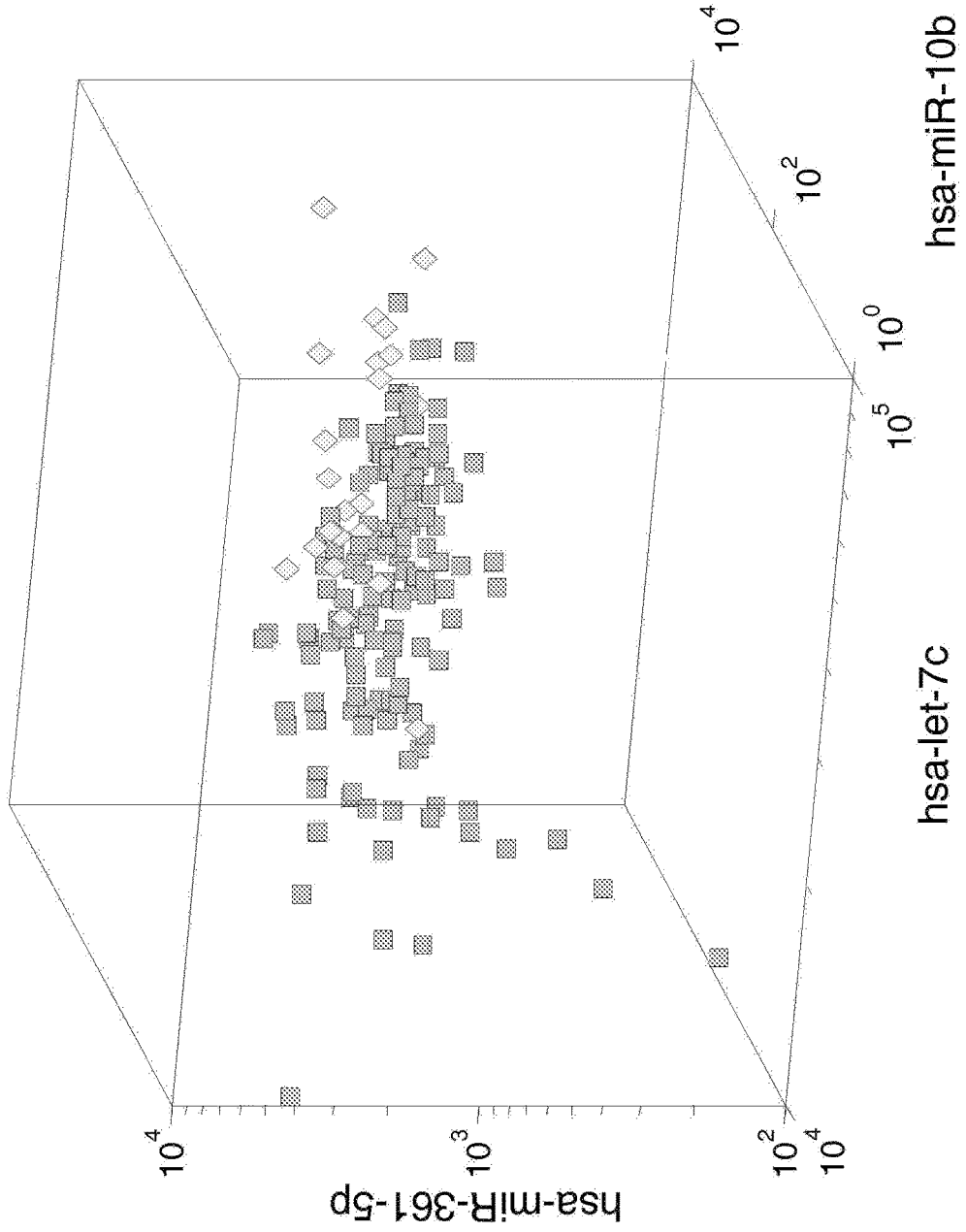

hsa-miR-361-5p
hsa-let-7c
hsa-miR-10b
10^4
10^3
10^2
10^4
10^5
10^0
10^2
10^4

FIG. 17

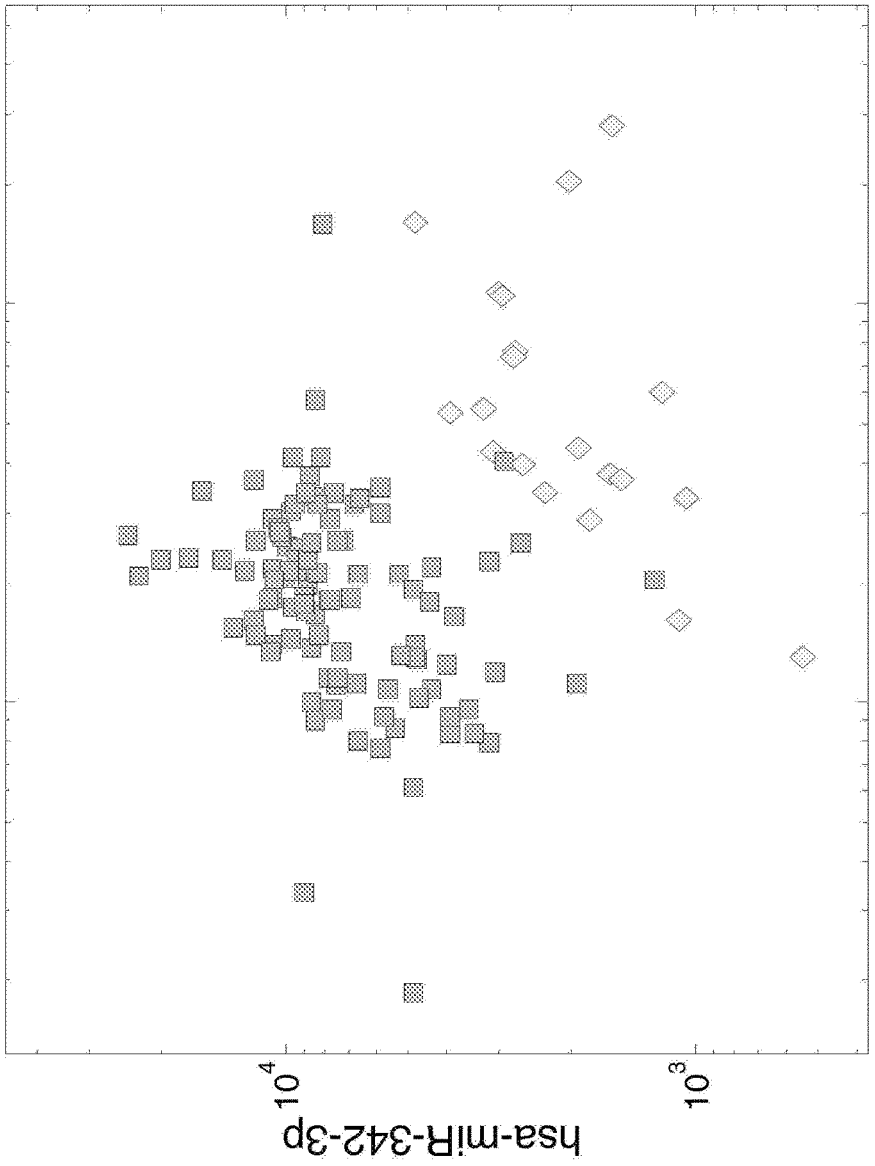
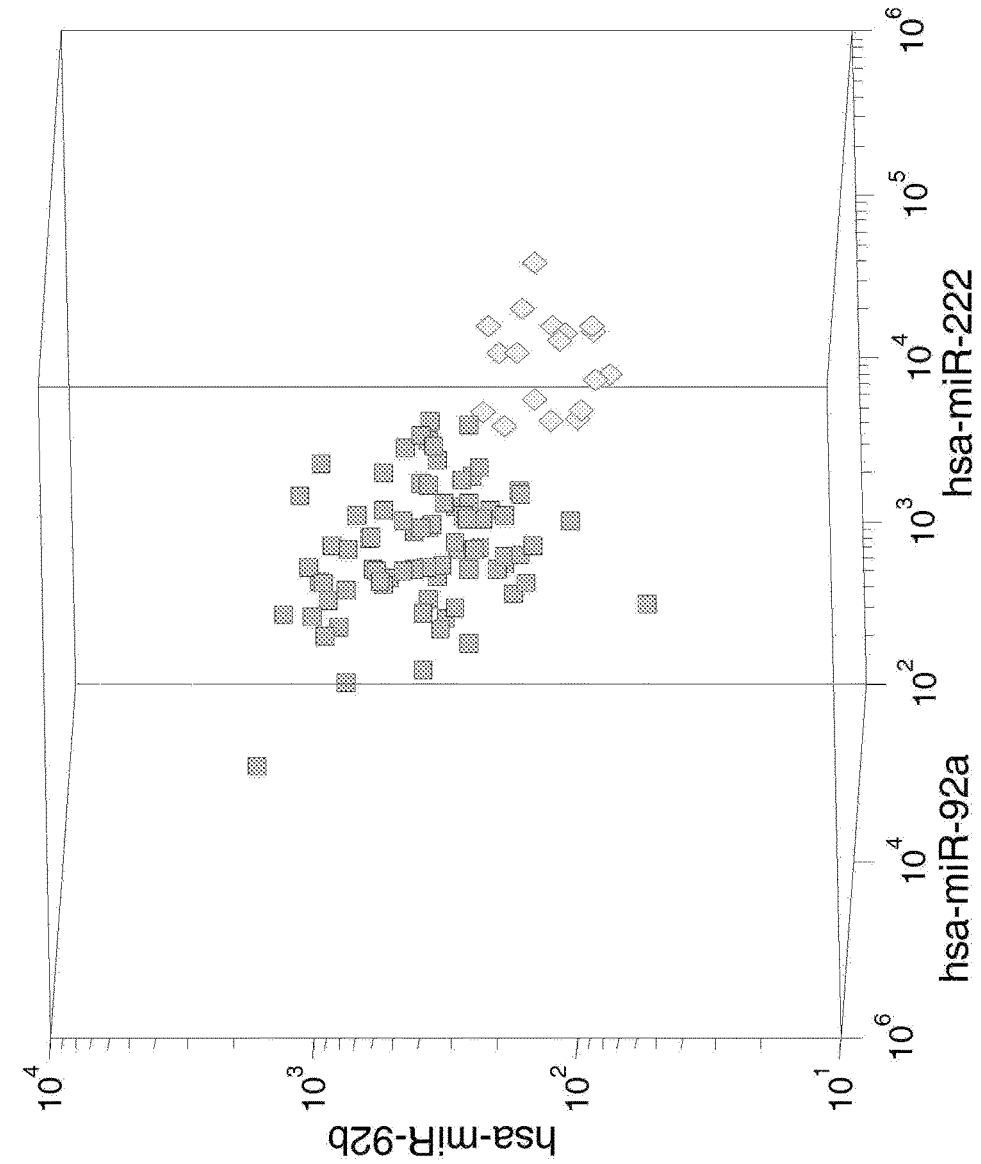


FIG.18

FIG. 19


hsa-miR-92b
10^4
10^3
10^2
10^1
hsa-miR-92a
10^6
10^4
10^2
hsa-miR-222
10^6
10^5
10^4
10^3

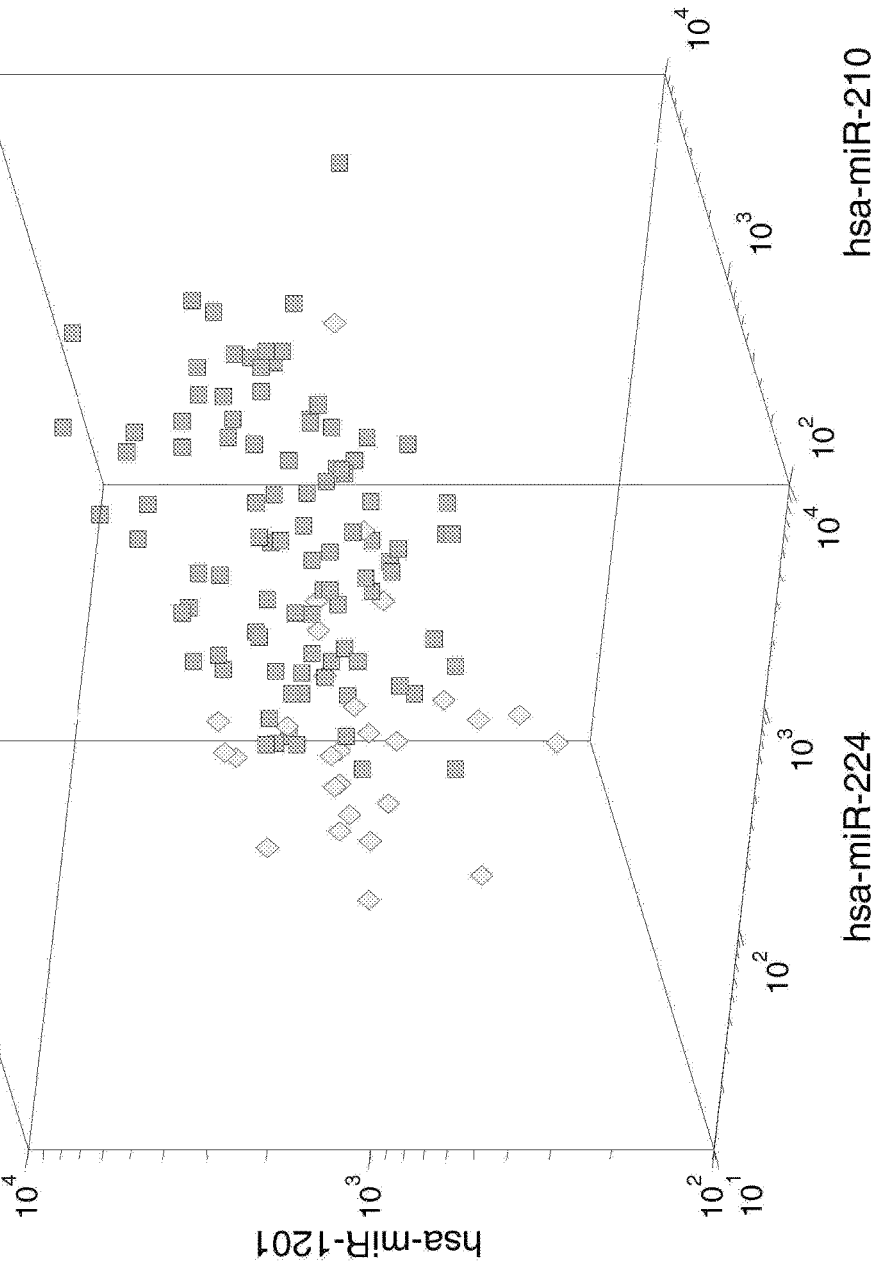


FIG. 20

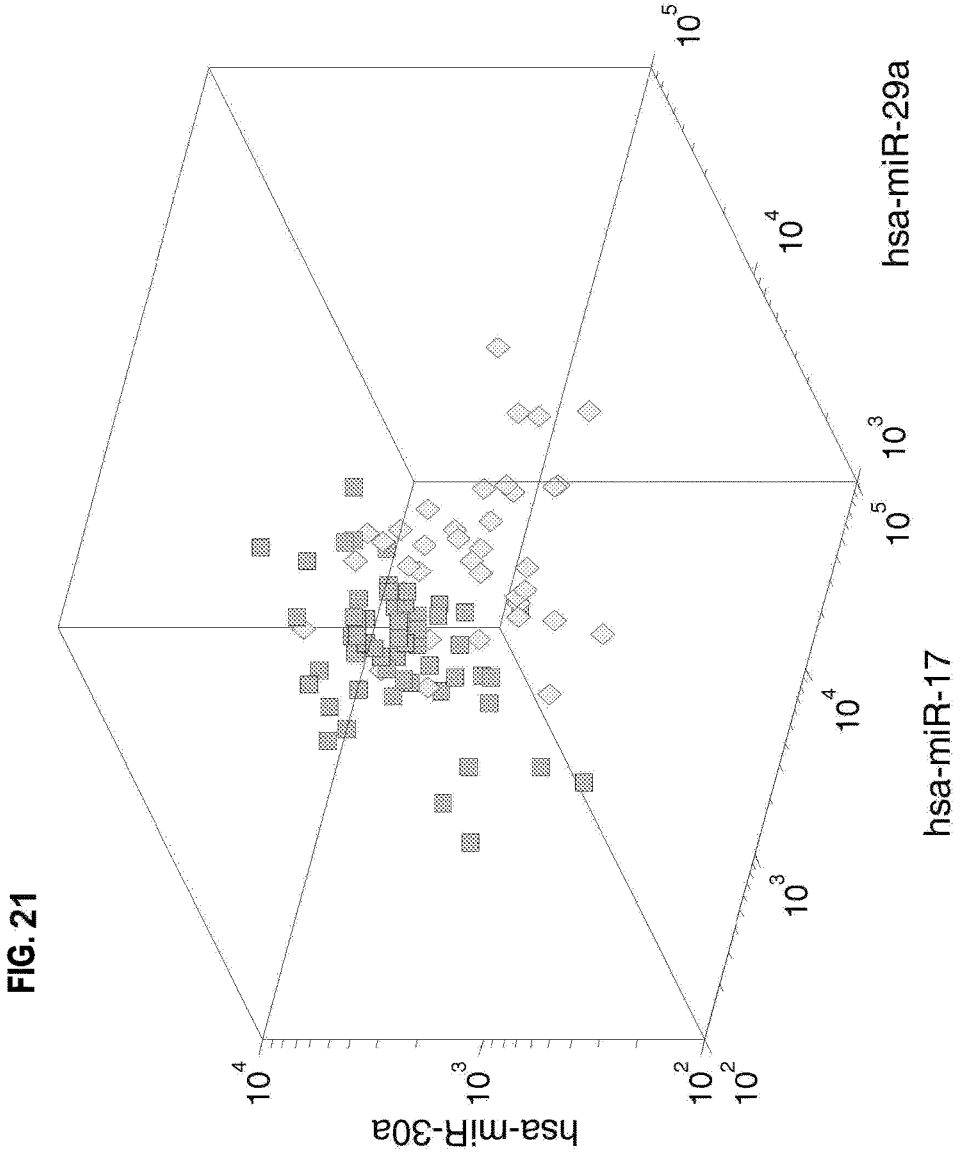
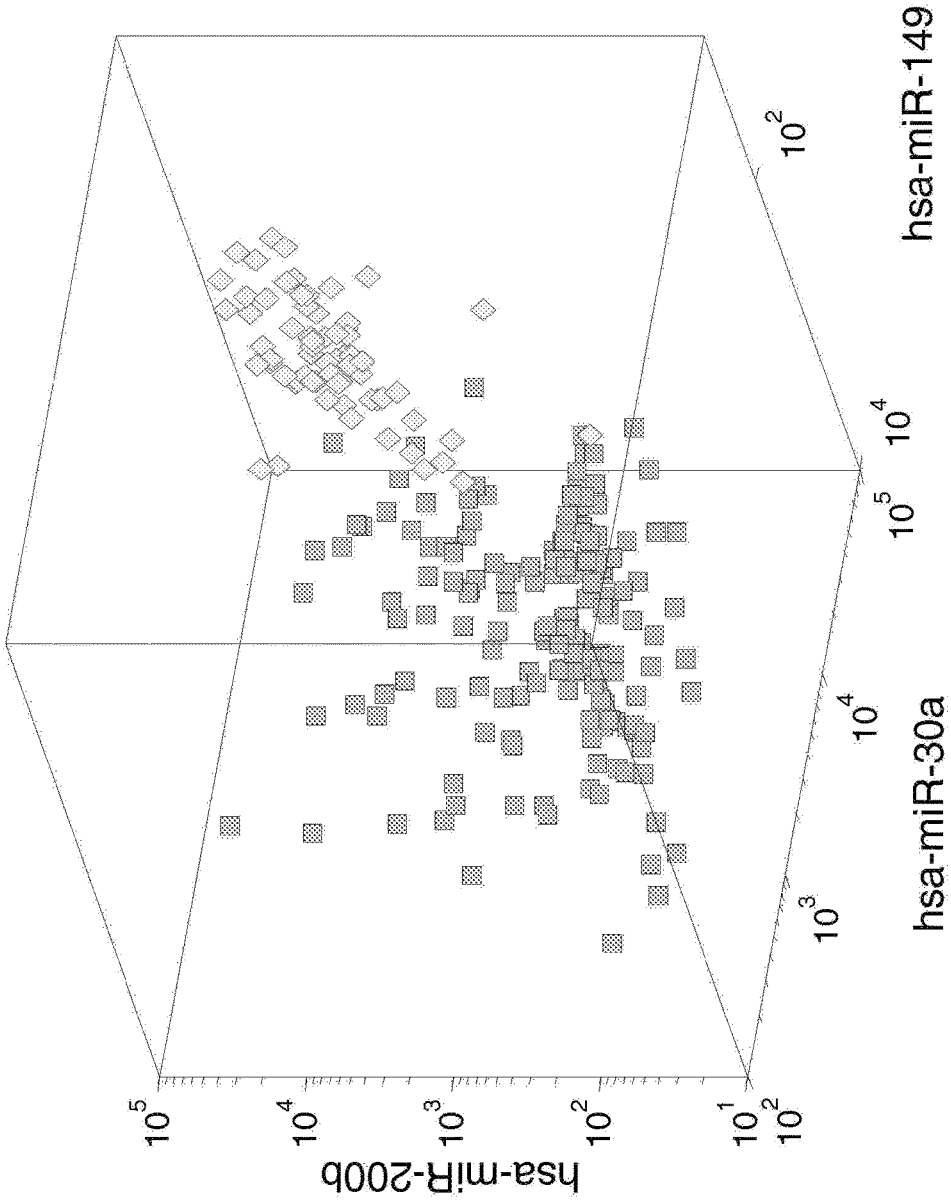


FIG. 21

FIG. 22


hsa-miR-200b
hsa-miR-30a
hsa-miR-149
10^5
10^4
10^3
10^2
10^1
10^2
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10^4
10^5
10^2

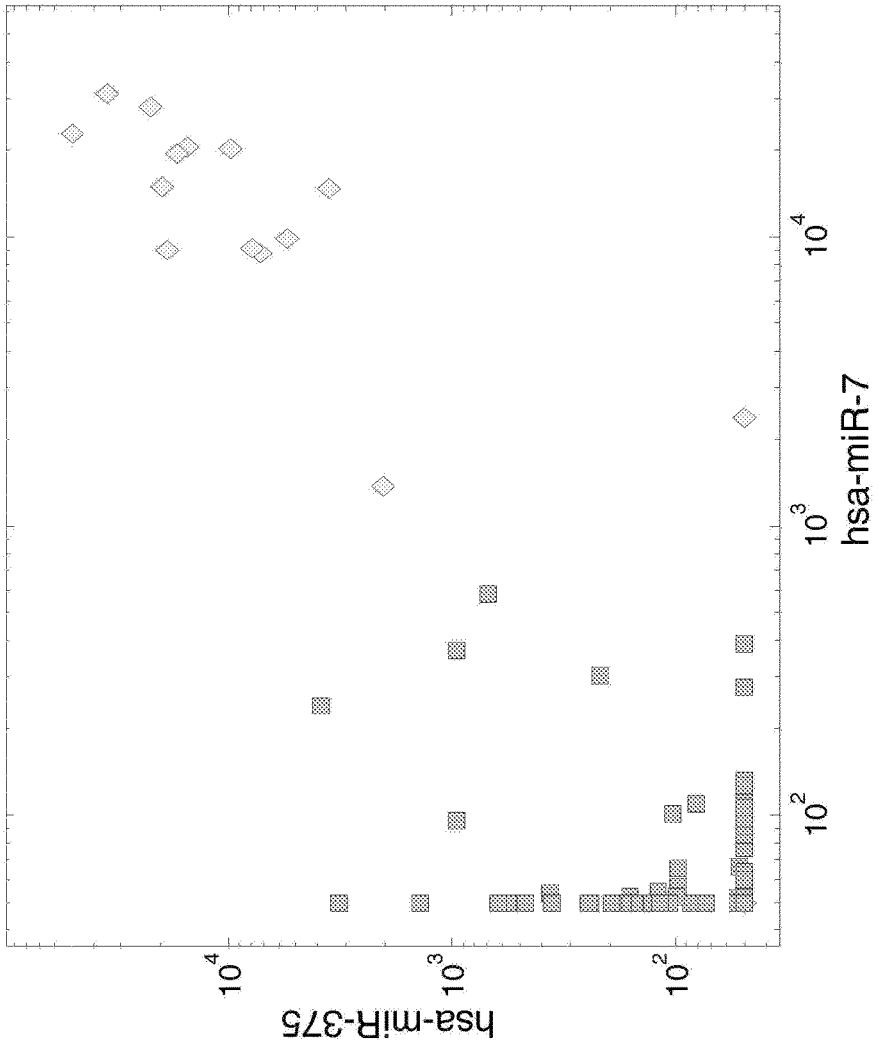

FIG.23

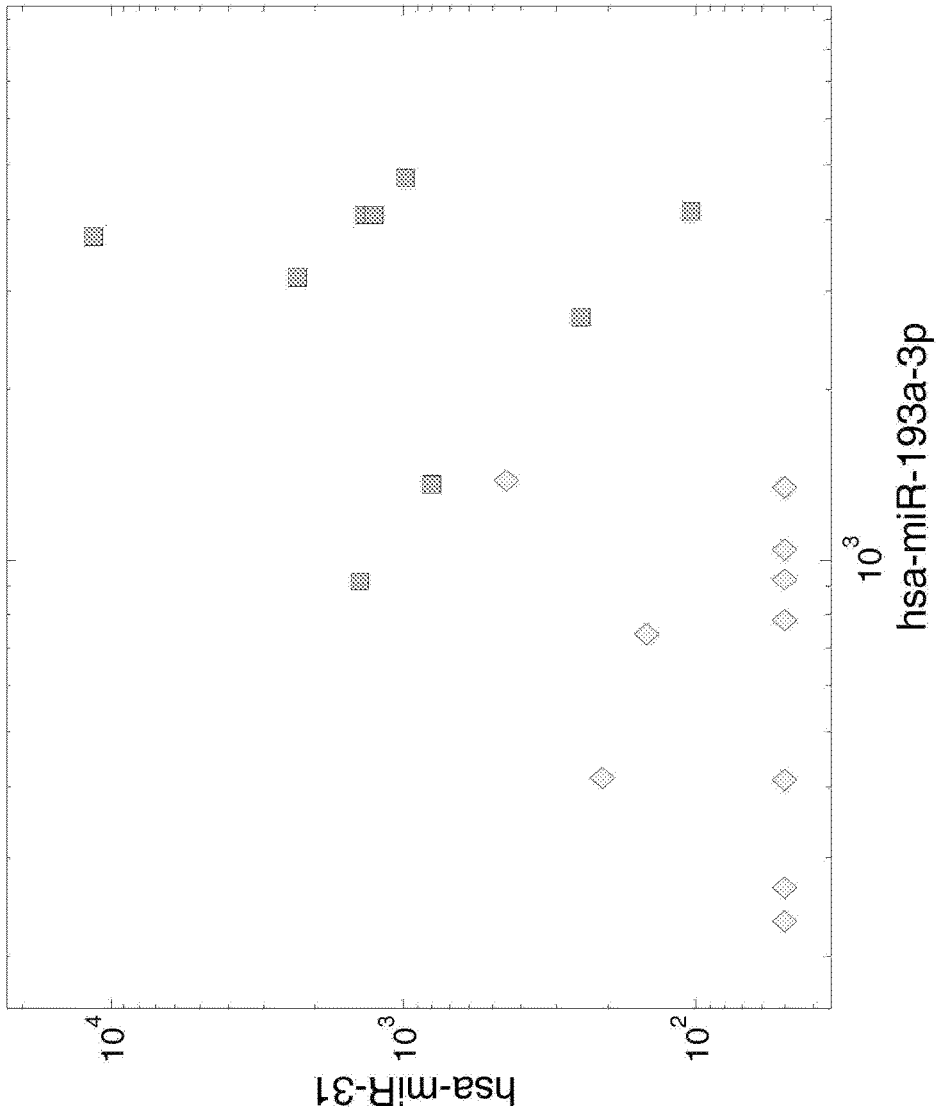

FIG.24

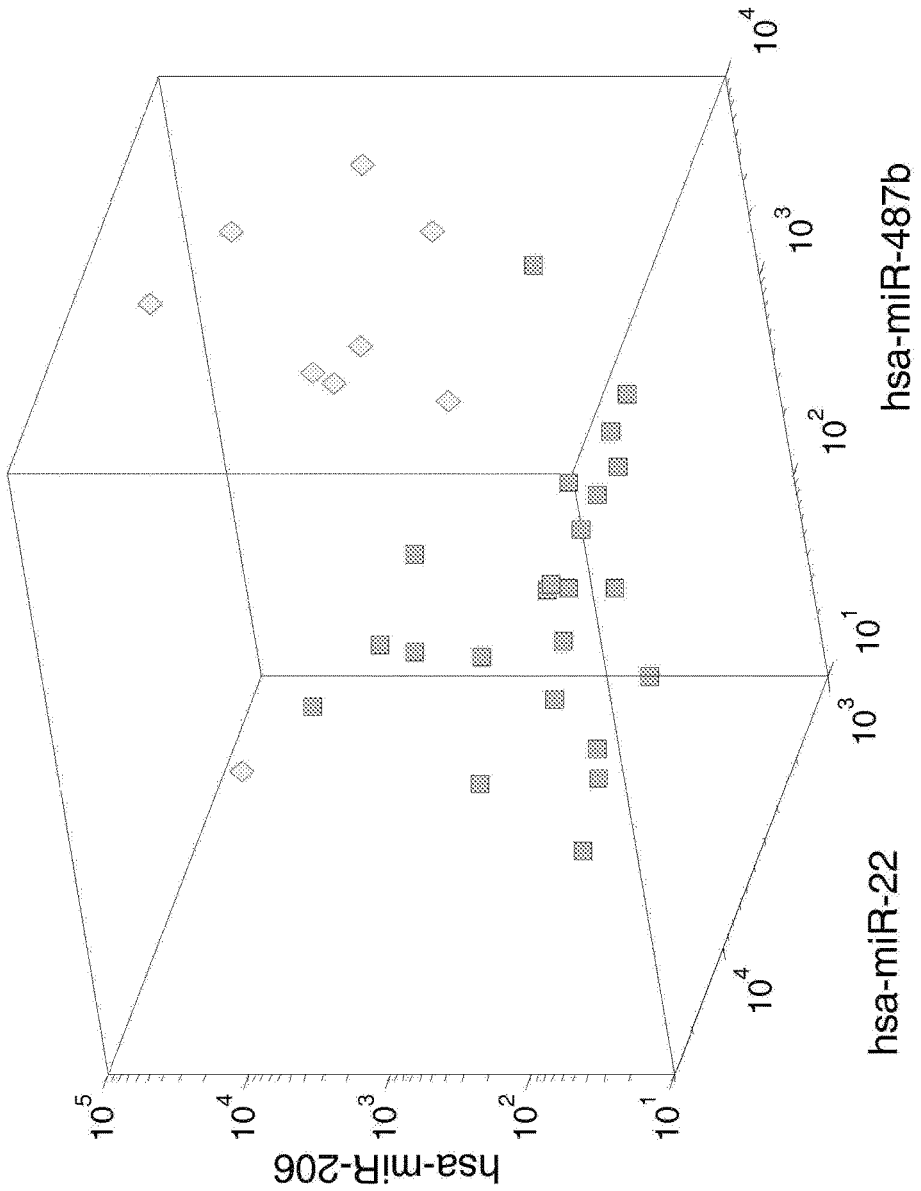
hsa-miR-206
10^5
10^4
10^3
10^2
10^1
hsa-miR-22
10^4
10^3
10^1
hsa-miR-487b
10^4
10^3
10^2

FIG. 25

METHODS AND MATERIALS FOR CLASSIFICATION OF TISSUE OF ORIGIN OF TUMOR SAMPLES

FIELD OF THE INVENTION

[0001] The present invention relates to methods and materials for classification of cancers and the identification of their tissue of origin. Specifically the invention relates to microRNA molecules associated with specific cancers, as well as various nucleic acid molecules relating thereto or derived therefrom.

BACKGROUND OF THE INVENTION

[0002] microRNAs (miRs, miRNAs) are a novel class of non-coding, regulatory RNA genes[1-3] which are involved in oncogenesis[4] and show remarkable tissue-specificity[5-7]. They have emerged as highly tissue-specific biomarkers[2,5,6] postulated to play important roles in encoding developmental decisions of differentiation. Various studies have tied microRNAs to the development of specific malignancies[4]. MicroRNAs are also stable in tissue, stored frozen or as formalin-fixed, paraffin-embedded (FFPE) samples, and in serum.

[0003] Hundreds of thousands of patients in the U.S. are diagnosed each year with a cancer that has already metastasized, without a clearly identified primary site. Oncologists and pathologists are constantly faced with a diagnostic dilemma when trying to identify the primary origin of a patient's metastasis. As metastases need to be treated according to their primary origin, accurate identification of the metastases' primary origin can be critical for determining appropriate treatment.

[0004] Once a metastatic tumor is found, the patient may undergo a wide range of costly, time consuming, and at times inefficient tests, including physical examination of the patient, histopathology analysis of the biopsy, imaging methods such as chest X-ray, CT and PET scans, in order to identify the primary origin of the metastasis.

[0005] Metastatic cancer of unknown primary (CUP) accounts for 3-5% of all new cancer cases, and as a group is usually a very aggressive disease with a poor prognosis[10]. The concept of CUP comes from the limitation of present methods to identify cancer origin, despite an often complicated and costly process which can significantly delay proper treatment of such patients. Recent studies revealed a high degree of variation in clinical management, in the absence of evidence based treatment for CUP[11]. Many protocols were evaluated[12] but have shown relatively small benefit[13]. Determining tumor tissue of origin is thus an important clinical application of molecular diagnostics[9].

[0006] Molecular classification studies for tumor tissue origin[14-17] have generally used classification algorithms that did not utilize domain-specific knowledge: tissues were treated as a-priori equivalents, ignoring underlying similarities between tissue types with a common developmental origin in embryogenesis. An exception of note is the study by Shedden and co-workers[18], that was based on a pathology classification tree. These studies used machine-learning methods that average effects of biological features (e.g., mRNA expression levels), an approach which is more amenable to automated processing but does not use or generate mechanistic insights.

[0007] Various markers have been proposed to indicate specific types of cancers and tumor tissue of origin. However, the diagnostic accuracy of tumor markers has not yet been defined. There is thus a need for a more efficient and effective method for diagnosing and classifying specific types of cancers.

SUMMARY OF THE INVENTION

[0008] The present invention provides specific nucleic acid sequences for use in the identification, classification and diagnosis of specific cancers and tumor tissue of origin. The nucleic acid sequences can also be used as prognostic markers for prognostic evaluation and determination of appropriate treatment of a subject based on the abundance of the nucleic acid sequences in a biological sample. The present invention provides a method for accurate identification of tumor tissue origin.

[0009] The invention is based in part on the development of a microRNA-based classifier for tumor classification. microRNA expression levels were measured in 1300 primary and metastatic tumor paraffin-embedded samples. microRNAs were profiled using a custom array platform. Using the custom array platform, a set of over 300 microRNAs was identified for the normalization of the array data and 65 microRNAs were used for the accurate classification of over 40 different tumor types. The accuracy of the assay exceeds 85%.

[0010] The findings demonstrate the utility of microRNA as novel biomarkers for the tissue of origin of a metastatic tumor. The classifier has wide biological as well as diagnostic applications.

[0011] According to a first aspect, the present invention provides a method of identifying a tissue of origin of a cancer, the method comprising obtaining a biological sample from a subject, measuring the relative abundance in said sample of nucleic acid sequences selected from the group consisting of SEQ ID NOS: 1-390, any combinations thereof, or a sequence having at least about 80% identity thereto; and comparing the measurement to a reference abundance of the nucleic acid by using a classifier algorithm, wherein the relative abundance of said nucleic acid sequences allows for the identification of the tissue of origin of said sample.

[0012] According to one aspect, the classifier algorithm is selected from the group consisting of decision tree classifier, K-nearest neighbor classifier (KNN), logistic regression classifier, nearest neighbor classifier, neural network classifier, Gaussian mixture model (GMM), Support Vector Machine (SVM) classifier, nearest centroid classifier, linear regression classifier and random forest classifier. According to one aspect, the sample is obtained from a subject with cancer of unknown primary (CUP), with a primary cancer or with a metastatic cancer. According to certain embodiments, the cancer is selected from the group consisting of adrenocortical carcinoma; anus or skin squamous cell carcinoma; biliary tract adenocarcinoma; Ewing sarcoma; gastrointestinal stromal tumor (GIST); gastrointestinal tract carcinoid; renal cell carcinoma: chromophobe, clear cell and papillary; pancreatic islet cell tumor; pheochromocytoma; urothelial cell carcinoma (TCC); lung, head & neck, or esophagus squamous cell carcinoma (SCC); brain: astrocytic tumor, oligodendroglioma; breast adenocarcinoma; uterine cervix squamous cell carcinoma; chondrosarcoma; germ cell cancer; sarcoma; colorectal adenocarcinoma; liposarcoma;

hepatocellular carcinoma (HCC); lung large cell or adenocarcinoma; lung carcinoid; pleural mesothelioma; lung small cell carcinoma; B-cell lymphoma; T-cell lymphoma; melanoma; malignant fibrous histiocytoma (MFH) or fibrosarcoma; osteosarcoma; ovarian primitive germ cell tumor; ovarian carcinoma; pancreatic adenocarcinoma; prostate adenocarcinoma; rhabdomyosarcoma; gastric or esophageal adenocarcinoma; synovial sarcoma; non-seminomatous testicular germ cell tumor; seminomatous testicular germ cell tumor; thymoma/thymic carcinoma; follicular thyroid carcinoma; medullary thyroid carcinoma; and papillary thyroid carcinoma.

[0013] The invention further provides a method for identifying a cancer of germ cell origin, comprising measuring the relative abundance of SEQ ID NO: 55 or a sequence having at least about 80% identity thereto in said sample; wherein the abundance of said nucleic acid sequence is indicative of a cancer of germ cell origin. According to some embodiments the germ cell is selected from the group consisting of an ovarian primitive cell and a testis cell. According to some embodiments the group of nucleic acid furthers consists of SEQ ID NOS: 29, 62 or a sequence having at least about 80% identity thereto, and the abundance of said nucleic acid sequence is indicative of a testis cell cancer origin selected from the group consisting of seminomatous testicular germ cell and non-seminomatous testicular germ cell.

[0014] The invention further provides a method for identifying a cancer origin selected from the group consisting of biliary tract adenocarcinoma and hepatocellular carcinoma, comprising measuring the relative abundance of a nucleic acid sequence selected from the group consisting of SEQ ID NOS: 55, 6, 9, 29 or a sequence having at least about 80% identity thereto in said sample; wherein the abundance of said nucleic acid sequence is indicative of a cancer origin selected from the group consisting of biliary tract adenocarcinoma and hepatocellular carcinoma.

[0015] The invention further provides a method for identifying a cancer of brain origin, the method comprising measuring the relative abundance of a nucleic acid sequence selected from the group consisting of SEQ ID NOS: 55, 6, 30, 46, 16, 156, 66, 68 or a sequence having at least about 80% identity thereto in said sample; wherein the abundance of said nucleic acid sequence is indicative of a cancer of brain origin.

[0016] According to some embodiments the group of nucleic acid furthers consists of SEQ ID NOS: 40, 60 or a sequence having at least about 80% identity thereto, and wherein the abundance of said nucleic acid sequence is indicative of a brain cancer origin selected from the group consisting of oligodendroglioma and astrocytoma.

[0017] The invention further provides a method for identifying a cancer of prostate adenocarcinoma origin, the method comprising measuring the relative abundance of a nucleic acid sequence selected from the group consisting of SEQ ID NOS: 55, 6, 30, 46, 56, 65, 25, 27, 35, 14, 21 or a sequence having at least about 80% identity thereto in said sample; wherein the abundance of said nucleic acid sequence is indicative of a cancer of prostate adenocarcinoma origin.

[0018] The invention further provides a method for identifying a cancer of breast adenocarcinoma origin, the method comprising measuring the relative abundance of a nucleic acid sequence selected from the group consisting of SEQ ID NOS: 55, 6, 30, 46, 56, 65, 27, 35, 14, 21, 32, 51, 7, 25, 50, 11, 148, 4, 49, 67 or a sequence having at least about 80% identity thereto in said sample; wherein the abundance of said nucleic acid sequence is indicative of a cancer of breast adenocarcinoma origin.

[0019] The invention further provides a method for identifying a cancer of ovarian carcinoma origin, the method comprising measuring the relative abundance of a nucleic acid sequence selected from the group consisting of SEQ ID NOS: 55, 6, 30, 46, 56, 65, 27, 35, 14, 21, 32, 51, 7, 25, 4, 39, 50, 11, 148, 49, 67, 57, 34 or a sequence having at least about 80% identity thereto in said sample; wherein the abundance of said nucleic acid sequence is indicative of a cancer of an ovarian carcinoma origin.

[0020] The invention further provides a method for identifying a cancer of thyroid carcinoma origin, the method comprising measuring the relative abundance of a nucleic acid sequence selected from the group consisting of SEQ ID NOS: 55, 6, 30, 46, 56, 65, 25, 27, 35, 14, 21, 32, 51, 7, 11, 148, 4 or a sequence having at least about 80% identity thereto in said sample; wherein the abundance of said nucleic acid sequence is indicative of a cancer of thyroid carcinoma origin.

[0021] According to some embodiments the group of nucleic acid furthers consists of SEQ ID NOS: 17, 34 or a sequence having at least about 80% identity thereto, and wherein said thyroid carcinoma origin is selected from the group consisting of follicular and papillary.

[0022] The invention further provides a method for identifying a cancer origin selected from the group consisting of lung large cell and lung adenocarcinoma, the method comprising measuring the relative abundance of a nucleic acid sequence selected from the group consisting of SEQ ID NOS: 55, 6, 30, 46, 56, 65, 25, 27, 35, 14, 21, 32, 51, 7, 11, 148, 4, 49, 67, 57, 34 or a sequence having at least about 80% identity thereto in said sample; wherein the abundance of said nucleic acid sequence is indicative of a cancer origin selected from the group consisting of lung large cell and lung adenocarcinoma.

[0023] The invention further provides a method for identifying a cancer origin selected from the group consisting of lung large cell and lung adenocarcinoma, the method comprising measuring the relative abundance of a nucleic acid sequence selected from the group consisting of SEQ ID NOS: 55, 6, 30, 46, 56, 65, 25, 27, 35, 14, 21, 32, 51, 7, 11, 148, 4, 49, 67, 57, 34 or a sequence having at least about 80% identity thereto in said sample; wherein the abundance of said nucleic acid sequence is indicative of a cancer origin selected from the group consisting of lung large cell and lung adenocarcinoma.

[0024] The invention further provides a method for identifying a cancer of thymic carcinoma origin, the method comprising measuring the relative abundance of a nucleic acid sequence selected from the group consisting of SEQ ID NOS: 55, 6, 30, 46, 56, 65, 25, 27, 35, 14, 21, 32, 51, 7, 50, 4, 39, 3, 34 or a sequence having at least about 80% identity thereto in said sample; wherein the abundance of said nucleic acid sequence is indicative of a cancer of a thymic carcinoma origin.

[0025] The invention further provides a method for identifying a cancer origin selected from the group consisting of a urothelial cell carcinoma and squamous cell carcinoma, the method comprising measuring the relative abundance of a nucleic acid sequence selected from the group consisting of

SEQ ID NOS: 55, 6, 30, 46, 56, 65, 25, 27, 35, 14, 21, 32, 51, 7, 50, 4, 39, 3, 34, 69, 24, 44 or a sequence having at least about 80% identity thereto in said sample; wherein the abundance of said nucleic acid sequence is indicative of is indicative of a cancer origin selected from the group consisting of urothelial cell carcinoma and squamous cell carcinoma.

[0026] According to some embodiments the group of nucleic acid further consists of SEQ ID NOS: 1, 5, 54 or a sequence having at least about 80% identity thereto, and wherein the abundance of said nucleic acid sequence is indicative of squamous-cell-carcinoma origin selected from the group consisting of uterine cervix squamous-cell-carcinoma and non uterine cervix squamous cell carcinoma.

[0027] According to some embodiments the group of nucleic acid further consists of SEQ ID NOS: 11, 23 or a sequence having at least about 80% identity thereto in said sample, and wherein the abundance of said nucleic acid sequence is indicative of a non-uterine cervix squamous cell carcinoma origin selected from the group consisting of anus or skin squamous cell carcinoma; and lung, head & neck, and esophagus squamous cell carcinoma.

[0028] The invention further provides a method for identifying a cancer origin selected from melanoma and lymphoma, the method comprising measuring the relative abundance of a nucleic acid sequence selected from the group consisting of SEQ ID NOS: 55, 6, 30, 46, 16, 2, 47, 50 or a sequence having at least about 80% identity thereto in said sample; wherein the abundance of said nucleic acid sequence is indicative of a cancer origin selected from the group consisting of melanoma and lymphoma.

[0029] According to some embodiments the group of nucleic acid further consists of SEQ ID NOS: 35, 48 or a sequence having at least about 80% identity thereto, and wherein the abundance of said nucleic acid sequence is indicative of a lymphoma cancer origin selected from the group consisting of B-cell lymphoma and T-cell lymphoma.

[0030] The invention further provides a method for identifying a cancer of lung small cell carcinoma origin, the method comprising measuring the relative abundance of a nucleic acid sequence selected from the group consisting of SEQ ID NOS: 55, 6, 30, 46, 56, 65, 25, 20, 45 or a sequence having at least about 80% identity thereto in said sample; wherein the abundance of said nucleic acid sequence is indicative of a cancer of lung small cell carcinoma origin.

[0031] The invention further provides a method for identifying a cancer of medullary thyroid carcinoma origin, the method comprising measuring the relative abundance of a nucleic acid sequence selected from the group consisting of SEQ ID NOS: 55, 6, 30, 46, 56, 65, 25, 20, 45, 40, 67, 68 or a sequence having at least about 80% identity thereto in said sample; wherein the abundance of said nucleic acid sequence is indicative of a cancer of medullary thyroid carcinoma origin.

[0032] The invention further provides a method for identifying a cancer of lung carcinoid origin, the method comprising measuring the relative abundance of a nucleic acid sequence selected from the group consisting of SEQ ID NOS: 55, 6, 30, 46, 56, 65, 25, 20, 45, 40, 67, 68, 64, 53, 37 or a sequence having at least about 80% identity thereto in said sample; wherein the abundance of said nucleic acid sequence is indicative of a cancer of lung carcinoid origin.

[0033] The invention further provides a method for identifying a cancer origin selected from the group consisting of gastrointestinal tract carcinoid and pancreatic islet cell tumor, the method comprising measuring the relative abundance of a nucleic acid sequence selected from the group consisting of SEQ ID NOS: 55, 6, 30, 46, 56, 65, 25, 20, 45, 40, 67, 68, 64, 53, 37, 34, 18 or a sequence having at least about 80% identity thereto in said sample; wherein the abundance of said nucleic acid sequence is indicative of a cancer origin selected from the group consisting of gastrointestinal tract carcinoid and pancreatic islet cell tumor.

[0034] The invention further provides a method for identifying a cancer origin selected from the group consisting of gastric and esophageal adenocarcinoma, the method comprising measuring the relative abundance of a nucleic acid sequence selected from the group consisting of SEQ ID NOS: 55, 6, 30, 46, 56, 65, 25, 27, 35, 42, 36, 146 or a sequence having at least about 80% identity thereto in said sample; wherein the abundance of said nucleic acid sequence is indicative of a cancer origin elected from the group consisting of gastric and esophageal adenocarcinoma.

[0035] The invention further provides a method for identifying a cancer of colorectal adenocarcinoma origin, the method comprising measuring the relative abundance of a nucleic acid sequence selected from the group consisting of SEQ ID NOS: 55, 6, 30, 46, 56, 65, 25, 27, 35, 42, 36, 146, 20, 43 or a sequence having at least about 80% identity thereto in said sample; wherein the abundance of said nucleic acid sequence is indicative of a cancer of colorectal adenocarcinoma origin.

[0036] The invention further provides a method for identifying a cancer origin selected from the group consisting of pancreatic adenocarcinoma and biliary tract adenocarcinoma, the method comprising measuring the relative abundance of a nucleic acid sequence selected from the group consisting of SEQ ID NOS: 55, 6, 30, 46, 56, 65, 25, 27, 35, 42, 36, 146, 20, 4351, 49, 16, or a sequence having at least about 80% identity thereto, and wherein the abundance of said nucleic acid sequence is indicative of a cancer origin selected from the group consisting of pancreatic adenocarcinoma or biliary tract adenocarcinoma.

[0037] The invention further provides a method for identifying a cancer of renal cell carcinoma origin, the method comprising measuring the relative abundance of a nucleic acid sequence selected from the group consisting of SEQ ID NOS: 55, 6, 30, 46, 16, 2, 66, 68, 19, 29 or a sequence having at least about 80% identity thereto in said sample; wherein the abundance of said nucleic acid sequence is indicative of a cancer of renal cell carcinoma origin.

[0038] According to some embodiments the group of nucleic acid further consists of SEQ ID NOS: 36, 147 or a sequence having at least about 80% identity thereto, and wherein the abundance of said nucleic acid sequence is indicative of a chromophobe renal cell carcinoma origin.

[0039] According to some embodiments the group of nucleic acid further consists of SEQ ID NOS: 49, 9 or a sequence having at least about 80% identity thereto, and wherein the abundance of said nucleic acid sequence is indicative of a renal cell carcinoma origin selected from the group consisting of clear cell and papillary.

[0040] The invention further provides a method for identifying a cancer of pheochromocytoma origin, the method comprising measuring the relative abundance of a nucleic acid sequence selected from the group consisting of SEQ ID NOS: 55, 6, 30, 46, 16, 2, 66, 68, 19, 29, 65, 56 or a sequence having at least about 80% identity thereto in said sample;

wherein the abundance of said nucleic acid sequence is indicative of a cancer of pheochromocytoma origin.

[0041] The invention further provides a method for identifying a cancer of adrenocortical origin, the method comprising measuring the relative abundance of a nucleic acid sequence selected from the group consisting of SEQ ID NOS: 55, 6, 30, 46, 16, 2, 66, 68, 19, 29, 65, 56, 31, 38, 61 or a sequence having at least about 80% identity thereto in said sample; wherein the abundance of said nucleic acid sequence is indicative of a cancer of adrenocortical origin.

[0042] The invention further provides a method for identifying a cancer of gastrointestinal stromal tumor origin, the method comprising measuring the relative abundance of a nucleic acid sequence selected from the group consisting of SEQ ID NOS: 55, 6, 30, 46, 16, 2, 66, 68, 19, 29, 65, 56, 31, 38, 61, 14, 45 or a sequence having at least about 80% identity thereto in said sample; wherein the abundance of said nucleic acid sequence is indicative of a cancer of gastrointestinal stromal tumor origin.

[0043] The invention further provides a method for identifying a cancer origin selected from the group consisting of pleural mesothelioma and sarcoma, the method comprising measuring the relative abundance of a nucleic acid sequence selected from the group consisting of SEQ ID NOS: 55, 6, 30, 46, 16, 2, 66, 68, 19, 29, 65, 56, 31, 38, 61, 14, 45, 35, 10, 5 or a sequence having at least about 80% identity thereto in said sample; wherein the abundance of said nucleic acid sequence is indicative of a cancer origin selected from the group consisting of pleural mesothelioma and sarcoma.

[0044] According to some embodiments the group of nucleic acid further consists of SEQ ID NOS: 3, 40, 15 or a sequence having at least about 80% identity thereto, and wherein said sarcoma is synovial sarcoma.

[0045] According to some embodiments the group of nucleic acid further consists of SEQ ID NOS: 3, 40, 15, 12, 58 or a sequence having at least about 80% identity thereto, and wherein said sarcoma is chondrosarcoma.

[0046] According to some embodiments the group of nucleic acid further consists of SEQ ID NOS: 3, 40, 15, 12, 58, 36, 26 or a sequence having at least about 80% identity thereto, and wherein said sarcoma is liposarcoma.

[0047] According to some embodiments the group of nucleic acid further consists of SEQ ID NOS: 3, 40, 15, 12, 58, 36, 26, 21, 25, 49 or a sequence having at least about 80% identity thereto and wherein said sarcoma is selected from the group consisting of Ewing sarcoma and osteosarcoma.

[0048] According to some embodiments the group of nucleic acid further consists of SEQ ID NOS: 3, 40, 15, 12, 58, 36, 26, 21, 59, 39, 33 or a sequence having at least about 80% identity thereto and wherein said sarcoma is selected from the group consisting of rhabdomyosarcoma; and malignant fibrous histiocytoma and fibrosarcoma.

[0049] According to another aspect, the present invention provides a method of distinguishing between cancers of different origins, said method comprising:

[0050] (a) obtaining a biological sample from a subject;

[0051] (b) measuring the relative abundance in said sample of nucleic acid sequences selected from the group consisting of SEQ ID NOS: 1-390 or a sequence having at least about 80% identity thereto; and

[0052] (c) comparing said measurement to a reference abundance of said nucleic acid by using a classifier algorithm;

[0053] wherein the relative abundance of said nucleic acid sequence in said sample allows for distinguishing between cancers of different origins.

[0054] According to some embodiments the measurement of the relative abundance of SEQ ID NOS: 372, 233, 55, 200, 201 or a sequence having at least about 80% identity thereto in said sample allows for distinguishing between a cancer originating from a germ-cell tumor and a cancer originating from the group consisting of non-germ-cell tumors.

[0055] According to some embodiments the measurement of the relative abundance of SEQ ID NOS: 6, 30, 13 or a sequence having at least about 80% identity thereto in said sample allows for distinguishing between a cancer originating from hepatobiliary tumors and a cancer originating from the group consisting of non-germ-cell non-hepatobiliary tumors.

[0056] According to some embodiments the measurement of the relative abundance of SEQ ID NOS: 28, 29, 231, 9 or a sequence having at least about 80% identity thereto in said sample allows for distinguishing between a cancer originating from liver tumors and a cancer originating from biliary-tract carcinomas.

[0057] According to some embodiments the measurement of the relative abundance of SEQ ID NOS: 46, 5, 12, 30, 29, 28, 32, 13, 152, 49 or a sequence having at least about 80% identity thereto in said sample allows for distinguishing between a cancer originating from the group consisting of tumors from an epithelial origin and a cancer originating from the group consisting of tumors from a non-epithelial origin.

[0058] According to some embodiments the measurement of the relative abundance of SEQ ID NOS: 164, 168, 170, 16, 198, 50, 176, 186, 11, 158, 20, 155, 231, 4, 8, 46, 3, 2, 7 or a sequence having at least about 80% identity thereto in said sample allows for distinguishing between a cancer originating from the group consisting of melanoma and lymphoma and a cancer originating from the group consisting of all other non-epithelial tumors.

[0059] According to some embodiments the measurement of the relative abundance of SEQ ID NOS: 159, 66, 225, 187, 162, 161, 68, 232, 173, 11, 8, 174, 155, 231, 4, 182, 181, 37 or a sequence having at least about 80% identity thereto in said sample allows for distinguishing between a cancer originating from brain tumors and a cancer originating from the group consisting of all non-brain, non-epithelial tumors.

[0060] According to some embodiments the measurement of the relative abundance of SEQ ID NOS: 40, 208, 60, 153, 230, 228, 147, 34, 206, 35, 52, 25, 229, 161, 187, 179 or a sequence having at least about 80% identity thereto in said sample allows for distinguishing between a cancer originating from astrocytoma and a cancer originating from oligodendroglioma.

[0061] According to some embodiments, measurement of the relative abundance of SEQ ID NOS: 56, 65, 25, 175, 152, 155, 32, 49, 35, 181, or a sequence having at least about 80% identity thereto in said sample allows for distinguishing between a cancer originating from the group consisting of

neuroendocrine tumors and a cancer originating from the group consisting of all non-neuroendocrine, epithelial tumors.

[0062] According to some embodiments, measurement of the relative abundance of SEQ ID NOS: 27, 177, 4, 32, 35 or a sequence having at least about 80% identity thereto in said sample allows for distinguishing between a cancer originating from the group consisting of gastrointestinal epithelial tumors and a cancer originating from the group consisting of non-gastrointestinal epithelial tumors.

[0063] According to some embodiments, measurement of the relative abundance of SEQ ID NOS: 56, 199, 14, 15, 165, 231, 36, 154, 21, 49 or a sequence having at least about 80% identity thereto in said sample allows for distinguishing between a cancer originating from prostate tumors and a cancer originating from the group consisting of all other non-gastrointestinal epithelial tumors.

[0064] According to some embodiments, measurement of the relative abundance of SEQ ID NOS: 222, 62, 29, 28, 211, 214, 227, 215, 218, 152, 216, 212, 224, 13, 194, 192, 221, 217, 205, 219, 32, 193, 223, 220, 210, 209, 213, 163, 30 or a sequence having at least about 80% identity thereto in said sample allows for distinguishing between a cancer originating from seminoma and a cancer originating from the group consisting of non-seminoma testis-tumors.

[0065] According to some embodiments, measurement of the relative abundance of SEQ ID NOS: 42, 32, 36, 178, 243, 242, 49, 240, 57, 11, 46, 17, 47, 51, 7, 8, 154, 190, 157, 196, 197, or a sequence having at least about 80% identity thereto in said sample allows for distinguishing between a cancer originating from the group consisting of squamous cell carcinoma, transitional cell carcinoma and thymoma, and a cancer originating from the group consisting of non gastrointestinal adenocarcinoma tumors.

[0066] According to some embodiments, measurement of the relative abundance of SEQ ID NOS: 56, 46, 25, 152, 50, 45, 191, 181, 179, 49, 32, 42, 184, 40, 147, 236, 57, 203, 36, or a sequence having at least about 80% identity thereto in said sample allows for distinguishing between a cancer originating from breast adenocarcinoma, and a cancer originating from the group consisting of squamous cell carcinoma, transitional cell carcinoma, thymomas and ovarian carcinoma.

[0067] According to some embodiments, measurement of the relative abundance of SEQ ID NOS: 253, 32, 4, 39, 10, 46, 5, 226, 2, 195, 32, 185, 11, 168, 184, 16, 242, 12, 237, 243, 250, 49, 246, 167 or a sequence having at least about 80% identity thereto in said sample allows for distinguishing between a cancer originating from ovarian carcinoma, and a cancer originating from the group consisting of squamous cell carcinoma, transitional cell carcinoma and thymomas.

[0068] According to some embodiments, measurement of the relative abundance of SEQ ID NOS: 11, 147, 17, 157, 40, 8, 49, 9, 191, 205, 207, 195, 51, 46, 45, 52, 234, 231, 21, 169, 43, 3, 196, 154, 390, 171, 255, 197, 190, 189, 39, 7, 48, 47, 32, 36, 4, 178, 37, 181, 25, 183, 182, 35, 240, 57, 242, 204, 236, 176, 158, 148, 206, 50, 20, 34, 186, 239, 251, 244, 24, 188, 172, 238 or a sequence having at least about 80% identity thereto in said sample allows for distinguishing between a cancer originating from thyroid carcinoma, and a cancer originating from the group consisting of breast adenocarcinoma, lung large cell carcinoma, lung adenocarcinoma and ovarian carcinoma.

[0069] According to some embodiments, measurement of the relative abundance of SEQ ID NOS: 249, 180, 65, 235, 241, 248, 254, 247, 160, 243, 245, 252, 17, 49, 166, 225, 168, 34 or a sequence having at least about 80% identity thereto in said sample allows for distinguishing between a cancer originating from follicular thyroid carcinoma and a cancer originating from papillary thyroid carcinoma.

[0070] According to some embodiments, measurement of the relative abundance of SEQ ID NOS: 32, 56, 50, 45, 25, 253, 152, 9, 46, 191, 178, 49, 40, 10, 147, 4, 36, 228, 236, 230, 189, 240, 67, 202, 17 or a sequence having at least about 80% identity thereto in said sample allows for distinguishing between a cancer originating from breast adenocarcinoma and a cancer originating from the group consisting of lung adenocarcinoma and ovarian carcinoma.

[0071] According to some embodiments, measurement of the relative abundance of SEQ ID NOS: 56, 11, 168, 16, 237, 21, 52, 12, 154, 279, 9, 39, 47, 23, 50, 167, 383, 34, 35, 388, 5, 359, 245, 254, 10, 240, 236, 202, 4, 25, 203, 231, 20, 158, 186, 258, 244, 172, 2, 235, 256, 28, 277, 296, 374, 153, 181 or a sequence having at least about 80% identity thereto in said sample allows for distinguishing between a cancer originating from lung adenocarcinoma and a cancer originating from ovarian carcinoma.

[0072] According to some embodiments, measurement of the relative abundance of SEQ ID NOS: 161, 164, 22, 53, 285, 3, 152, 191, 154, 21, 206, 174, 19, 45, 171, 179, 8, 296, 284, 18, 51, 258, 49, 184, 35, 34, 37, 42, 228, 15, 14, 242, 230, 253, 36, 182, 293, 292, 4, 294, 297, 354, 377, 189, 30, 386, 249, 5, 274 or a sequence having at least about 80% identity thereto in said sample allows for distinguishing between a cancer originating from thymic carcinoma and a cancer originating from the group consisting of transitional cell carcinoma and squamous cell carcinoma.

[0073] According to some embodiments, measurement of the relative abundance of SEQ ID NOS: 69, 28, 280, 13, 191, 152, 29, 175, 30, 204, 4, 24, 5, 329, 273, 170, 184, 26, 231, 368, 37, 16, 169, 155, 35, 40, 17 or a sequence having at least about 80% identity thereto in said sample allows for distinguishing between a cancer originating from transitional cell carcinoma and a cancer originating from the group consisting of squamous cell carcinoma.

[0074] According to some embodiments, measurement of the relative abundance of SEQ ID NOS: 164, 5, 231, 54, 1, 242, 372, 249, 167, 254, 354, 381, 380, 245, 358, 364, 240, 11, 378 or a sequence having at least about 80% identity thereto in said sample allows for distinguishing between squamous cell carcinoma cancers originating from the uterine cervix, and squamous cell carcinoma cancers originating from the group consisting of anus and skin, lung, head & neck and esophagus.

[0075] According to some embodiments, measurement of the relative abundance of SEQ ID NOS: 305, 184, 41, 183, 49, 382, 235, 291, 181, 5, 296, 289, 206, 338, 334, 25, 11, 19, 198, 23 or a sequence having at least about 80% identity thereto in said sample allows for distinguishing between squamous cell carcinoma cancers originating from the group consisting of anus and skin, and between squamous cell carcinoma cancers originating from the group consisting of lung, head & neck and esophagus.

[0076] According to some embodiments, measurement of the relative abundance of SEQ ID NOS: 4, 11, 46, 8, 274, 169, 36, 47, 363, 231, 303, 349, 10, 7, 3, 16, 164, 170, 168, 198, 50, 245, 365, 45, 382, 259, 296, 364, 314, 12 or a

sequence having at least about 80% identity thereto in said sample allows for distinguishing between a cancer originating from melanoma and a cancer originating from lymphoma.

[0077] According to some embodiments, measurement of the relative abundance of SEQ ID NOS: 11, 191, 48, 35, 228 or a sequence having at least about 80% identity thereto in said sample allows for distinguishing between a cancer originating from B-cell lymphoma and a cancer originating from T-cell lymphoma.

[0078] According to some embodiments, measurement of the relative abundance of SEQ ID NOS: 158, 20, 176, 186, 148, 36, 51, 172, 260, 265, 67, 188, 277, 284, 302, 68, 168, 242, 204, 162, 177, 27, 65, 263, 155, 191, 190, 45, 59, 43, 56, 266, 14, 15, 8, 7, 39, 189, 249, 231, 293, 2 or a sequence having at least about 80% identity thereto in said sample allows for distinguishing between a cancer originating from lung small cell carcinoma and a cancer originating from the group consisting of lung carcinoid, medullary thyroid carcinoma, gastrointestinal tract carcinoid and pancreatic islet cell tumor.

[0079] According to some embodiments, measurement of the relative abundance of SEQ ID NOS: 159, 40, 147, 11, 311, 4, 8, 231, 301, 297, 68, 67, 265, 36 or a sequence having at least about 80% identity thereto in said sample allows for distinguishing between a cancer originating from medullary thyroid carcinoma and a cancer originating from other neuroendocrine tumors selected from the group consisting of lung carcinoid, gastrointestinal tract carcinoid and pancreatic islet cell tumor.

[0080] According to some embodiments, measurement of the relative abundance of SEQ ID NOS: 331, 162, 59, 326, 306, 350, 317, 155, 325, 318, 339, 264, 332, 262, 336, 324, 322, 330, 321, 263, 309, 53, 320, 275, 352, 312, 355, 367, 269, 64, 308, 175, 190, 54, 302, 152, 301, 266, 47, 313, 359, 65, 307, 191, 242, 4, 147, 40, 372, 168, 16, 182, 167, 356, 148, 382, 37, 364, 35 or a sequence having at least about 80% identity thereto in said sample allows for distinguishing between a cancer originating from lung carcinoid tumors, and a cancer originating from gastrointestinal neuroendocrine tumors selected from the group consisting of gastrointestinal tract carcinoid and pancreatic islet cell tumor.

[0081] According to some embodiments, measurement of the relative abundance of SEQ ID NOS: 263, 288, 18, 286, 162, 225, 287, 206, 205, 296, 258, 313, 377, 373, 256, 153, 259, 265, 303, 268, 267, 165, 15, 272, 14, 202, 236, 203, 4, 168, 310, 298, 27, 29, 34, 228, 3, 349, 35, 26 or a sequence having at least about 80% identity thereto in said sample allows for distinguishing between a cancer originating from pancreatic islet cell tumors and a Gastrointestinal neuroendocrine carcinoid cancer originating from the group consisting of small intestine and duodenum; appendicitis, stomach and pancreas.

[0082] According to some embodiments, measurement of the relative abundance of SEQ ID NOS: 36, 267, 268, 165, 15, 14, 356, 167, 372, 272, 370, 42, 41, 146 or a sequence having at least about 80% identity thereto in said sample allows for distinguishing between adenocarcinoma tumors of the gastrointestinal system originating from:

[0083] the group consisting of gastric and esophageal adenocarcinoma, and

[0084] the group consisting of cholangiocarcinoma or adenocarcinoma of the extrahepatic biliary tract, pancreatic adenocarcinoma and colorectal adenocarcinoma.

[0085] According to some embodiments, measurement of the relative abundance of SEQ ID NOS: 42, 184, 67, 158, 20, 186, 284, 389, 203, 240, 236, 146, 204, 43, 176, 202, 49, 46, 38, 363 or a sequence having at least about 80% identity thereto in said sample allows for distinguishing between a cancer originating from colorectal adenocarcinoma and a cancer originating from the group consisting of adenocarcinoma of biliary tract or pancreas.

[0086] According to some embodiments, measurement of the relative abundance of SEQ ID NOS: 49, 11, 13, 373, 154, 5, 30, 45, 178, 147, 274, 16, 40, 21, 43, 253, 245, 256, 12, 374, 379, 180, 153, 51, 52, 1, 295, 257, 385, 293, 294 or a sequence having at least about 80% identity thereto in said sample allows for distinguishing between a cancer originating from pancreatic adenocarcinoma, and a cancer originating from the group consisting of cholangiocarcinoma or adenocarcinoma of the extrahepatic biliary tract.

[0087] According to some embodiments, measurement of the relative abundance of SEQ ID NOS: 29, 28, 30, 46, 49, 195, 152, 175, 47, 4, 387, 196, 177, 375, 27, 304, 40, 191, 147, 35, 16, 34, 5, 155, 181, 312, 183, 182, 320, 59, 38, 324, 323, 37, 322, 325, 19, 42, 334, 265, 22 or a sequence having at least about 80% identity thereto in said sample allows for distinguishing between a cancer originating from:

[0088] renal cell tumors selected from the group consisting of chromophobe renal cell carcinoma, clear cell renal cell carcinoma and papillary renal cell carcinoma, and

[0089] the group consisting of sarcomas, adrenal tumors and pleural mesothelioma.

[0090] According to some embodiments, measurement of the relative abundance of SEQ ID NOS: 65, 56, 11, 162, 59, 331, 350, 155, 335, 159, 336, 332, 263, 306, 339, 337, 275, 301, 276, 330, 317, 309, 45, 318, 324, 352, 191, 262, 269, 313, 19, 367, 326, 325, 322, 327, 190, 261, 321, 360, 353, 312, 371, 5, 328, 205, 183, 38, 181, 37, 40, 182, 147, 17, 42, 382, 34, 18, 3 or a sequence having at least about 80% identity thereto in said sample allows for distinguishing between a cancer originating from pheochromocytoma, and a cancer originating from the group consisting of all sarcoma, adrenal carcinoma and mesothelioma tumors.

[0091] According to some embodiments, measurement of the relative abundance of SEQ ID NOS: 61, 333, 31, 347, 346, 344, 345, 387, 334, 351, 324, 326, 269, 155, 320, 322, 59, 318, 325, 245, 254, 331, 275, 180, 355, 370, 323, 312, 178, 249, 183, 181, 38, 182, 37, 3, 25 or a sequence having at least about 80% identity thereto in said sample allows for distinguishing between a cancer originating from adrenal carcinoma and a cancer originating from the group consisting of mesothelioma and sarcoma tumors.

[0092] According to some embodiments, measurement of the relative abundance of SEQ ID NOS: 165, 14, 15, 333, 272, 270, 45, 301, 191, 46, 195, 266, 190, 19, 334, 155, 25, 147, 40, 34 or a sequence having at least about 80% identity thereto in said sample allows for distinguishing between a cancer originating from a gastrointestinal stromal tumor and a cancer originating from the group consisting of mesothelioma and sarcoma tumors.

[0093] According to some embodiments, measurement of the relative abundance of SEQ ID NOS: 13, 30, 361, 280, 362, 147, 40, 291, 387, 290, 299, 152, 178, 303, 242, 49, 11, 35, 34, 36, 206, 16, 170, 177, 17 or a sequence having at least about 80% identity thereto in said sample allows for distinguishing between a cancer originating from a chromo-

phobe renal cell carcinoma tumor and a cancer originating from the group consisting of clear cell and papillary renal cell carcinoma tumors.

[0094] According to some embodiments, measurement of the relative abundance of SEQ ID NOS: 344, 382, 9, 338, 29, 49, 28, 195, 46, 4, 11, 254 or a sequence having at least about 80% identity thereto in said sample allows for distinguishing between a renal carcinoma cancer originating from a clear cell tumor and a cancer originating from a papillary tumor.

[0095] According to some embodiments, measurement of the relative abundance of SEQ ID NOS: 49, 35, 17, 34, 25, 36, 168, 170, 26, 4, 190, 46, 10, 240, 43, 39, 385, 63, 202, 181, 37, 5, 183, 182, 38, 206, 296, 1 or a sequence having at least about 80% identity thereto in said sample allows for distinguishing between a cancer originating from pleural mesothelioma and a cancer originating from the group consisting of sarcoma tumors.

[0096] According to some embodiments, measurement of the relative abundance of SEQ ID NOS: 152, 29, 159, 28, 339, 275, 352, 19, 320, 155, 262, 38, 37, 182, 331, 317, 323, 355, 3, 282, 312, 181, 269, 318, 59, 266, 322, 8, 324, 10, 40, 147, 169, 205, 34, 168, 14, 15, 12, 46, 255, 39, 23, 190, 236, 386, 379, 202 or a sequence having at least about 80% identity thereto in said sample allows for distinguishing between a cancer originating from a synovial sarcoma and a cancer originating from the group consisting of other sarcoma tumors.

[0097] According to some embodiments, measurement of the relative abundance of SEQ ID NOS: 12, 271, 206, 333, 11, 58, 36, 18, 178, 293, 189, 382, 381, 240, 249, 5, 377, 235, 17, 20, 385, 384, 46, 283 or a sequence having at least about 80% identity thereto in said sample allows for distinguishing between a cancer originating from chondrosarcoma and a cancer originating from the group consisting of other non-synovial sarcoma tumors.

[0098] According to some embodiments, measurement of the relative abundance of SEQ ID NOS: 295, 205, 25, 26, 231, 183, 42, 254, 168, 64, 14, 178, 15, 39, 36, 154, 265, 174, 384, 67 or a sequence having at least about 80% identity thereto in said sample allows for distinguishing between a cancer originating from liposarcoma and a cancer originating from the group consisting of other non chondrosarcoma and non synovial sarcoma tumors.

[0099] According to some embodiments, measurement of the relative abundance of SEQ ID NOS: 22, 154, 21, 174, 205, 158, 186, 148, 20, 59, 8, 183, 231 or a sequence having at least about 80% identity thereto in said sample allows for distinguishing between a cancer originating from:

[0100] the group consisting of Ewing sarcoma and osteosarcoma, and

[0101] the group consisting of rhabdomyosarcoma, malignant fibrous histiocytoma and fibrosarcoma.

[0102] According to some embodiments, measurement of the relative abundance of SEQ ID NOS: 155, 179, 43, 208, 278, 17, 385, 174, 5, 52, 257, 366, 48, 49, 12, 25, 169, 34, 35, 23, 384, 189, 377, 265, 294, 293, 292 or a sequence having at least about 80% identity thereto in said sample allows for distinguishing between a cancer originating from Ewing sarcoma and a cancer originating from osteosarcoma.

[0103] According to some embodiments, measurement of the relative abundance of SEQ ID NOS: 33, 268, 267, 333, 276, 319, 306, 320, 334, 323, 300, 281, 59, 339, 316, 176, 348, 352, 349, 67, 357, 315, 343, 342, 355, 340, 344, 10, 341, 331, 20, 277, 318, 158, 265, 284, 36, 183, 40, 63, 147, 43, 289, 52, 190, 4, 5, 39, 169, 208 or a sequence having at least about 80% identity thereto in said sample allows for distinguishing between a cancer originating from rhabdomyosarcoma and a cancer originating from the group consisting of malignant fibrous histiocytoma and fibrosarcoma.

[0104] According to some aspects of the invention the biological sample is selected from the group consisting of bodily fluid, a cell line, a tissue sample, a biopsy sample, a needle biopsy sample, a fine needle biopsy (FNA) sample, a surgically removed sample, and a sample obtained by tissue-sampling procedures such as endoscopy, bronchoscopy, or laparoscopic methods. According to some embodiments, the tissue is a fresh, frozen, fixed, wax-embedded or formalin-fixed paraffin-embedded (FFPE) tissue.

[0105] According to additional aspects of the invention the nucleic acid sequence relative abundance is determined by a method selected from the group consisting of nucleic acid hybridization and nucleic acid amplification. According to some embodiments, the nucleic acid hybridization is performed using a solid-phase nucleic acid biochip array or in situ hybridization. According to some embodiments, the nucleic acid amplification method is real-time PCR. According to some embodiments, the real-time PCR comprises forward and reverse primers. According to additional embodiments, the real-time PCR method further comprises a probe. According to additional embodiments, the probe comprises a sequence selected from the group consisting of a sequence that is complementary to a sequence selected from SEQ ID NOS: 1-390; a fragment thereof and a sequence having at least about 80% identity thereto.

[0106] According to another aspect, the present invention provides a kit for cancer origin identification, the kit comprising a probe comprising a sequence selected from the group consisting of a sequence that is complementary to a sequence selected from SEQ ID NOS: 1-390; a fragment thereof and a sequence having at least about 80% identity thereto.

[0107] These and other embodiments of the present invention will become apparent in conjunction with the figures, description and claims that follow.

BRIEF DESCRIPTION OF THE DRAWINGS

[0108] FIGS. **1**A-**1**F demonstrate the structure of the binary decision-tree classifier, with 45 nodes and 46 leaves. Each node is a binary decision between two sets of samples, those to the left and right of the node. A series of binary decisions, starting at node #1 and moving downwards, lead to one of the possible tumor types, which are the "leaves" of the tree. A sample which is classified to the right branch at node #1 continues to node #2, otherwise it continues to node #11. A sample which is classified to the right branch at node #2 continues to node #4, otherwise it continues to node #3. A sample that reaches node #3, is further classified to either the left branch at node #3, and is assigned to the "hepatocellular carcinoma" class, or to the right branch at node #3, and is assigned to the "biliary tract adenocarcinoma" class. Decisions are made at consecutive nodes using microRNA expression levels, until an end-point ("leaf" of the tree) is reached, indicating the predicted class for this sample. In specifying the tree structure, clinico-pathological considerations were combined with properties observed in the training set data.

[0109] FIGS. **2**A-**2**D demonstrate binary decisions at node #1 of the decision-tree. When training a decision algorithm for a given node, only samples from classes which are possible outcomes of this node are used for training. The "non germ cell" classes (right branch at node #1); are easily distinguished from tumors of the "germ cell" classes (left branch at node #1) using the expression levels of hsa-miR-373 (SEQ ID NO: 233, **2**A), hsa-miR-372 (SEQ ID NO: 55, **2**B), hsa-miR-371-3p (SEQ ID NO: 200, **2**C), and hsa-miR-371-5p (SEQ ID NO: 201, **2**D). The boxplot presentations comparing distribution of the expression of the statistically significant miRs in tumor samples from the "germ cell" classes (left box) and "non germ cell" classes (right box). The line in the box indicates the median value. The box contains 50% of the data and the horizontal lines and crosses (outliers) show the full range of signals in this group.

[0110] FIG. **3** demonstrates binary decisions at node #3 of the decision-tree. Tumors of hepatocellular carcinoma (HCC) origin (left branch at node #3, marked by squares) are easily distinguished from tumors of biliary tract adenocarcinoma origin (right branch at node #3, marked by diamonds) using the expression levels of hsa-miR-200b (SEQ ID NO: 29, y-axis) and hsa-miR-126 (SEQ ID NO: 9, x-axis).

[0111] FIG. **4** demonstrates binary decisions at node #4 of the decision-tree. Tumors originating in epithelial (diamonds) are easily distinguished from tumors of non-epithelial origin (squares) using the expression levels of hsa-miR-30a (SEQ ID NO: 46, y-axis) and hsa-miR-200c (SEQ ID NO: 30, x-axis).

[0112] FIG. **5** demonstrates binary decisions at node #5 of the decision-tree. Tumors originating in the lymphoma or melanoma (diamonds) are easily distinguished from tumors of non epithelial, non lymphoma/melanoma origin (squares) using the expression levels of hsa-miR-146a (SEQ ID NO: 16, y-axis), hsa-miR-30a (SEQ ID NO: 46, x-axis) and hsa-let-7e (SEQ ID NO: 2, z-axis).

[0113] FIG. **6** demonstrates binary decisions at node #6 of the decision-tree. Tumors originating in the brain (left branch at node #6, marked by diamonds) are easily distinguished from tumors of non epithelial, non brain (right branch at node #6, marked by squares) using the expression levels of hsa-miR-9* (SEQ ID NO: 66, y-axis) and hsa-miR-92b (SEQ ID NO: 68, x-axis).

[0114] FIG. **7** demonstrates binary decisions at node #7 of the decision-tree. Tumors originating in astrocytoma (right branch at node #7, marked by diamonds) are easily distinguished from tumors of oligodendroglioma origins (left branch at node #7, marked by squares) using the expression levels of hsa-miR-497 (SEQ ID NO: 60, y-axis) and hsa-miR-222 (SEQ ID NO: 40, x-axis).

[0115] FIG. **8** demonstrates binary decisions at node #8 of the decision-tree. Tumors originating in the neuroendocrine (diamonds) are easily distinguished from tumors of epithelial, origin (squares) using the expression levels of hsa-miR-193a-3p (SEQ ID NO: 181, y-axis), hsa-miR-7 (SEQ ID NO: 65, x-axis) and hsa-miR-375 (SEQ ID NO: 56, z-axis).

[0116] FIG. **9** demonstrates binary decisions at node #9 of the decision-tree. Tumors originating in gastro-intestinal (GI) (left branch at node #9, marked by diamonds) are easily distinguished from tumors of non GI origins (right branch at node #9, marked by squares) using the expression levels of hsa-miR-21* (SEQ ID NO: 35, y-axis) and hsa-miR-194 (SEQ ID NO: 27, x-axis).

[0117] FIG. **10** demonstrates binary decisions at node #10 of the decision-tree. Tumors originating in prostate adenocarcinoma (left branch at node #10, marked by diamonds) are easily distinguished from tumors of non prostate origins (right branch at node #10, marked by squares) using the expression levels of hsa-miR-181a (SEQ ID NO: 21, y-axis) and hsa-miR-143 (SEQ ID NO: 14, x-axis).

[0118] FIG. **11** demonstrates binary decisions at node #12 of the decision-tree. Tumors originating in seminomatous testicular germ cell (left branch at node #12, marked by diamonds) are easily distinguished from tumors of non seminomatous origins (right branch at node #12, marked by squares) using the expression levels of hsa-miR-516a-5p (SEQ ID NO: 62, y-axis) and hsa-miR-200b (SEQ ID NO: 29, x-axis).

[0119] FIG. **12** demonstrates binary decisions at node #16 of the decision-tree. Tumors originating in thyroid carcinoma (diamonds) are easily distinguished from tumors of adenocarcinoma of the lung, breast and ovarian origin (squares) using the expression levels of hsa-miR-93 (SEQ ID NO: 148, y-axis), hsa-miR-138 (SEQ ID NO: 11, x-axis) and hsa-miR-10a (SEQ ID NO: 4, z-axis).

[0120] FIG. **13** demonstrates binary decisions at node #17 of the decision-tree. Tumors originating in follicular thyroid carcinoma (left branch at node #17, marked by diamonds) are easily distinguished from tumors of papillary thyroid carcinoma origins (right branch at node #17, marked by squares) using the expression levels of hsa-miR-21 (SEQ ID NO: 34, y-axis) and hsa-miR-146b-5p (SEQ ID NO: 17, x-axis).

[0121] FIG. **14** demonstrates binary decisions at node #18 of the decision-tree. Tumors originating in breast (diamonds) are easily distinguished from tumors of lung and ovarian origin (squares) using the expression levels of hsa-miR-92a (SEQ ID NO: 67, y-axis), hsa-miR-193a-3p (SEQ ID NO: 25, x-axis) and hsa-miR-31 (SEQ ID NO: 49, z-axis).

[0122] FIG. **15** demonstrates binary decisions at node #19 of the decision-tree. Tumors originating in lung adenocarcinoma (diamonds) are easily distinguished from tumors of ovarian carcinoma origin (squares) using the expression levels of hsa-miR-21 (SEQ ID NO: 34, y-axis), hsa-miR-378 (SEQ ID NO: 57, x-axis) and hsa-miR-138 (SEQ ID NO: 11, z-axis).

[0123] FIG. **16** demonstrates binary decisions at node #20 of the decision-tree. Tumors originating in thymic carcinoma (left branch at node #20, marked by diamonds) are easily distinguished from tumors of urothelial carcinoma, transitional cell carcinoma (TCC) carcinoma and squamous cell carcinoma (SCC) origins (right branch at node #20, marked by squares) using the expression levels of hsa-miR-21 (SEQ ID NO: 34, y-axis) and hsa-miR-100 (SEQ ID NO: 3, x-axis).

[0124] FIG. **17** demonstrates binary decisions at node #22 of the decision-tree. Tumors originating in SCC of the uterine cervix (diamonds) are easily distinguished from tumors of other SCC origin (squares) using the expression levels of hsa-miR-361-5p (SEQ ID NO: 54, y-axis), hsa-let-7c (SEQ ID NO: 1, x-axis) and hsa-miR-10b (SEQ ID NO: 5, z-axis).

[0125] FIG. **18** demonstrates binary decisions at node #24 of the decision-tree. Tumors originating in melanoma (diamonds) are easily distinguished from tumors of lymphoma

origin (squares) using the expression levels of hsa-miR-342-3p (SEQ ID NO: 50, y-axis) and hsa-miR-30d (SEQ ID NO: 47, x-axis).

[0126] FIG. **19** demonstrates binary decisions at node #27 of the decision-tree. Tumors originating in thyroid carcinoma, medullary (diamonds) are easily distinguished from tumors of other neuroendocrine origin (squares) using the expression levels of hsa-miR-92b (SEQ ID NO: 68, y-axis), hsa-miR-222 (SEQ ID NO: 40, x-axis) and hsa-miR-92a (SEQ ID NO: 67, z-axis).

[0127] FIG. **20** demonstrates binary decisions at node #30 of the decision-tree. Tumors originating in gastric or esophageal adenocarcinoma (diamonds) are easily distinguished from tumors of other GI adenocarcinoma origin (squares) using the expression levels of hsa-miR-1201 (SEQ ID NO: 146, y-axis), hsa-miR-224 (SEQ ID NO: 42, x-axis) and hsa-miR-210 (SEQ ID NO: 36, z-axis).

[0128] FIG. **21** demonstrates binary decisions at node #31 of the decision-tree. Tumors originating in colorectal adenocarcinoma (diamonds) are easily distinguished from tumors of adenocarcinoma of biliary tract or pancreas origin (squares) using the expression levels of hsa-miR-30a (SEQ ID NO: 46, y-axis), hsa-miR-17 (SEQ ID NO: 20, x-axis) and hsa-miR-29a (SEQ ID NO: 43, z-axis).

[0129] FIG. **22** demonstrates binary decisions at node #33 of the decision-tree. Tumors originating in kidney (diamonds) are easily distinguished from tumors of adrenal, mesothelioma and sarcoma origin (squares) using the expression levels of hsa-miR-200b (SEQ ID NO: 29, y-axis), hsa-miR-30a (SEQ ID NO: 46, x-axis) and hsa-miR-149 (SEQ ID NO: 19, z-axis).

[0130] FIG. **23** demonstrates binary decisions at node #34 of the decision-tree. Tumors originating in pheochromocytoma (diamonds) are easily distinguished from tumors of adrenal, mesothelioma and sarcoma origin (squares) using the expression levels of hsa-miR-375 (SEQ ID NO: 56, y-axis) and hsa-miR-7 (SEQ ID NO: 65, x-axis).

[0131] FIG. **24** demonstrates binary decisions at node #44 of the decision-tree. Tumors originating in Ewing sarcoma (diamonds) are easily distinguished from tumors of osteosarcoma origin (squares) using the expression levels of hsa-miR-31 (SEQ ID NO: 49, y-axis) and hsa-miR-193a-3p (SEQ ID NO: 25, x-axis).

[0132] FIG. **25** demonstrates binary decisions at node #45 of the decision-tree. Tumors originating in Rhabdomyosarcoma (diamonds) are easily distinguished from tumors of malignant fibrous histiocytoma (MFH) or fibrosarcoma origin (squares) using the expression levels of hsa-miR-206 (SEQ ID NO: 33, y-axis), hsa-miR-22 (SEQ ID NO: 39, x-axis) and hsa-miR-487b (SEQ ID NO: 59, z-axis).

DETAILED DESCRIPTION OF THE INVENTION

[0133] Identification of the tissue-of-origin of a tumor is vital to its management. The present invention is based in part on the discovery that specific nucleic acid sequences can be used for the identification of the tissue-of-origin of a tumor. The present invention provides a sensitive, specific and accurate method which can be used to distinguish between different tumor origins. A new microRNA-based classifier was developed for determining tissue origin of tumors based on 65 microRNAs markers. The classifier uses a specific algorithm and allows a clear interpretation of the specific biomarkers.

[0134] According to the present invention each node in the classification tree may be used as an independent differential diagnosis tool, for example in the identification of different types of lung cancers. The possibility to distinguish between different tumor origins facilitates providing the patient with the best and most suitable treatment.

[0135] The present invention provides diagnostic assays and methods, both quantitative and qualitative for detecting, diagnosing, monitoring, staging and prognosticating cancers by comparing the levels of the specific microRNA molecules of the invention. Such levels are preferably measured in at least one of biopsies, tumor samples, fine-needle aspiration (FNA), cells, tissues and/or bodily fluids. The methods provided in the present invention are particularly useful for discriminating between different cancers.

[0136] All the methods of the present invention may optionally further include measuring levels of additional cancer markers. The cancer markers measured in addition to said microRNA molecules depend on the cancer being tested and are known to those of skill in the art.

[0137] Assay techniques can be used to determine levels of gene expression, such as genes encoding the nucleic acids of the present invention in a sample derived from a patient. Such assay methods, which are well known to those of skill in the art, include, but are not limited to, nucleic acid microarrays and biochip analysis, reverse transcriptase PCR (RT-PCR) assays, immunohistochemistry assays, in situ hybridization assays, competitive-binding assays, northern blot analyses and ELISA assays.

[0138] According to one embodiment, the assay is based on expression level of 65 microRNAs in RNA extracted from FFPE metastatic tumor tissue.

[0139] The expression levels are used to infer the sample origin using analysis techniques such as, but not limited to, decision-tree classifier, K nearest neighbors classifier, logistic regression classifier, linear regression classifier, nearest neighbor classifier, neural network classifier and nearest centroid classifier.

[0140] In use of the decision tree classifier the expression levels are used to make binary decisions (at each relevant node) following the pre-defined structure of the binary decision-tree (defined using a training set).

[0141] At each node, the expressions of one or several microRNAs are combined together using a function of the form P=exp (β0+β1*miR1+β2*miR2+β3*miR3 . . .)/(1−exp (β0+β1*miR1+β2*miR2+β3*miR3 . . .)), where the values of (30, (31, (32 . . . and the identities of the microRNAs have been pre-determined (using a training set). The resulting P is compared to a probability threshold level (P_{TH}, which was also determined using the training set), and the classification continues to the left or right branch according to whether P is larger or smaller than the P_{TH} for that node. This continues until an end-point ("leaf") of the tree is reached. According to some embodiments, P_{TH}=0.5 for all nodes, and the value of (30 is adjusted accordingly. According to further embodiments, β0, β1, β2, . . . are adjusted so that the slope of the log of the odds ratio function is limited.

[0142] Training the tree algorithm means determining the tree structure—which nodes there are and what is on each side, and, for each node: which miRs are used, the values of β0, β1, β2 . . . and the P_{TH}. These are determined by a combination of machine learning, optimization algorithm, and trial and error by experts in machine learning and diagnostic algorithms

[0143] An arbitrary threshold of the expression level of one or more nucleic acid sequences can be set for assigning a sample to one of two groups. Alternatively, in a preferred embodiment, expression levels of one or more nucleic acid sequences of the invention are combined by a method such as logistic regression to define a metric which is then compared to previously measured samples or to a threshold. The threshold is treated as a parameter that can be used to quantify the confidence with which samples are assigned to each class. The threshold can be scaled to favor sensitivity or specificity, depending on the clinical scenario. The correlation value to the reference data generates a continuous score that can be scaled and provides diagnostic information on the likelihood that a sample belongs to a certain class of cancer origin or type. In multivariate analysis the microRNA signature provides a high level of prognostic information.

[0144] In another preferred embodiment, expression level of nucleic acids is used to classify a test sample by comparison to a training set of samples. In this embodiment, the test sample is compared in turn to each one of the training set samples. The comparison is performed by comparing the expression levels of one or multiple nucleic acids between the test sample and the specific training sample. Each such pairwise comparison generates a combined metric for the multiple nucleic acids, which can be calculated by various numeric methods such as correlation, cosine, Euclidian distance, mean square distance, or other methods known to those skilled in the art. The training samples are then ranked according to this metric, and the samples with the highest values of the metric (or lowest values, according to the type of metric) are identified, indicating those samples that are most similar to the test sample. By choosing a parameter K, this generates a list that includes the K training samples that are most similar to the test sample. Various methods can then be applied to identify from this list the predicted class of the test sample. In a favored embodiment, the test sample is predicted to belong to the class that has the highest number of representative in the list of K most-similar training samples (this method is known as the K Nearest Neighbors method). Other embodiments may provide a list of predictions including all or part of the classes represented in the list, those classes that are represented more than a given minimum number of times, or other voting schemes whereby classes are grouped together.

I. Definitions

[0145] It is to be understood that the terminology used herein is for the purpose of describing particular embodiments only and is not intended to be limiting. It must be noted that, as used in the specification and the appended claims, the singular forms "a," "an" and "the" include plural referents unless the context clearly dictates otherwise.

[0146] For the recitation of numeric ranges herein, each intervening number there between with the same degree of precision is explicitly contemplated. For example, for the range of 6-9, the numbers 7 and 8 are contemplated in addition to 6 and 9, and for the range 6.0-7.0, the number 6.0, 6.1, 6.2, 6.3, 6.4, 6.5, 6.6, 6.7, 6.8, 6.9 and 7.0 are explicitly contemplated.

[0147] About

[0148] As used herein, the term "about" refers to +/−10%.

[0149] Attached

[0150] "Attached" or "immobilized", as used herein, to refer to a probe and a solid support means that the binding between the probe and the solid support is sufficient to be stable under conditions of binding, washing, analysis, and removal. The binding may be covalent or non-covalent. Covalent bonds may be formed directly between the probe and the solid support or may be formed by a cross linker or by inclusion of a specific reactive group on either the solid support or the probe or both molecules. Non-covalent binding may be one or more of electrostatic, hydrophilic, and hydrophobic interactions. Included in non-covalent binding is the covalent attachment of a molecule, such as streptavidin, to the support and the non-covalent binding of a biotinylated probe to the streptavidin. Immobilization may also involve a combination of covalent and non-covalent interactions.

[0151] Baseline

[0152] "Baseline", as used herein, means the initial cycles of PCR, in which there is little change in fluorescence signal.

[0153] Biological Sample

[0154] "Biological sample", as used herein, means a sample of biological tissue or fluid that comprises nucleic acids. Such samples include, but are not limited to, tissue or fluid isolated from subjects. Biological samples may also include sections of tissues such as biopsy and autopsy samples, FFPE samples, frozen sections taken for histological purposes, blood, blood fraction, plasma, serum, sputum, stool, tears, mucus, hair, skin, urine, effusions, ascitic fluid, amniotic fluid, saliva, cerebrospinal fluid, cervical secretions, vaginal secretions, endometrial secretions, gastrointestinal secretions, bronchial secretions, cell line, tissue sample, or secretions from the breast. A biological sample may be provided by fine-needle aspiration (FNA), pleural effusion or bronchial brushing. A biological sample may be provided by removing a sample of cells from a subject but can also be accomplished by using previously isolated cells (e.g., isolated by another person, at another time, and/or for another purpose), or by performing the methods described herein in vivo. Archival tissues, such as those having treatment or outcome history, may also be used. Biological samples also include explants and primary and/or transformed cell cultures derived from animal or human tissues.

[0155] Cancer

[0156] The term "cancer" is meant to include all types of cancerous growths or oncogenic processes, metastatic tissues or malignantly transformed cells, tissues, or organs, irrespective of histopathologic type or stage of invasiveness. Examples of cancers include, but are not limited, to solid tumors and leukemias, including: apudoma, choristoma, branchioma, malignant carcinoid syndrome, carcinoid heart disease, carcinoma (e.g., Walker, basal cell, basosquamous, Brown-Pearce, ductal, Ehrlich tumor, non-small cell lung (e.g., lung squamous cell carcinoma, lung adenocarcinoma and lung undifferentiated large cell carcinoma), oat cell, papillary, bronchiolar, bronchogenic, squamous cell, and transitional cell), histiocytic disorders, leukemia (e.g., B cell, mixed cell, null cell, T cell, T-cell chronic, HTLV-II-associated, lymphocytic acute, lymphocytic chronic, mast cell, and myeloid), histiocytosis malignant, Hodgkin disease, immunoproliferative small, non-Hodgkin lymphoma, plasmacytoma, reticuloendotheliosis, melanoma, chondroblastoma, chondroma, chondrosarcoma, fibroma, fibrosarcoma, giant cell tumors, histiocytoma, lipoma, liposarcoma, mesothelioma, myxoma, myxosarcoma, osteoma, osteosarcoma, Ewing sarcoma, synovioma, adenofibroma, adenolymphoma, carcinosarcoma, chordoma, craniopharyn-

gioma, dysgerminoma, hamartoma, mesenchymoma, mesonephroma, myosarcoma, ameloblastoma, cementoma, odontoma, teratoma, thymoma, trophoblastic tumor, adenocarcinoma, adenoma, cholangioma, cholesteatoma, cylindroma, cystadenocarcinoma, cystadenoma, granulosa cell tumor, gynandroblastoma, hepatoma, hidradenoma, islet cell tumor, Leydig cell tumor, papilloma, Sertoli cell tumor, theca cell tumor, leiomyoma, leiomyosarcoma, myoblastoma, myosarcoma, rhabdomyoma, rhabdomyosarcoma, ependymoma, ganglioneuroma, glioma, medulloblastoma, meningioma, neurilemmoma, neuroblastoma, neuroepithelioma, neurofibroma, neuroma, paraganglioma, paraganglioma nonchromaffin, angiokeratoma, angiolymphoid hyperplasia with eosinophilia, angioma sclerosing, angiomatosis, glomangioma, hemangioendothelioma, hemangioma, hemangiopericytoma, hemangiosarcoma, lymphangioma, lymphangiomyoma, lymphangiosarcoma, pinealoma, carcinosarcoma, chondrosarcoma, cystosarcoma, phyllodes, fibrosarcoma, hemangiosarcoma, leimyosarcoma, leukosarcoma, liposarcoma, lymphangiosarcoma, myosarcoma, myxosarcoma, ovarian carcinoma, rhabdomyosarcoma, sarcoma (e.g., Ewing, experimental, Kaposi, and mast cell), neurofibromatosis, and cervical dysplasia, and other conditions in which cells have become immortalized or transformed.

[0157] Classification

[0158] The term classification refers to a procedure and/or algorithm in which individual items are placed into groups or classes based on quantitative information on one or more characteristics inherent in the items (referred to as traits, variables, characters, features, etc.) and based on a statistical model and/or a training set of previously labeled items. A "classification tree" places categorical variables into classes.

[0159] Complement

[0160] "Complement" or "complementary" is used herein to refer to a nucleic acid may mean Watson-Crick (e.g., A-T/U and C-G) or Hoogsteen base pairing between nucleotides or nucleotide analogs of nucleic acid molecules. A full complement or fully complementary means 100% complementary base pairing between nucleotides or nucleotide analogs of nucleic acid molecules. In some embodiments, the complementary sequence has a reverse orientation (5'-3').

[0161] Ct

[0162] Ct signals represent the first cycle of PCR where amplification crosses a threshold (cycle threshold) of fluorescence. Accordingly, low values of Ct represent high abundance or expression levels of the microRNA.

[0163] In some embodiments the PCR Ct signal is normalized such that the normalized Ct remains inversed from the expression level. In other embodiments the PCR Ct signal may be normalized and then inverted such that low normalized-inverted Ct represents low abundance or low expression levels of the microRNA.

[0164] Data Processing Routine

[0165] As used herein, a "data processing routine" refers to a process that can be embodied in software that determines the biological significance of acquired data (i.e., the ultimate results of an assay or analysis). For example, the data processing routine can determine a tissue of origin based upon the data collected. In the systems and methods herein, the data processing routine can also control the data collection routine based upon the results determined. The data processing routine and the data collection routines can be integrated and provide feedback to operate the data acquisition, and hence provide assay-based judging methods.

[0166] Data Set

[0167] As use herein, the term "data set" refers to numerical values obtained from the analysis. These numerical values associated with analysis may be values such as peak height and area under the curve.

[0168] Data Structure

[0169] As used herein, the term "data structure" refers to a combination of two or more data sets, an application of one or more mathematical manipulation to one or more data sets to obtain one or more new data sets, or a manipulation of two or more data sets into a form that provides a visual illustration of the data in a new way. An example of a data structure prepared from manipulation of two or more data sets would be a hierarchical cluster.

[0170] Detection

[0171] "Detection" means detecting the presence of a component in a sample. Detection also means detecting the absence of a component. Detection also means determining the level of a component, either quantitatively or qualitatively.

[0172] Differential Expression

[0173] "Differential expression" means qualitative or quantitative differences in the temporal and/or spatial gene expression patterns within and among cells and tissue. Thus, a differentially expressed gene may qualitatively have its expression altered, including an activation or inactivation, in, e.g., normal versus diseased tissue. Genes may be turned on or turned off in a particular state, relative to another state, thus permitting comparison of two or more states. A qualitatively regulated gene may exhibit an expression pattern within a state or cell type which may be detectable by standard techniques. Some genes may be expressed in one state or cell type, but not in both. Alternatively, the difference in expression may be quantitative, e.g., in that expression is modulated: up-regulated, resulting in an increased amount of transcript, or down-regulated, resulting in a decreased amount of transcript. The degree to which expression differs needs only to be large enough to quantify via standard characterization techniques such as expression arrays, quantitative reverse transcriptase PCR, northern blot analysis, real-time PCR, in situ hybridization and RNase protection.

[0174] Epithelial Tumors

[0175] "Epithelial tumors" is meant to include all types of tumors from epithelial origin. Examples of epithelial tumors include, but are not limited to cholangioca or adenoca of extrahepatic biliary tract, urothelial carcinoma, adenocarcinoma of the breast, lung large cell or adenocarcinoma, lung small cell carcinoma, carcinoid, lung, ovarian carcinoma, pancreatic adenocarcinoma, prostatic adenocarcinoma, gastric or esophageal adenocarcinoma, thymoma/thymic carcinoma, follicular thyroid carcinoma, papillary thyroid carcinoma, medullary thyroid carcinoma, anus or skin squamous cell carcinoma, lung, head&neck, or esophagus squamous cell carcinoma, uterine cervix squamous cell carcinoma, gastrointestinal tract carcinoid, pancreatic islet cell tumor and colorectal adenocarcinoma.

[0176] Non Epithelial Tumors

[0177] "Non epithelial tumors" is meant to include all types of tumors from non epithelial origin. Examples of non epithelial tumors include, but are not limited to adrenocor-

tical carcinoma, chromophobe renal cell carcinoma, clear cell renal cell carcinoma, papillary renal cell carcinoma, pleural mesothelioma, astrocytic tumor, oligodendroglioma, pheochromocytoma, B-cell lymphoma, T-cell lymphoma, melanoma, gastrointestinal stromal tumor (GIST), Ewing Sarcoma, chondrosarcoma, malignant fibrous histiocytoma (MFH) or fibrosarcoma, osteosarcoma, rhabdomyosarcoma, synovial sarcoma and liposarcoma.

[0178] Expression Profile

[0179] The term "expression profile" is used broadly to include a genomic expression profile, e.g., an expression profile of microRNAs. Profiles may be generated by any convenient means for determining a level of a nucleic acid sequence, e.g., quantitative hybridization of microRNA, labeled microRNA, amplified microRNA, cDNA, etc., quantitative PCR, ELISA for quantitation, and the like, and allow the analysis of differential gene expression between two samples. A subject or patient tumor sample, e.g., cells or collections thereof, e.g., tissues, is assayed. Samples are collected by any convenient method, as known in the art. Nucleic acid sequences of interest are nucleic acid sequences that are found to be predictive, including the nucleic acid sequences provided above, where the expression profile may include expression data for 5, 10, 20, 25, 50, 100 or more of the nucleic acid sequences, including all of the listed nucleic acid sequences. According to some embodiments, the term "expression profile" means measuring the relative abundance of the nucleic acid sequences in the measured samples.

[0180] Expression Ratio

[0181] "Expression ratio", as used herein, refers to relative expression levels of two or more nucleic acids as determined by detecting the relative expression levels of the corresponding nucleic acids in a biological sample.

[0182] FDR (False Discovery Rate)

[0183] When performing multiple statistical tests, for example in comparing between the signal of two groups in multiple data features, there is an increasingly high probability of obtaining false positive results, by random differences between the groups that can reach levels that would otherwise be considered statistically significant. In order to limit the proportion of such false discoveries, statistical significance is defined only for data features in which the differences reached a p-value (by two-sided t-test) below a threshold, which is dependent on the number of tests performed and the distribution of p-values obtained in these tests.

[0184] Fragment

[0185] "Fragment" is used herein to indicate a non-full-length part of a nucleic acid. Thus, a fragment is itself also a nucleic acid.

[0186] Gastrointestinal Tumors

[0187] "gastrointestinal tumors" is meant to include all types of tumors from gastrointestinal origin. Examples of gastrointestinal tumors include, but are not limited to cholangioca. or adenoca of extrahepatic biliary tract, pancreatic adenocarcinoma, gastric or esophageal adenocarcinoma, and colorectal adenocarcinoma.

[0188] Gene

[0189] "Gene", as used herein, may be a natural (e.g., genomic) or synthetic gene comprising transcriptional and/or translational regulatory sequences and/or a coding region and/or non-translated sequences (e.g., introns, 5'- and 3'-untranslated sequences). The coding region of a gene may be a nucleotide sequence coding for an amino acid sequence or a functional RNA, such as tRNA, rRNA, catalytic RNA, siRNA, miRNA or antisense RNA. A gene may also be an mRNA or cDNA corresponding to the coding regions (e.g., exons and miRNA) optionally comprising 5'- or 3'-untranslated sequences linked thereto. A gene may also be an amplified nucleic acid molecule produced in vitro, comprising all or a part of the coding region and/or 5'- or 3'-untranslated sequences linked thereto.

[0190] Germ Cell Tumors

[0191] "Germ cell tumors" as used herein, include, but are not limited, to non-seminomatous testicular germ cell tumors, seminomatous testicular germ cell tumors and ovarian primitive germ cell tumors.

[0192] Groove Binder/Minor Groove Binder (MGB)

[0193] "Groove binder" and/or "minor groove binder" may be used interchangeably and refer to small molecules that fit into the minor groove of double-stranded DNA, typically in a sequence-specific manner Minor groove binders may be long, flat molecules that can adopt a crescent-like shape and thus fit snugly into the minor groove of a double helix, often displacing water. Minor groove binding molecules may typically comprise several aromatic rings connected by bonds with torsional freedom such as furan, benzene, or pyrrole rings. Minor groove binders may be antibiotics such as netropsin, distamycin, berenil, pentamidine and other aromatic diamidines, Hoechst 33258, SN 6999, aureolic anti-tumor drugs such as chromomycin and mithramycin, CC-1065, dihydrocyclopyrroloindole tripeptide (DPI_3), 1,2-dihydro-(3H)-pyrrolo[3,2-e]indole-7-carboxylate ($CDPI_3$), and related compounds and analogues, including those described in Nucleic Acids in Chemistry and Biology, 2nd ed., Blackburn and Gait, eds., Oxford University Press, 1996, and PCT Published Application No. WO 03/078450, the contents of which are incorporated herein by reference. A minor groove binder may be a component of a primer, a probe, a hybridization tag complement, or combinations thereof. Minor groove binders may increase the T_m of the primer or a probe to which they are attached, allowing such primers or probes to effectively hybridize at higher temperatures.

[0194] High Expression miR-205 Tumors

[0195] "High expression miR-205 tumors" as used herein include, but are not limited, to urothelial carcinoma (TCC), thymoma/thymic carcinoma, anus or skin squamous cell carcinoma, lung, head&neck, or esophagus squamous cell carcinoma and uterine cervix squamous cell carcinoma.

[0196] Low Expression 205 Tumors

[0197] "Low expression miR-205 tumors" as used herein include, but are not limited, to lung, large cell or adenocarcinoma, follicular thyroid carcinoma and papillary thyroid carcinoma.

[0198] Host Cell

[0199] "Host cell", as used herein, may be a naturally occurring cell or a transformed cell that may contain a vector and may support replication of the vector. Host cells may be cultured cells, explants, cells in vivo, and the like. Host cells may be prokaryotic cells, such as *E. coli*, or eukaryotic cells, such as yeast, insect, amphibian, or mammalian cells, such as CHO and HeLa cells.

[0200] Identity

[0201] "Identical" or "identity", as used herein, in the context of two or more nucleic acids or polypeptide sequences mean that the sequences have a specified percent-

age of residues that are the same over a specified region. The percentage may be calculated by optimally aligning the two sequences, comparing the two sequences over the specified region, determining the number of positions at which the identical residue occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the specified region, and multiplying the result by 100 to yield the percentage of sequence identity. In cases where the two sequences are of different lengths or the alignment produces one or more staggered ends and the specified region of comparison includes only a single sequence, the residues of single sequence are included in the denominator but not the numerator of the calculation. When comparing DNA and RNA sequences, thymine (T) and uracil (U) may be considered equivalent. Identity may be performed manually or by using a computer sequence algorithm such as BLAST or BLAST 2.0.

[0202] In Situ Detection

[0203] "In situ detection", as used herein, means the detection of expression or expression levels in the original site, hereby meaning in a tissue sample such as biopsy.

[0204] K-Nearest Neighbor

[0205] The phrase "K-nearest neighbor" refers to a classification method that classifies a point by calculating the distances between it and points in the training data set. It then assigns the point to the class that is most common among its K-nearest neighbors (where K is an integer).

[0206] Leaf

[0207] A leaf, as used herein, is the terminal group in a classification or decision tree.

[0208] Label

[0209] "Label", as used herein, means a composition detectable by spectroscopic, photochemical, biochemical, immunochemical, chemical, or other physical means. For example, useful labels include ^{32}P, fluorescent dyes, electron-dense reagents, enzymes (e.g., as commonly used in an ELISA), biotin, digoxigenin, or haptens and other entities which can be made detectable. A label may be incorporated into nucleic acids and proteins at any position.

[0210] Logistic Regression

[0211] Logistic regression is part of a category of statistical models called generalized linear models. Logistic regression can allow one to predict a discrete outcome, such as group membership, from a set of variables that may be continuous, discrete, dichotomous, or a mix of any of these. The dependent or response variable can be dichotomous, for example, one of two possible types of cancer. Logistic regression models the natural log of the odds ratio, i.e., the ratio of the probability of belonging to the first group (P) over the probability of belonging to the second group (1−P), as a linear combination of the different expression levels (in log-space). The logistic regression output can be used as a classifier by prescribing that a case or sample will be classified into the first type if P is greater than 0.5 or 50%. Alternatively, the calculated probability P can be used as a variable in other contexts, such as a 1D or 2D threshold classifier.

[0212] Metastasis

[0213] "Metastasis" means the process by which cancer spreads from the place at which it first arose as a primary tumor to other locations in the body. The metastatic progression of a primary tumor reflects multiple stages, including dissociation from neighboring primary tumor cells, survival in the circulation, and growth in a secondary location.

[0214] Neuroendocrine Tumors

[0215] "Neuroendocrine tumors" is meant to include all types of tumors from neuroendocrine origin. Examples of neuroendocrine tumors include, but are not limited to lung small cell carcinoma, lung carcinoid, gastrointestinal tract carcinoid, pancreatic islet cell tumor and medullary thyroid carcinoma.

[0216] Node

[0217] A "node" is a decision point in a classification (i.e., decision) tree. Also, a point in a neural net that combines input from other nodes and produces an output through application of an activation function.

[0218] Nucleic Acid

[0219] "Nucleic acid" or "oligonucleotide" or "polynucleotide", as used herein, mean at least two nucleotides covalently linked together. The depiction of a single strand also defines the sequence of the complementary strand. Thus, a nucleic acid also encompasses the complementary strand of a depicted single strand. Many variants of a nucleic acid may be used for the same purpose as a given nucleic acid. Thus, a nucleic acid also encompasses substantially identical nucleic acids and complements thereof. A single strand provides a probe that may hybridize to a target sequence under stringent hybridization conditions. Thus, a nucleic acid also encompasses a probe that hybridizes under stringent hybridization conditions.

[0220] Nucleic acids may be single-stranded or double-stranded, or may contain portions of both double-stranded and single-stranded sequences. The nucleic acid may be DNA, both genomic and cDNA, RNA, or a hybrid, where the nucleic acid may contain combinations of deoxyribo- and ribo-nucleotides, and combinations of bases including uracil, adenine, thymine, cytosine, guanine, inosine, xanthine hypoxanthine, isocytosine and isoguanine. Nucleic acids may be obtained by chemical synthesis methods or by recombinant methods.

[0221] A nucleic acid will generally contain phosphodiester bonds, although nucleic acid analogs may be included that may have at least one different linkage, e.g., phosphoramidate, phosphorothioate, phosphorodithioate, or O-methylphosphoroamidite linkages and peptide nucleic acid backbones and linkages. Other analog nucleic acids include those with positive backbones, non-ionic backbones and non-ribose backbones, including those described in U.S. Pat. Nos. 5,235,033 and 5,034,506, which are incorporated herein by reference. Nucleic acids containing one or more non-naturally occurring or modified nucleotides are also included within one definition of nucleic acids. The modified nucleotide analog may be located for example at the 5'-end and/or the 3'-end of the nucleic acid molecule. Representative examples of nucleotide analogs may be selected from sugar- or backbone-modified ribonucleotides. It should be noted, however, that also nucleobase-modified ribonucleotides, i.e., ribonucleotides, containing a non-naturally occurring nucleobase instead of a naturally occurring nucleobase such as uridine or cytidine modified at the 5-position, e.g., 5-(2-amino) propyl uridine, 5-bromo uridine; adenosine and guanosine modified at the 8-position, e.g., 8-bromo guanosine; deaza nucleotides, e.g., 7-deaza-adenosine; O- and N-alkylated nucleotides, e.g., N6-methyl adenosine are suitable. The 2'-OH-group may be replaced by a group

selected from H, OR, R, halo, SH, SR, NH_2, NHR, NR_2 or CN, wherein R is C1-C6 alkyl, alkenyl or alkynyl and halo is F, Cl, Br or I. Modified nucleotides also include nucleotides conjugated with cholesterol through, e.g., a hydroxyprolinol linkage as described in Krutzfeldt et al., Nature 2005; 438:685-689, Soutschek et al., Nature 2004; 432:173-178, and U.S. Patent Publication No. 20050107325, which are incorporated herein by reference. Additional modified nucleotides and nucleic acids are described in U.S. Patent Publication No. 20050182005, which is incorporated herein by reference. Modifications of the ribose-phosphate backbone may be done for a variety of reasons, e.g., to increase the stability and half-life of such molecules in physiological environments, to enhance diffusion across cell membranes, or as probes on a biochip. The backbone modification may also enhance resistance to degradation, such as in the harsh endocytic environment of cells. The backbone modification may also reduce nucleic acid clearance by hepatocytes, such as in the liver and kidney. Mixtures of naturally occurring nucleic acids and analogs may be made; alternatively, mixtures of different nucleic acid analogs, and mixtures of naturally occurring nucleic acids and analogs may be made.

[0222] Probe

[0223] "Probe", as used herein, means an oligonucleotide capable of binding to a target nucleic acid of complementary sequence through one or more types of chemical bonds, usually through complementary base pairing, usually through hydrogen bond formation. Probes may bind target sequences lacking complete complementarity with the probe sequence depending upon the stringency of the hybridization conditions. There may be any number of base pair mismatches which will interfere with hybridization between the target sequence and the single-stranded nucleic acids described herein. However, if the number of mutations is so great that no hybridization can occur under even the least stringent of hybridization conditions, the sequence is not a complementary target sequence. A probe may be single-stranded or partially single- and partially double-stranded. The strandedness of the probe is dictated by the structure, composition, and properties of the target sequence. Probes may be directly labeled or indirectly labeled such as with biotin to which a streptavidin complex may later bind.

[0224] Reference Value

[0225] As used herein, the term "reference value" or "reference expression profile" refers to a criterion expression value to which measured values are compared in order to identify a specific cancer. The reference value may be based on the abundance of the nucleic acids, or may be based on a combined metric score thereof.

[0226] In preferred embodiments the reference value is determined from statistical analysis of studies that compare microRNA expression with known clinical outcomes.

[0227] Sarcoma

[0228] Sarcoma is meant to include all types of tumors from sarcoma origin. Examples of sarcoma tumors include, but are not limited to gastrointestinal stromal tumor (GIST), Ewing sarcoma, chondrosarcoma, malignant fibrous histiocytoma (MFH) or fibrosarcoma, osteosarcoma, rhabdomyosarcoma, synovial sarcoma and liposarcoma.

[0229] Sensitivity

[0230] "Sensitivity", as used herein, may mean a statistical measure of how well a binary classification test correctly identifies a condition, for example, how frequently it correctly classifies a cancer into the correct class out of two possible classes. The sensitivity for class A is the proportion of cases that are determined to belong to class "A" by the test out of the cases that are in class "A", as determined by some absolute or gold standard.

[0231] Specificity

[0232] "Specificity", as used herein, may mean a statistical measure of how well a binary classification test correctly identifies a condition, for example, how frequently it correctly classifies a cancer into the correct class out of two possible classes. The specificity for class A is the proportion of cases that are determined to belong to class "not A" by the test out of the cases that are in class "not A", as determined by some absolute or gold standard.

[0233] Stringent Hybridization Conditions

[0234] "Stringent hybridization conditions", as used herein, mean conditions under which a first nucleic acid sequence (e.g., probe) will hybridize to a second nucleic acid sequence (e.g., target), such as in a complex mixture of nucleic acids. Stringent conditions are sequence-dependent and will be different in different circumstances. Stringent conditions may be selected to be about 5-10° C. lower than the thermal melting point (T_m) for the specific sequence at a defined ionic strength pH. The T_m may be the temperature (under defined ionic strength, pH, and nucleic concentration) at which 50% of the probes complementary to the target hybridize to the target sequence at equilibrium (as the target sequences are present in excess, at T_m, 50% of the probes are occupied at equilibrium). Stringent conditions may be those in which the salt concentration is less than about 1.0 M sodium ion, such as about 0.01-1.0 M sodium ion concentration (or other salts) at pH 7.0 to 8.3 and the temperature is at least about 30° C. for short probes (e.g., about 10-50 nucleotides) and at least about 60° C. for long probes (e.g., greater than about 50 nucleotides). Stringent conditions may also be achieved with the addition of destabilizing agents such as formamide. For selective or specific hybridization, a positive signal may be at least 2 to 10 times background hybridization. Exemplary stringent hybridization conditions include the following: 50% formamide, 5×SSC, and 1% SDS, incubating at 42° C., or, 5×SSC, 1% SDS, incubating at 65° C., with wash in 0.2×SSC, and 0.1% SDS at 65° C.

[0235] Substantially Complementary

[0236] "Substantially complementary", as used herein, means that a first sequence is at least 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, 97%, 98% or 99% identical to the complement of a second sequence over a region of 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100 or more nucleotides, or that the two sequences hybridize under stringent hybridization conditions.

[0237] Substantially Identical

[0238] "Substantially identical", as used herein, means that a first and a second sequence are at least 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, 97%, 98% or 99% identical over a region of 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100 or more nucleotides or amino acids, or with respect to nucleic acids, if the first sequence is substantially complementary to the complement of the second sequence.

[0239] Subject

[0240] As used herein, the term "subject" refers to a mammal, including both human and other mammals. The methods of the present invention are preferably applied to human subjects.

[0241] Target Nucleic Acid

[0242] "Target nucleic acid", as used herein, means a nucleic acid or variant thereof that may be bound by another nucleic acid. A target nucleic acid may be a DNA sequence. The target nucleic acid may be RNA. The target nucleic acid may comprise a mRNA, tRNA, shRNA, siRNA or Piwi-interacting RNA, or a pri-miRNA, pre-miRNA, miRNA, or anti-miRNA.

[0243] The target nucleic acid may comprise a target miRNA binding site or a variant thereof. One or more probes may bind the target nucleic acid. The target binding site may comprise 5-100 or 10-60 nucleotides. The target binding site may comprise a total of 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15,16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30-40, 40-50, 50-60, 61, 62 or 63 nucleotides. The target site sequence may comprise at least 5 nucleotides of the sequence of a target miRNA binding site disclosed in U.S. patent application Ser. Nos. 11/384,049, 11/418,870 or 11/429,720, the contents of which are incorporated herein.

[0244] 1D/2D Threshold Classifier

[0245] "1D/2D threshold classifier", as used herein, may mean an algorithm for classifying a case or sample such as a cancer sample into one of two possible types such as two types of cancer. For a 1D threshold classifier, the decision is based on one variable and one predetermined threshold value; the sample is assigned to one class if the variable exceeds the threshold and to the other class if the variable is less than the threshold. A 2D threshold classifier is an algorithm for classifying into one of two types based on the values of two variables. A threshold may be calculated as a function (usually a continuous or even a monotonic function) of the first variable; the decision is then reached by comparing the second variable to the calculated threshold, similar to the 1D threshold classifier.

[0246] Tissue Sample

[0247] As used herein, a tissue sample is tissue obtained from a tissue biopsy using methods well known to those of ordinary skill in the related medical arts. The phrase "suspected of being cancerous", as used herein, means a cancer tissue sample believed by one of ordinary skill in the medical arts to contain cancerous cells. Methods for obtaining the sample from the biopsy include gross apportioning of a mass, microdissection, laser-based microdissection, or other art-known cell-separation methods.

[0248] Tumor

[0249] "Tumor", as used herein, refers to all neoplastic cell growth and proliferation, whether malignant or benign, and all pre-cancerous and cancerous cells and tissues.

[0250] Variant

[0251] "Variant", as used herein, referring to a nucleic acid means (i) a portion of a referenced nucleotide sequence; (ii) the complement of a referenced nucleotide sequence or portion thereof; (iii) a nucleic acid that is substantially identical to a referenced nucleic acid or the complement thereof; or (iv) a nucleic acid that hybridizes under stringent conditions to the referenced nucleic acid, complement thereof, or a sequence substantially identical thereto.

[0252] Wild Type

[0253] As used herein, the term "wild-type" sequence refers to a coding, a non-coding or an interface sequence which is an allelic form of sequence that performs the natural or normal function for that sequence. Wild-type sequences include multiple allelic forms of a cognate sequence, for example, multiple alleles of a wild type sequence may encode silent or conservative changes to the protein sequence that a coding sequence encodes.

[0254] The present invention employs miRNAs for the identification, classification and diagnosis of specific cancers and the identification of their tissues of origin.

[0255] 1. microRNA Processing

[0256] A gene coding for microRNA (miRNA) may be transcribed leading to production of a miRNA primary transcript known as the pri-miRNA. The pri-miRNA may comprise a hairpin with a stem and loop structure. The stem of the hairpin may comprise mismatched bases. The pri-miRNA may comprise several hairpins in a polycistronic structure.

[0257] The hairpin structure of the pri-miRNA may be recognized by Drosha, which is an RNase III endonuclease. Drosha may recognize terminal loops in the pri-miRNA and cleave approximately two helical turns into the stem to produce a 60-70 nt precursor known as the pre-miRNA. Drosha may cleave the pri-miRNA with a staggered cut typical of RNase III endonucleases yielding a pre-miRNA stem loop with a 5' phosphate and ~2 nucleotide 3' overhang. Approximately one helical turn of stem (~10 nucleotides) extending beyond the Drosha cleavage site may be essential for efficient processing. The pre-miRNA may then be actively transported from the nucleus to the cytoplasm by Ran-GTP and the export receptor Ex-portin-5.

[0258] The pre-miRNA may be recognized by Dicer, which is also an RNase III endonuclease. Dicer may recognize the double-stranded stem of the pre-miRNA. Dicer may also cut off the terminal loop two helical turns away from the base of the stem loop, leaving an additional 5' phosphate and a ~2 nucleotide 3' overhang. The resulting siRNA-like duplex, which may comprise mismatches, comprises the mature miRNA and a similar-sized fragment known as the miRNA*. The miRNA and miRNA* may be derived from opposing arms of the pri-miRNA and pre-miRNA. MiRNA* sequences may be found in libraries of cloned miRNAs, but typically at lower frequency than the miRNAs.

[0259] Although initially present as a double-stranded species with miRNA*, the miRNA may eventually become incorporated as a single-stranded RNA into a ribonucleoprotein complex known as the RNA-induced silencing complex (RISC). Various proteins can form the RISC, which can lead to variability in specificity for miRNA/miRNA* duplexes, binding site of the target gene, activity of miRNA (repress or activate), and which strand of the miRNA/miRNA* duplex is loaded in to the RISC.

[0260] When the miRNA strand of the miRNA:miRNA* duplex is loaded into the RISC, the miRNA* may be removed and degraded. The strand of the miRNA:miRNA* duplex that is loaded into the RISC may be the strand whose 5' end is less tightly paired. In cases where both ends of the miRNA:miRNA* have roughly equivalent 5' pairing, both miRNA and miRNA* may have gene silencing activity.

[0261] The RISC may identify target nucleic acids based on high levels of complementarity between the miRNA and the mRNA, especially by nucleotides 2-7 of the miRNA.

Only one case has been reported in animals where the interaction between the miRNA and its target was along the entire length of the miRNA. This was shown for miR-196 and Hox B8 and it was further shown that miR-196 mediates the cleavage of the Hox B8 mRNA (Yekta et al. Science 2004; 304:594-596). Otherwise, such interactions are known only in plants (Bartel & Bartel 2003; 132:709-717).

[0262] A number of studies have looked at the base-pairing requirement between miRNA and its mRNA target for achieving efficient inhibition of translation (reviewed by Bartel 2004; 116:281-297). In mammalian cells, the first 8 nucleotides of the miRNA may be important (Doench & Sharp GenesDev 2004; 18:504-511). However, other parts of the microRNA may also participate in mRNA binding. Moreover, sufficient base pairing at the 3' can compensate for insufficient pairing at the 5' (Brennecke et al., PloS Biol 2005; 3:e85). Computation studies, analyzing miRNA binding on whole genomes have suggested a specific role for bases 2-7 at the 5' of the miRNA in target binding but the role of the first nucleotide, found usually to be "A" was also recognized (Lewis et al. Cell 2005; 120:15-20). Similarly, nucleotides 1-7 or 2-8 were used to identify and validate targets by Krek et al. (Nat Genet 2005; 37:495-500).

[0263] The target sites in the mRNA may be in the 5' UTR, the 3' UTR or in the coding region. Interestingly, multiple miRNAs may regulate the same mRNA target by recognizing the same or multiple sites. The presence of multiple miRNA binding sites in most genetically identified targets may indicate that the cooperative action of multiple RISCs provides the most efficient translational inhibition.

[0264] miRNAs may direct the RISC to down-regulate gene expression by either of two mechanisms: mRNA cleavage or translational repression. The miRNA may specify cleavage of the mRNA if the mRNA has a certain degree of complementarity to the miRNA. When a miRNA guides cleavage, the cut may be between the nucleotides pairing to residues 10 and 11 of the miRNA. Alternatively, the miRNA may repress translation if the miRNA does not have the requisite degree of complementarity to the miRNA. Translational repression may be more prevalent in animals since animals may have a lower degree of complementarity between the miRNA and binding site.

[0265] It should be noted that there may be variability in the 5' and 3' ends of any pair of miRNA and miRNA*. This variability may be due to variability in the enzymatic processing of Drosha and Dicer with respect to the site of cleavage. Variability at the 5' and 3' ends of miRNA and miRNA* may also be due to mismatches in the stem structures of the pri-miRNA and pre-miRNA. The mismatches of the stem strands may lead to a population of different hairpin structures. Variability in the stem structures may also lead to variability in the products of cleavage by Drosha and Dicer.

[0266] 2. Nucleic Acids

[0267] Nucleic acids are provided herein. The nucleic acids comprise the sequences of SEQ ID NOS: 1-390 or variants thereof. The variant may be a complement of the referenced nucleotide sequence. The variant may also be a nucleotide sequence that is substantially identical to the referenced nucleotide sequence or the complement thereof. The variant may also be a nucleotide sequence which hybridizes under stringent conditions to the referenced nucleotide sequence, complements thereof, or nucleotide sequences substantially identical thereto.

[0268] The nucleic acid may have a length of from about 10 to about 250 nucleotides. The nucleic acid may have a length of at least 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 35, 40, 45, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200 or 250 nucleotides. The nucleic acid may be synthesized or expressed in a cell (in vitro or in vivo) using a synthetic gene described herein. The nucleic acid may be synthesized as a single-strand molecule and hybridized to a substantially complementary nucleic acid to form a duplex. The nucleic acid may be introduced to a cell, tissue or organ in a single- or double-stranded form or capable of being expressed by a synthetic gene using methods well known to those skilled in the art, including as described in U.S. Pat. No. 6,506,559, which is incorporated herein by reference.

TABLE 1

SEQ ID NOS of sequences used in the invention

miR name	miR SEQ ID NO	hairpin SEQ ID NO
hsa-let-7c	1	70
hsa-let-7e	2, 156	71
hsa-miR-100	3	72
hsa-miR-10a	4	73
hsa-miR-10b	5	74
hsa-miR-122	6	75
hsa-miR-125a-5p	7	76
hsa-miR-125b	8	77, 78
hsa-miR-126	9	79
hsa-miR-130a	10	80
hsa-miR-138	11	81, 82
hsa-miR-140-3p	12	83
hsa-miR-141	13	84
hsa-miR-143	14	85
hsa-miR-145	15	86
hsa-miR-146a	16	87
hsa-miR-146b-5p	17	88
hsa-miR-148a	18	89
hsa-miR-149	19	90
hsa-miR-17	20	91
hsa-miR-181a	21	92, 93
hsa-miR-181a*	22	92, 93
hsa-miR-185	23	94
hsa-miR-191	24	95
hsa-miR-193a-3p	25	96
hsa-miR-193a-5p	26	96
hsa-miR-194	27	97, 98
hsa-miR-200a	28	99
hsa-miR-200b	29	100
hsa-miR-200c	30	101
hsa-miR-202	31	102
hsa-miR-205	32	103
hsa-miR-206	33	104
hsa-miR-21	34	105
hsa-miR-21*	35	105
hsa-miR-210	36	106
hsa-miR-214	37	107
hsa-miR-214*	38	107
hsa-miR-22	39	108
hsa-miR-222	40	109
hsa-miR-223	41	110
hsa-miR-224	42	111
hsa-miR-29a	43	112
hsa-miR-29c	44, 191	113
hsa-miR-29c*	45	113
hsa-miR-30a	46	114
hsa-miR-30d	47	115
hsa-miR-30e	48	116
hsa-miR-31	49	117
hsa-miR-342-3p	50	118
hsa-miR-345	51	119
hsa-miR-34a	52	120
hsa-miR-34c-5p	53	121

TABLE 1-continued

SEQ ID NOS of sequences used in the invention

miR name	miR SEQ ID NO	hairpin SEQ ID NO
hsa-miR-361-5p	54	122
hsa-miR-372	55	123
hsa-miR-375	56	124
hsa-miR-378	57, 202	125
hsa-miR-455-5p	58	126
hsa-miR-487b	59	127
hsa-miR-497	60, 208	128
hsa-miR-509-3p	61	129, 130, 131
hsa-miR-516a-5p	62, 211	132, 133
hsa-miR-574-5p	63	134
hsa-miR-652	64	135
hsa-miR-7	65	136, 137, 138
hsa-miR-9*	66	139, 140, 141
hsa-miR-92a	67	142, 143
hsa-miR-92b	68	144
hsa-miR-934	69	145
hsa-miR-1201	146	149
hsa-miR-221	147	150
hsa-miR-93	148	151
hsa-miR-182	152	
hsa-let-7d	153	
hsa-miR-181b	154	
hsa-miR-127-3p	155	
hsa-let-7i	157	
hsa-miR-106a	158	
hsa-miR-124	159	
hsa-miR-1248	160	
hsa-miR-128	161	
hsa-miR-129-3p	162	
hsa-miR-1323	163	
hsa-miR-142-5p	164	
hsa-miR-143*	165	
hsa-miR-146b-3p	166	
hsa-miR-149*	167	
hsa-miR-150	168	
hsa-miR-152	169	
hsa-miR-155	170	
hsa-miR-15a	171	
hsa-miR-15b	172	
hsa-miR-181c	173	
hsa-miR-181d	174	
hsa-miR-183	175	
hsa-miR-18a	176	
hsa-miR-192	177	
hsa-miR-193b	178	
hsa-miR-195	179	
hsa-miR-1973	180	
hsa-miR-199a-3p	181	
hsa-miR-199a-5p	182	
hsa-miR-199b-5p	183	
hsa-miR-203	184	
hsa-miR-205*	185	
hsa-miR-20a	186	
hsa-miR-219-2-3p	187	
hsa-miR-25	188	
hsa-miR-27b	189	
hsa-miR-29b	190	
hsa-miR-302a	192	
hsa-miR-302a*	193	
hsa-miR-302d	194	
hsa-miR-30a*	195	
hsa-miR-30c	196	
hsa-miR-331-3p	197	
hsa-miR-342-5p	198	
hsa-miR-363	199	
hsa-miR-371-3p	200	
hsa-miR-371-5p	201	
hsa-miR-422a	203	
hsa-miR-425	204	
hsa-miR-451	205	
hsa-miR-455-3p	206	
hsa-miR-486-5p	207	
hsa-miR-498	209	

TABLE 1-continued

SEQ ID NOS of sequences used in the invention

miR name	miR SEQ ID NO	hairpin SEQ ID NO
hsa-miR-512-5p	210	
hsa-miR-516b	212	
hsa-miR-517a	213	
hsa-miR-517c	214	
hsa-miR-518a-3p	215	
hsa-miR-518e	216	
hsa-miR-518f*	217	
hsa-miR-519a	218	
hsa-miR-519d	219	
hsa-miR-520a-5p	220	
hsa-miR-520c-3p	221	
hsa-miR-520d-5p	222	
hsa-miR-524-5p	223	
hsa-miR-527	224	
hsa-miR-551b	225	
hsa-miR-625	226	
hsa-miR-767-5p	227	
hsa-miR-886-3p	228	
hsa-miR-9	229	
hsa-miR-886-5p	230	
hsa-miR-99a	231	
hsa-miR-99a*	232	
hsa-miR-373	233	
hsa-miR-1977	234	
hsa-miR-1978	235	
MID-00689	236	
MID-15684	237, 369	
MID-15867	238	
MID-15907	239	
MID-15965	240	
MID-16318	241	
MID-16489	242	
MID-16869	243	
MID-17144	244	
MID-18336	245	
MID-18422	246	
MID-19340	247	
MID-19533	248	
MID-20524	249	
MID-20703	250	
MID-21271	251	
MID-22664	252	
MID-23256	253	
MID-23291	254	
MID-23794	255	
MID-00405	390	
hsa-let-7a	256	
hsa-let-7b	257	
hsa-let-7f	258	
hsa-let-7g	259	
hsa-miR-106b	260	
hsa-miR-1180	261	
hsa-miR-127-5p	262	
hsa-miR-129*	263	
hsa-miR-129-5p	264	
hsa-miR-130b	265	
hsa-miR-132	266	
hsa-miR-133a	267	
hsa-miR-133b	268	
hsa-miR-134	269	
hsa-miR-139-5p	270	
hsa-miR-140-5p	271	
hsa-miR-145*	272	
hsa-miR-148b	273	
hsa-miR-151-3p	274	
hsa-miR-154	275	
hsa-miR-154*	276	
hsa-miR-17*	277	
hsa-miR-181a-2*	278	
hsa-miR-1826	279	
hsa-miR-187	280	
hsa-miR-188-5p	281	
hsa-miR-196a	282	

TABLE 1-continued

SEQ ID NOS of sequences used in the invention

miR name	miR SEQ ID NO	hairpin SEQ ID NO
hsa-miR-1979	283	
hsa-miR-19b	284	
hsa-miR-20b	285	
hsa-miR-216a	286	
hsa-miR-216b	287	
hsa-miR-217	288	
hsa-miR-22*	289	
hsa-miR-221*	290	
hsa-miR-222*	291	
hsa-miR-23a	292	
hsa-miR-23b	293	
hsa-miR-24	294	
hsa-miR-26a	295	
hsa-miR-26b	296	
hsa-miR-27a	297	
hsa-miR-28-3p	298	
hsa-miR-296-5p	299	
hsa-miR-299-3p	300	
hsa-miR-29b-2*	301	
hsa-miR-301a	302	
hsa-miR-30b	303	
hsa-miR-30e*	304	
hsa-miR-31*	305	
hsa-miR-323-3p	306	
hsa-miR-324-5p	307	
hsa-miR-328	308	
hsa-miR-329	309	
hsa-miR-330-3p	310	
hsa-miR-335	311	
hsa-miR-337-5p	312	
hsa-miR-338-3p	313	
hsa-miR-361-3p	314	
hsa-miR-362-3p	315	
hsa-miR-362-5p	316	
hsa-miR-369-5p	317	
hsa-miR-370	318	
hsa-miR-376a	319	
hsa-miR-376c	320	
hsa-miR-377*	321	
hsa-miR-379	322	
hsa-miR-381	323	
hsa-miR-382	324	
hsa-miR-409-3p	325	
hsa-miR-409-5p	326	
hsa-miR-410	327	
hsa-miR-411	328	
hsa-miR-425*	329	
hsa-miR-431*	330	
hsa-miR-432	331	
hsa-miR-433	332	
hsa-miR-483-3p	333	
hsa-miR-483-5p	334	
hsa-miR-485-3p	335	
hsa-miR-485-5p	336	
hsa-miR-487a	337	
hsa-miR-494	338	
hsa-miR-495	339	
hsa-miR-500	340	
hsa-miR-500*	341	
hsa-miR-501-3p	342	
hsa-miR-502-3p	343	
hsa-miR-503	344	
hsa-miR-506	345	
hsa-miR-509-3-5p	346	
hsa-miR-513a-5p	347	
hsa-miR-532-3p	348	
hsa-miR-532-5p	349	
hsa-miR-539	350	
hsa-miR-542-5p	351	
hsa-miR-543	352	
hsa-miR-598	353	
hsa-miR-612	354	
hsa-miR-654-3p	355	

TABLE 1-continued

SEQ ID NOS of sequences used in the invention

miR name	miR SEQ ID NO	hairpin SEQ ID NO
hsa-miR-658	356	
hsa-miR-660	357	
hsa-miR-665	358	
hsa-miR-708	359	
hsa-miR-873	360	
hsa-miR-874	361	
hsa-miR-891a	362	
hsa-miR-99b	363	
MID-00064	364	
MID-00078	365	
MID-00144	366	
MID-00465	367	
MID-00672	368	
MID-15986	370	
MID-16270	371	
MID-16469	372	
MID-16582	373	
MID-16748	374	
MID-17356 (3651)	389	
MID-17375	375	
MID-17576	376	
MID-17866	377	
MID-18307	378	
MID-18395	379	
MID-19898	380	
MID-19962	381	
MID-22331	382	
MID-22912	383	
MID-23017	384	
MID-23168	385	
MID-23178	386	
MID-23751	387	
hsa-miR-423-5p	388	

[0269] SEQ ID NOs 1-34 are in accordance with Sanger database version 10; SEQ ID NOs 35-390 are in accordance with Sanger database version 11;

[0270] 3. Nucleic Acid Complexes

[0271] The nucleic acid may further comprise one or more of the following: a peptide, a protein, a RNA-DNA hybrid, an antibody, an antibody fragment, a Fab fragment, and an aptamer.

[0272] 4. Pri-miRNA

[0273] The nucleic acid may comprise a sequence of a pri-miRNA or a variant thereof. The pri-miRNA sequence may comprise from 45-30,000, 50-25,000, 100-20,000, 1,000-1,500 or 80-100 nucleotides. The sequence of the pri-miRNA may comprise a pre-miRNA, miRNA and miRNA*, as set forth herein, and variants thereof. The sequence of the pri-miRNA may comprise any of the sequences of SEQ ID NOS: 1-390 or variants thereof.

[0274] The pri-miRNA may comprise a hairpin structure. The hairpin may comprise a first and a second nucleic acid sequence that are substantially complimentary. The first and second nucleic acid sequence may be from 37-50 nucleotides. The first and second nucleic acid sequence may be separated by a third sequence of from 8-12 nucleotides. The hairpin structure may have a free energy of less than −25 Kcal/mole, as calculated by the Vienna algorithm with default parameters, as described in Hofacker et al. (Monatshefte f. Chemie 1994; 125:167-188), the contents of which are incorporated herein by reference. The hairpin may comprise a terminal loop of 4-20, 8-12 or 10 nucleotides. The pri-miRNA may comprise at least 19% adenosine

nucleotides, at least 16% cytosine nucleotides, at least 23% thymine nucleotides and at least 19% guanine nucleotides.

[0275] 5. Pre-miRNA

[0276] The nucleic acid may also comprise a sequence of a pre-miRNA or a variant thereof. The pre-miRNA sequence may comprise from 45-90, 60-80 or 60-70 nucleotides. The sequence of the pre-miRNA may comprise a miRNA and a miRNA* as set forth herein. The sequence of the pre-miRNA may also be that of a pri-miRNA excluding from 0-160 nucleotides from the 5' and 3' ends of the pri-miRNA. The sequence of the pre-miRNA may comprise the sequence of SEQ ID NOS: 1-390 or variants thereof.

[0277] 6. miRNA

[0278] The nucleic acid may also comprise a sequence of a miRNA (including miRNA*) or a variant thereof. The miRNA sequence may comprise from 13-33, 18-24 or 21-23 nucleotides. The miRNA may also comprise a total of at least 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39 or 40 nucleotides. The sequence of the miRNA may be the first 13-33 nucleotides of the pre-miRNA. The sequence of the miRNA may also be the last 13-33 nucleotides of the pre-miRNA. The sequence of the miRNA may comprise the sequence of SEQ ID NOS: 1-69, 146-148, 152-390 or variants thereof.

[0279] 7. Probes

[0280] A probe comprising a nucleic acid described herein is also provided. Probes may be used for screening and diagnostic methods, as outlined below. The probe may be attached or immobilized to a solid substrate, such as a biochip.

[0281] The probe may have a length of from 8 to 500, 10 to 100 or 20 to 60 nucleotides. The probe may also have a length of at least 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 35, 40, 45, 50, 60, 70, 80, 90, 100, 120, 140, 160, 180, 200, 220, 240, 260, 280 or 300 nucleotides. The probe may further comprise a linker sequence of from 10-60 nucleotides. The probe may comprise a nucleic acid that is complementary to a sequence selected from the group consisting of SEQ ID NOS: 1-390 or variants thereof.

[0282] 8. Biochip

[0283] A biochip is also provided. The biochip may comprise a solid substrate comprising an attached probe or plurality of probes described herein. The probes may be capable of hybridizing to a target sequence under stringent hybridization conditions. The probes may be attached at spatially defined addresses on the substrate. More than one probe per target sequence may be used, with either overlapping probes or probes to different sections of a particular target sequence. The probes may be capable of hybridizing to target sequences associated with a single disorder appreciated by those in the art. The probes may either be synthesized first, with subsequent attachment to the biochip, or may be directly synthesized on the biochip.

[0284] The solid substrate may be a material that may be modified to contain discrete individual sites appropriate for the attachment or association of the probes and is amenable to at least one detection method. Representative examples of substrates include glass and modified or functionalized glass, plastics (including acrylics, polystyrene and copolymers of styrene and other materials, polypropylene, polyethylene, polybutylene, polyurethanes, TeflonJ, etc.), polysaccharides, nylon or nitrocellulose, resins, silica or silica-based materials including silicon and modified silicon, carbon, metals, inorganic glasses and plastics. The substrates may allow optical detection without appreciably fluorescing.

[0285] The substrate may be planar, although other configurations of substrates may be used as well. For example, probes may be placed on the inside surface of a tube, for flow-through sample analysis to minimize sample volume. Similarly, the substrate may be flexible, such as flexible foam, including closed cell foams made of particular plastics.

[0286] The biochip and the probe may be derivatized with chemical functional groups for subsequent attachment of the two. For example, the biochip may be derivatized with a chemical functional group including, but not limited to, amino groups, carboxyl groups, oxo groups or thiol groups. Using these functional groups, the probes may be attached using functional groups on the probes either directly or indirectly using a linker. The probes may be attached to the solid support by either the 5' terminus, 3' terminus, or via an internal nucleotide.

[0287] The probe may also be attached to the solid support non-covalently. For example, biotinylated oligonucleotides can be made, which may bind to surfaces covalently coated with streptavidin, resulting in attachment. Alternatively, probes may be synthesized on the surface using techniques such as photopolymerization and photolithography.

[0288] 9. Diagnostics

[0289] As used herein, the term "diagnosing" refers to classifying pathology, or a symptom, determining a severity of the pathology (e.g., grade or stage), monitoring pathology progression, forecasting an outcome of pathology and/or prospects of recovery.

[0290] As used herein, the phrase "subject in need thereof" refers to an animal or human subject who is known to have cancer, at risk of having cancer (e.g., a genetically predisposed subject, a subject with medical and/or family history of cancer, a subject who has been exposed to carcinogens, occupational hazard, environmental hazard) and/or a subject who exhibits suspicious clinical signs of cancer (e.g., blood in the stool or melena, unexplained pain, sweating, unexplained fever, unexplained loss of weight up to anorexia, changes in bowel habits (constipation and/or diarrhea), tenesmus (sense of incomplete defecation, for rectal cancer specifically), anemia and/or general weakness). Additionally or alternatively, the subject in need thereof can be a healthy human subject undergoing a routine well-being check up.

[0291] Analyzing presence of malignant or pre-malignant cells can be effected in vivo or ex vivo, whereby a biological sample (e.g., biopsy, blood) is retrieved. Such biopsy samples comprise cells and may be an incisional or excisional biopsy. Alternatively, the cells may be retrieved from a complete resection.

[0292] While employing the present teachings, additional information may be gleaned pertaining to the determination of treatment regimen, treatment course and/or to the measurement of the severity of the disease.

[0293] As used herein the phrase "treatment regimen" refers to a treatment plan that specifies the type of treatment, dosage, follow-up plans, schedule and/or duration of a treatment provided to a subject in need thereof (e.g., a subject diagnosed with a pathology). The selected treatment regimen can be an aggressive one which is expected to result in the best clinical outcome (e.g., complete cure of the pathology) or a more moderate one which may relieve

symptoms of the pathology yet results in incomplete cure of the pathology. It will be appreciated that in certain cases the treatment regimen may be associated with some discomfort to the subject or adverse side effects (e.g., damage to healthy cells or tissue). The type of treatment can include a surgical intervention (e.g., removal of lesion, diseased cells, tissue, or organ), a cell replacement therapy, an administration of a therapeutic drug (e.g., receptor agonists, antagonists, hormones, chemotherapy agents) in a local or a systemic mode, an exposure to radiation therapy using an external source (e.g., external beam) and/or an internal source (e.g., brachytherapy) and/or any combination thereof. The dosage, schedule and duration of treatment can vary, depending on the severity of pathology and the selected type of treatment, and those of skill in the art are capable of adjusting the type of treatment with the dosage, schedule and duration of treatment.

[0294] A method of diagnosis is also provided. The method comprises detecting an expression level of a specific cancer-associated nucleic acid in a biological sample. The sample may be derived from a patient. Diagnosis of a specific cancer state in a patient may allow for prognosis and selection of therapeutic strategy. Further, the developmental stage of cells may be classified by determining temporarily expressed specific cancer-associated nucleic acids.

[0295] In situ hybridization of labeled probes to tissue arrays may be performed. When comparing the fingerprints between individual samples the skilled artisan can make a diagnosis, a prognosis, or a prediction based on the findings. It is further understood that the nucleic acid sequences which indicate the diagnosis may differ from those which indicate the prognosis and molecular profiling of the condition of the cells or exosomes may lead to distinctions between responsive or refractory conditions or may be predictive of outcomes.

[0296] 10. Kits

[0297] A kit is also provided and may comprise a nucleic acid described herein together with any or all of the following: assay reagents, buffers, probes and/or primers, and sterile saline or another pharmaceutically acceptable emulsion and suspension base. In addition, the kits may include instructional materials containing directions (e.g., protocols) for the practice of the methods described herein. The kit may further comprise a software package for data analysis of expression profiles.

[0298] For example, the kit may be a kit for the amplification, detection, identification or quantification of a target nucleic acid sequence. The kit may comprise a poly (T) primer, a forward primer, a reverse primer, and a probe.

[0299] Any of the compositions described herein may be comprised in a kit. In a non-limiting example, reagents for isolating miRNA, labeling miRNA, and/or evaluating a miRNA population using an array are included in a kit. The kit may further include reagents for creating or synthesizing miRNA probes. The kits will thus comprise, in suitable container means, an enzyme for labeling the miRNA by incorporating labeled nucleotide or unlabeled nucleotides that are subsequently labeled. It may also include one or more buffers, such as reaction buffer, labeling buffer, washing buffer, or a hybridization buffer, compounds for preparing the miRNA probes, components for in situ hybridization and components for isolating miRNA. Other kits of the invention may include components for making a nucleic acid array comprising miRNA, and thus may include, for example, a solid support.

[0300] The following examples are presented in order to more fully illustrate some embodiments of the invention. They should, in no way be construed, however, as limiting the broad scope of the invention.

EXAMPLES

Methods

1. Tumor Samples

[0301] 1300 primary and metastatic tumor FFPE were used in the study. Tumor samples were obtained from several sources. Institutional review approvals were obtained for all samples in accordance with each institute's institutional review board or IRB equivalent guidelines. Samples included primary tumors and metastases of defined origins, according to clinical records. Tumor content was at least 50% for >95% of samples, as determined by a pathologist based on hematoxylin-eosin (H&E) stained slides.

2. RNA Extraction

[0302] For FFPE samples, total RNA was isolated from seven to ten 10-μm-thick tissue sections using the miR extraction protocol developed at Rosetta Genomics. Briefly, the sample was incubated a few times in xylene at 57° C. to remove paraffin excess, followed by ethanol washes. Proteins were degraded by proteinase K solution at 45° C. for a few hours. The RNA was extracted with acid phenol: chloroform followed by ethanol precipitation and DNAse digestion. Total RNA quantity and quality was checked by spectrophotometer (Nanodrop ND-1000).

3. miR Array Platform

[0303] Custom microarrays (Agilent Technologies, Santa Clara, Calif.) were produced by printing DNA oligonucleotide probes to: 982 miRs sequences, 17 negative controls, 23 spikes, and 10 positive controls (total of 1032 probes). Each probe, printed in triplicate, carried up to 28-nucleotide (nt) linker at the 3' end of the microRNA's complement sequence. 17 negative control probes were designed using as sequences which do not match the genome. Two groups of positive control probes were designed to hybridize to miR array: (i) synthetic small RNAs were spiked to the RNA before labeling to verify the labeling efficiency; and (ii) probes for abundant small RNA (e.g., small nuclear RNAs (U43, U24, Z30, U6, U48, U44), 5.8 s and 5 s ribosomal RNA are spotted on the array to verify RNA quality.

4. Cy-Dye Labeling of miRNA for miR Array

[0304] One μg of total RNA were labeled by ligation (Thomson et al. Nature Methods 2004; 1:47-53) of an RNA-linker, p-rCrU-Cy/dye (Eurogentec or equivalent), to the 3' end with Cy3 or Cy5. The labeling reaction contained total RNA, spikes (0.1-100 fmoles), 400 ng RNA-linker-dye, 15% DMSO, lx ligase buffer and 20 units of T4 RNA ligase (NEB), and proceeded at 4° C. for 1 h, followed by 1 h at 37° C., followed by 4° C. up to 40 min.

[0305] The labeled RNA was mixed with 30 μl hybridization mixture (mixture of 45 μL of the 10× GE Agilent Blocking Agent and 246 μL of 2×Hi-RPM Hybridization). The labeling mixture was incubated at 100° C. for 5 minutes

followed by ice incubation in water bath for 5 minutes. Slides were Hybridize at 54° C. for 16-20 hours, followed by two washes. The first wash was conducted at room temperature with Agilent GE Wash Buffer 1 for 5 min followed by a second wash with Agilent GE Wash Buffer 2 at 37° C. for 5 min.

[0306] Arrays were scanned using an Agilent Microarray Scanner Bundle G2565BA (resolution of 5 μm at XDR Hi 100%, XDR Lo 5%). Array images were analyzed using Feature Extraction 10.7 software (Agilent).

5. Array Signal Calculation and Normalization

[0307] Triplicate spots were combined to produce one signal for each probe by taking the logarithmic mean of reliable spots. All data were log 2-transformed and the analysis was performed in log 2-space. A reference data vector for normalization R was calculated by taking the median expression level for each probe across all samples. For each sample data vector S, a 2nd degree polynomial F was found so as to provide the best fit between the sample data and the reference data, such that R≈F(S). Remote data points ("outliers") were not used for fitting the polynomial F. For each probe in the sample (element Si in the vector S), the normalized value (in log-space) Mi was calculated from the initial value Si by transforming it with the polynomial function F, so that Mi=F(Si).

6. Logistic Regression

[0308] The aim of a logistic regression model is to use several features, such as expression levels of several microRNAs, to assign a probability of belonging to one of two possible groups, such as two branches of a node in a binary decision-tree. Logistic regression models the natural log of the odds ratio, i.e., the ratio of the probability of belonging to the first group, for example, the left branch in a node of a binary decision-tree (P) over the probability of belonging to the second group, for example, the right branch in such a node (1−P), as a linear combination of the different expression levels (in log-space). The logistic regression assumes that:

$$\ln\left(\frac{P}{1-P}\right)=\beta_0+\sum_{i=1}^{N}\beta_i\cdot M_i=\beta_0+\beta_1\cdot M_1+\beta_2\cdot M_2+\ldots\ ,$$

[0309] where β_0 is the bias, M_i is the expression level (normalized, in log 2-space) of the i-th microRNA used in the decision node, and β_i its corresponding coefficient. βi>0 indicates that the probability to take the left branch (P) increases when the expression level of this microRNA (Mi) increases, and the opposite for βi<0. If a node uses only a single microRNA (M), then solving for P results in:

$$P=\frac{e^{\beta_0+\beta_1\cdot M}}{1+e^{\beta_0+\beta_1\cdot M}}.$$

[0310] The regression error on each sample is the difference between the assigned probability P and the true "probability" of this sample, i.e., 1 if this sample is in the left branch group and 0 otherwise. The training and optimization of the logistic regression model calculates the parameters β and the p-values [for each microRNA by the Wald statistic and for the overall model by the χ2 (chi-square) difference], maximizing the likelihood of the data given the model and minimizing the total regression error

$$\sum_{\substack{Samples\ in\\ first\ group}}(1-P_j)+\sum_{\substack{Samples\ in\\ second\ group}}P_j.$$

[0311] The probability output of the logistic model is here converted to a binary decision by comparing P to a threshold, denoted by P_{TH} i.e., $P>P_{TH}$ then the sample belongs to the left branch ("first group") and vice versa. Choosing at each node the branch which has a probability >0.5, i.e., using a probability threshold of 0.5, leads to a minimization of the sum of the regression errors. However, as the goal was the minimization of the overall number of misclassifications (and not of their probability), a modification which adjusts the probability threshold (P_{TH}) was used in order to minimize the overall number of mistakes at each node (Table 2). For each node the threshold to a new probability threshold P_{TH} was optimized such that the number of classification errors is minimized. This change of probability threshold is equivalent (in terms of classifications) to a modification of the bias β_0, which may reflect a change in the prior frequencies of the classes. Once the threshold was chosen β_0 was modified such that the threshold will be shifted back to 0.5. In addition, β0, β1, β2, . . . were adjusted so that the slope of the log of the odds ratio function is limited.

7. Stepwise Logistic Regression and Feature Selection

[0312] The original data contain the expression levels of multiple microRNAs for each sample, i.e., multiple of data features. In training the classifier for each node, only a small subset of these features was selected and used for optimizing a logistic regression model. In the initial training this was done using a forward stepwise scheme. The features were sorted in order of decreasing log-likelihoods, and the logistic model was started off and optimized with the first feature. The second feature was then added, and the model re-optimized. The regression error of the two models was compared: if the addition of the feature did not provide a significant advantage (a χ2 difference less than 7.88, p-value of 0.005), the new feature was discarded. Otherwise, the added feature was kept. Adding a new feature may make a previous feature redundant (e.g., if they are very highly correlated). To check for this, the process iteratively checks if the feature with lowest likelihood can be discarded (without losing χ2 difference as above). After ensuring that the current set of features is compact in this sense, the process continues to test the next feature in the sorted list, until features are exhausted. No limitation on the number of features was inserted into the algorithm.

[0313] The stepwise logistic regression method was used on subsets of the training set samples by re-sampling the training set with repetition ("bootstrap"), so that each of the 20 runs contained somewhat different training set. All the features that took part in one of the 20 models were collected. A robust set of 1-3 features per each node was selected by comparing features that were repeatedly chosen in the bootstrap sets to previous evidence, and considering their signal strengths and reliability. When using these

selected features to construct the classifier, the stepwise process was not used and the training optimized the logistic regression model parameters only.

8. K-Nearest-Neighbors (KNN) Classification Algorithm

[0314] The KNN algorithm (see e.g., Ma et al., Arch Pathol Lab Med 2006; 130:465-73) calculates the distance (Pearson correlation) of any sample to all samples in the training set, and classifies the sample by the majority vote of the k samples which are most similar (k being a parameter of the classifier). The correlation is calculated on the predefined set of microRNAs (the microRNAs that were used by the decision-tree). KNN algorithms with k=1;10 were compared, and the optimal performer was selected, using k=5. The KNN was based on comparing the expression of all 65 microRNAs in each sample to all other samples in the training database.

9. Reporting a Final Answer (Prediction):

[0315] The decision-tree and KNN each return a predicted tissue of origin and histological type where applicable. The tissue of origin and histological type may be one of the exact origins and types in the training or a variant thereof. For example, whereas the training includes brain oligodendrioglioma and brain astrocytoma, the answer may simply be brain carcinoma. In addition to the tissue of origin and histological type, the KNN and decision-tree each return a confidence measure. The KNN returns the number of samples within the K nearest neighbors that agreed with the answer reported by the KNN (denoted by V), and the decision-tree returns the probability of the result (P), which is the multiplication of the probabilities at each branch point made on the way to that answer. The classifier returns the two different predictions or a single prediction in case the predictions concur, can be unified into a single answer (for example into the prediction brain if the KNN returned brain oligodendrioglioma and the decision-tree brain astrocytoma), or if based on V and P, one answer is chosen to override the other.

Example 1

Decision-Tree Classification Algorithm

[0316] A tumor classifier was built using the microRNA expression levels by applying a binary tree classification scheme (FIGS. **1**A-F). This framework is set up to utilize the specificity of microRNAs in tissue differentiation and embryogenesis: different microRNAs are involved in various stages of tissue specification, and are used by the algorithm at different decision points or "nodes". The tree breaks up the complex multi-tissue classification problem into a set of simpler binary decisions. At each node, classes which branch out earlier in the tree are not considered, reducing interference from irrelevant samples and further simplifying the decision. The decision at each node can then be accomplished using only a small number of microRNA biomarkers, which have well-defined roles in the classification (Table 2). The structure of the binary tree was based on a hierarchy of tissue development and morphological similarity[18], which was modified by prominent features of the microRNA expression patterns. For example, the expression patterns of microRNAs indicated a significant difference between germ cell tumors and tumors of non-germ cell origin, and these are therefore distinguished at node #1 (FIG. **2**) into separate branches (FIG. **1**A).

[0317] For each of the individual nodes logistic regression models were used, a robust family of classifiers which are frequently used in epidemiological and clinical studies to combine continuous data features into a binary decision (FIGS. **2**-**25** and Methods). Since gene expression classifiers have an inherent redundancy in selecting the gene features, bootstrapping was used on the training sample set as a method to select a stable microRNA set for each node (Methods). This resulted in a small number (usually 2-3) of microRNA features per node, totaling 65 microRNAs for the full classifier (Table 2). This approach provides a systematic process for identifying new biomarkers for differential expression.

TABLE 2

microRNAs used per class in the tree classifier

miR List:	Class
hsa-miR-372 (SEQ ID NO: 55)	Germ cell cancer
hsa-miR-372, hsa-miR-122 (SEQ ID NO: 6), hsa-miR-126 (SEQ ID NO: 9), hsa-miR-200b (SEQ ID NO: 29)	Biliary tract adenocarcinoma
hsa-miR-372, hsa-miR-122, hsa-miR-126, hsa-miR-200b	Hepatocellular carcinoma (HCC)
hsa-miR-372, hsa-miR-122, hsa-miR-200c (SEQ ID NO: 30), hsa-miR-30a (SEQ ID NO: 46), hsa-miR-146a (SEQ ID NO: 16), hsa-let-7e (SEQ ID NO: 156), hsa-miR-9* (SEQ ID NO: 66), hsa-miR-92b (SEQ ID NO: 68)	Brain tumor
hsa-miR-372, hsa-miR-122, hsa-miR-200c, hsa-miR-30a, hsa-miR-146a, hsa-let-7e, hsa-miR-9*, hsa-miR-92b, hsa-miR-222 (SEQ ID NO: 40), hsa-miR-497 (SEQ ID NO: 60)	Brain - oligodendroglioma
hsa-miR-372, hsa-miR-122, hsa-miR-200c, hsa-miR-30a, hsa-miR-146a, hsa-let-7e, hsa-miR-9*, hsa-miR-92b, hsa-miR-222, hsa-miR-497	Brain - astrocytoma
hsa-miR-372, hsa-miR-122, hsa-miR-200c, hsa-miR-30a, hsa-miR-375 (SEQ ID NO: 56), hsa-miR-7 (SEQ ID NO: 65), hsa-miR-193a-3p (SEQ ID NO: 25), hsa-miR-194 (SEQ ID NO: 27), hsa-miR-21* (SEQ ID NO: 35), hsa-miR-143 (SEQ ID NO: 14), hsa-miR-181a (SEQ ID NO: 21)	Prostate Adenocarcinoma
hsa-miR-372	Ovarian primitive germ cell tumor

TABLE 2-continued

microRNAs used per class in the tree classifier

miR List:	Class
hsa-miR-372	Testis
hsa-miR-372, hsa-miR-200b, hsa-miR-516a-5p (SEQ ID NO: 62)	Seminomatous testicular germ cell tumor
hsa-miR-372, hsa-miR-200b, hsa-miR-516a-5p	Non seminomatous testicular germ cell tumor
hsa-miR-372, hsa-miR-122, hsa-miR-200c, hsa-miR-30a, hsa-miR-7, hsa-miR-194, hsa-miR-21*, hsa-miR-143, hsa-miR-181a, hsa-miR-205 (SEQ ID NO: 32), hsa-miR-345 (SEQ ID NO: 51), hsa-miR-125a-5p (SEQ ID NO: 7), hsa-miR-193a-3p (SEQ ID NO: 25), hsa-miR-375, hsa-miR-342-3p (SEQ ID NO: 50)	Breast adenocarcinoma
hsa-miR-372, hsa-miR-122, hsa-miR-200c, hsa-miR-30a, hsa-miR-7, hsa-miR-193a-3p, hsa-miR-194, hsa-miR-21*, hsa-miR-143, hsa-miR-181a, hsa-miR-345, hsa-miR-125a-5p, hsa-miR-193a-3p, hsa-miR-375, hsa-miR-342-3p, hsa-miR-205 (SEQ ID NO: 32), hsa-miR-10a (SEQ ID NO: 4), hsa-miR-22 (SEQ ID NO: 39)	Ovarian carcinoma
hsa-miR-372, hsa-miR-122, hsa-miR-200c, hsa-miR-30a, hsa-miR-375, hsa-miR-7, hsa-miR-193a-3p, hsa-miR-194, hsa-miR-21*, hsa-miR-143, hsa-miR-181a, hsa-miR-205, hsa-miR-345, hsa-miR-125a-5p, hsa-miR-138 (SEQ ID NO: 11), hsa-miR-93 (SEQ ID NO: 148), hsa-miR-10a (SEQ ID NO: 4)	Thyroid carcinoma
hsa-miR-372, hsa-miR-122, hsa-miR-200c, hsa-miR-30a, hsa-miR-375, hsa-miR-7, hsa-miR-193a-3p, hsa-miR-194, hsa-miR-21*, hsa-miR-143, hsa-miR-181a, hsa-miR-205, hsa-miR-345, hsa-miR-125a-5p, hsa-miR-138, hsa-miR-93, hsa-miR-10a, hsa-miR-146b-5p (SEQ ID NO: 17), hsa-miR-21 (SEQ ID NO: 34)	Thyroid carcinoma follicular
hsa-miR-372, hsa-miR-122, hsa-miR-200c, hsa-miR-30a, hsa-miR-375, hsa-miR-7, hsa-miR-193a-3p, hsa-miR-194, hsa-miR-21*, hsa-miR-143, hsa-miR-181a, hsa-miR-205, hsa-miR-345, hsa-miR-125a-5p, hsa-miR-138, hsa-miR-93, hsa-miR-10a, hsa-miR-146b-5p, hsa-miR-21	Thyroid carcinoma papillary
hsa-miR-372, hsa-miR-122, hsa-miR-200c, hsa-miR-30a, hsa-miR-375, hsa-miR-7, hsa-miR-194, hsa-miR-21*, hsa-miR-143, hsa-miR-181a, hsa-miR-205, hsa-miR-345, hsa-miR-125a-5p, hsa-miR-138, hsa-miR-93, hsa-miR-10a, hsa-miR-193a-3p (SEQ ID NO: 25), hsa-miR-31 (SEQ ID NO: 49), hsa-miR-92a (SEQ ID NO: 67)	Breast adenocarcinoma
hsa-miR-372, hsa-miR-122, hsa-miR-200c, hsa-miR-30a, hsa-miR-375, hsa-miR-7, hsa-miR-193a-3p, hsa-miR-194, hsa-miR-21*, hsa-miR-143, hsa-miR-181a, hsa-miR-205, hsa-miR-345, hsa-miR-125a-5p, hsa-miR-93, hsa-miR-10a, hsa-miR-193a-3p, hsa-miR-31, hsa-miR-92a, hsa-miR-138 (SEQ ID NO: 11), hsa-miR-378 (SEQ ID NO: 57), hsa-miR-21 (SEQ ID NO: 34)	Lung large cell or adenocarcinoma
hsa-miR-372, hsa-miR-122, hsa-miR-200c, hsa-miR-30a, hsa-miR-375, hsa-miR-7, hsa-miR-194, hsa-miR-21*, hsa-miR-143, hsa-miR-181a, hsa-miR-205, hsa-miR-345, hsa-miR-125a-5p, hsa-miR-93, hsa-miR-10a, hsa-miR-193a-3p, hsa-miR-31, hsa-miR-92a, hsa-miR-138, hsa-miR-378, hsa-miR-21	Ovarian carcinoma
hsa-miR-372, hsa-miR-122, hsa-miR-200c, hsa-miR-30a, hsa-miR-375, hsa-miR-7, hsa-miR-193a-3p, hsa-miR-194, hsa-miR-21*, hsa-miR-143, hsa-miR-181a, hsa-miR-205, hsa-miR-345, hsa-miR-125a-5p, hsa-miR-342-3p, hsa-miR-10a, hsa-miR-22, hsa-miR-100, hsa-miR-21	Thymoma
hsa-miR-372, hsa-miR-122, hsa-miR-200c, hsa-miR-30a, hsa-miR-375, hsa-miR-7, hsa-miR-193a-3p, hsa-miR-194, hsa-miR-21*, hsa-miR-143, hsa-miR-181a, hsa-miR-205, hsa-miR-345, hsa-miR-125a-5p, hsa-miR-342-3p, hsa-miR-205, hsa-miR-10a, hsa-miR-22, hsa-miR-100, hsa-miR-21, hsa-miR-934 (SEQ ID NO: 69), hsa-miR-191 (SEQ ID NO: 24), hsa-miR-29c (SEQ ID NO: 44)	Urothelial carcinoma (TCC)
hsa-miR-372, hsa-miR-122, hsa-miR-200c, hsa-miR-30a, hsa-miR-375, hsa-miR-7, hsa-miR-193a-3p, hsa-miR-194, hsa-miR-21*, hsa-miR-143, hsa-miR-181a, hsa-miR-205, hsa-miR-345, hsa-miR-125a-5p, hsa-miR-342-3p, hsa-miR-10a, hsa-miR-22, hsa-miR-100, hsa-miR-21, hsa-miR-934, hsa-miR-191, hsa-miR-29c	Squamous cell carcinoma (SCC)
hsa-miR-372, hsa-miR-122, hsa-miR-200c, hsa-miR-30a, hsa-miR-375, hsa-miR-7, hsa-miR-193a-3p, hsa-miR-194, hsa-miR-21*, hsa-miR-143, hsa-miR-181a, hsa-miR-205, hsa-miR-345, hsa-miR-125a-5p, hsa-miR-342-3p, hsa-miR-10a, hsa-miR-22, hsa-miR-100, hsa-miR-21, hsa-miR-934, hsa-miR-191, hsa-miR-29c, hsa-miR-10b (SEQ ID NO: 5), hsa-let-7c (SEQ ID NO: 1), hsa-miR-361-5p (SEQ ID NO: 54)	Uterine cervix SCC
hsa-miR-372, hsa-miR-122, hsa-miR-200c, hsa-miR-30a, hsa-miR-375, hsa-miR-7, hsa-miR-193a-3p, hsa-miR-194, hsa-miR-21*, hsa-miR-143, hsa-miR-181a, hsa-miR-205, hsa-miR-345, hsa-miR-125a-5p, hsa-miR-193a-3p, hsa-miR-375, hsa-miR-342-3p, hsa-miR-205, hsa-miR-10a, hsa-miR-22, hsa-miR-100, hsa-miR-21, hsa-miR-934, hsa-miR-	Anus or Skin SCC

TABLE 2-continued

microRNAs used per class in the tree classifier

miR List:	Class
191, hsa-miR-29c, hsa-miR-10b, hsa-let-7c, hsa-miR-361-5p, hsa-miR-138, hsa-miR-185 (SEQ ID NO: 23)	
hsa-miR-372, hsa-miR-122, hsa-miR-200c, hsa-miR-30a, hsa-miR-375, hsa-miR-7, hsa-miR-193a-3p, hsa-miR-194, hsa-miR-21*, hsa-miR-143, hsa-miR-181a, hsa-miR-205, hsa-miR-345, hsa-miR-125a-5p, hsa-miR-342-3p, hsa-miR-10a, hsa-miR-22, hsa-miR-100, hsa-miR-21, hsa-miR-934, hsa-miR-191, hsa-miR-29c, hsa-let-7c, hsa-miR-361-5p, hsa-miR-10b, hsa-miR-138, hsa-miR-185	Lung, Head& Neck or Esophagus SCC
hsa-miR-372, hsa-miR-122, hsa-miR-200c, hsa-miR-30a, hsa-miR-146a (SEQ ID NO: 16), hsa-let-7e (SEQ ID NO: 2), hsa-miR-30d (SEQ ID NO: 47), hsa-miR-342-3p	Melanoma
hsa-miR-372, hsa-miR-122, hsa-miR-200c, hsa-miR-30a, hsa-miR-146a, hsa-let-7e, hsa-miR-30d, hsa-miR-342-3p	Lymphoma
hsa-miR-372, hsa-miR-122, hsa-miR-200c, hsa-miR-30a, hsa-miR-146a, hsa-let-7e, hsa-miR-30d, hsa-miR-342-3p, hsa-miR-21*, hsa-miR-30e (SEQ ID NO: 48)	B cell lymphoma
hsa-miR-372, hsa-miR-122, hsa-miR-200c, hsa-miR-30a, hsa-miR-146a, hsa-let-7e, hsa-miR-30a, hsa-miR-30d, hsa-miR-342-3p, hsa-miR-21*, hsa-miR-30e	T cell lymphoma
hsa-miR-372, hsa-miR-122, hsa-miR-200c, hsa-miR-30a, hsa-miR-375, hsa-miR-7, hsa-miR-193a-3p, hsa-miR-17 (SEQ ID NO: 20), hsa-miR-29c* (SEQ ID NO: 45)	Lung small cell carcinoma
hsa-miR-372, hsa-miR-122, hsa-miR-200c, hsa-miR-30a, hsa-miR-375, hsa-miR-7, hsa-miR-193a-3p, hsa-miR-17, hsa-miR-29c*, hsa-miR-222 (SEQ ID NO: 40), hsa-miR-92a (SEQ ID NO: 67), hsa-miR-92b (SEQ ID NO: 68)	Medullary thyroid carcinoma
hsa-miR-372, hsa-miR-122, hsa-miR-200c, hsa-miR-30a, hsa-miR-375, hsa-miR-7, hsa-miR-193a-3p, hsa-miR-17, hsa-miR-29c*, hsa-miR-222, hsa-miR-92a, hsa-miR-92b, hsa-miR-652 (SEQ ID NO: 64), hsa-miR-34c-5p (SEQ ID NO: 53), hsa-miR-214 (SEQ ID NO: 37)	Lung carcinoid
hsa-miR-372, hsa-miR-122, hsa-miR-200c, hsa-miR-30a, hsa-miR-375, hsa-miR-7, hsa-miR-193a-3p, hsa-miR-17, hsa-miR-29c*, hsa-miR-222, hsa-miR-92a, hsa-miR-92b, hsa-miR-652, hsa-miR-34c-5p, hsa-miR-214, hsa-miR-21 (SEQ ID NO: 34), hsa-miR-148a (SEQ ID NO: 18)	Gastrointestinal (GI) tract carcinoid
hsa-miR-372, hsa-miR-122, hsa-miR-200c, hsa-miR-30a, hsa-miR-375, hsa-miR-7, hsa-miR-193a-3p, hsa-miR-17, hsa-miR-29c*, hsa-miR-222, hsa-miR-92a, hsa-miR-92b, hsa-miR-652, hsa-miR-34c-5p, hsa-miR-214, hsa-miR-21, hsa-miR-148a	Pancreas islet cell tumor
hsa-miR-372, hsa-miR-122, hsa-miR-200c, hsa-miR-30a, hsa-miR-375, hsa-miR-7, hsa-miR-193a-3p, hsa-miR-194 (SEQ ID NO: 27), hsa-miR-21* (SEQ ID NO: 35), hsa-miR-224 (SEQ ID NO: 42), hsa-miR-210 (SEQ ID NO: 36), hsa-miR-1201 (SEQ ID NO: 146)	Gastric or Esophageal Adenocarcinoma
hsa-miR-372, hsa-miR-122, hsa-miR-200c, hsa-miR-30a, hsa-miR-375, hsa-miR-7, hsa-miR-193a-3p, hsa-miR-194, hsa-miR-21*, hsa-miR-224, hsa-miR-210, hsa-miR-1201, hsa-miR-17 (SEQ ID NO: 20), hsa-miR-29a (SEQ ID NO: 43)	Colorectal Adenocarcinoma
hsa-miR-372, hsa-miR-122, hsa-miR-200c, hsa-miR-30a, hsa-miR-375, hsa-miR-7, hsa-miR-193a-3p, hsa-miR-194, hsa-miR-21*, hsa-miR-224, hsa-miR-210, hsa-miR-1201, hsa-miR-17, hsa-miR-29a	Pancreas or bile
hsa-miR-372, hsa-miR-122, hsa-miR-200c, hsa-miR-30a, hsa-miR-375, hsa-miR-7, hsa-miR-193a-3p, hsa-miR-194, hsa-miR-21*, hsa-miR-224, hsa-miR-210, hsa-miR-1201, hsa-miR-17, hsa-miR-29a, hsa-miR-345 (SEQ ID NO: 51), hsa-miR-31 (SEQ ID NO: 49), hsa-miR-146a (SEQ ID NO: 16)	Pancreatic adenocarcinoma
hsa-miR-372, hsa-miR-122, hsa-miR-200c, hsa-miR-30a, hsa-miR-375, hsa-miR-7, hsa-miR-193a-3p, hsa-miR-194, hsa-miR-21*, hsa-miR-224, hsa-miR-210, hsa-miR-1201, hsa-miR-17, hsa-miR-29a, hsa-miR-345, hsa-miR-31, hsa-miR-146a	Biliary tract adenocarcinoma
hsa-miR-372, hsa-miR-122, hsa-miR-200c, hsa-miR-30a, hsa-miR-146a (SEQ ID NO: 16), hsa-let-7e, hsa-miR-9* (SEQ ID NO: 66), hsa-miR-92b (SEQ ID NO: 68), hsa-miR-149 (SEQ ID NO: 19), hsa-miR-200b (SEQ ID NO: 29)	Renal cell carcinoma chromophobe
hsa-miR-372, hsa-miR-122, hsa-miR-200c, hsa-miR-30a, hsa-miR-146a, hsa-let-7e, hsa-miR-9*, hsa-miR-92b, hsa-miR-30a, hsa-miR-149, hsa-miR-200b, hsa-miR-7 (SEQ ID NO: 65), hsa-miR-375	Pheochromocytoma
hsa-miR-372, hsa-miR-122, hsa-miR-200c, hsa-miR-30a, hsa-miR-146a, hsa-let-7e, hsa-miR-9*, hsa-miR-92b, hsa-miR-149, hsa-miR-200b, hsa-miR-7, hsa-miR-375, hsa-miR-202 (SEQ ID NO: 31), hsa-miR-214* (SEQ ID NO: 38), hsa-miR-509-3p (SEQ ID NO: 61)	Adrenocortical

TABLE 2-continued

microRNAs used per class in the tree classifier

miR List:	Class
hsa-miR-372, hsa-miR-122, hsa-miR-200c, hsa-miR-30a, hsa-miR-146a, hsa-let-7e, hsa-miR-9*, hsa-miR-92b, hsa-miR-149, hsa-miR-200b, hsa-miR-7, hsa-miR-375, hsa-miR-202, hsa-miR-214*, hsa-miR-509-3p, hsa-miR-143 (SEQ ID NO: 14), hsa-miR-29c*	Gastrointestinal stromal tumor (GIST)
hsa-miR-372, hsa-miR-122, hsa-miR-200c, hsa-miR-30a, hsa-miR-146a, hsa-let-7e, hsa-miR-9*, hsa-miR-92b, hsa-miR-149, hsa-miR-200b, hsa-miR-210 (SEQ ID NO: 36), hsa-miR-221 (SEQ ID NO: 147)	Renal cell carcinoma chromophobe
hsa-miR-372, hsa-miR-122, hsa-miR-200c, hsa-miR-30a, hsa-miR-146a, hsa-let-7e, hsa-miR-9*, hsa-miR-92b, hsa-miR-149, hsa-miR-200b, hsa-miR-210, hsa-miR-221, hsa-miR-31 (SEQ ID NO: 49), hsa-miR-126 (SEQ ID NO: 9)	Renal cell carcinoma clear cell
hsa-miR-372, hsa-miR-122, hsa-miR-200c, hsa-miR-30a, hsa-miR-146a, hsa-let-7e, hsa-miR-9*, hsa-miR-92b, hsa-miR-149, hsa-miR-200b, hsa-miR-210, hsa-miR-221, hsa-miR-31, hsa-miR-126	Renal cell carcinoma papillary
hsa-miR-372, hsa-miR-122, hsa-miR-200c, hsa-miR-30a, hsa-miR-146a, hsa-let-7e, hsa-miR-9*, hsa-miR-92b, hsa-miR-149, hsa-miR-200b, hsa-miR-7 (SEQ ID NO: 65), hsa-miR-375, hsa-miR-202 (SEQ ID NO: 31), hsa-miR-214* (SEQ ID NO: 38), hsa-miR-509-3p (SEQ ID NO: 61), hsa-miR-143 (SEQ ID NO: 14), hsa-miR-29c*, hsa-miR-21* (SEQ ID NO: 35), hsa-miR-130a (SEQ ID NO: 10), hsa-miR-10b (SEQ ID NO: 5)	Pleural mesothelioma
hsa-miR-372, hsa-miR-122, hsa-miR-200c, hsa-miR-30a, hsa-miR-146a, hsa-let-7e, hsa-miR-9*, hsa-miR-92b, hsa-miR-149, hsa-miR-200b, hsa-miR-7, hsa-miR-375, hsa-miR-202, hsa-miR-214*, hsa-miR-509-3p, hsa-miR-143, hsa-miR-29c*, hsa-miR-21*, hsa-miR-130a, hsa-miR-10b	Sarcoma
hsa-miR-372, hsa-miR-122, hsa-miR-200c, hsa-miR-30a, hsa-miR-146a, hsa-let-7e, hsa-miR-9*, hsa-miR-92b, hsa-miR-149, hsa-miR-200b, hsa-miR-7, hsa-miR-375, hsa-miR-202, hsa-miR-214*, hsa-miR-509-3p, hsa-miR-143, hsa-miR-29c*, hsa-miR-21*, hsa-miR-130a, hsa-miR-10b, hsa-miR-100 (SEQ ID NO: 3), hsa-miR-222 (SEQ ID NO: 40), hsa-miR-145 (SEQ ID NO: 15)	Synovial sarcoma
hsa-miR-372, hsa-miR-122, hsa-miR-200c, hsa-miR-30a, hsa-miR-146a, hsa-let-7e, hsa-miR-9*, hsa-miR-92b, hsa-miR-149, hsa-miR-200b, hsa-miR-7, hsa-miR-375, hsa-miR-202, hsa-miR-214*, hsa-miR-509-3p, hsa-miR-143, hsa-miR-29c*, hsa-miR-21*, hsa-miR-130a, hsa-miR-10b, hsa-miR-100, hsa-miR-222, hsa-miR-145, hsa-miR-140-3p (SEQ ID NO: 12), hsa-miR-455-5p (SEQ ID NO: 58)	Chondrosarcoma
hsa-miR-372, hsa-miR-122, hsa-miR-200c, hsa-miR-30a, hsa-miR-146a, hsa-let-7e, hsa-miR-9*, hsa-miR-92b, hsa-miR-149, hsa-miR-200b, hsa-miR-7, hsa-miR-375, hsa-miR-202, hsa-miR-214*, hsa-miR-509-3p, hsa-miR-143, hsa-miR-29c*, hsa-miR-21*, hsa-miR-130a, hsa-miR-10b, hsa-miR-100, hsa-miR-222, hsa-miR-145, hsa-miR-140-3p, hsa-miR-455-5p, hsa-miR-210 (SEQ ID NO: 36), hsa-miR-193a-5p (SEQ ID NO: 26)	Liposarcoma
hsa-miR-372, hsa-miR-122, hsa-miR-200c, hsa-miR-30a, hsa-miR-146a, hsa-let-7e, hsa-miR-9*, hsa-miR-92b, hsa-miR-149, hsa-miR-200b, hsa-miR-7, hsa-miR-375, hsa-miR-202, hsa-miR-214*, hsa-miR-509-3p, hsa-miR-143, hsa-miR-29c*, hsa-miR-21*, hsa-miR-130a, hsa-miR-10b, hsa-miR-100, hsa-miR-222, hsa-miR-145, hsa-miR-140-3p, hsa-miR-455-5p, hsa-miR-210, hsa-miR-193a-5p, hsa-miR-181a, hsa-miR-193a-3p (SEQ ID NO: 25), hsa-miR-31 (SEQ ID NO: 49)	Ewing sarcoma
hsa-miR-372, hsa-miR-122, hsa-miR-200c, hsa-miR-30a, hsa-miR-146a, hsa-let-7e, hsa-miR-9*, hsa-miR-92b, hsa-miR-149, hsa-miR-200b, hsa-miR-7, hsa-miR-375, hsa-miR-202, hsa-miR-214*, hsa-miR-509-3p, hsa-miR-143, hsa-miR-29c*, hsa-miR-21*, hsa-miR-130a, hsa-miR-10b, hsa-miR-100, hsa-miR-222, hsa-miR-145, hsa-miR-140-3p, hsa-miR-455-5p, hsa-miR-210, hsa-miR-193a-5p, hsa-miR-181a, hsa-miR-193a-3p, hsa-miR-31	Osteosarcoma
hsa-miR-372, hsa-miR-122, hsa-miR-200c, hsa-miR-30a, hsa-miR-146a, hsa-let-7e, hsa-miR-30a, hsa-miR-9*, hsa-miR-92b, hsa-miR-30a, hsa-miR-149, hsa-miR-200b, hsa-miR-7, hsa-miR-375, hsa-miR-202, hsa-miR-214*, hsa-miR-509-3p, hsa-miR-143, hsa-miR-29c*, hsa-miR-21*, hsa-miR-130a, hsa-miR-10b, hsa-miR-100, hsa-miR-222, hsa-miR-145, hsa-miR-140-3p, hsa-miR-455-5p, hsa-miR-210, hsa-miR-193a-5p, hsa-miR-181a, hsa-miR-487b (SEQ ID NO: 59), hsa-miR-22 (SEQ ID NO: 39), hsa-miR-206 (SEQ ID NO: 33)	Rhabdomyo sarcoma
hsa-miR-372, hsa-miR-122, hsa-miR-200c, hsa-miR-30a, hsa-miR-146a, hsa-let-7e, hsa-miR-30a, hsa-miR-9*, hsa-miR-92b, hsa-miR-30a, hsa-miR-149, hsa-miR-200b, hsa-miR-7, hsa-miR-375, hsa-miR-202, hsa-miR-214*, hsa-miR-509-3p, hsa-miR-143, hsa-miR-29c*, hsa-miR-21*, hsa-miR-130a, hsa-miR-10b, hsa-miR-100, hsa-miR-222, hsa-	Malignant fibrous histiocytoma (MFH) or fibrosarcoma

TABLE 2-continued

microRNAs used per class in the tree classifier	
miR List:	Class
miR-145, hsa-miR-140-3p, hsa-miR-455-5p, hsa-miR-210, hsa-miR-193a-5p, hsa-miR-181a, hsa-miR-487b, hsa-miR-22, hsa-miR-206	

Example 2

[0318] Expression of miRs Provides for Distinguishing Between Tumors

TABLE 3

miR expression (in fluorescence units) distinguishing between the group consisting of germ-cell tumors and the group consisting of all other tumors

median values	fold-change	p-value	SEQ ID NO.	miR name
2.7e+004-5.0e+001	545.73 (+)	<e-240	233	hsa-miR-373
1.8e+004-5.0e+001	365.93 (+)	<e-240	55	hsa-miR-372
8.6e+003-5.0e+001	171.72 (+)	<e-240	200	hsa-miR-371-3p
5.9e+003-5.1e+001	115.94 (+)	7.3e-249	201	hsa-miR-371-5p

(+) for all the listed miRs, the higher expression is in tumors from a germ-cell origin.

[0319] hsa-miR-372 (SEQ ID NO: 55) is used at node 1 of the binary-tree-classifier detailed in the invention to distinguish between germ-cell tumors and all other tumors.

[0320] FIGS. **2**A-D are boxplot presentations comparing distribution of the expression of the statistically significant miRs in tumor samples from the "germ cell" class (left box) and "non germ cell" class (right box).

TABLE 4

miR expression (in fluorescence units) distinguishing between the group consisting of hepatobiliary tumors and the group consisting of non germ-cell non-hepatobiliary tumors

median values	fold-change	p-value	SEQ ID NO.	miR name
1.0e+005-5.0e+001	2024.31 (+)	1.1e-123	6	hsa-miR-122
7.4e+001-8.1e+003	109.63 (-)	3.6e-010	30	hsa-miR-200c
5.0e+001-1.4e+003	27.92 (-)	4.8e-010	13	hsa-miR-141

(+) the higher expression of this miR is in tumors from a hepatobiliary origin

(-) the higher expression of this miR is in tumors from a non germ-cell, non-hepatobiliary origin

[0321] hsa-miR-122 (SEQ ID NO: 6) is used at node 2 of the binary-tree-classifier detailed in the invention to distinguish between hepatobiliary tumors and non germ-cell non-hepatobiliary tumors.

TABLE 5

miR expression (in fluorescence units) distinguishing between the group consisting of liver tumors and the group consisting of biliary-tract carcinomas (cholangiocarcinoma or gallbladder adenocarcinoma)

median values	fold-change	p-value	SEQ ID NO.	miR name
6.1e+003-4.1e+002	14.74 (+)	5.5e-005	28	hsa-miR-200a
9.7e+003-9.0e+002	10.74 (+)	2.4e-004	29	hsa-miR-200b

TABLE 5-continued

miR expression (in fluorescence units) distinguishing between the group consisting of liver tumors and the group consisting of biliary-tract carcinomas (cholangiocarcinoma or gallbladder adenocarcinoma)

median values	fold-change	p-value	SEQ ID NO.	miR name
1.9e+003-7.0e+003	3.67 (-)	8.5e-004	231	hsa-miR-99a
3.3e+003-7.5e+003	2.28 (-)	6.2e-004	9	hsa-miR-126

(+) the higher expression of this miR is in biliary tract carcinomas

(-) the higher expression of this miR is in liver tumors

[0322] hsa-miR-126 (SEQ ID NO: 9) and hsa-miR-200b (SEQ ID NO: 29) are used at node 3 of the binary-tree-classifier detailed in the invention to distinguish between liver tumors and biliary-tract carcinoma.

[0323] FIG. **3** demonstrates that tumors of hepatocellular carcinoma (HCC) origin (marked by squares) are easily distinguished from tumors of biliary tract adenocarcinoma origin (marked by diamonds) using the expression levels of hsa-miR-200b (SEQ ID NO: 29, y-axis) and hsa-miR-126 (SEQ ID NO: 9, x-axis).

TABLE 6

miR expression (in fluorescence units) distinguishing between the group consisting of tumors from an epithelial origin and the group consisting of tumors from a non-epithelial origin

median values	fold-change	p-value	SEQ ID NO.	miR name
1.5e+004-7.7e+001	196.43 (+)	1.5e-300	30	hsa-miR-200c
9.0e+003-5.0e+001	180.07 (+)	1.3e-208	29	hsa-miR-200b
3.9e+003-5.0e+001	78.09 (+)	2.2e-187	28	hsa-miR-200a
2.7e+003-5.0e+001	54.64 (+)	7.0e-078	32	hsa-miR-205
2.6e+003-5.0e+001	51.98 (+)	1.2e-265	13	hsa-miR-141
5.4e+002-9.2e+001	5.90 (+)	6.3e-048	152	hsa-miR-182
1.1e+003-2.5e+002	4.35 (+)	4.8e-022	49	hsa-miR-31

(+) for all the listed miRs, the higher expression is in tumors from epithelial origins

[0324] A combination of the expression level of any of the miRs detailed in table 6 with the expression level of any of hsa-miR-30a (SEQ ID NO: 46), hsa-miR-10b (SEQ ID NO: 5) and hsa-miR-140-3p (SEQ ID NO: 12) also provides for distinguishing between tumors from epithelial origins and tumors from non-epithelial origins. This is demonstrated at node 4 of the binary-tree-classifier detailed in the invention with hsa-miR-200c (SEQ ID NO: 30) and hsa-miR-30a (SEQ ID NO: 46) (FIG. **4**). Tumors originating in epithelial (diamonds) are easily distinguished from tumors of non-epithelial origin (squares) using the expression levels of hsa-miR-30a (SEQ ID NO: 46, y-axis) and hsa-miR-200c (SEQ ID NO: 30, x-axis).

TABLE 7

miR expression (in fluorescence units) distinguishing between the group consisting of melanoma and lymphoma (B-cell, T-cell), and the group consisting of all other non-epithelial tumors

median values	fold-change	p-value	SEQ ID NO.	miR name
2.0e+003-7.0e+001	28.25 (−)	1.9e−074	164	hsa-miR-142-5p
1.2e+004-6.3e+002	18.86 (−)	6.0e−061	168	hsa-miR-150
5.4e+003-3.1e+002	17.29 (−)	5.6e−060	170	hsa-miR-155
4.2e+003-3.5e+002	12.03 (−)	8.4e−068	16	hsa-miR-146a
5.9e+002-1.4e+002	4.25 (−)	8.2e−048	198	hsa-miR-342-5p
7.5e+003-1.9e+003	4.02 (−)	4.8e−056	50	hsa-miR-342-3p
8.9e+002-2.5e+002	3.53 (−)	6.0e−035	176	hsa-miR-18a
4.4e+003-1.4e+003	3.28 (−)	8.0e−038	186	hsa-miR-20a
7.9e+002-2.6e+002	3.03 (−)	7.3e−005	11	hsa-miR-138
6.6e+003-2.3e+003	2.82 (−)	4.0e−039	158	hsa-miR-106a
4.1e+003-1.4e+003	2.82 (−)	2.4e−037	20	hsa-miR-17
6.2e+001-5.9e+002	9.53 (+)	3.7e−027	155	hsa-miR-127-3p
1.2e+003-7.0e+003	5.71 (+)	1.5e−047	231	hsa-miR-99a
3.9e+002-1.7e+003	4.25 (+)	6.6e−022	4	hsa-miR-10a
1.0e+004-4.1e+004	3.91 (+)	3.2e−037	8	hsa-miR-125b
6.5e+002-2.2e+003	3.37 (+)	2.4e−023	46	hsa-miR-30a
1.9e+003-5.6e+003	2.98 (+)	1.0e−025	3	hsa-miR-100
2.5e+003-7.1e+003	2.89 (+)	1.8e−051	2	hsa-let-7e
2.9e+003-8.4e+003	2.86 (+)	8.1e−047	7	hsa-miR-125a-5p

(+) the higher expression of this miR is in the group of non-epithelial tumors excluding melanoma and lymphoma

(−) the higher expression of this miR is in the group consisting of melanoma and lymphoma

[0325] hsa-miR-146a (SEQ ID NO: 16), hsa-let-7e (SEQ ID NO: 2) and hsa-miR-30a (SEQ ID NO: 46) are used at node 5 of the binary-tree-classifier detailed in the invention to distinguish between the group consisting of melanoma and lymphoma, and the group consisting of all other non-epithelial tumors. FIG. **5** demonstrates that tumors originating in the lymphoma or melanoma (diamonds) are easily distinguished from tumors of non epithelial, non lymphoma/melanoma origin (squares) using the expression levels of hsa-miR-146a (SEQ ID NO: 16, y-axis), hsa-miR-30a (SEQ ID NO: 46, x-axis) and hsa-let-7e (SEQ ID NO: 2, z-axis).

TABLE 8

miR expression (in fluorescence units) distinguishing between the group consisting of brain tumors (astrocytic tumor and oligodendroglioma) and the group consisting of all non-brain, non-epithelial tumors

median values	fold-change	p-value	SEQ ID NO.	miR name
9.1e+003-5.0e+001	182.94 (+)	3.8e−059	159	hsa-miR-124
4.4e+003-5.0e+001	88.33 (+)	1.1e−125	66	hsa-miR-9*
2.1e+003-6.0e+001	34.97 (+)	6.0e−035	225	hsa-miR-551b
9.9e+002-5.0e+001	19.73 (+)	3.0e−116	187	hsa-miR-219-2-3p
6.5e+002-5.0e+001	12.95 (+)	1.8e−021	162	hsa-miR-129-3p
1.1e+003-1.0e+002	10.52 (+)	2.0e−034	161	hsa-miR-128
2.3e+003-2.5e+002	9.45 (+)	2.2e−052	68	hsa-miR-92b
5.2e+002-6.8e+001	7.61 (+)	6.7e−019	232	hsa-miR-99a*
6.9e+002-9.2e+001	7.45 (+)	5.5e−023	173	hsa-miR-181c
2.2e+003-3.5e+002	6.34 (+)	7.4e−007	11	hsa-miR-138
1.2e+005-2.4e+004	4.78 (+)	1.7e−014	8	hsa-miR-125b
1.8e+003-3.9e+002	4.70 (+)	7.2e−014	174	hsa-miR-181d
8.5e+002-1.8e+002	4.64 (+)	2.2e−002	155	hsa-miR-127-3p
1.6e+004-3.5e+003	4.60 (+)	2.4e−010	231	hsa-miR-99a
8.5e+001-1.1e+003	13.55 (−)	2.4e−014	4	hsa-miR-10a
7.7e+002-6.6e+003	8.58 (−)	8.4e−017	182	hsa-miR-199a-5p

TABLE 8-continued

miR expression (in fluorescence units) distinguishing between the group consisting of brain tumors (astrocytic tumor and oligodendroglioma) and the group consisting of all non-brain, non-epithelial tumors

median values	fold-change	p-value	SEQ ID NO.	miR name
5.7e+002-4.7e+003	8.12 (−)	1.8e−013	181	hsa-miR-199a-3p
2.8e+002-1.9e+003	6.81 (−)	1.4e−012	37	hsa-miR-214

(+) the higher expression of this miR is in the group consisting of brain tumors

(−) the higher expression of this miR is in the group consisting of all non-brain, non-epithelial tumors

[0326] hsa-miR-9* (SEQ ID NO: 66) and hsa-miR-92b (SEQ ID NO: 68) are used at node 6 of the binary-tree-classifier detailed in the invention to distinguish between brain tumors and the group consisting of all non-brain, non-epithelial tumors. FIG. **6** demonstrates that tumors originating in the brain (marked by diamonds) are easily distinguished from tumors of non epithelial, non brain origin (marked by squares) using the expression levels of hsa-miR-9* (SEQ ID NO: 66, y-axis) and hsa-miR-92b (SEQ ID NO: 68, x-axis).

TABLE 9

miR expression (in fluorescence units) distinguishing between astrocytic tumors and oligodendrogliomas

median values	fold-change	p-value	SEQ ID NO.	miR name
2.5e+003-2.3e+002	11.10 (+)	5.1e−011	230	hsa-miR-886-5p
4.4e+003-4.9e+002	9.06 (+)	1.1e−009	228	hsa-miR-886-3p
1.0e+004-1.7e+003	5.99 (+)	7.7e−008	147	hsa-miR-221
1.3e+004-2.6e+003	5.03 (+)	2.6e−006	40	hsa-miR-222
3.3e+004-7.3e+003	4.54 (+)	3.9e−004	34	hsa-miR-21
8.4e+002-2.2e+002	3.78 (+)	3.7e−006	206	hsa-miR-455-3p
6.0e+002-1.8e+002	3.30 (+)	1.3e−002	35	hsa-miR-21*
5.8e+003-1.8e+003	3.15 (+)	2.4e−005	52	hsa-miR-34a
1.1e+003-3.5e+002	3.04 (+)	1.0e−003	25	hsa-miR-193a-3p
1.6e+002-8.2e+002	5.17 (−)	1.2e−004	229	hsa-miR-9
4.6e+002-2.3e+003	5.09 (−)	7.1e−003	161	hsa-miR-128
4.1e+002-1.8e+003	4.43 (−)	1.3e−002	187	hsa-miR-219-2-3p
3.8e+003-1.3e+004	3.31 (−)	1.9e−002	179	hsa-miR-195

(+) the higher expression of this miR is in astrocytic tumors

(−) the higher expression of this miR is in oligodendrogliomas

[0327] A combination of the expression level of any of the miRs detailed in table 9 with the expression level of hsa-miR-497 (SEQ ID NO: 208) or hsa-let-7d (SEQ ID NO: 153) also provides for classification of brain tumors as astrocytic tumors or oligodendrogliomas. This is demonstrated at node 7 of the binary-tree-classifier detailed in the invention with hsa-miR-222 (SEQ ID NO: 40) and hsa-miR-497 (SEQ ID NO: 208). In another embodiment of the invention, the expression levels of hsa-miR-222 (SEQ ID NO: 40) and hsa-let-7d (SEQ ID NO: 153) are combined to distinguish between astrocytic tumors and oligodendrogliomas.

[0328] FIG. **7** demonstrates that tumors originating in astrocytoma (marked by diamonds) are easily distinguished from tumors of oligodendroglioma origins (marked by squares) using the expression levels of hsa-miR-497 (SEQ ID NO: 208, y-axis) and hsa-miR-222 (SEQ ID NO: 40, x-axis).

TABLE 10

miR expression (in fluorescence units) distinguishing between the group consisting of neuroendocrine tumors and the group consisting of all non-neuroendocrine, epithelial tumors

median values	fold-change	p-value	SEQ ID NO.	miR name
3.8e+004-1.5e+002	259.47 (+)	5.3e−086	56	hsa-miR-375
3.6e+003-5.2e+001	70.47 (+)	4.4e−145	65	hsa-miR-7
1.3e+003-1.8e+002	6.89 (+)	4.7e−044	175	hsa-miR-183
1.9e+003-4.4e+002	4.42 (+)	3.5e−025	152	hsa-miR-182
1.2e+003-3.0e+002	4.16 (+)	5.5e−028	155	hsa-miR-127-3p
5.6e+001-7.0e+003	124.66 (−)	1.4e−023	32	hsa-miR-205
1.5e+002-1.4e+003	9.25 (−)	1.8e−019	49	hsa-miR-31
3.4e+002-1.4e+003	4.12 (−)	9.5e−032	35	hsa-miR-21*

(+) the higher expression of this miR is in the group consisting of neuroendocrine tumors

(−) the higher expression of this miR is in the group consisting of all non-neuroendocrine, epithelial tumors

[0329] hsa-miR-375 (SEQ ID NO: 56), hsa-miR-7 (SEQ ID NO: 65) and hsa-miR-193a-3p (SEQ ID NO: 25) are used at node 8 of the binary-tree-classifier detailed in the invention to distinguish between the group consisting of neuroendocrine tumors and the group consisting of all non-neuroendocrine, epithelial tumors. FIG. **8** demonstrates that tumors originating in the neuroendocrine (diamonds) are easily distinguished from tumors of epithelial, origin (squares) using the expression levels of hsa-miR-193a-3p (SEQ ID NO: 25, y-axis), hsa-miR-7 (SEQ ID NO: 65, x-axis) and hsa-miR-375 (SEQ ID NO: 56, z-axis).

TABLE 11

miR expression (in fluorescence units) distinguishing between the group consisting of gastrointestinal (GI) epithelial tumors and the group consisting of non-GI epithelial tumors

median values	fold-change	p-value	SEQ ID NO.	miR name
2.6e+003-7.1e+001	36.09 (+)	2.5e−127	27	hsa-miR-194
3.9e+003-1.2e+002	33.26 (+)	1.6e−117	177	hsa-miR-192
2.6e+003-6.7e+002	3.88 (+)	3.3e−021	4	hsa-miR-10a
5.0e+001-2.1e+004	411.76 (−)	6.5e−045	32	hsa-miR-205

(+) the higher expression of this miR is in the group consisting of GI epithelial tumors

(−) the higher expression of this miR is in the group consisting of non-GI epithelial tumors

hsa-miR-194 (SEQ ID NO: 27) and hsa-miR-21* (SEQ ID NO: 35) are used at node 9 of the binary-tree-classifier detailed in the invention to distinguish between GI epithelial tumors and non-GI epithelial tumors.

[0330] FIG. **9** demonstrates that tumors originating in gastro-intestinal (GI) (marked by diamonds) are easily distinguished from tumors of non GI origins (marked by squares) using the expression levels of hsa-miR-21* (SEQ ID NO: 35, y-axis) and hsa-miR-194 (SEQ ID NO: 27, x-axis).

TABLE 12

miR expression (in fluorescence units) distinguishing between prostate tumors and all other non-GI epithelial tumors

median values	fold-change	p-value	SEQ ID NO.	miR name
5.1e+003-5.2e+001	96.76 (+)	3.7e−016	56	hsa-miR-375
1.0e+003-5.5e+001	18.27 (+)	4.0e−025	199	hsa-miR-363
6.8e+004-7.2e+003	9.41 (+)	1.0e−025	14	hsa-miR-143
1.2e+005-1.4e+004	8.14 (+)	7.8e−022	15	hsa-miR-145
2.8e+003-3.5e+002	7.89 (+)	1.5e−012	165	hsa-miR-143*

TABLE 12-continued

miR expression (in fluorescence units) distinguishing between prostate tumors and all other non-GI epithelial tumors

median values	fold-change	p-value	SEQ ID NO.	miR name
2.1e+004-4.4e+003	4.76 (+)	2.2e−011	231	hsa-miR-99a
4.6e+002-2.1e+003	4.58 (−)	8.0e−007	36	hsa-miR-210
2.7e+002-1.1e+003	3.84 (−)	7.8e−017	154	hsa-miR-181b
1.2e+003-4.3e+003	3.76 (−)	1.2e−014	21	hsa-miR-181a
5.5e+002-2.0e+003	3.63 (−)	2.3e−002	49	hsa-miR-31

(+) the higher expression of this miR is in prostate tumors

(−) the higher expression of this miR is in the group consisting of all other non-GI epithelial tumors

[0331] hsa-miR-143 (SEQ ID NO: 14) and hsa-miR-181a (SEQ ID NO: 21) are used at node 10 of the binary-tree-classifier detailed in the invention to distinguish between prostate tumors and all other non-GI epithelial tumors.

[0332] FIG. **10** demonstrates that tumors originating in prostate adenocarcinoma (marked by diamonds) are easily distinguished from tumors of non prostate origins (marked by squares) using the expression levels of hsa-miR-181a (SEQ ID NO: 21, y-axis) and hsa-miR-143 (SEQ ID NO: 14, x-axis).

TABLE 13

miR expression (in fluorescence units) distinguishing between seminomatous and non-seminomatous testicular tumors

median values	fold-change	p-value	SEQ ID NO.	miR name
4.3e+003-7.6e+002	5.63 (+)	6.6e−004	152	hsa-miR-182
1.0e+002-2.1e+003	20.46 (−)	6.2e−005	216	hsa-miR-518e
7.8e+001-1.2e+003	15.29 (−)	4.5e−005	212	hsa-miR-516b
6.8e+001-8.2e+002	11.94 (−)	2.2e−005	224	hsa-miR-527
2.1e+002-2.2e+003	10.40 (−)	1.9e−006	13	hsa-miR-141
5.3e+002-5.0e+003	9.48 (−)	5.0e−004	194	hsa-miR-302d
1.4e+002-1.3e+003	8.97 (−)	4.1e−006	192	hsa-miR-302a
2.7e+002-2.3e+003	8.78 (−)	2.9e−003	221	hsa-miR-520c-3p
1.3e+002-1.2e+003	8.65 (−)	8.3e−004	217	hsa-miR-518f*
3.4e+003-2.9e+004	5.98 (−)	2.6e−007	205	hsa-miR-451
2.8e+002-1.7e+003	5.98 (−)	1.1e−002	219	hsa-miR-519d
2.0e+002-1.2e+003	5.90 (−)	6.8e−005	32	hsa-miR-205
2.0e+002-1.1e+003	5.59 (−)	5.8e−006	193	hsa-miR-302a*
1.9e+002-1.0e+003	5.27 (−)	6.7e−003	223	hsa-miR-524-5p
1.5e+002-8.0e+002	5.22 (−)	5.4e−003	220	hsa-miR-520a-5p
2.2e+002-1.1e+003	5.21 (−)	4.1e−003	210	hsa-miR-512-5p
3.2e+002-1.4e+003	4.57 (−)	9.2e−003	209	hsa-miR-498
7.2e+002-3.2e+003	4.51 (−)	3.1e−002	213	hsa-miR-517a
6.4e+002-2.9e+003	4.47 (−)	2.9e−002	163	hsa-miR-1323
9.5e+002-4.1e+003	4.29 (−)	1.3e−004	30	hsa-miR-200c

(+) the higher expression of this miR is in seminoma tumors

(−) the higher expression of this miR is in non-seminoma tumors

[0333] A combination of the expression level of any of the miRs detailed in table 13 with the expression level of hsa-miR-200b (SEQ ID NO: 29), hsa-miR-200a (SEQ ID NO: 28), hsa-miR-516a-5p (SEQ ID NO: 211), hsa-miR-767-5p (SEQ ID NO: 227), hsa-miR-518a-3p (SEQ ID NO: 215), hsa-miR-520d-5p (SEQ ID NO: 222), hsa-miR-519a (SEQ ID NO: 218) and hsa-miR-517c (SEQ ID NO: 214) also provides for classification of seminoma and non-seminoma testis-tumors.

[0334] hsa-miR-516a-5p (SEQ ID NO: 211) and hsa-miR-200b (SEQ ID NO: 29) are used at node 12 of the binary-tree-classifier detailed in the invention to distinguish between seminoma and non-seminoma testis-tumors.

[0335] FIG. **11** demonstrates that tumors originating in seminomatous testicular germ cell (marked by diamonds) are easily distinguished from tumors of non seminomatous origins (marked by squares) using the expression levels of hsa-miR-516a-5p (SEQ ID NO: 211, y-axis) and hsa-miR-200b (SEQ ID NO: 29, x-axis).

TABLE 14

miR expression (in fluorescence units) distinguishing between the group consisting of squamous cell carcinoma (SCC), transitional cell carcinoma (TCC), thymoma and the group consisting of non gastrointestinal (GI) adenocarcinoma tumors

miR name	SEQ ID NO.	p-value	fold-change	median values
hsa-miR-205	32	1.6e−059	321.76 (+)	4.6e+004-1.4e+002
hsa-miR-210	36	8.6e−015	5.96 (+)	2.9e+003-4.9e+002
hsa-miR-193b	178	2.6e−016	3.82 (+)	2.5e+003-6.6e+002
MID-16869	243	1.8e−008	3.67 (+)	2.5e+003-6.8e+002
MID-16489	242	2.2e−011	3.53 (+)	3.4e+003-9.7e+002
hsa-miR-31	49	8.2e−004	2.82 (+)	3.7e+003-1.3e+003
MID-15965	240	1.7e−010	2.78 (+)	6.4e+003-2.3e+003
hsa-miR-378	57	2.7e−017	2.71 (+)	1.4e+003-5.2e+002
hsa-miR-138	11	2.9e−023	8.05 (−)	2.8e+002-2.2e+003
hsa-miR-30a	46	1.5e−018	3.70 (−)	7.3e+002-2.7e+003
hsa-miR-146b-5p	17	4.0e−013	2.60 (−)	8.6e+002-2.2e+003
hsa-miR-30d	47	1.5e−021	2.44 (−)	1.8e+003-4.3e+003
hsa-miR-345	51	2.6e−019	2.38 (−)	4.5e+002-1.1e+003
hsa-miR-125a-5p	7	3.8e−014	2.30 (−)	4.2e+003-9.6e+003
hsa-miR-125b	8	3.0e−009	2.26 (−)	1.9e+004-4.3e+004
hsa-miR-181b	154	3.2e−008	2.24 (−)	9.4e+002-2.1e+003
hsa-miR-29b	190	3.3e−010	2.13 (−)	7.4e+002-1.6e+003
hsa-let-7i	157	4.6e−014	2.04 (−)	6.6e+003-1.3e+004
hsa-miR-30c	196	7.9e−010	2.04 (−)	2.4e+003-4.8e+003

(+) the higher expression of this miR is in SCC, TCC and thymoma
(−) the higher expression of this miR is in non GI adenocarcinoma

[0336] Node 13 of the binary-tree-classifier separates tissues with high expression of miR-205 (SCC marker) such as SCC, TCC and thymomas from adenocarcinomas.

[0337] Breast adenocarcinoma and ovarian carcinoma are excluded from this separation due to a wide range of expression of miR-205.

[0338] A combination of the expression level of any of the miRs detailed in table 14 with the expression level of hsa-miR-331-3p (SEQ ID NO: 197) also provides for this classification.

[0339] hsa-miR-205 (SEQ ID NO: 32), hsa-miR-345 (SEQ ID NO: 51) and hsa-miR-125a-5p (SEQ ID NO: 7) are used at node 13 of the binary-tree-classifier detailed in the invention.

TABLE 15

miR expression (in fluorescence units) distinguishing between the group consisting of breast adenocarcinoma and the group consisting of SCC, TCC, thymomas and ovarian carcinoma

miR name	SEQ ID NO.	p-value	fold-change	median values
hsa-miR-375	56	4.1e−029	25.95 (+)	1.3e+003-5.0e+001
hsa-miR-30a	46	1.6e−014	3.25 (+)	2.7e+003-8.3e+002
hsa-miR-193a-3p	25	9.5e−022	3.09 (+)	4.4e+003-1.4e+003
hsa-miR-182	152	2.1e−009	2.94 (+)	1.2e+003-4.1e+002
hsa-miR-342-3p	50	7.3e−014	2.48 (+)	5.5e+003-2.2e+003
hsa-miR-29c*	45	6.3e−008	2.48 (+)	6.6e+002-2.7e+002
hsa-miR-29c	191	5.8e−007	2.26 (+)	5.0e+002-2.2e+002

TABLE 15-continued

miR expression (in fluorescence units) distinguishing between the group consisting of breast adenocarcinoma and the group consisting of SCC, TCC, thymomas and ovarian carcinoma

miR name	SEQ ID NO.	p-value	fold-change	median values
hsa-miR-199a-3p	181	1.3e−004	2.19 (+)	7.3e+003-3.3e+003
hsa-miR-195	179	2.0e−006	2.05 (+)	2.2e+003-1.1e+003
hsa-miR-31	49	9.6e−014	13.81 (−)	2.2e+002-3.1e+003
hsa-miR-205	32	9.3e−008	6.32 (−)	6.3e+003-4.0e+004
hsa-miR-224	42	5.3e−010	5.72 (−)	8.9e+001-5.1e+002
hsa-miR-203	184	6.7e−007	4.05 (−)	1.5e+002-6.3e+002
hsa-miR-222	40	5.8e−018	2.64 (−)	5.7e+003-1.5e+004
hsa-miR-221	147	1.0e−018	2.41 (−)	3.8e+003-9.2e+003
MID-00689	236	4.9e−010	2.39 (−)	4.8e+002-1.1e+003
hsa-miR-378	57	1.2e−010	2.37 (−)	6.0e+002-1.4e+003
hsa-miR-422a	203	2.2e−008	2.24 (−)	2.3e+002-5.2e+002
hsa-miR-210	36	1.5e−007	2.22 (−)	1.2e+003-2.6e+003

(+) the higher expression of this miR is in breast adenocarcinoma
(−) the higher expression of this miR is in SCC, TCC, thymomas and ovarian carcinoma

[0340] hsa-miR-193a-3p (SEQ ID NO: 25), hsa-miR-375 (SEQ ID NO: 56) and hsa-miR-342-3p (SEQ ID NO: 50) are used at node 14 of the binary-tree-classifier detailed in the invention. According to another embodiment, hsa-miR-193a-3p (SEQ ID NO: 25), hsa-miR-375 (SEQ ID NO: 56) and hsa-miR-224 (SEQ ID NO: 42) may be used at node 14 of the binary-tree-classifier detailed in the invention.

TABLE 16

miR expression (in fluorescence units) distinguishing between the group consisting of ovarian carcinoma and the group consisting of SCC, TCC and thymomas

miR name	SEQ ID NO.	p-value	fold-change	median values
hsa-miR-10a	4	1.2e−012	5.57 (+)	3.1e+003-5.5e+002
hsa-miR-130a	10	1.7e−014	3.41 (+)	5.1e+003-1.5e+003
hsa-miR-30a*	195	1.3e−014	3.39 (+)	2.5e+002-7.5e+001
hsa-miR-10b	5	5.5e−009	2.68 (+)	2.4e+003-8.8e+002
hsa-miR-625	226	2.5e−012	2.48 (+)	2.9e+002-1.2e+002
hsa-let-7e	2	7.7e−012	2.28 (+)	8.8e+003-3.9e+003
hsa-miR-30a	46	3.6e−007	2.20 (+)	1.6e+003-7.3e+002
hsa-miR-205	32	1.0e−033	37.52 (−)	1.2e+003-4.6e+004
hsa-miR-205*	185	4.2e−018	5.42 (−)	5.0e+001-2.7e+002
hsa-miR-138	11	1.1e−009	4.63 (−)	6.0e+001 2.8e+002
hsa-miR-150	168	5.2e−010	4.18 (−)	5.7e+002-2.4e+003
hsa-miR-203	184	2.5e−003	2.74 (−)	2.9e+002-8.0e+002
hsa-miR-146a	16	2.1e−006	2.62 (−)	2.9e+002-7.6e+002
MID-16489	242	1.9e−007	2.49 (−)	1.4e+003-3.4e+003
hsa-miR-140-3p	12	2.3e−015	2.42 (−)	9.5e+002-2.3e+003
MID-15684	237	5.2e−006	2.37 (−)	7.6e+002-1.8e+003
MID-16869	243	9.8e−005	2.23 (−)	1.1e+003-2.5e+003
MID-20703	250	5.9e−004	2.18 (−)	2.1e+003-4.6e+003
hsa-miR-22	39	6.5e−012	2.13 (−)	2.7e+003-5.8e+003
MID-23256	253	1.0e−003	2.13 (−)	4.3e+002-9.2e+002
hsa-miR-31	49	1.4e−002	2.12 (−)	1.7e+003-3.7e+003
MID-18422	246	1.3e−003	2.06 (−)	1.7e+003-3.6e+003
hsa-miR-149*	167	1.4e−007	2.04 (−)	2.1e+003-4.4e+003

(+) the higher expression of this miR is in ovarian carcinoma
(−) the higher expression of this miR is in SCC, TCC and thymomas

[0341] hsa-miR-205 (SEQ ID NO: 32), hsa-miR-10a (SEQ ID NO: 4) and hsa-miR-22 (SEQ ID NO: 39) are used at node 15 of the binary-tree-classifier detailed in the invention.

TABLE 17

miR expression (in fluorescence units) distinguishing between the group consisting of thyroid carcinoma (follicular and papillary) and the group consisting of breast adenocarcinoma, lung large cell carcinoma, lung adenocarcinoma and ovarian carcinoma

miR name	SEQ ID NO.	p-value	fold-change	median values
hsa-miR-138	11	7.4e−033	33.86 (+)	4.1e+003-1.2e+002
hsa-miR-221	147	1.4e−009	5.03 (+)	3.4e+004-6.7e+003
hsa-miR-146b-5p	17	1.0e−006	4.74 (+)	4.9e+003-1.0e+003
hsa-let-7i	157	2.8e−027	3.71 (+)	2.2e+004-5.8e+003
hsa-miR-222	40	7.9e−009	3.63 (+)	3.9e+004-1.1e+004
hsa-miR-125b	8	1.5e−014	2.78 (+)	5.4e+004-1.9e+004
hsa-miR-31	49	5.0e−003	2.78 (+)	1.3e+003-4.9e+002
hsa-miR-126	9	1.3e−008	2.48 (+)	6.9e+003-2.8e+003
hsa-miR-29c	191	4.8e−007	2.36 (+)	8.1e+002-3.4e+002
hsa-miR-451	205	3.8e−003	2.33 (+)	1.3e+004-5.7e+003
hsa-miR-486-5p	207	1.3e−003	2.16 (+)	4.8e+002-2.2e+002
hsa-miR-30a*	195	8.0e−006	2.12 (+)	4.9e+002-2.3e+002
hsa-miR-345	51	2.7e−011	2.11 (+)	1.4e+003-6.6e+002
hsa-miR-30a	46	1.5e−006	2.10 (+)	.5e+003-1.7e+003
hsa-miR-29c*	45	1.5e−006	1.97 (+)	6.4e+002-3.2e+002
hsa-miR-34a	52	3.4e−007	1.88 (+)	7.4e+003-4.0e+003
hsa-miR-1977	234	5.9e−008	1.88 (+)	6.1e+003-3.3e+003
hsa-miR-99a	231	1.5e−005	1.85 (+)	7.5e+003-4.1e+003
hsa-miR-181a	21	2.7e−004	1.85 (+)	7.6e+003-4.1e+003
hsa-miR-152	169	5.1e−008	1.82 (+)	1.0e+003-5.5e+002
hsa-miR-29a	43	3.7e−008	1.79 (+)	1.1e+004-6.0e+003
hsa-miR-100	3	2.9e−005	1.77 (+)	5.4e+003-3.0e+003
hsa-miR-30c	196	7.3e−007	1.73 (+)	5.9e+003-3.4e+003
hsa-miR-181b	154	4.6e−004	1.69 (+)	2.1e+003-1.2e+003
MID-00405	390	6.4e−003	1.66 (+)	4.4e+002-2.6e+002
hsa-miR-15a	171	5.3e−006	1.65 (+)	5.5e+002-3.3e+002
MID-23794	255	6.0e−003	1.60 (+)	1.3e+003-8.1e+002
hsa-miR-331-3p	197	8.3e−007	1.57 (+)	2.3e+003-1.4e+003
hsa-miR-29b	190	1.4e−005	1.57 (+)	1.8e+003-1.1e+003
hsa-miR-27b	189	1.4e−003	1.56 (+)	3.6e+003-2.3e+003
hsa-miR-22	39	3.6e−005	1.52 (+)	6.6e+003-4.3e+003
hsa-miR-125a-5p	7	2.2e−006	1.52 (+)	9.9e+003-6.5e+003
hsa-miR-30e	48	6.2e−006	1.51 (+)	7.8e+002-5.2e+002
hsa-miR-30d	47	1.2e−002	1.51 (+)	4.3e+003-2.8e+003
hsa-miR-205	32	2.2e−005	22.05 (−)	1.0e+002-2.2e+003
hsa-miR-210	36	4.8e−020	8.83 (−)	2.1e+002-1.8e+003
hsa-miR-10a	4	8.7e−011	4.34 (−)	3.2e+002-1.4e+003
hsa-miR-193b	178	4.6e−014	3.59 (−)	4.9e+002-1.8e+003
hsa-miR-214	37	8.3e−006	2.74 (−)	1.0e+003-2.8e+003
hsa-miR-199a-3p	181	4.4e−005	2.67 (−)	2.0e+003-5.5e+003
hsa-miR-193a-3p	25	3.1e−011	2.65 (−)	1.1e+003-2.8e+003
hsa-miR-199b-5p	183	1.3e−004	2.63 (−)	2.7e+002-7.2e+002
hsa-miR-199a-5p	182	1.6e−005	2.57 (−)	3.1e+003-8.1e+003
hsa-miR-21*	35	4.7e−006	2.41 (−)	5.1e+002-1.2e+003
MID-15965	240	9.3e−003	2.39 (−)	2.0e+003-4.8e+003
hsa-miR-378	57	3.0e−006	2.35 (−)	3.4e+002-8.0e+002
MID-16489	242	1.2e−003	2.25 (−)	8.2e+002-1.9e+003
hsa-miR-425	204	1.4e−011	2.18 (−)	6.0e+002-1.3e+003
MID-00689	236	5.3e−006	2.06 (−)	3.0e+002-6.1e+002
hsa-miR-18a	176	2.0e−006	1.96 (−)	2.3e+002-4.5e+002
hsa-miR-106a	158	3.5e−006	1.85 (−)	2.3e+003-4.3e+003
hsa-miR-93	148	1.9e−010	1.79 (−)	2.4e+003-4.4e+003
hsa-miR-455-3p	206	1.9e−007	1.79 (−)	2.9e+002-5.2e+002
hsa-miR-342-3p	50	7.8e−005	1.78 (−)	1.3e+003-2.3e+003
hsa-miR-17	20	6.0e−006	1.75 (−)	1.4e+003-2.5e+003
hsa-miR-21	34	5.1e−006	1.75 (−)	2.8e+004-4.8e+004
hsa-miR-20a	186	1.1e−004	1.74 (−)	1.4e+003-2.4e+003
MID-15907	239	8.4e−004	1.72 (−)	2.4e+002-4.1e+002
MID-21271	251	9.9e−003	1.62 (−)	3.0e+002-4.8e+002
MID-17144	244	4.3e−002	1.60 (−)	2.2e+003-3.6e+003
hsa-miR-191	24	4.7e−006	1.59 (−)	3.8e+003-6.1e+003
hsa-miR-25	188	2.0e−005	1.59 (−)	1.0e+003-1.6e+003
hsa-miR-15b	172	1.9e−002	1.57 (−)	2.1e+003-3.2e+003
MID-15867	238	9.5e−003	1.56 (−)	2.6e+003-4.0e+003

(+) the higher expression of this miR is in thyroid carcinoma

(−) the higher expression of this miR is in breast adenocarcinoma, lung large cell carcinoma, lung adenocarcinoma and ovarian carcinoma

[0342] FIG. **12** demonstrates binary decisions at node #16 of the decision-tree. Tumors originating in thyroid carcinoma (diamonds) are easily distinguished from tumors of adenocarcinoma of the lung, breast and ovarian origin (squares) using the expression levels of hsa-miR-93 (SEQ ID NO: 148, y-axis), hsa-miR-138 (SEQ ID NO: 11, x-axis) and hsa-miR-10a (SEQ ID NO: 4, z-axis).

TABLE 18

miR expression (in fluorescence units) distinguishing between follicular thyroid carcinoma and papillary thyroid carcinoma

miR name	SEQ ID NO.	p-value	fold-change	median values
MID-20524	249	4.5e−011	9.34 (+)	6.6e+003-7.1e+002
hsa-miR-1973	180	1.9e−008	7.80 (+)	1.7e+003-2.2e+002
hsa-miR-7	65	8.3e−005	7.58 (+)	4.5e+002-5.9e+001
hsa-miR-1978	235	4.8e−007	6.52 (+)	2.5e+003-3.8e+002
MID-16318	241	1.5e−008	6.14 (+)	2.2e+003-3.6e+002
MID-19533	248	3.0e−004	6.00 (+)	4.2e+002-7.1e+001
MID-23291	254	1.6e−008	5.76 (+)	9.6e+002-1.7e+002
MID-19340	247	3.2e−005	5.33 (+)	9.9e+002-1.9e+002
hsa-miR-1248	160	6.8e−009	5.17 (+)	6.4e+002-1.2e+002
MID-16869	243	1.1e−006	4.97 (+)	1.5e+003-3.0e+002
MID-18336	245	1.4e−010	4.48 (+)	2.7e+003-6.1e+002
MID-22664	252	7.0e−004	4.00 (+)	5.0e+002-1.2e+002
hsa-miR-146b-5p	17	6.7e−011	62.88 (−)	4.0e+002-2.5e+004
hsa-miR-31	49	2.5e−008	18.72 (−)	4.4e+002-8.2e+003
hsa-miR-146b-3p	166	5.0e−012	18.69 (−)	5.0e+001-9.3e+002
hsa-miR-551b	225	4.8e−006	10.86 (−)	7.6e+001-8.3e+002
hsa-miR-150	168	3.2e−007	10.71 (−)	3.1e+002-3.3e+003
hsa-miR-21	34	3.4e−007	4.40 (−)	1.1e+004-4.7e+004

(+) the higher expression of this miR is in follicular thyroid carcinoma

(−) the higher expression of this miR is in papillary thyroid carcinoma

[0343] FIG. **13** demonstrates binary decisions at node #17 of the decision-tree. Tumors originating in follicular thyroid carcinoma (marked by diamonds) are easily distinguished from tumors of papillary thyroid carcinoma origins (marked by squares) using the expression levels of hsa-miR-21 (SEQ ID NO: 34, y-axis) and hsa-miR-146b-5p (SEQ ID NO: 17, x-axis).

TABLE 19

miR expression (in fluorescence units) distinguishing between the group consisting of breast adenocarcinoma and the group consisting of lung adenocarcinoma and ovarian carcinoma

miR name	SEQ ID NO.	p-value	fold-change	median values
hsa-miR-205	32	8.8e−005	10.55 (+)	6.3e+003-6.0e+002
hsa-miR-375	56	7.9e−006	8.43 (+)	1.3e+003-1.5e+002
hsa-miR-342-3p	50	7.7e−012	3.17 (+)	5.5e+003-1.7e+003
hsa-miR-29c*	45	2.2e−008	2.52 (+)	6.6e+002-2.6e+002
hsa-miR-193a-3p	25	2.2e−012	2.23 (+)	4.4e+003-2.0e+003
MID-23256	253	7.9e−005	2.20 (+)	9.5e+002-4.3e+002
hsa-miR-182	152	4.9e−005	2.15 (+)	1.2e+003-5.6e+002
hsa-miR-126	9	5.3e−005	1.94 (+)	3.7e+003-1.9e+003
hsa-miR-30a	46	2.9e−004	1.90 (+)	2.7e+003-1.4e+003
hsa-miR-29c	191	1.1e−004	1.78 (+)	5.0e+002-2.8e+002
hsa-miR-193b	178	1.5e−006	1.72 (+)	2.4e+003-1.4e+003
hsa-miR-31	49	7.7e−006	5.79 (−)	2.2e+002-1.3e+003
hsa-miR-222	40	3.0e−010	2.69 (−)	5.7e+003-1.5e+004
hsa-miR-130a	10	1.6e−006	2.50 (−)	1.4e+003-3.4e+003
hsa-miR-221	147	1.2e−009	2.41 (−)	3.8e+003-9.3e+003
hsa-miR-10a	4	2.2e−002	2.33 (−)	9.3e+002-2.2e+003
hsa-miR-210	36	1.5e−005	2.09 (−)	1.2e+003-2.5e+003
hsa-miR-886-3p	228	9.9e−005	2.01 (−)	1.3e+003-2.6e+003
MID-00689	236	4.6e−004	1.95 (−)	4.8e+002-9.4e+002
hsa-miR-886-5p	230	6.3e−004	1.92 (−)	5.3e+002-1.0e+003

TABLE 19-continued

miR expression (in fluorescence units) distinguishing between the group consisting of breast adenocarcinoma and the group consisting of lung adenocarcinoma and ovarian carcinoma

miR name	SEQ ID NO.	p-value	fold-change	median values
hsa-miR-27b	189	7.1e−005	1.86 (−)	1.8e+003-3.3e+003
MID-15965	240	6.1e−003	1.79 (−)	3.6e+003-6.4e+003
hsa-miR-92a	67	3.5e−005	1.75 (−)	2.7e+003-4.7e+003
hsa-miR-378	202	3.0e−004	1.73 (−)	6.0e+002-1.0e+003
hsa-miR-146b-5p	17	2.9e−004	1.71 (−)	8.0e+002-1.4e+003

(+) the higher expression of this miR is in breast adenocarcinoma

(−) the higher expression of this miR is in lung adenocarcinoma and ovarian carcinoma

[0344] FIG. **14** demonstrates binary decisions at node #18 of the decision-tree. Tumors originating in breast (diamonds) are easily distinguished from tumors of lung and ovarian origin (squares) using the expression levels of hsa-miR-92a (SEQ ID NO: 67, y-axis), hsa-miR-193a-3p (SEQ ID NO: 25, x-axis) and hsa-miR-31 (SEQ ID NO: 49, z-axis).

TABLE 20

miR expression (in fluorescence units) distinguishing between lung adenocarcinoma and ovarian carcinoma

median values	fold-change	p-value	SEQ ID NO.	miR name
1.4e+003-5.2e+001	27.96 (+)	3.5e−008	56	hsa-miR-375
5.5e+002-6.0e+001	9.19 (+)	8.1e−009	11	hsa-miR-138
3.2e+003-5.7e+002	5.65 (+)	5.6e−004	168	hsa-miR-150
9.7e+002-2.9e+002	3.35 (+)	2.2e−004	16	hsa-miR-146a
2.3e+003-7.6e+002	2.96 (+)	3.2e−003	237	MID-15684
8.4e+003-2.9e+003	2.88 (+)	1.7e−010	21	hsa-miR-181a
7.0e+003-2.6e+003	2.69 (+)	9.2e−008	52	hsa-miR-34a
2.4e+003-9.5e+002	2.58 (+)	3.2e−007	12	hsa-miR-140-3p
2.1e+003-8.8e+002	2.39 (+)	2.1e−007	154	hsa-miR-181b
1.4e+005-6.3e+004	2.28 (+)	1.9e−003	279	hsa-miR-1826
3.2e+003-1.4e+003	2.25 (+)	6.1e−003	9	hsa-miR-126
6.1e+003-2.7e+003	2.24 (+)	2.3e−006	39	hsa-miR-22
4.2e+003-2.2e+003	1.93 (+)	8.9e−005	47	hsa-miR-30d
1.9e+003-1.0e+003	1.90 (+)	3.5e−006	23	hsa-miR-185
2.8e+003-1.5e+003	1.88 (+)	1.4e−003	50	hsa-miR-342-3p
3.6e+003-2.1e+003	1.69 (+)	1.8e−002	167	hsa-miR-149*
9.7e+002-5.9e+002	1.66 (+)	8.7e−005	383	MID-22912
6.8e+004-4.2e+004	1.64 (+)	5.4e−004	34	hsa-miR-21
1.8e+003-1.2e+003	1.55 (+)	5.1e−004	35	hsa-miR-21*
1.4e+003-8.9e+002	1.54 (+)	1.7e−004	388	hsa-miR-423-5p
4.4e+002-2.4e+003	5.38 (−)	1.0e−007	5	hsa-miR-10b
1.9e+002-7.2e+002	3.77 (−)	3.3e−006	359	hsa-miR-708
6.4e+002-2.1e+003	3.27 (−)	5.8e−003	245	MID-18336
1.8e+002-5.4e+002	2.96 (−)	6.6e−003	254	MID-23291
1.7e+003-5.1e+003	2.95 (−)	3.4e−005	10	hsa-miR-130a
2.8e+003-8.1e+003	2.86 (−)	3.7e−003	240	MID-15965
5.1e+002-1.3e+003	2.65 (−)	3.7e−004	236	MID-00689
6.1e+002-1.6e+003	2.63 (−)	1.8e−004	202	hsa-miR-378
1.3e+003-3.1e+003	2.39 (−)	1.2e−002	4	hsa-miR-10a
1.0e+003-2.3e+003	2.30 (−)	1.8e−006	25	hsa-miR-193a-3p
2.6e+002-5.6e+002	2.15 (−)	4.1e−004	203	hsa-miR-422a
3.0e+003-6.1e+003	2.04 (−)	1.8e−002	231	hsa-miR-99a
2.0e+003-3.9e+003	2.01 (−)	3.5e−005	20	hsa-miR-17
3.3e+003-6.4e+003	1.96 (−)	3.5e−005	158	hsa-miR-106a
1.8e+003-3.5e+003	1.88 (−)	3.1e−005	186	hsa-miR-20a
3.2e+003-5.9e+003	1.85 (−)	1.2e−004	258	hsa-let-7f
2.4e+003-4.4e+003	1.85 (−)	2.0e−003	244	MID-17144
2.0e+003-3.5e+003	1.72 (−)	8.7e−004	172	hsa-miR-15b
5.2e+003-8.8e+003	1.69 (−)	5.3e−004	2	hsa-let-7e
4.1e+002-6.8e+002	1.66 (−)	1.2e−002	235	hsa-miR-1978
3.3e+004-5.4e+004	1.66 (−)	3.3e−005	256	hsa-let-7a
2.8e+003-4.7e+003	1.65 (−)	3.5e−003	28	hsa-miR-200a
5.2e+002-8.5e+002	1.62 (−)	1.6e−004	277	hsa-miR-17*

TABLE 20-continued

miR expression (in fluorescence units) distinguishing between lung adenocarcinoma and ovarian carcinoma

median values	fold-change	p-value	SEQ ID NO.	miR name
3.7e+002-5.8e+002	1.57 (−)	1.9e−003	296	hsa-miR-26b
1.0e+005-1.6e+005	1.56 (−)	3.7e−002	374	MID-16748
6.0e+003-9.1e+003	1.53 (−)	2.1e−005	153	hsa-let-7d
3.8e+003-5.7e+003	1.50 (−)	4.1e−003	181	hsa-miR-199a-3p

(+) the higher expression of this miR is in lung adenocarcinoma

(−) the higher expression of this miR is in ovarian carcinoma

[0345] FIG. **15** demonstrates binary decisions at node #19 of the decision-tree. Tumors originating in lung adenocarcinoma (diamonds) are easily distinguished from tumors of ovarian carcinoma origin (squares) using the expression levels of hsa-miR-21 (SEQ ID NO: 34, y-axis), hsa-miR-378 (SEQ ID NO: 202, x-axis) and hsa-miR-138 (SEQ ID NO: 11, z-axis).

TABLE 21

miR expression (in fluorescence units) distinguishing between the group consisting of thymic carcinoma and the group consisting of TCC and SCC

median values	fold-change	p-value	SEQ ID NO.	miR name
5.3e+002-5.9e+001	9.00 (+)	5.7e−026	161	hsa-miR-128
7.4e+002-9.2e+001	8.04 (+)	2.2e−007	164	hsa-miR-142-5p
6.8e+002-8.8e+001	7.82 (+)	2.6e−021	22	hsa-miR-181a*
7.1e+002-1.2e+002	6.09 (+)	1.2e−006	53	hsa-miR-34c-5p
9.1e+002-1.8e+002	5.06 (+)	2.2e−008	285	hsa-miR-20b
1.3e+004-2.8e+003	4.59 (+)	7.5e−014	3	hsa-miR-100
1.6e+003-3.6e+002	4.39 (+)	7.1e−007	152	hsa-miR-182
8.7e+002-2.0e+002	4.37 (+)	6.4e−010	191	hsa-miR-29c
3.7e+003-9.1e+002	4.09 (+)	2.6e−014	154	hsa-miR-181b
1.5e+004-3.8e+003	3.82 (+)	4.8e−009	21	hsa-miR-181a
2.1e+003-6.4e+002	3.25 (+)	6.4e−006	206	hsa-miR-455-3p
8.7e+002-2.7e+002	3.23 (+)	1.5e−010	174	hsa-miR-181d
9.4e+002-2.9e+002	3.23 (+)	1.9e−004	19	hsa-miR-149
7.3e+002-2.6e+002	2.80 (+)	2.5e−008	45	hsa-miR-29c*
8.7e+002-3.2e+002	2.69 (+)	2.2e−007	171	hsa-miR-15a
2.7e+003-1.0e+003	2.66 (+)	5.1e−005	179	hsa-miR-195
4.4e+004-1.8e+004	2.46 (+)	8.2e−008	8	hsa-miR-125b
7.3e+002-3.2e+002	2.26 (+)	2.8e−004	296	hsa-miR-26b
2.7e+003-1.2e+003	2.22 (+)	2.4e−003	284	hsa-miR-19b
5.7e+002-2.6e+002	2.17 (+)	7.8e−005	18	hsa-miR-148a
9.1e+002-4.4e+002	2.06 (+)	1.4e−006	51	hsa-miR-345
7.5e+003-3.8e+003	2.00 (+)	1.6e−002	258	hsa-let-7f
1.8e+002-4.4e+003	24.66 (−)	3.9e−008	49	hsa-miR-31
5.8e+001-1.0e+003	17.65 (−)	1.0e−007	184	hsa-miR-203
2.2e+002-1.6e+003	7.43 (−)	4.5e−018	35	hsa-miR-21*
1.1e+004-5.5e+004	4.97 (−)	1.5e−032	34	hsa-miR-21
6.2e+002-2.5e+003	4.06 (−)	2.0e−008	37	hsa-miR-214
1.6e+002-5.8e+002	3.69 (−)	6.3e−005	42	hsa-miR-224
6.9e+002-2.5e+003	3.58 (−)	2.3e−009	228	hsa-miR-886-3p
4.8e+003-1.7e+004	3.47 (−)	3.9e−009	15	hsa-miR-145
2.7e+003-8.2e+003	3.08 (−)	2.7e−008	14	hsa-miR-143
1.3e+003-3.7e+003	2.93 (−)	6.7e−005	242	MID-16489
2.5e+002-7.4e+002	2.91 (−)	4.3e−006	230	hsa-miR-886-5p
3.5e+002-1.0e+003	2.90 (−)	5.6e−004	253	MID-23256
1.1e+003-3.0e+003	2.82 (−)	7.9e−006	36	hsa-miR-210
2.2e+003-5.8e+003	2.63 (−)	1.2e−007	182	hsa-miR-199a-5p
5.0e+003-1.2e+004	2.48 (−)	3.8e−006	293	hsa-miR-23b
7.5e+003-1.8e+004	2.44 (−)	1.1e−008	292	hsa-miR-23a
2.7e+002-6.6e+002	2.43 (−)	5.4e−003	4	hsa-miR-10a
9.0e+003-2.2e+004	2.43 (−)	5.5e−015	294	hsa-miR-24
3.8e+003-8.8e+003	2.35 (−)	3.0e−004	297	hsa-miR-27a
2.3e+002-5.2e+002	2.28 (−)	1.6e−002	354	hsa-miR-612
1.8e+003-3.9e+003	2.22 (−)	1.1e−006	377	MID-17866
1.6e+003-3.3e+003	2.11 (−)	2.4e−004	189	hsa-miR-27b

TABLE 21-continued

miR expression (in fluorescence units) distinguishing between the group consisting of thymic carcinoma and the group consisting of TCC and SCC

median values	fold-change	p-value	SEQ ID NO.	miR name
6.9e+003-1.4e+004	2.08 (−)	1.5e−004	30	hsa-miR-200c
3.8e+004-7.9e+004	2.05 (−)	1.8e−008	386	MID-23178
1.5e+003-3.1e+003	2.04 (−)	2.6e−002	249	MID-20524
4.6e+002-9.3e+002	2.03 (−)	5.6e−002	5	hsa-miR-10b
2.5e+002-5.0e+002	2.03 (−)	3.2e−005	274	hsa-miR-151-3p

(+) the higher expression of this miR is in thymic carcinoma

(−) the higher expression of this miR is in TCC and SCC

[0346] FIG. **16** demonstrates binary decisions at node #20 of the decision-tree. Tumors originating in thymic carcinoma (marked by diamonds) are easily distinguished from tumors of urothelial carcinoma, transitional cell carcinoma (TCC) carcinoma and squamous cell carcinoma (SCC) origins (marked by squares) using the expression levels of hsa-miR-21 (SEQ ID NO: 34, y-axis) and hsa-miR-100 (SEQ ID NO: 3, x-axis).

TABLE 22

miR expression (in fluorescence units) distinguishing between TCC and SCC (of anus, skin, lung, head&neck, esophagus or uterine cervix)

median values	fold-change	p-value	SEQ ID NO.	miR name
2.5e+002-5.0e+001	5.05 (+)	7.4e−036	69	hsa-miR-934
9.1e+003-2.2e+003	4.14 (+)	1.2e−012	28	hsa-miR-200a
2.1e+002-5.3e+001	3.87 (+)	8.4e−007	280	hsa-miR-187

TABLE 22-continued

miR expression (in fluorescence units) distinguishing between TCC and SCC (of anus, skin, lung, head&neck, esophagus or uterine cervix)

median values	fold-change	p-value	SEQ ID NO.	miR name
6.0e+003-1.9e+003	3.19 (+)	9.8e−008	13	hsa-miR-141
5.6e+002-1.8e+002	3.15 (+)	4.7e−013	191	hsa-miR-29c
9.4e+002-3.0e+002	3.13 (+)	8.1e−008	152	hsa-miR-182
1.8e+004-6.2e+003	2.99 (+)	3.9e−010	29	hsa-miR-200b
3.2e+002-1.1e+002	2.81 (+)	8.8e−009	175	hsa-miR-183
3.1e+004-1.2e+004	2.65 (+)	8.1e−005	30	hsa-miR-200c
2.1e+003-8.1e+002	2.63 (+)	6.2e−020	204	hsa-miR-425
1.2e+003-4.8e+002	2.41 (+)	6.3e−007	4	hsa-miR-10a
8.5e+003-3.7e+003	2.30 (+)	2.4e−024	24	hsa-miR-191
1.8e+003-8.4e+002	2.14 (+)	2.7e−006	5	hsa-miR-10b
3.5e+002-1.7e+002	2.09 (+)	2.0e−006	329	hsa-miR-425*
3.4e+002-1.6e+002	2.08 (+)	8.0e−005	273	hsa-miR-148b
3.1e+002-8.1e+002	2.60 (−)	1.6e−005	170	hsa-miR-155
5.0e+002-1.2e+003	2.49 (−)	1.0e−002	184	hsa-miR-203
1.5e+002-3.5e+002	2.39 (−)	3.0e−011	26	hsa-miR-193a-5p
1.9e+003-4.5e+003	2.35 (−)	1.3e−008	231	hsa-miR-99a
1.2e+002-2.7e+002	2.28 (−)	1.6e−003	368	MID-00672
1.4e+003-3.2e+003	2.25 (−)	1.3e−005	37	hsa-miR-214
3.9e+002-8.7e+002	2.23 (−)	1.5e−004	16	hsa-miR-146a
3.5e+002-7.6e+002	2.15 (−)	4.2e−005	169	hsa-miR-152
1.5e+002-3.3e+002	2.15 (−)	4.4e−004	155	hsa-miR-127-3p
8.4e+002-1.7e+003	2.08 (−)	1.6e−005	35	hsa-miR-21*
7.7e+003-1.6e+004	2.07 (−)	5.3e−012	40	hsa-miR-222
4.4e+002-9.0e+002	2.06 (−)	1.5e−005	17	hsa-miR-146b-5p

(+) the higher expression of this miR is in TCC

(−) the higher expression of this miR is in SCC

[0347] hsa-miR-934 (SEQ ID NO: 69), hsa-miR-191 (SEQ ID NO: 24) and hsa-miR-29c (SEQ ID NO: 191) are used at node #21 of the binary-tree-classifier detailed in the invention to distinguish between TCC and SCC.

TABLE 23

miR expression (in fluorescence units) distinguishing between SCC of the uterine cervix and other SCC tumors (anus, skin, lung, head& neck or esophagus)

median values	auROC	fold-change	p-value	SEQ ID NO.	miR name
2.4e+002-9.2e+001	0.65	2.57 (+)	2.0e−002	164	hsa-miR-142-5p
1.6e+003-7.6e+002	0.85	2.13 (+)	1.7e−005	5	hsa-miR-10b
8.9e+003-4.4e+003	0.74	2.01 (+)	2.1e−004	231	hsa-miR-99a
1.2e+003-9.8e+002	0.71	1.24 (+)	1.2e−002	54	hsa-miR-361-5p
3.4e+004-2.7e+004	0.71	1.24 (+)	3.9e−004	1	hsa-let-7c
1.3e+003-4.3e+003	0.81	3.39 (−)	9.9e−006	242	MID-16489
3.9e+002-1.2e+003	0.74	3.10 (−)	2.1e−003	372	MID-16469
1.1e+003-3.3e+003	0.84	3.09 (−)	1.3e−008	249	MID-20524
1.7e+003-5.2e+003	0.78	3.01 (−)	2.4e−005	167	hsa-miR-149*
2.7e+002-8.0e+002	0.79	2.97 (−)	1.4e−004	254	MID-23291
2.2e+002-6.2e+002	0.76	2.77 (−)	1.7e−004	354	hsa-miR-612
5.7e+002-1.5e+003	0.76	2.65 (−)	7.8e−006	381	MID-19962
2.3e+002-6.0e+002	0.79	2.63 (−)	2.1e−005	380	MID-19898
9.8e+002-2.4e+003	0.78	2.44 (−)	2.8e−005	245	MID-18336
1.2e+002-2.8e+002	0.73	2.34 (−)	5.3e−003	358	hsa-miR-665
6.1e+002-1.4e+003	0.70	2.31 (−)	6.1e−003	364	MID-00064
2.9e+003-6.7e+003	0.81	2.30 (−)	8.8e−008	240	MID-15965
1.2e+002-2.8e+002	0.66	2.26 (−)	1.5e−002	11	hsa-miR-138
1.0e+002-2.3e+002	0.77	2.24 (−)	8.9e−005	378	MID-18307

(+) the higher expression of this miR is in SCC of the uterine cervix

(−) the higher expression of this miR is in other SCC tumors

[0348] FIG. **17** demonstrates binary decisions at node #22 of the decision-tree. Tumors originating in SCC of the uterine cervix (diamonds) are easily distinguished from tumors of other SCC origin (squares) using the expression levels of hsa-miR-361-5p (SEQ ID NO: 54, y-axis), hsa-let-7c (SEQ ID NO: 1, x-axis) and hsa-miR-10b (SEQ ID NO: 5, z-axis).

TABLE 24

miR expression (in fluorescence units) distinguishing between anus or skin SCC and upper SCC tumors (lung, head& neck or esophagus)

median values	auROC	fold-change	p-value	SEQ ID NO.	miR name
3.2e+002-5.0e+001	0.78	6.38 (+)	3.0e−006	305	hsa-miR-31*
4.3e+003-8.0e+002	0.80	5.39 (+)	1.8e−006	184	hsa-miR-203
8.6e+002-2.5e+002	0.78	3.49 (+)	1.8e−006	41	hsa-miR-223
1.7e+003-5.4e+002	0.80	3.12 (+)	3.5e−006	183	hsa-miR-199b-5p
9.4e+003-3.5e+003	0.70	2.73 (+)	2.4e−003	49	hsa-miR-31
8.7e+003-3.2e+003	0.86	2.71 (+)	3.6e−007	382	MID-22331
1.9e+003-7.1e+002	0.87	2.68 (+)	1.7e−008	235	hsa-miR-1978
2.4e+002-9.2e+001	0.83	2.55 (+)	9.6e−009	291	hsa-miR-222*
6.8e+003-2.9e+003	0.74	2.31 (+)	7.4e−004	181	hsa-miR-199a-3p
1.5e+003-6.7e+002	0.88	2.28 (+)	7.1e−007	5	hsa-miR-10b
5.3e+002-2.4e+002	0.75	2.21 (+)	1.4e−004	296	hsa-miR-26b
3.4e+002-1.6e+002	0.74	2.19 (+)	7.7e−005	289	hsa-miR-22*
1.3e+003-6.0e+002	0.71	2.13 (+)	1.2e−003	206	hsa-miR-455-3p
7.9e+003-3.8e+003	0.84	2.11 (+)	4.2e−006	338	hsa-miR-494
2.9e+002-1.4e+002	0.73	2.08 (+)	1.1e−004	334	hsa-miR-483-5p
2.8e+003-1.3e+003	0.82	2.07 (+)	4.5e−006	25	hsa-miR-193a-3p
1.1e+002-3.3e+002	0.77	3.03 (−)	2.3e−005	11	hsa-miR-138
1.3e+002-3.1e+002	0.65	2.29 (−)	1.5e−002	19	hsa-miR-149
9.7e+001-2.1e+002	0.75	2.16 (−)	4.0e−005	198	hsa-miR-342-5p
1.1e+003-1.8e+003	0.83	1.63 (−)	1.1e−006	23	hsa-miR-185

(+) the higher expression of this miR is in anus or skin SCC

(−) the higher expression of this miR is in upper SCC tumors

[0349] hsa-miR-10b (SEQ ID NO: 5), hsa-miR-138 (SEQ ID NO: 11) and hsa-miR-185 (SEQ ID NO: 23) are used at node 23 of the binary-tree-classifier detailed in the invention to distinguish between anus or skin SCC and upper SCC tumors.

TABLE 25

miR expression (in fluorescence units) distinguishing between melanoma and lymphoma (B-cell or T-cell) tumors

median values	auROC	fold-change	p-value	SEQ ID NO.	miR name
1.7e+003-3.0e+002	0.89	5.81 (+)	2.8e−010	4	hsa-miR-10a
1.9e+003-6.0e+002	0.80	3.13 (+)	7.9e−005	11	hsa-miR-138
1.7e+003-5.7e+002	0.94	2.98 (+)	2.3e−011	46	hsa-miR-30a
2.5e+004-8.8e+003	0.87	2.83 (+)	1.1e−009	8	hsa-miR-125b
6.2e+002-2.3e+002	0.94	2.74 (+)	9.2e−011	274	hsa-miR-151-3p
9.2e+002-3.4e+002	0.87	2.70 (+)	1.9e−007	169	hsa-miR-152
1.6e+003-6.0e+002	0.77	2.60 (+)	2.0e−004	36	hsa-miR-210
4.8e+003-1.9e+003	0.90	2.56 (+)	2.1e−011	47	hsa-miR-30d
1.2e+003-5.5e+002	0.88	2.26 (+)	2.5e−008	363	hsa-miR-99b
2.4e+003-1.1e+003	0.85	2.24 (+)	1.4e−006	231	hsa-miR-99a
6.5e+003-3.0e+003	0.80	2.17 (+)	2.2e−005	303	hsa-miR-30b
6.4e+002-3.0e+002	0.86	2.14 (+)	2.9e−008	349	hsa-miR-532-5p
2.1e+003-1.0e+003	0.86	2.08 (+)	1.6e−006	10	hsa-miR-130a
5.4e+003-2.6e+003	0.81	2.06 (+)	8.3e−006	7	hsa-miR-125a-5p
3.6e+003-1.8e+003	0.82	2.05 (+)	2.5e−006	3	hsa-miR-100
7.9e+003-3.9e+003	0.69	2.04 (+)	1.5e−002	16	hsa-miR-146a
1.6e+002-2.2e+003	0.93	13.84 (−)	1.1e−014	164	hsa-miR-142-5p
7.2e+002-7.5e+003	0.93	10.40 (−)	1.1e−013	170	hsa-miR-155
2.0e+003-1.4e+004	0.90	7.18 (−)	2.2e−010	168	hsa-miR-150
1.7e+002-7.0e+002	0.91	4.14 (−)	5.2e−011	198	hsa-miR-342-5p
2.2e+003-8.3e+003	0.97	3.83 (−)	6.2e−019	50	hsa-miR-342-3p
9.1e+002-2.6e+003	0.86	2.87 (−)	1.3e−008	245	MID-18336
2.3e+002-6.4e+002	0.77	2.74 (−)	2.4e−004	365	MID-00078
1.9e+002-5.2e+002	0.78	2.68 (−)	4.7e−004	45	hsa-miR-29c*
2.8e+003-6.6e+003	0.74	2.34 (−)	1.6e−003	382	MID-22331

TABLE 25-continued

miR expression (in fluorescence units) distinguishing between melanoma and lymphoma (B-cell or T-cell) tumors

median values	auROC	fold-change	p-value	SEQ ID NO.	miR name
3.4e+003-7.9e+003	0.85	2.30 (−)	1.2e−004	259	hsa-let-7g
3.8e+002-8.5e+002	0.75	2.25 (−)	4.3e−003	296	hsa-miR-26b
7.5e+002-1.6e+003	0.78	2.16 (−)	2.3e−004	364	MID-00064
6.3e+002-1.3e+003	0.79	2.08 (−)	7.9e−005	314	hsa-miR-361-3p
2.7e+003-5.4e+003	0.80	2.05 (−)	7.5e−007	12	hsa-miR-140-3p

(+) the higher expression of this miR is in melanoma
(−) the higher expression of this miR is in lymphoma

[0350] FIG. **18** demonstrates binary decisions at node #24 of the decision-tree. Tumors originating in melanoma (diamonds) are easily distinguished from tumors of lymphoma origin (squares) using the expression levels of hsa-miR-342-3p (SEQ ID NO: 50, y-axis) and hsa-miR-30d (SEQ ID NO: 47, x-axis).

TABLE 26

miR expression (in fluorescence units) distinguishing between B-cell lymphoma and T-cell lymphoma

median values	auROC	fold-change	p-value	SEQ ID NO.	miR name
8.3e+002-2.8e+002	0.74	2.96 (+)	3.7e−005	11	hsa-miR-138
6.7e+002-2.8e+002	0.72	2.37 (+)	2.2e−003	191	hsa-miR-29c
1.2e+003-5.9e+002	0.76	2.02 (+)	1.4e−003	48	hsa-miR-30e

TABLE 26-continued

miR expression (in fluorescence units) distinguishing between B-cell lymphoma and T-cell lymphoma

median values	auROC	fold-change	p-value	SEQ ID NO.	miR name
6.7e+002-1.8e+003	0.79	2.77 (−)	1.1e−006	35	hsa-miR-21*
1.5e+003-3.9e+003	0.68	2.68 (−)	2.6e−003	228	hsa-miR-886-3p

(+) the higher expression of this miR is in B-cell lymphoma
(−) the higher expression of this miR is in T-cell lymphoma

[0351] hsa-miR-30e (SEQ ID NO: 48) and hsa-miR-21* (SEQ ID NO: 35) are used at node 25 of the binary-tree-classifier detailed in the invention to distinguish between B-cell lymphoma and T-cell lymphoma.

TABLE 27

miR expression (in fluorescence units) distinguishing between lung small cell carcinoma and other neuroendocrine tumors selected from the group consisting of lung carcinoid, medullary thyroid carcinoma, gastrointestinal tract carcinoid and pancreatic islet cell tumor

median values	auROC	fold-change	p-value	SEQ ID NO.	miR name
1.2e+004-1.2e+003	0.99	9.68 (+)	3.3e−021	158	hsa-miR-106a
7.3e+003-7.9e+002	1.00	9.17 (+)	3.4e−022	20	hsa-miR-17
1.4e+003-1.6e+002	0.99	8.53 (+)	8.2e−022	176	hsa-miR-18a
5.8e+003-7.0e+002	1.00	8.38 (+)	7.4e−021	186	hsa-miR-20a
1.1e+004-1.5e+003	0.98	7.71 (+)	1.7e−022	148	hsa-miR-93
4.7e+003-6.7e+002	0.89	6.99 (+)	1.0e−008	36	hsa-miR-210
2.2e+003-3.7e+002	0.95	5.87 (+)	2.8e−016	51	hsa-miR-345
8.9e+003-1.8e+003	0.95	4.96 (+)	1.6e−010	172	hsa-miR-15b
8.2e+003-1.8e+003	0.98	4.68 (+)	6.3e−020	260	hsa-miR-106b
1.1e+003-2.4e+002	0.91	4.62 (+)	7.7e−010	265	hsa-miR-130b
8.0e+003-1.8e+003	0.94	4.33 (+)	2.7e−013	67	hsa-miR-92a
4.1e+003-9.8e+002	0.98	4.15 (+)	2.6e−019	188	hsa-miR-25
1.1e+003-3.4e+002	0.98	3.40 (+)	7.9e−016	277	hsa-miR-17*
2.5e+003-8.3e+002	0.99	2.96 (+)	1.8e−011	284	hsa-miR-19b
5.1e+002-1.8e+002	0.74	2.84 (+)	6.1e−004	302	hsa-miR-301a
7.9e+002-2.9e+002	0.91	2.78 (+)	8.7e−010	68	hsa-miR-92b
9.9e+002-4.3e+002	0.69	2.28 (+)	5.1e−002	168	hsa-miR-150
2.5e+003-1.1e+003	0.70	2.24 (+)	4.5e−003	242	MID-16489
1.4e+003-6.6e+002	0.91	2.12 (+)	1.1e−009	204	hsa-miR-425
5.0e+001-1.6e+003	0.91	31.23 (−)	4.5e−009	162	hsa-miR-129-3p
1.1e+002-1.6e+003	0.91	14.13 (−)	8.6e−009	177	hsa-miR-192
7.6e+001-7.9e+002	0.91	10.42 (−)	1.5e−008	27	hsa-miR-194
5.5e+002-5.0e+003	0.92	9.14 (−)	1.7e−009	65	hsa-miR-7
7.1e+001-5.7e+002	0.78	8.02 (−)	5.8e−005	263	hsa-miR-129*
2.5e+002-1.6e+003	0.80	6.30 (−)	3.5e−005	155	hsa-miR-127-3p
1.5e+002-9.1e+002	0.96	6.05 (−)	3.5e−015	191	hsa-miR-29c
3.3e+002-2.0e+003	0.93	5.99 (−)	3.3e−013	190	hsa-miR-29b
1.7e+002-9.9e+002	0.99	5.76 (−)	1.3e−020	45	hsa-miR-29c*

TABLE 27-continued

miR expression (in fluorescence units) distinguishing between lung small cell carcinoma and other neuroendocrine tumors selected from the group consisting of lung carcinoid, medullary thyroid carcinoma, gastrointestinal tract carcinoid and pancreatic islet cell tumor

median values	auROC	fold-change	p-value	SEQ ID NO.	miR name
1.2e+002-6.6e+002	0.75	5.60 (−)	8.0e−004	59	hsa-miR-487b
1.8e+003-8.0e+003	0.90	4.44 (−)	1.6e−012	43	hsa-miR-29a
1.3e+004-4.9e+004	0.88	3.87 (−)	3.3e−006	56	hsa-miR-375
1.6e+002-5.5e+002	0.95	3.37 (−)	9.6e−011	266	hsa-miR-132
4.0e+003-1.2e+004	0.82	2.98 (−)	9.4e−006	14	hsa-miR-143
7.8e+003-2.3e+004	0.85	2.89 (−)	6.1e−006	15	hsa-miR-145
1.2e+004-3.4e+004	0.79	2.83 (−)	4.3e−005	8	hsa-miR-125b
4.5e+003-1.2e+004	0.97	2.70 (−)	1.7e−014	7	hsa-miR-125a-5p
1.9e+003-5.0e+003	0.89	2.67 (−)	3.6e−010	39	hsa-miR-22
2.5e+003-5.7e+003	0.79	2.25 (−)	8.7e−004	189	hsa-miR-27b
1.1e+003-2.4e+003	0.64	2.18 (−)	4.1e−002	249	MID-20524
2.2e+003-4.8e+003	0.72	2.14 (−)	8.5e−003	231	hsa-miR-99a
9.6e+003-2.0e+004	0.82	2.12 (−)	1.3e−003	293	hsa-miR-23b
5.1e+003-1.0e+004	0.80	2.01 (−)	6.3e−005	2	hsa-let-7e

(+) the higher expression of this miR is in lung small cell carcinoma

(−) the higher expression of this miR is in other neuroendocrine tumors

[0352] hsa-miR-17 (SEQ ID NO: 20) and hsa-miR-29c* (SEQ ID NO: 45) are used at node #26 of the binary-tree-classifier detailed in the invention to distinguish between lung small cell carcinoma and other neuroendocrine tumors.

TABLE 28

miR expression (in fluorescence units) distinguishing between medullary thyroid carcinoma and other neuroendocrine tumors selected from the group consisting of lung carcinoid, gastrointestinal tract carcinoid and pancreatic islet cell tumor

median values	auROC	fold-change	p-value	SEQ ID NO.	miR name
4.4e+003-5.5e+001	0.84	79.70 (+)	1.5e−007	159	hsa-miR-124
4.0e+004-4.9e+003	0.98	8.07 (+)	1.6e−015	40	hsa-miR-222
1.9e+004-2.8e+003	0.98	6.85 (+)	4.8e−016	147	hsa-miR-221
1.1e+003-2.0e+002	0.70	5.55 (+)	1.1e−003	11	hsa-miR-138
3.2e+002-7.8e+001	0.83	4.12 (+)	7.6e−007	311	hsa-miR-335
5.8e+003-1.5e+003	0.86	3.91 (+)	1.3e−006	4	hsa-miR-10a
6.3e+004-1.7e+004	0.83	3.61 (+)	3.9e−006	8	hsa-miR-125b
1.1e+004-3.2e+003	0.79	3.43 (+)	5.5e−005	231	hsa-miR-99a
4.3e+002-2.0e+002	0.78	2.10 (+)	2.8e−004	301	hsa-miR-29b-2*
7.9e+003-3.8e+003	0.82	2.06 (+)	4.4e−005	297	hsa-miR-27a
1.4e+002-4.0e+002	0.95	2.95 (−)	7.5e−011	68	hsa-miR-92b
1.1e+003-2.8e+003	0.87	2.50 (−)	3.2e−006	67	hsa-miR-92a
1.8e+002-3.7e+002	0.76	2.07 (−)	2.0e−003	265	hsa-miR-130b
4.4e+002-9.0e+002	0.75	2.04 (−)	2.1e−003	36	hsa-miR-210

(+) the higher expression of this miR is in medullary thyroid carcinoma

(−) the higher expression of this miR is in other neuroendocrine tumors

[0353] FIG. **19** demonstrates binary decisions at node #27 of the decision-tree. Tumors originating in medullary thyroid carcinoma (diamonds) are easily distinguished from tumors of other neuroendocrine origin (squares) using the expression levels of hsa-miR-92b (SEQ ID NO: 68, y-axis), hsa-miR-222 (SEQ ID NO: 40, x-axis) and hsa-miR-92a (SEQ ID NO: 67, z-axis).

TABLE 29

miR expression (in fluorescence units) distinguishing between lung carcinoid tumors and GI neuroendocrine tumors selected from the group consisting of gastrointestinal tract carcinoid and pancreatic islet cell tumor

median values	auROC	fold-change	p-value	SEQ ID NO.	miR name
4.0e+003-9.9e+001	0.90	40.08 (+)	1.9e−010	331	hsa-miR-432
6.0e+003-1.5e+002	0.86	39.24 (+)	4.6e−008	162	hsa-miR-129-3p
6.3e+003-1.9e+002	0.87	34.16 (+)	7.8e−009	59	hsa-miR-487b
1.3e+003-5.5e+001	0.88	23.36 (+)	2.9e−010	326	hsa-miR-409-5p
1.1e+003-5.0e+001	0.88	21.14 (+)	5.2e−010	306	hsa-miR-323-3p
1.0e+003-5.5e+001	0.87	18.59 (+)	1.5e−009	350	hsa-miR-539
7.9e+002-5.6e+001	0.84	14.25 (+)	1.4e−008	317	hsa-miR-369-5p
1.0e+004-7.2e+002	0.86	13.95 (+)	3.2e−007	155	hsa-miR-127-3p
1.7e+003-1.2e+002	0.86	13.60 (+)	2.1e−008	325	hsa-miR-409-3p
1.6e+003-1.2e+002	0.88	13.10 (+)	4.2e−009	318	hsa-miR-370
9.5e+002-7.3e+001	0.81	13.03 (+)	3.1e−006	339	hsa-miR-495
9.5e+002-7.4e+001	0.84	12.92 (+)	5.7e−007	264	hsa-miR-129-5p
6.4e+002-5.0e+001	0.91	12.84 (+)	1.6e−013	332	hsa-miR-433
6.5e+002-5.7e+001	0.88	11.52 (+)	5.1e−011	262	hsa-miR-127-5p
5.6e+002-5.2e+001	0.90	10.76 (+)	2.7e−012	336	hsa-miR-485-5p
2.0e+003-1.9e+002	0.86	10.44 (+)	4.2e−008	324	hsa-miR-382
7.9e+002-7.8e+001	0.83	10.20 (+)	1.3e−007	322	hsa-miR-379
6.0e+002-5.9e+001	0.89	10.15 (+)	9.6e−012	330	hsa-miR-431*
4.7e+002-5.0e+001	0.90	9.41 (+)	6.1e−012	321	hsa-miR-377*
1.3e+003-1.4e+002	0.80	9.40 (+)	1.5e−005	263	hsa-miR-129*
4.7e+002-5.0e+001	0.86	9.35 (+)	1.8e−008	309	hsa-miR-329
4.9e+002-5.3e+001	0.79	9.24 (+)	3.1e−005	53	hsa-miR-34c-5p
1.1e+003-1.2e+002	0.83	9.05 (+)	6.4e−007	320	hsa-miR-376c
1.1e+003-1.2e+002	0.86	8.81 (+)	2.3e−008	275	hsa-miR-154
6.5e+002-8.4e+001	0.83	7.73 (+)	8.1e−007	352	hsa-miR-543
9.9e+002-1.3e+002	0.82	7.49 (+)	3.2e−007	312	hsa-miR-337-5p
6.2e+002-8.8e+001	0.86	7.10 (+)	3.0e−008	355	hsa-miR-654-3p
3.5e+002-5.0e+001	0.91	7.05 (+)	3.2e−013	367	MID-00465
6.0e+002-1.0e+002	0.84	5.76 (+)	5.9e−007	269	hsa-miR-134
3.2e+003-8.5e+002	0.91	3.84 (+)	1.2e−011	64	hsa-miR-652
3.2e+002-1.1e+002	0.83	2.84 (+)	2.3e−005	308	hsa-miR-328
2.6e+003-9.4e+002	0.74	2.78 (+)	1.1e−003	175	hsa-miR-183
2.8e+003-1.0e+003	0.87	2.73 (+)	3.0e−006	190	hsa-miR-29b
3.9e+003-1.6e+003	0.88	2.49 (+)	6.9e−010	54	hsa-miR-361-5p
4.1e+002-1.7e+002	0.67	2.44 (+)	2.1e−002	302	hsa-miR-301a
4.0e+003-1.7e+003	0.79	2.41 (+)	5.9e−004	152	hsa-miR-182
4.0e+002-1.7e+002	0.88	2.39 (+)	4.7e−007	301	hsa-miR-29b-2*
8.7e+002-3.7e+002	0.77	2.36 (+)	6.8e−005	266	hsa-miR-132
7.7e+003-3.3e+003	0.82	2.34 (+)	5.4e−006	47	hsa-miR-30d
3.7e+002-1.6e+002	0.70	2.32 (+)	5.8e−003	313	hsa-miR-338-3p
3.3e+002-1.5e+002	0.66	2.16 (+)	1.3e−002	359	hsa-miR-708
5.5e+003-2.5e+003	0.68	2.16 (+)	4.2e−002	65	hsa-miR-7
2.1e+003-9.9e+002	0.78	2.13 (+)	7.0e−005	307	hsa-miR-324-5p
1.2e+003-5.9e+002	0.81	2.02 (+)	1.6e−004	191	hsa-miR-29c
3.5e+002-1.9e+003	0.88	5.36 (−)	1.0e−007	242	MID-16489
6.5e+002-1.9e+003	0.76	2.96 (−)	4.9e−004	4	hsa-miR-10a
1.3e+003-3.6e+003	0.84	2.79 (−)	1.9e−006	147	hsa-miR-221
2.2e+003-5.9e+003	0.81	2.75 (−)	8.5e−006	40	hsa-miR-222
2.6e+002-6.8e+002	0.76	2.56 (−)	7.4e−004	372	MID-16469
3.5e+002-8.9e+002	0.71	2.56 (−)	4.7e−003	168	hsa-miR-150
1.5e+002-3.7e+002	0.83	2.55 (−)	4.8e−005	16	hsa-miR-146a
1.9e+003-4.7e+003	0.82	2.40 (−)	1.7e−005	182	hsa-miR-199a-5p
1.3e+003-3.0e+003	0.79	2.35 (−)	1.2e−004	167	hsa-miR-149*
2.1e+002-4.8e+002	0.84	2.26 (−)	3.1e−005	356	hsa-miR-658
1.2e+003-2.8e+003	0.74	2.25 (−)	1.4e−003	148	hsa-miR-93
1.4e+003-3.1e+003	0.70	2.23 (−)	1.9e−002	382	MID-22331
8.0e+002-1.8e+003	0.83	2.21 (−)	2.9e−005	37	hsa-miR-214
4.4e+002-8.9e+002	0.79	2.01 (−)	2.1e−004	364	MID-00064
2.1e+002-4.2e+002	0.78	2.01 (−)	1.1e−003	35	hsa-miR-21*

(+) the higher expression of this miR is in lung carcinoid tumors

(−) the higher expression of this miR is in GI neuroendocrine tumors

[0354] hsa-miR-652 (SEQ ID NO: 64), hsa-miR-34c-5p (SEQ ID NO: 53) and hsa-miR-214 (SEQ ID NO: 37) are used at node 28 of the binary-tree-classifier detailed in the invention to distinguish between lung carcinoid tumors and GI neuroendocrine tumors.

TABLE 30

miR expression (in fluorescence units) distinguishing between pancreatic islet cell tumors and GI neuroendocrine carcinoid tumors selected from the group consisting of small intestine and duodenum; appendicitis, stomach and pancreas

miR name	SEQ ID NO.	p-value	fold-change	auROC	median values	
hsa-miR-129*	263	2.8e−004	20.91 (+)	0.80	2.3e+003	1.1e+002
hsa-miR-217	288	6.6e−003	9.61 (+)	0.72	4.8e+002	5.0e+001
hsa-miR-148a	18	6.8e−006	8.54 (+)	0.90	1.6e+003	1.9e+002
hsa-miR-216a	286	2.7e−002	8.34 (+)	0.68	4.3e+002	5.2e+001
hsa-miR-129-3p	162	4.4e−003	7.22 (+)	0.74	1.8e+003	2.5e+002
hsa-miR-551b	225	2.3e−003	6.65 (+)	0.74	6.6e+002	9.9e+001
hsa-miR-216b	287	5.4e−003	6.04 (+)	0.75	3.0e+002	5.0e+001
hsa-miR-455-3p	206	7.3e−007	3.75 (+)	0.92	7.1e+002	1.9e+002
hsa-miR-451	205	2.5e−003	3.65 (+)	0.79	1.3e+004	3.4e+003
hsa-miR-26b	296	2.8e−004	3.43 (+)	0.83	8.9e+002	2.6e+002
hsa-let-7f	258	3.6e−004	3.29 (+)	0.91	8.7e+003	2.6e+003
hsa-miR-338-3p	313	3.2e−003	3.25 (+)	0.78	5.2e+002	1.6e+002
MID-17866	377	5.0e−005	2.71 (+)	0.85	6.6e+003	2.4e+003
MID-16582	373	1.2e−005	2.45 (+)	0.88	1.9e+004	7.6e+003
hsa-let-7a	256	1.0e−003	2.42 (+)	0.80	6.4e+004	2.7e+004
hsa-let-7d	153	1.8e−004	2.36 (+)	0.89	1.1e+004	4.7e+003
hsa-let-7g	259	2.2e−003	2.28 (+)	0.86	6.4e+003	2.8e+003
hsa-miR-130b	265	1.0e−002	2.11 (+)	0.69	4.8e+002	2.3e+002
hsa-miR-30b	303	7.5e−003	2.09 (+)	0.75	6.4e+003	3.1e+003
hsa-miR-133b	268	5.4e−004	9.40 (−)	0.81	1.0e+002	9.7e+002
hsa-miR-133a	267	5.4e−004	9.22 (−)	0.80	1.1e+002	1.0e+003
hsa-miR-143*	165	2.1e−006	8.37 (−)	0.93	2.3e+002	1.9e+003
hsa-miR-145	15	3.7e−008	8.18 (−)	0.94	1.1e+004	9.2e+004
hsa-miR-145*	272	7.0e−006	8.05 (−)	0.91	6.6e+001	5.3e+002
hsa-miR-143	14	3.7e−009	7.30 (−)	0.96	5.2e+003	3.8e+004
hsa-miR-378	202	6.2e−006	6.35 (−)	0.88	3.1e+002	2.0e+003
MID-00689	236	8.1e−006	4.99 (−)	0.88	2.9e+002	1.4e+003
hsa-miR-422a	203	7.9e−006	4.74 (−)	0.88	1.4e+002	6.4e+002
hsa-miR-10a	4	2.4e−004	3.91 (−)	0.82	9.2e+002	3.6e+003
hsa-miR-150	168	4.4e−003	3.78 (−)	0.78	3.0e+002	1.1e+003
hsa-miR-330-3p	310	3.4e−004	3.23 (−)	0.81	1.1e+002	3.6e+002
hsa-miR-28-3p	298	4.6e−007	3.16 (−)	0.95	2.1e+002	6.7e+002
hsa-miR-194	27	1.4e−002	3.09 (−)	0.74	7.2e+002	2.2e+003
hsa-miR-200b	29	7.6e−005	2.72 (−)	0.91	7.5e+003	2.1e+004
hsa-miR-21	34	2.8e−006	2.57 (−)	0.87	8.5e+003	2.2e+004
hsa-miR-886-3p	228	8.0e−003	2.56 (−)	0.74	6.7e+002	1.7e+003
hsa-miR-100	3	3.6e−003	2.50 (−)	0.77	1.5e+003	3.8e+003
hsa-miR-532-5p	349	4.3e−007	2.14 (−)	0.94	2.5e+002	5.3e+002
hsa-miR-21*	35	8.5e−004	2.06 (−)	0.82	2.4e+002	5.0e+002
hsa-miR-193a-5p	26	5.7e−003	2.01 (−)	0.77	1.6e+002	3.3e+002

(+) the higher expression of this miR is in pancreatic islet cell tumors

(−) the higher expression of this miR is in GI neuroendocrine carcinoid tumors

[0355] hsa-miR-21 (SEQ ID NO: 34), and hsa-miR-148a (SEQ ID NO: 18) are used at node 29 of the binary-tree-classifier detailed in the invention to distinguish between pancreatic islet cell tumors and GI neuroendocrine carcinoid tumors.

TABLE 31

miR expression (in fluorescence units) distinguishing between gastric or esophageal adenocarcinoma and other adenocarcinoma tumors of the gastrointestinal system selected from the group consisting of cholangiocarcinoma or adenocarcinoma of extrahepatic biliary tract, pancreatic adenocarcinoma and colorectal adenocarcinoma

miR name	SEQ ID NO.	p-value	fold-change	auROC	median values	
hsa-miR-133a	267	4.6e−008	9.14 (+)	0.74	6.2e+002	6.7e+001
hsa-miR-133b	268	3.9e−008	8.73 (+)	0.74	5.5e+002	6.3e+001
hsa-miR-143*	165	3.9e−007	4.26 (+)	0.75	2.5e+003	5.9e+002
hsa-miR-145	15	4.5e−004	2.82 (+)	0.71	7.9e+004	2.8e+004
hsa-miR-143	14	1.3e−003	2.55 (+)	0.68	3.2e+004	1.3e+004
hsa-miR-658	356	8.2e−004	2.53 (+)	0.71	1.3e+003	5.1e+002
hsa-miR-149*	167	2.2e−004	2.33 (+)	0.72	7.2e+003	3.1e+003
MID-17576	376	7.2e−004	2.22 (+)	0.69	3.1e+003	1.4e+003
MID-16469	372	3.0e−004	2.20 (+)	0.71	1.4e+003	6.5e+002
hsa-miR-145*	272	3.0e−004	2.14 (+)	0.69	3.2e+002	1.5e+002
MID-15986	370	3.8e−004	2.11 (+)	0.74	2.9e+003	1.4e+003
hsa-miR-224	42	5.4e−008	6.57 (−)	0.83	5.5e+001	3.6e+002
hsa-miR-223	41	1.1e−004	2.61 (−)	0.73	1.5e+002	4.0e+002
hsa-miR-1201	146	1.2e−002	1.28 (−)	0.67	9.0e+002	1.2e+003

(+) the higher expression of this miR is in gastric or esophageal adenocarcinoma

(−) the higher expression of this miR is in other adenocarcinoma tumors of the gastrointestinal system

[0356] FIG. **20** demonstrates binary decisions at node #30 of the decision-tree. Tumors originating in gastric or esophageal adenocarcinoma (diamonds) are easily distinguished from tumors of other GI adenocarcinoma origin (squares) using the expression levels of hsa-miR-1201 (SEQ ID NO: 146, y-axis), hsa-miR-224 (SEQ ID NO: 42, x-axis) and hsa-miR-210 (SEQ ID NO: 36, z-axis).

TABLE 32

miR expression (in fluorescence units) distinguishing between colorectal adenocarcinoma and cholangiocarcinoma or adenocarcinoma of biliary tract or pancreas

miR name	SEQ ID NO.	p-value	fold-change	auROC	median values	
hsa-miR-224	42	4.0e−003	2.55 (+)	0.69	5.4e+002	2.1e+002
hsa-miR-203	184	1.2e−003	2.28 (+)	0.70	4.2e+002	1.8e+002
hsa-miR-92a	67	5.1e−007	1.91 (+)	0.77	6.2e+003	3.2e+003
hsa-miR-106a	158	4.6e−007	1.81 (+)	0.81	5.6e+003	3.1e+003
hsa-miR-17	20	1.3e−007	1.81 (+)	0.81	3.2e+003	1.8e+003
hsa-miR-20a	186	7.9e−005	1.80 (+)	0.76	3.2e+003	1.8e+003
hsa-miR-19b	284	1.4e−005	1.75 (+)	0.76	1.9e+003	1.1e+003
MID-17356	389	3.0e−003	1.67 (+)	0.70	2.6e+003	1.6e+003
hsa-miR-422a	203	2.1e−005	1.63 (+)	0.75	5.1e+002	3.1e+002
MID-15965	240	5.6e−003	1.60 (+)	0.67	7.2e+003	4.5e+003
MID-00689	236	1.7e−005	1.59 (+)	0.76	1.1e+003	6.9e+002
hsa-miR-1201	146	2.5e−003	1.53 (+)	0.68	1.6e+003	1.1e+003
hsa-miR-425	204	5.2e−004	1.49 (+)	0.69	1.4e+003	9.1e+002
hsa-miR-29a	43	1.2e−005	1.44 (+)	0.77	9.3e+003	6.5e+003
hsa-miR-18a	176	7.3e−006	1.44 (+)	0.75	6.4e+002	4.5e+002
hsa-miR-378	202	1.4e−004	1.41 (+)	0.72	1.3e+003	9.1e+002
hsa-miR-31	49	2.0e−003	3.39 (−)	0.69	5.3e+002	1.8e+003
hsa-miR-30a	46	2.2e−008	2.39 (−)	0.82	8.2e+002	2.0e+003
hsa-miR-214*	38	1.3e−002	1.47 (−)	0.66	2.5e+002	3.7e+002
hsa-miR-99b	363	2.2e−003	1.41 (−)	0.73	9.0e+002	1.3e+003

(+) the higher expression of this miR is in colorectal adenocarcinoma

(−) the higher expression of this miR is in other cholangiocarcinoma or adenocarcinoma tumors of biliary tract or pancreas

[0357] FIG. **21** demonstrates binary decisions at node #31 of the decision-tree. Tumors originating in colorectal adenocarcinoma (diamonds) are easily distinguished from tumors of cholangiocarcinoma or adenocarcinoma of biliary tract or pancreas origin (squares) using the expression levels of hsa-miR-30a (SEQ ID NO: 46, y-axis), hsa-miR-17 (SEQ ID NO: 20, x-axis) and hsa-miR-29a (SEQ ID NO: 43, z-axis).

TABLE 33

miR expression (in fluorescence units) distinguishing between cholangiocarcinoma or adenocarcinoma of extrahepatic biliary tract and pancreatic adenocarcinoma

miR name	SEQ ID NO.	p-value	fold-change	auROC	median values	
hsa-miR-31	49	1.5e−003	3.06 (+)	0.81	3.4e+003	1.1e+003
hsa-miR-138	11	1.1e−002	2.36 (+)	0.71	3.3e+002	1.4e+002
hsa-miR-141	13	1.7e−002	1.77 (+)	0.70	3.0e+003	1.7e+003
MID-16582	373	1.5e−002	1.65 (+)	0.70	1.8e+004	1.1e+004
hsa-miR-181b	154	9.6e−002	1.63 (+)	0.69	1.4e+003	8.4e+002
hsa-miR-10b	5	5.1e−001	1.62 (+)	0.69	7.0e+002	4.3e+002
hsa-miR-200c	30	7.4e−002	1.61 (+)	0.68	1.5e+004	9.3e+003
hsa-miR-29c*	45	1.3e−002	1.58 (+)	0.72	4.2e+002	2.7e+002
hsa-miR-193b	178	1.1e−001	1.47 (+)	0.66	1.5e+003	1.0e+003
hsa-miR-221	147	1.2e−002	1.36 (+)	0.75	9.0e+003	6.6e+003
hsa-miR-151-3p	274	4.0e−002	1.36 (+)	0.70	6.4e+002	4.7e+002
hsa-miR-146a	16	2.4e−002	1.34 (+)	0.66	7.3e+002	5.4e+002
hsa-miR-222	40	3.7e−002	1.32 (+)	0.71	1.5e+004	1.1e+004
hsa-miR-181a	21	8.4e−002	1.30 (+)	0.71	4.9e+003	3.8e+003
hsa-miR-29a	43	6.3e−002	1.14 (+)	0.66	6.8e+003	6.0e+003
MID-23256	253	2.1e−002	1.81 (−)	0.74	3.3e+002	5.9e+002
MID-18336	245	8.0e−002	1.70 (−)	0.66	1.1e+003	1.9e+003
hsa-let-7a	256	7.4e−003	1.68 (−)	0.73	2.7e+004	4.5e+004
hsa-miR-140-3p	12	9.2e−002	1.51 (−)	0.65	1.8e+003	2.7e+003
MID-16748	374	5.4e−003	1.47 (−)	0.75	9.3e+004	1.4e+005
MID-18395	379	2.9e−002	1.45 (−)	0.66	6.1e+004	8.9e+004
hsa-miR-1973	180	6.6e−002	1.41 (−)	0.69	3.3e+002	4.7e+002
hsa-let-7d	153	2.6e−002	1.40 (−)	0.68	4.3e+003	6.0e+003
hsa-miR-345	51	7.1e−002	1.39 (−)	0.75	3.2e+002	4.4e+002
hsa-miR-34a	52	3.9e−002	1.38 (−)	0.70	4.4e+003	6.1e+003
hsa-let-7c	1	1.4e−002	1.37 (−)	0.73	2.4e+004	3.3e+004
hsa-miR-26a	295	2.8e−002	1.36 (−)	0.68	1.5e+004	2.0e+004
hsa-let-7b	257	3.3e−003	1.35 (−)	0.77	2.9e+004	3.9e+004
MID-23168	385	6.5e−002	1.26 (−)	0.66	4.8e+003	6.1e+003
hsa-miR-23b	293	9.0e−002	1.21 (−)	0.67	1.0e+004	1.3e+004
hsa-miR-24	294	2.6e−002	1.18 (−)	0.68	2.1e+004	2.4e+004

(+) the higher expression of this miR is in pancreatic adenocarcinoma

(−) the higher expression of this miR is in cholangiocarcinoma or adenocarcinoma of extrahepatic biliary tract

[0358] hsa-miR-345 (SEQ ID NO: 51), hsa-miR-31 (SEQ ID NO: 49) and hsa-miR-146a (SEQ ID NO: 16) are used at node #32 of the binary-tree-classifier detailed in the invention to distinguish between cholangio cancer or adenocarcinoma of extrahepatic biliary tract and pancreatic adenocarcinoma.

TABLE 34

miR expression (in fluorescence units) distinguishing between kidney tumors selected from the group consisting of chromophobe renal cell carcinoma, clear cell renal cell carcinoma and papillary renal cell carcinoma and other tumors selected from the group consisting of sarcoma, adrenal (pheochromocytoma, adrenocortical carcinoma) and mesothelioma (pleural mesothelioma)

miR name	SEQ ID NO.	p-value	fold-change	auROC	median values	
hsa-miR-200b	29	7.6e−042	96.12 (+)	0.94	4.8e+003	5.0e+001
hsa-miR-200a	28	3.3e−044	45.03 (+)	0.94	2.3e+003	5.0e+001
hsa-miR-200c	30	1.1e−015	15.36 (+)	0.82	7.7e+002	5.0e+001
hsa-miR-30a	46	8.6e−041	9.73 (+)	0.96	1.1e+004	1.2e+003
hsa-miR-31	49	1.1e−008	9.21 (+)	0.74	1.1e+003	1.2e+002
hsa-miR-30a*	195	8.6e−039	8.87 (+)	0.94	1.7e+003	1.9e+002
hsa-miR-182	152	1.1e−009	6.58 (+)	0.74	5.0e+002	7.5e+001
hsa-miR-183	175	9.8e−011	5.07 (+)	0.76	2.5e+002	5.0e+001
hsa-miR-30d	47	5.0e−033	3.81 (+)	0.92	8.3e+003	2.2e+003

TABLE 34-continued

miR expression (in fluorescence units) distinguishing between kidney tumors selected from the group consisting of chromophobe renal cell carcinoma, clear cell renal cell carcinoma and papillary renal cell carcinoma and other tumors selected from the group consisting of sarcoma, adrenal (pheochromocytoma, adrenocortical carcinoma) and mesothelioma (pleural mesothelioma)

miR name	SEQ ID NO.	p-value	fold-change	auROC	median values	
hsa-miR-10a	4	2.5e−016	3.52 (+)	0.83	5.1e+003	1.5e+003
MID-23751	387	6.4e−011	3.15 (+)	0.75	2.3e+002	7.3e+001
hsa-miR-30c	196	1.1e−025	2.95 (+)	0.89	9.5e+003	3.2e+003
hsa-miR-192	177	2.1e−012	2.80 (+)	0.76	4.0e+002	1.4e+002
MID-17375	375	1.7e−015	2.52 (+)	0.79	2.5e+002	9.8e+001
hsa-miR-194	27	2.1e−012	2.43 (+)	0.75	2.2e+002	9.0e+001
hsa-miR-30e*	304	6.5e−013	2.40 (+)	0.76	2.8e+002	1.2e+002
hsa-miR-222	40	1.6e−012	2.37 (+)	0.75	1.6e+004	6.7e+003
hsa-miR-29c	191	9.5e−006	2.33 (+)	0.69	5.9e+002	2.5e+002
hsa-miR-221	147	1.4e−011	2.20 (+)	0.74	9.8e+003	4.5e+003
hsa-miR-21*	35	7.6e−003	2.19 (+)	0.61	9.8e+002	4.5e+002
hsa-miR-146a	16	3.7e−007	2.15 (+)	0.71	6.1e+002	2.8e+002
hsa-miR-21	34	1.2e−003	2.07 (+)	0.64	4.9e+004	2.4e+004
hsa-miR-10b	5	5.4e−004	2.06 (+)	0.66	4.7e+003	2.3e+003
hsa-miR-127-3p	155	2.1e−018	9.53 (−)	0.85	1.2e+002	1.2e+003
hsa-miR-199a-3p	181	4.9e−023	7.57 (−)	0.89	1.6e+003	1.2e+004
hsa-miR-337-5p	312	1.2e−019	7.45 (−)	0.86	5.0e+001	3.7e+002
hsa-miR-199b-5p	183	1.7e−015	7.21 (−)	0.82	1.4e+002	1.0e+003
hsa-miR-199a-5p	182	1.4e−017	6.48 (−)	0.86	2.6e+003	1.7e+004
hsa-miR-376c	320	3.5e−019	5.73 (−)	0.86	5.0e+001	2.9e+002
hsa-miR-487b	59	2.6e−016	5.23 (−)	0.86	6.5e+001	3.4e+002
hsa-miR-214*	38	9.7e−016	5.18 (−)	0.82	9.4e+001	4.9e+002
hsa-miR-382	324	2.2e−017	4.83 (−)	0.86	5.0e+001	2.4e+002
hsa-miR-381	323	6.6e−017	4.27 (−)	0.83	5.0e+001	2.1e+002
hsa-miR-214	37	2.7e−013	4.22 (−)	0.81	1.2e+003	5.0e+003
hsa-miR-379	322	8.5e−018	4.21 (−)	0.86	5.0e+001	2.1e+002
hsa-miR-409-3p	325	1.2e−015	4.14 (−)	0.83	5.0e+001	2.1e+002
hsa-miR-149	19	2.8e−016	3.76 (−)	0.86	6.7e+001	2.5e+002
hsa-miR-224	42	2.8e−007	3.51 (−)	0.71	7.5e+001	2.6e+002
hsa-miR-483-5p	334	1.3e−011	3.25 (−)	0.79	9.9e+001	3.2e+002
hsa-miR-130b	265	9.5e−012	2.08 (−)	0.79	1.5e+002	3.0e+002
hsa-miR-181a*	22	4.8e−009	2.00 (−)	0.76	1.0e+002	2.0e+002

(+) the higher expression of this miR is in the kidney tumors

(−) the higher expression of this miR is in sarcoma, adrenal and mesothelioma tumors

[0359] FIG. **22** demonstrates binary decisions at node #33 of the decision-tree. Tumors originating in kidney (diamonds) are easily distinguished from tumors of adrenal, mesothelioma and sarcoma origin (squares) using the expression levels of hsa-miR-200b (SEQ ID NO: 29, y-axis), hsa-miR-30a (SEQ ID NO: 46, x-axis) and hsa-miR-149 (SEQ ID NO: 19, z-axis).

TABLE 35

miR expression (in fluorescence units) distinguishing between pheochromocytoma (neuroendocrine tumor of the adrenal) and all sarcoma, adrenal carcinoma and mesothelioma tumors

miR name	SEQ ID NO.	p-value	fold-change	auROC	median values	
hsa-miR-7	65	6.7e−067	295.36 (+)	0.96	1.5e+004	5.0e+001
hsa-miR-375	56	5.0e−036	196.58 (+)	0.91	9.8e+003	5.0e+001
hsa-miR-138	11	3.2e−009	29.73 (+)	0.85	4.0e+003	1.3e+002
hsa-miR-129-3p	162	1.5e−021	20.53 (+)	0.94	1.0e+003	5.0e+001
hsa-miR-487b	59	3.0e−008	15.11 (+)	0.84	4.0e+003	2.7e+002
hsa-miR-432	331	7.4e−008	14.54 (+)	0.81	2.2e+003	1.5e+002
hsa-miR-539	350	9.4e−011	12.45 (+)	0.84	8.7e+002	7.0e+001
hsa-miR-127-3p	155	8.3e−005	12.36 (+)	0.80	1.2e+004	9.6e+002
hsa-miR-485-3p	335	1.2e−008	11.61 (+)	0.80	6.8e+002	5.8e+001
hsa-miR-124	159	2.7e−008	11.48 (+)	0.87	5.7e+002	5.0e+001
hsa-miR-485-5p	336	2.3e−014	10.67 (+)	0.86	5.6e+002	5.3e+001
hsa-miR-433	332	1.2e−012	10.38 (+)	0.83	5.2e+002	5.0e+001
hsa-miR-129*	263	1.1e−029	10.28 (+)	0.94	5.1e+002	5.0e+001
hsa-miR-323-3p	306	9.6e−008	9.55 (+)	0.82	4.8e+002	5.0e+001
hsa-miR-495	339	1.0e−005	9.22 (+)	0.79	1.2e+003	1.2e+002
hsa-miR-487a	337	4.4e−006	9.01 (+)	0.80	5.2e+002	5.8e+001

TABLE 35-continued

miR expression (in fluorescence units) distinguishing between pheochromocytoma (neuroendocrine tumor of the adrenal) and all sarcoma, adrenal carcinoma and mesothelioma tumors

miR name	SEQ ID NO.	p-value	fold-change	auROC	median values	
hsa-miR-154	275	4.8e−006	8.75 (+)	0.80	1.4e+003	1.6e+002
hsa-miR-29b-2*	301	6.0e−013	8.56 (+)	0.90	6.1e+002	7.1e+001
hsa-miR-154*	276	3.7e−005	8.54 (+)	0.78	4.5e+002	5.3e+001
hsa-miR-431*	330	4.7e−009	7.77 (+)	0.83	4.1e+002	5.3e+001
hsa-miR-369-5p	317	1.3e−006	7.56 (+)	0.81	7.4e+002	9.8e+001
hsa-miR-329	309	1.4e−007	7.56 (+)	0.80	4.8e+002	6.4e+001
hsa-miR-29c*	45	1.4e−009	7.28 (+)	0.90	1.8e+003	2.4e+002
hsa-miR-370	318	1.5e−005	7.24 (+)	0.79	1.1e+003	1.5e+002
hsa-miR-382	324	1.5e−005	6.74 (+)	0.80	1.5e+003	2.2e+002
hsa-miR-543	352	3.1e−004	6.53 (+)	0.76	8.6e+002	1.3e+002
hsa-miR-29c	191	2.6e−008	6.44 (+)	0.89	1.5e+003	2.3e+002
hsa-miR-127-5p	262	1.1e−005	6.40 (+)	0.79	6.2e+002	9.6e+001
hsa-miR-134	269	2.3e−004	6.39 (+)	0.77	9.6e+002	1.5e+002
hsa-miR-338-3p	313	2.1e−012	6.03 (+)	0.90	3.3e+002	5.4e+001
hsa-miR-149	19	4.8e−008	5.80 (+)	0.84	1.3e+003	2.2e+002
MID-00465	367	7.5e−012	5.32 (+)	0.82	2.7e+002	5.0e+001
hsa-miR-409-5p	326	5.3e−005	5.27 (+)	0.78	5.6e+002	1.1e+002
hsa-miR-409-3p	325	3.1e−004	5.26 (+)	0.76	9.6e+002	1.8e+002
hsa-miR-379	322	8.2e−004	5.25 (+)	0.76	9.2e+002	1.8e+002
hsa-miR-410	327	4.6e−008	5.05 (+)	0.79	2.5e+002	5.0e+001
hsa-miR-29b	190	3.4e−011	4.95 (+)	0.97	4.0e+003	8.1e+002
hsa-miR-1180	261	7.6e−019	4.85 (+)	0.93	3.7e+002	7.6e+001
hsa-miR-377*	321	1.0e−005	4.43 (+)	0.79	2.8e+002	6.4e+001
hsa-miR-873	360	2.9e−009	4.09 (+)	0.81	2.0e+002	5.0e+001
hsa-miR-598	353	1.2e−012	4.08 (+)	0.88	2.1e+002	5.3e+001
hsa-miR-337-5p	312	3.0e−003	4.01 (+)	0.73	1.3e+003	3.3e+002
MID-16270	371	8.8e−005	3.96 (+)	0.77	2.6e+002	6.6e+001
hsa-miR-10b	5	6.2e−005	3.51 (+)	0.85	7.2e+003	2.1e+003
hsa-miR-411	328	2.6e−002	3.40 (+)	0.68	2.3e+002	6.7e+001
hsa-miR-451	205	4.3e−004	3.17 (+)	0.77	2.2e+004	6.9e+003
hsa-miR-199b-5p	183	2.9e−008	12.33 (−)	0.90	1.1e+002	1.3e+003
hsa-miR-214*	38	2.4e−006	4.75 (−)	0.86	1.1e+002	5.5e+002
hsa-miR-199a-3p	181	2.9e−005	4.48 (−)	0.84	3.2e+003	1.5e+004
hsa-miR-214	37	6.8e−005	4.47 (−)	0.85	1.3e+003	5.9e+003
hsa-miR-222	40	5.9e−004	4.23 (−)	0.80	1.8e+003	7.8e+003
hsa-miR-199a-5p	182	9.0e−006	4.13 (−)	0.87	4.5e+003	1.8e+004
hsa-miR-221	147	6.4e−004	4.11 (−)	0.80	1.3e+003	5.2e+003
hsa-miR-146b-5p	17	4.7e−007	3.72 (−)	0.85	1.9e+002	7.0e+002
hsa-miR-224	42	2.3e−003	3.48 (−)	0.72	8.9e+001	3.1e+002
MID-22331	382	3.8e−005	3.42 (−)	0.81	8.0e+002	2.7e+003
hsa-miR-21	34	1.1e−004	3.35 (−)	0.79	7.9e+003	2.6e+004
hsa-miR-148a	18	1.3e−003	3.08 (−)	0.74	1.4e+002	4.2e+002
hsa-miR-100	3	2.6e−005	3.03 (−)	0.83	2.1e+003	6.3e+003

(+) the higher expression of this miR is in pheochromocytoma

(−) the higher expression of this miR is in sarcoma, adrenal carcinoma and mesothelioma tumors

[0360] FIG. **23** demonstrates binary decisions at node #34 of the decision-tree. Tumors originating in pheochromocytoma (diamonds) are easily distinguished from tumors of adrenal, mesothelioma and sarcoma origin (squares) using the expression levels of hsa-miR-375 (SEQ ID NO: 56, y-axis) and hsa-miR-7 (SEQ ID NO: 65, x-axis).

TABLE 36

miR expression (in fluorescence units) distinguishing between adrenal carcinoma and mesothelioma or sarcoma tumors

miR name	SEQ ID NO.	p-value	fold-change	auROC	median values	
hsa-miR-509-3p	61	1.3e−040	51.10 (+)	0.98	2.6e+003	5.0e+001
hsa-miR-483-3p	333	4.9e−007	24.55 (+)	0.76	1.3e+003	5.4e+001
hsa-miR-202	31	8.1e−066	24.01 (+)	0.99	1.2e+003	5.0e+001
hsa-miR-513a-5p	347	2.6e−024	21.83 (+)	0.95	1.4e+003	6.4e+001
hsa-miR-509-3-5p	346	9.3e−030	12.08 (+)	0.96	6.0e+002	5.0e+001
hsa-miR-503	344	2.2e−016	11.82 (+)	0.92	2.2e+003	1.9e+002
hsa-miR-506	345	3.8e−033	10.25 (+)	0.98	5.1e+002	5.0e+001
MID-23751	387	1.2e−026	9.70 (+)	0.96	5.9e+002	6.1e+001
hsa-miR-483-5p	334	6.0e−005	8.66 (+)	0.71	2.7e+003	3.1e+002

TABLE 36-continued

miR expression (in fluorescence units) distinguishing between adrenal carcinoma and mesothelioma or sarcoma tumors

miR name	SEQ ID NO.	p-value	fold-change	auROC	median values	
hsa-miR-542-5p	351	1.1e−015	7.79 (+)	0.91	1.1e+003	1.4e+002
hsa-miR-382	324	8.5e−005	5.77 (+)	0.72	1.2e+003	2.0e+002
hsa-miR-409-5p	326	3.1e−007	5.44 (+)	0.75	5.5e+002	1.0e+002
hsa-miR-134	269	2.7e−004	5.31 (+)	0.73	7.2e+002	1.4e+002
hsa-miR-127-3p	155	8.9e−003	4.98 (+)	0.69	3.9e+003	7.9e+002
hsa-miR-376c	320	6.4e−003	4.93 (+)	0.68	1.0e+003	2.1e+002
hsa-miR-379	322	2.6e−003	4.84 (+)	0.69	7.8e+002	1.6e+002
hsa-miR-487b	59	4.9e−005	4.53 (+)	0.72	1.0e+003	2.2e+002
hsa-miR-370	318	1.3e−003	4.49 (+)	0.69	6.6e+002	1.5e+002
hsa-miR-409-3p	325	2.9e−004	4.45 (+)	0.71	7.8e+002	1.7e+002
MID-18336	245	3.9e−011	4.19 (+)	0.92	4.7e+003	1.1e+003
MID-23291	254	1.8e−007	3.79 (+)	0.84	1.1e+003	2.9e+002
hsa-miR-432	331	1.5e−004	3.71 (+)	0.70	5.0e+002	1.4e+002
hsa-miR-154	275	1.6e−003	3.60 (+)	0.69	5.3e+002	1.5e+002
hsa-miR-1973	180	7.2e−011	3.48 (+)	0.90	1.1e+003	3.1e+002
hsa-miR-654-3p	355	6.9e−002	3.22 (+)	0.63	5.4e+002	1.7e+002
MID-15986	370	8.6e−009	3.14 (+)	0.86	3.5e+003	1.1e+003
hsa-miR-381	323	4.5e−002	3.07 (+)	0.64	5.4e+002	1.8e+002
hsa-miR-337-5p	312	5.8e−002	3.07 (+)	0.63	8.9e+002	2.9e+002
hsa-miR-193b	178	1.0e−008	3.03 (+)	0.88	5.6e+003	1.8e+003
MID-20524	249	1.6e−006	3.02 (+)	0.81	4.2e+003	1.4e+003
hsa-miR-199b-5p	183	1.3e−015	18.32 (−)	0.96	9.5e+001	1.7e+003
hsa-miR-199a-3p	181	9.7e−014	10.80 (−)	0.95	1.7e+003	1.9e+004
hsa-miR-214*	38	2.6e−016	10.75 (−)	0.97	6.1e+001	6.5e+002
hsa-miR-199a-5p	182	1.9e−015	9.43 (−)	0.97	2.5e+003	2.4e+004
hsa-miR-214	37	1.2e−011	7.89 (−)	0.96	9.0e+002	7.1e+003
hsa-miR-100	3	1.8e−012	4.87 (−)	0.90	1.5e+003	7.5e+003
hsa-miR-193a-3p	25	3.6e−006	3.37 (−)	0.83	7.6e+002	2.5e+003
hsa-miR-152	169	2.5e−006	3.05 (−)	0.80	4.3e+002	1.3e+003

(+) the higher expression of this miR is in adrenal carcinoma

(−) the higher expression of this miR is in sarcoma and mesothelioma tumors

[0361] hsa-miR-202 (SEQ ID NO: 31), hsa-miR-509-3p (SEQ ID NO: 61) and hsa-miR-214* (SEQ ID NO: 38) are used at node 35 of the binary-tree-classifier detailed in the invention to distinguish between adrenal carcinoma and sarcoma or mesothelioma tumors.

TABLE 37

miR expression (in fluorescence units) distinguishing between GIST and mesothelioma or sarcoma tumors

median values		auROC	fold-change	p-value	SEQ ID NO.	miR name
2.4e+002	5.6e+003	0.97	23.39 (+)	4.2e−033	165	hsa-miR-143*
4.9e+003	1.0e+005	0.97	21.41 (+)	1.7e−025	14	hsa-miR-143
8.1e+003	1.5e+005	0.99	18.42 (+)	4.2e−026	15	hsa-miR-145
5.0e+001	7.9e+002	0.87	15.77 (+)	1.5e−010	333	hsa-miR-483-3p
6.2e+001	8.4e+002	0.98	13.54 (+)	1.5e−037	272	hsa-miR-145*
1.6e+002	1.6e+003	0.99	9.58 (+)	2.7e−024	270	hsa-miR-139-5p
1.8e+002	1.8e+003	0.96	9.49 (+)	2.7e−019	45	hsa-miR-29c*
6.1e+001	5.8e+002	0.95	9.48 (+)	7.9e−028	301	hsa-miR-29b-2*
1.9e+002	1.5e+003	0.94	7.89 (+)	1.9e−015	191	hsa-miR-29c
1.2e+003	6.3e+003	0.96	5.12 (+)	8.8e−014	46	hsa-miR-30a
1.9e+002	7.3e+002	0.93	3.84 (+)	6.6e−013	195	hsa-miR-30a*
2.4e+002	8.7e+002	0.92	3.66 (+)	1.8e−008	266	hsa-miR-132
6.1e+002	2.2e+003	0.91	3.52 (+)	4.2e−008	190	hsa-miR-29b
1.9e+002	6.5e+002	0.82	3.50 (+)	1.5e−006	19	hsa-miR-149
2.6e+002	9.0e+002	0.82	3.47 (+)	4.8e−005	334	hsa-miR-483-5p
9.3e+002	1.9e+002	0.70	5.00 (−)	2.1e−003	155	hsa-miR-127-3p
3.4e+003	7.1e+002	0.88	4.74 (−)	2.3e−007	25	hsa-miR-193a-3p
7.0e+003	1.9e+003	0.79	3.64 (−)	5.5e−004	147	hsa-miR-221
9.8e+003	2.8e+003	0.78	3.54 (−)	1.1e−003	40	hsa-miR-222
3.2e+004	9.8e+003	0.75	3.26 (−)	1.1e−003	34	hsa-miR-21

(+) the higher expression of this miR is in GIST

(−) the higher expression of this miR is in sarcoma and mesothelioma tumors

[0362] hsa-miR-29C* (SEQ ID NO: 45) and hsa-miR-143 (SEQ ID NO: 14) are used at node 36 of the binary-tree-classifier detailed in the invention to distinguish between GIST and sarcoma or mesothelioma tumors.

TABLE 38

miR expression (in fluorescence units) distinguishing between chromophobe renal cell carcinoma tumors and clear cell or papillary renal cell carcinoma tumors

median values		auROC	fold-change	p-value	SEQ ID NO.	miR name
8.8e+001	2.1e+003	0.99	23.68 (+)	4.7e−017	13	hsa-miR-141
3.0e+002	5.7e+003	0.99	18.81 (+)	8.4e−012	30	hsa-miR-200c
6.6e+001	9.8e+002	0.99	14.85 (+)	7.5e−019	361	hsa-miR-874
5.0e+001	7.4e+002	0.97	14.80 (+)	1.0e−014	280	hsa-miR-187
5.0e+001	7.2e+002	0.98	14.47 (+)	4.7e−018	362	hsa-miR-891a
5.3e+003	7.4e+004	0.98	13.97 (+)	5.3e−017	147	hsa-miR-221
7.6e+003	9.0e+004	0.97	11.89 (+)	1.4e−015	40	hsa-miR-222
5.3e+001	5.1e+002	0.98	9.66 (+)	1.2e−017	291	hsa-miR-222*
1.4e+002	1.1e+003	0.94	8.01 (+)	2.7e−010	387	MID-23751
7.4e+001	5.4e+002	0.97	7.32 (+)	4.4e−015	290	hsa-miR-221*
1.1e+002	5.6e+002	0.93	4.97 (+)	3.2e−010	299	hsa-miR-296-5p
3.2e+002	1.5e+003	0.90	4.90 (+)	3.1e−007	152	hsa-miR-182
8.4e+002	3.3e+003	0.73	3.89 (+)	6.3e−003	178	hsa-miR-193b
5.4e+003	1.7e+004	0.92	3.26 (+)	2.2e−007	303	hsa-miR-30b
1.1e+003	3.5e+003	0.74	3.20 (+)	8.1e−003	242	MID-16489
6.2e+003	3.3e+002	0.85	18.53 (−)	4.3e−006	49	hsa-miR-31
6.1e+002	5.0e+001	0.90	12.13 (−)	2.1e−007	11	hsa-miR-138
1.8e+003	2.2e+002	0.98	8.38 (−)	6.7e−014	35	hsa-miR-21*
7.9e+004	1.0e+004	0.95	7.54 (−)	3.1e−013	34	hsa-miR-21
3.7e+003	5.4e+002	0.92	6.79 (−)	3.1e−009	36	hsa-miR-210
9.8e+002	1.7e+002	0.97	5.71 (−)	3.1e−013	206	hsa-miR-455-3p
1.0e+003	2.5e+002	0.91	4.07 (−)	4.7e−008	16	hsa-miR-146a
6.0e+002	1.7e+002	0.89	3.64 (−)	7.1e−007	170	hsa-miR-155
7.5e+002	2.1e+002	0.78	3.48 (−)	1.6e−003	177	hsa-miR-192
8.6e+002	2.5e+002	0.86	3.39 (−)	6.6e−006	17	hsa-miR-146b-5p

(+) the higher expression of this miR is in chromophobe renal cell carcinoma tumors
(−) the higher expression of this miR is in clear cell or papillary renal cell carcinoma tumors

[0363] hsa-miR-210 (SEQ ID NO: 36) and hsa-miR-221 (SEQ ID NO: 147) are used at node #37 of the binary-tree-classifier detailed in the invention to distinguish between chromophobe renal cell carcinoma tumors and clear cell or papillary renal cell carcinoma tumors.

TABLE 39

miR expression (in fluorescence units) distinguishing between clear cell and papillary renal cell carcinoma tumors

miR name	SEQ ID NO.	p-value	fold-change	auROC	median values	
hsa-miR-503	344	2.3e−005	4.81 (+)	0.89	5.7e+002	1.2e+002
MID-22331	382	5.8e−003	3.65 (+)	0.81	5.9e+003	1.6e+003
hsa-miR-126	9	1.1e−005	3.54 (+)	0.94	6.4e+003	1.8e+003
hsa-miR-494	338	3.0e−003	3.45 (+)	0.82	5.7e+003	1.7e+003
hsa-miR-200b	29	3.1e−004	8.35 (−)	0.87	1.3e+003	1.1e+004
hsa-miR-31	49	3.0e−002	6.61 (−)	0.81	1.3e+003	8.7e+003
hsa-miR-200a	28	5.0e−005	5.30 (−)	0.92	9.5e+002	5.1e+003
hsa-miR-30a*	195	1.1e−009	4.10 (−)	1.00	5.1e+002	2.1e+003
hsa-miR-30a	46	4.5e−010	3.70 (−)	1.00	5.0e+003	1.9e+004
hsa-miR-10a	4	6.9e−004	3.39 (−)	0.86	1.6e+003	5.3e+003
hsa-miR-138	11	2.0e−002	3.23 (−)	0.76	2.3e+002	7.6e+002
MID-23291	254	7.4e−003	3.17 (−)	0.79	2.0e+002	6.4e+002

(+) the higher expression of this miR is in renal clear cell carcinoma tumors
(−) the higher expression of this miR is in papillary renal cell carcinoma tumors

[0364] hsa-miR-31 (SEQ ID NO: 49) and hsa-miR-126 (SEQ ID NO: 9) are used at node 38 of the binary-tree-classifier detailed in the invention to distinguish between renal clear cell and papillary cell carcinoma tumors.

TABLE 40

miR expression (in fluorescence units) distinguishing between pleural mesothelioma and sarcoma tumors

miR name	SEQ ID NO.	p-value	fold-change	auROC	median values	
hsa-miR-31	49	1.7e−006	13.97 (+)	0.78	1.7e+003	1.2e+002
hsa-miR-21*	35	2.0e−011	5.01 (+)	0.89	2.1e+003	4.3e+002
hsa-miR-146b-5p	17	2.1e−008	2.75 (+)	0.84	1.6e+003	5.9e+002
hsa-miR-21	34	4.8e−010	2.71 (+)	0.89	6.9e+004	2.5e+004
hsa-miR-193a-3p	25	2.3e−005	2.57 (+)	0.77	6.1e+003	2.4e+003
hsa-miR-210	36	5.9e−005	2.49 (+)	0.75	3.1e+003	1.2e+003
hsa-miR-150	168	9.7e−004	2.33 (+)	0.70	1.1e+003	4.6e+002
hsa-miR-155	170	1.4e−004	2.33 (+)	0.75	6.8e+002	2.9e+002
hsa-miR-193a-5p	26	1.4e−005	2.25 (+)	0.76	7.3e+002	3.2e+002
hsa-miR-10a	4	1.7e−004	2.13 (+)	0.76	2.4e+003	1.1e+003
hsa-miR-29b	190	1.1e−003	2.03 (+)	0.70	1.0e+003	5.1e+002
hsa-miR-30a	46	1.5e−005	1.99 (+)	0.77	1.8e+003	9.0e+002
hsa-miR-130a	10	8.9e−003	1.90 (+)	0.71	4.9e+003	2.6e+003
MID-15965	240	1.6e−003	1.88 (+)	0.69	5.2e+003	2.8e+003
hsa-miR-29a	43	1.5e−002	1.71 (+)	0.67	7.3e+003	4.3e+003
hsa-miR-22	39	1.1e−004	1.65 (+)	0.72	8.2e+003	5.0e+003
MID-23168	385	2.9e−002	1.57 (+)	0.64	5.9e+003	3.8e+003
hsa-miR-574-5p	63	1.4e−002	1.55 (+)	0.66	1.5e+003	9.9e+002
hsa-miR-378	202	2.8e−002	1.53 (+)	0.66	1.2e+003	7.5e+002
hsa-miR-199a-3p	181	3.3e−007	3.62 (−)	0.84	7.4e+003	2.7e+004
hsa-miR-214	37	3.2e−006	3.45 (−)	0.81	3.1e+003	1.1e+004
hsa-miR-10b	5	6.7e−008	3.36 (−)	0.85	8.3e+002	2.8e+003
hsa-miR-199b-5p	183	2.0e−004	3.19 (−)	0.74	9.1e+002	2.9e+003
hsa-miR-199a-5p	182	6.0e−005	2.84 (−)	0.80	1.1e+004	3.0e+004
hsa-miR-214*	38	5.7e−005	2.22 (−)	0.78	3.8e+002	8.4e+002
hsa-miR-455-3p	206	2.8e−004	1.69 (−)	0.75	7.0e+002	1.2e+003
hsa-miR-26b	296	2.9e−003	1.61 (−)	0.75	4.4e+002	7.0e+002
hsa-let-7c	1	4.3e−003	1.58 (−)	0.71	3.2e+004	5.0e+004

(+) the higher expression of this miR is in pleural mesothelioma tumors
(−) the higher expression of this miR is in sarcoma tumors

[0365] hsa-miR-21* (SEQ ID NO: 35) hsa-miR-130a (SEQ ID NO: 10) and hsa-miR-10b (SEQ ID NO: 5) are used at node 39 of the binary-tree-classifier detailed in the invention to distinguish between pleural mesothelioma tumors and sarcoma tumors.

TABLE 41

miR expression (in fluorescence units) distinguishing between synovial sarcoma and other sarcoma tumors

miR name	SEQ ID NO.	p-value	fold-change	auROC	median values	
hsa-miR-182	152	2.9e−009	25.03 (+)	0.89	1.3e+003	5.1e+001
hsa-miR-200b	29	9.2e−009	21.59 (+)	0.92	1.1e+003	5.0e+001
hsa-miR-124	159	5.9e−007	19.35 (+)	0.88	9.7e+002	5.0e+001
hsa-miR-200a	28	1.5e−008	12.81 (+)	0.92	6.4e+002	5.0e+001
hsa-miR-495	339	8.2e−005	7.00 (+)	0.88	8.9e+002	1.3e+002
hsa-miR-154	275	1.6e−005	6.94 (+)	0.89	1.1e+003	1.6e+002
hsa-miR-543	352	2.8e−004	6.53 (+)	0.87	7.3e+002	1.1e+002
hsa-miR-149	19	6.1e−006	6.51 (+)	0.91	8.8e+002	1.4e+002
hsa-miR-376c	320	9.6e−005	6.22 (+)	0.86	2.0e+003	3.3e+002
hsa-miR-127-3p	155	1.5e−003	6.05 (+)	0.84	6.2e+003	1.0e+003
hsa-miR-127-5p	262	1.7e−004	5.40 (+)	0.84	5.2e+002	9.7e+001
hsa-miR-214*	38	2.5e−004	5.33 (+)	0.86	4.2e+003	7.8e+002
hsa-miR-214	37	7.3e−003	5.29 (+)	0.84	5.0e+004	9.5e+003
hsa-miR-199a-5p	182	4.7e−003	4.90 (+)	0.87	1.4e+005	2.9e+004
hsa-miR-432	331	1.9e−003	4.56 (+)	0.81	6.4e+002	1.4e+002
hsa-miR-369-5p	317	2.7e−004	4.43 (+)	0.84	5.0e+002	1.1e+002
hsa-miR-381	323	9.6e−003	4.19 (+)	0.78	8.9e+002	2.1e+002
hsa-miR-654-3p	355	2.7e−003	3.96 (+)	0.81	7.7e+002	1.9e+002
hsa-miR-100	3	9.6e−006	3.79 (+)	0.91	2.1e+004	5.6e+003
hsa-miR-196a	282	2.8e−004	3.76 (+)	0.86	6.5e+002	1.7e+002
hsa-miR-337-5p	312	6.0e−003	3.55 (+)	0.80	1.5e+003	4.1e+002
hsa-miR-199a-3p	181	7.4e−003	3.52 (+)	0.86	9.1e+004	2.6e+004
hsa-miR-134	269	6.5e−003	3.41 (+)	0.80	5.5e+002	1.6e+002

TABLE 41-continued

miR expression (in fluorescence units) distinguishing between synovial sarcoma and other sarcoma tumors

miR name	SEQ ID NO.	p-value	fold-change	auROC	median values	
hsa-miR-370	318	8.3e−003	3.32 (+)	0.79	6.4e+002	1.9e+002
hsa-miR-487b	59	7.6e−003	3.08 (+)	0.78	1.0e+003	3.2e+002
hsa-miR-132	266	7.1e−007	3.02 (+)	0.87	6.4e+002	2.1e+002
hsa-miR-379	322	1.1e−002	2.92 (+)	0.78	6.3e+002	2.2e+002
hsa-miR-125b	8	1.6e−004	2.83 (+)	0.92	1.2e+005	4.4e+004
hsa-miR-382	324	8.4e−003	2.58 (+)	0.78	6.1e+002	2.4e+002
hsa-miR-130a	10	1.8e−003	2.45 (+)	0.80	6.0e+003	2.4e+003
hsa-miR-222	40	2.1e−010	10.95 (−)	0.96	8.4e+002	9.2e+003
hsa-miR-221	147	7.9e−010	10.19 (−)	0.96	6.7e+002	6.8e+003
hsa-miR-152	169	2.1e−005	4.92 (−)	0.88	3.6e+002	1.8e+003
hsa-miR-451	205	2.8e−002	4.72 (−)	0.72	1.7e+003	7.9e+003
hsa-miR-21	34	4.4e−005	4.59 (−)	0.84	5.9e+003	2.7e+004
hsa-miR-150	168	9.2e−004	4.32 (−)	0.83	1.4e+002	5.9e+002
hsa-miR-143	14	2.2e−007	4.15 (−)	0.92	1.3e+003	5.5e+003
hsa-miR-145	15	2.7e−007	3.30 (−)	0.93	2.9e+003	9.5e+003
hsa-miR-140-3p	12	1.6e−003	3.30 (−)	0.91	1.0e+003	3.5e+003
hsa-miR-30a	46	6.1e−003	2.92 (−)	0.78	3.5e+002	1.0e+003
MID-23794	255	4.1e−004	2.86 (−)	0.82	3.6e+002	1.0e+003
hsa-miR-22	39	1.9e−005	2.82 (−)	0.88	2.0e+003	5.8e+003
hsa-miR-185	23	3.9e−003	2.74 (−)	0.77	4.0e+002	1.1e+003
hsa-miR-29b	190	6.8e−003	2.45 (−)	0.80	2.4e+002	5.8e+002
MID-00689	236	4.9e−003	2.27 (−)	0.79	3.1e+002	7.1e+002
MID-23178	386	2.2e−004	2.10 (−)	0.85	3.2e+004	6.7e+004
MID-18395	379	2.9e−003	2.08 (−)	0.80	3.7e+004	7.7e+004
hsa-miR-378	202	7.4e−003	2.07 (−)	0.78	3.8e+002	7.8e+002

(+) the higher expression of this miR is in synovial sarcoma tumors

(−) the higher expression of this miR is in other sarcoma tumors

[0366] hsa-miR-100 (SEQ ID NO: 3) hsa-miR-145 (SEQ ID NO: 15) and hsa-miR-222 (SEQ ID NO: 40) are used at node 40 of the binary-tree-classifier detailed in the invention to distinguish between synovial sarcoma tumors and other sarcoma tumors.

TABLE 42

miR expression (in fluorescence units) distinguishing between chondrosarcoma and other non synovial sarcoma tumors

miR name	SEQ ID NO.	p-value	fold-change	auROC	median values	
hsa-miR-140-3p	12	2.1e−022	75.69 (+)	1.00	2.2e+005	2.9e+003
hsa-miR-140-5p	271	8.5e−015	35.23 (+)	0.91	5.1e+003	1.5e+002
hsa-miR-455-3p	206	6.1e−015	14.49 (+)	0.98	1.6e+004	1.1e+003
hsa-miR-483-3p	333	3.1e−003	11.03 (+)	0.71	5.5e+002	5.0e+001
hsa-miR-138	11	1.2e−006	11.01 (+)	0.88	1.1e+003	9.5e+001
hsa-miR-455-5p	58	6.3e−012	8.87 (+)	0.87	8.2e+002	9.2e+001
hsa-miR-210	36	1.5e−006	4.37 (+)	0.91	4.7e+003	1.1e+003
hsa-miR-148a	18	3.1e−004	3.98 (+)	0.83	1.4e+003	3.6e+002
hsa-miR-193b	178	2.3e−002	2.36 (+)	0.72	3.6e+003	1.5e+003
hsa-miR-23b	293	1.5e−004	2.13 (+)	0.84	2.8e+004	1.3e+004
hsa-miR-27b	189	5.8e−004	2.05 (+)	0.80	5.5e+003	2.7e+003
MID-22331	382	1.1e−004	5.01 (−)	0.70	6.7e+002	3.4e+003
MID-19962	381	1.2e−004	3.91 (−)	0.81	1.7e+002	6.6e+002
MID-15965	240	1.9e−004	3.76 (−)	0.83	8.5e+002	3.2e+003
MID-20524	249	8.0e−004	3.47 (−)	0.79	4.2e+002	1.5e+003
hsa-miR-10b	5	1.3e−005	3.27 (−)	0.85	9.0e+002	2.9e+003
MID-17866	377	6.9e−005	2.92 (−)	0.78	1.0e+003	2.9e+003
hsa-miR-1978	235	1.3e−003	2.62 (−)	0.75	2.7e+002	7.1e+002
hsa-miR-146b-5p	17	4.4e−005	2.48 (−)	0.81	2.8e+002	7.0e+002
hsa-miR-17	20	2.7e−002	2.36 (−)	0.71	5.7e+002	1.3e+003
MID-23168	385	8.2e−003	2.36 (−)	0.73	1.9e+003	4.5e+003
MID-23017	384	4.8e−003	2.16 (−)	0.74	5.0e+003	1.1e+004

TABLE 42-continued

miR expression (in fluorescence units) distinguishing between chondrosarcoma and other non synovial sarcoma tumors

miR name	SEQ ID NO.	p-value	fold-change	auROC	median values	
hsa-miR-30a	46	3.2e−004	2.04 (−)	0.79	5.4e+002	1.1e+003
hsa-miR-1979	283	3.0e−004	2.02 (−)	0.83	8.1e+003	1.6e+004

(+) the higher expression of this miR is in chondrosarcoma tumors

(−) the higher expression of this miR is in other non-synovial sarcoma tumors

[0367] hsa-miR-140-3p (SEQ ID NO: 12) and hsa-miR-455-5p (SEQ ID NO: 58) are used at node 41 of the binary-tree-classifier detailed in the invention to distinguish between chondrosarcoma tumors and other non-synovial sarcoma tumors.

TABLE 43

miR expression (in fluorescence units) distinguishing between liposarcoma and other non chondrosarcoma and non synovial sarcoma tumors

miR name	SEQ ID NO.	p-value	fold-change	auROC	median values	
hsa-miR-26a	295	1.6e−011	6.18 (+)	0.93	1.2e+005	1.9e+004
hsa-miR-451	205	8.1e−003	4.20 (+)	0.73	1.8e+004	4.2e+003
hsa-miR-193a-3p	25	6.5e−006	3.94 (+)	0.84	5.9e+003	1.5e+003
hsa-miR-193a-5p	26	7.5e−007	3.70 (+)	0.88	8.8e+002	2.4e+002
hsa-miR-99a	231	2.2e−005	3.24 (+)	0.88	2.0e+004	6.1e+003
hsa-miR-199b-5p	183	1.9e−003	2.60 (+)	0.75	5.9e+003	2.3e+003
hsa-miR-224	42	1.7e−004	2.54 (+)	0.79	7.9e+002	3.1e+002
MID-23291	254	9.9e−003	2.54 (+)	0.71	7.4e+002	2.9e+002
hsa-miR-150	168	1.5e−002	2.38 (+)	0.71	1.0e+003	4.2e+002
hsa-miR-652	64	1.1e−004	2.36 (+)	0.77	7.7e+002	3.2e+002
hsa-miR-143	14	5.4e−006	2.27 (+)	0.84	1.1e+004	4.8e+003
hsa-miR-193b	178	2.7e−004	2.20 (+)	0.76	3.0e+003	1.4e+003
hsa-miR-145	15	1.1e−004	2.13 (+)	0.78	1.7e+004	7.9e+003
hsa-miR-22	39	9.8e−004	2.12 (+)	0.79	9.7e+003	4.6e+003
hsa-miR-210	36	1.8e−004	4.49 (−)	0.79	3.1e+002	1.4e+003
hsa-miR-181b	154	1.2e−002	2.60 (−)	0.71	9.0e+002	2.4e+003
hsa-miR-130b	265	4.0e−003	2.29 (−)	0.75	2.6e+002	5.9e+002
hsa-miR-181d	174	3.2e−003	2.16 (−)	0.75	3.0e+002	6.5e+002
MID-23017	384	2.0e−004	2.14 (−)	0.79	5.6e+003	1.2e+004
hsa-miR-92a	67	6.6e−004	2.04 (−)	0.80	1.6e+003	3.3e+003

(+) the higher expression of this miR is in liposarcoma tumors

(−) the higher expression of this miR is in other non-chondrosarcoma and non-synovial sarcoma tumors

[0368] hsa-miR-210 (SEQ ID NO: 36) and hsa-miR-193a-5p (SEQ ID NO: 26) are used at node 42 of the binary-tree-classifier detailed in the invention to distinguish between liposarcoma tumors and other non-chondrosarcoma and non-synovial sarcoma tumors.

TABLE 44

miR expression (in fluorescence units) distinguishing between Ewing sarcoma or osteosarcoma; and rhabdomyosarcoma, malignant fibrous histiocytoma (MFH) or fibrosarcoma

miR name	SEQ ID NO.	p-value	fold-change	auROC	median values	
hsa-miR-181a*	22	1.1e−006	6.62 (+)	0.87	1.2e+003	1.9e+002
hsa-miR-181b	154	8.7e−009	5.68 (+)	0.91	6.4e+003	1.1e+003
hsa-miR-181a	21	2.9e−010	5.67 (+)	0.93	2.1e+004	3.7e+003
hsa-miR-181d	174	3.5e−006	4.19 (+)	0.85	1.8e+003	4.2e+002
hsa-miR-451	205	1.2e−002	3.27 (+)	0.72	9.4e+003	2.9e+003
hsa-miR-106a	158	2.9e−003	2.63 (+)	0.78	4.7e+003	1.8e+003
hsa-miR-20a	186	2.9e−003	2.52 (+)	0.78	2.8e+003	1.1e+003

TABLE 44-continued

miR expression (in fluorescence units) distinguishing between Ewing sarcoma or osteosarcoma; and rhabdomyosarcoma, malignant fibrous histiocytoma (MFH) or fibrosarcoma

miR name	SEQ ID NO.	p-value	fold-change	auROC	median values	
hsa-miR-93	148	9.2e−005	2.45 (+)	0.81	4.9e+003	2.0e+003
hsa-miR-17	20	5.1e−003	2.32 (+)	0.77	2.6e+003	1.1e+003
hsa-miR-487b	59	1.1e−002	4.54 (−)	0.71	1.3e+002	6.0e+002
hsa-miR-125b	8	2.9e−005	2.86 (−)	0.84	1.7e+004	4.9e+004
hsa-miR-199b-5p	183	9.4e−003	2.70 (−)	0.72	1.3e+003	3.4e+003
hsa-miR-99a	231	1.1e−003	2.34 (−)	0.76	3.5e+003	8.1e+003

(+) the higher expression of this miR is in Ewing sarcoma or osteosarcoma tumors

(−) the higher expression of this miR is in rhabdomyosarcoma, malignant fibrous histiocytoma (MFH) or fibrosarcoma tumors

[0369] hsa-miR-181a (SEQ ID NO: 21) is used at node 43 of the binary-tree-classifier detailed in the invention to distinguish between Ewing sarcoma or osteosarcoma tumors and rhabdomyosarcoma, malignant fibrous histiocytoma (MFH) or fibrosarcoma tumors.

TABLE 45

miR expression (in fluorescence units) distinguishing between Ewing sarcoma and osteosarcoma

miR name	SEQ ID NO.	p-value	fold-change	auROC	median values	
hsa-miR-127-3p	155	3.7e−006	6.60 (+)	1.00	1.1e+003	1.6e+002
hsa-miR-195	179	8.9e−004	5.85 (+)	0.97	8.5e+003	1.4e+003
hsa-miR-29a	43	1.4e−002	4.90 (+)	0.86	1.4e+004	2.8e+003
hsa-miR-497	208	1.1e−004	4.58 (+)	1.00	6.5e+003	1.4e+003
hsa-miR-181a-2*	278	1.0e−003	4.42 (+)	0.88	7.6e+002	1.7e+002
hsa-miR-146b-5p	17	6.0e−003	4.05 (+)	0.86	1.6e+003	4.0e+002
MID-23168	385	1.4e−002	2.64 (+)	0.81	8.9e+003	3.4e+003
hsa-miR-181d	174	1.5e−002	2.60 (+)	0.77	2.1e+003	8.0e+002
hsa-miR-10b	5	1.3e−002	2.55 (+)	0.82	4.1e+003	1.6e+003
hsa-miR-34a	52	7.1e−003	2.19 (+)	0.84	4.9e+003	2.2e+003
hsa-let-7b	257	2.7e−004	2.16 (+)	0.97	5.4e+004	2.5e+004
MID-00144	366	2.1e−003	2.12 (+)	0.88	5.2e+002	2.5e+002
hsa-miR-30e	48	6.2e−003	2.06 (+)	0.84	9.4e+002	4.5e+002
hsa-miR-31	49	7.9e−005	25.44 (−)	0.96	5.0e+001	1.3e+003
hsa-miR-140-3p	12	1.4e−003	5.72 (−)	0.89	2.0e+003	1.2e+004
hsa-miR-193a-3p	25	5.2e−005	4.92 (−)	0.94	7.6e+002	3.8e+003
hsa-miR-152	169	3.3e−003	4.09 (−)	0.89	4.4e+002	1.8e+003
hsa-miR-21	34	3.2e−003	3.00 (−)	0.89	1.2e+004	3.7e+004
hsa-miR-21*	35	1.7e−003	2.96 (−)	0.83	2.7e+002	8.1e+002
hsa-miR-185	23	4.2e−003	2.55 (−)	0.88	6.7e+002	1.7e+003
MID-23017	384	1.7e−002	2.53 (−)	0.82	8.2e+003	2.1e+004
hsa-miR-27b	189	3.8e−003	2.52 (−)	0.84	1.7e+003	4.3e+003
MID-17866	377	3.0e−002	2.18 (−)	0.80	2.3e+003	5.1e+003
hsa-miR-130b	265	3.0e−002	2.17 (−)	0.78	4.4e+002	9.6e+002
hsa-miR-24	294	3.3e−003	2.07 (−)	0.82	1.8e+004	3.7e+004
hsa-miR-23b	293	9.0e−003	2.03 (−)	0.86	8.8e+003	1.8e+004
hsa-miR-23a	292	1.6e−002	2.02 (−)	0.80	1.5e+004	3.0e+004

(+) the higher expression of this miR is in Ewing sarcoma tumors

(−) the higher expression of this miR is in osteosarcoma tumors

[0370] FIG. **24** demonstrates binary decisions at node #44 of the decision-tree. Tumors originating in Ewing sarcoma (diamonds) are easily distinguished from tumors of osteosarcoma origin (squares) using the expression levels of hsa-miR-31 (SEQ ID NO: 49, y-axis) and hsa-miR-193a-3p (SEQ ID NO: 25, x-axis).

TABLE 46

miR expression (in fluorescence units) distinguishing between rhabdomyosarcoma and malignant fibrous histiocytoma (MFH) or fibrosarcoma

median values		auROC	fold-change	p-value	SEQ ID NO.	miR name
5.0e+001	4.1e+003	0.96	81.34 (+)	1.9e−007	33	hsa-miR-206
5.7e+001	4.3e+003	0.89	74.89 (+)	1.8e−004	268	hsa-miR-133b
5.9e+001	3.9e+003	0.88	66.65 (+)	3.2e−004	267	hsa-miR-133a
5.0e+001	1.3e+003	0.89	25.89 (+)	3.9e−006	333	hsa-miR-483-3p
5.3e+001	5.2e+002	0.85	9.90 (+)	1.3e−004	276	hsa-miR-154*
5.8e+001	5.6e+002	0.85	9.63 (+)	1.2e−004	319	hsa-miR-376a
5.7e+001	5.1e+002	0.86	9.00 (+)	4.8e−005	306	hsa-miR-323-3p
2.5e+002	1.8e+003	0.84	7.01 (+)	2.8e−003	320	hsa-miR-376c
2.6e+002	1.7e+003	0.82	6.52 (+)	3.9e−003	334	hsa-miR-483-5p
3.1e+002	1.9e+003	0.87	6.22 (+)	5.1e−004	323	hsa-miR-381
1.0e+002	6.3e+002	0.85	6.19 (+)	5.4e−004	300	hsa-miR-299-3p
1.3e+002	7.9e+002	0.82	6.18 (+)	1.4e−003	281	hsa-miR-188-5p
4.1e+002	2.3e+003	0.86	5.73 (+)	1.4e−003	59	hsa-miR-487b
1.5e+002	8.4e+002	0.85	5.68 (+)	8.1e−004	339	hsa-miR-495
3.7e+002	1.7e+003	0.79	4.57 (+)	3.1e−002	316	hsa-miR-362-5p
2.0e+002	9.2e+002	0.80	4.49 (+)	2.4e−003	176	hsa-miR-18a
2.9e+002	1.3e+003	0.82	4.39 (+)	1.4e−003	348	hsa-miR-532-3p
1.8e+002	7.8e+002	0.85	4.27 (+)	4.0e−004	352	hsa-miR-543
4.0e+002	1.7e+003	0.81	4.18 (+)	2.3e−002	349	hsa-miR-532-5p
1.9e+003	7.8e+003	0.87	4.14 (+)	4.9e−004	67	hsa-miR-92a
5.7e+002	2.4e+003	0.86	4.13 (+)	9.2e−004	357	hsa-miR-660
1.3e+002	5.6e+002	0.78	4.13 (+)	4.2e−003	315	hsa-miR-362-3p
2.3e+002	8.6e+002	0.81	3.73 (+)	2.8e−003	343	hsa-miR-502-3p
2.0e+002	7.2e+002	0.84	3.64 (+)	1.5e−003	342	hsa-miR-501-3p
2.3e+002	8.5e+002	0.82	3.62 (+)	6.7e−003	355	hsa-miR-654-3p
1.9e+002	6.7e+002	0.79	3.56 (+)	1.3e−002	340	hsa-miR-500
2.4e+002	8.4e+002	0.80	3.56 (+)	7.9e−003	344	hsa-miR-503
2.2e+003	7.6e+003	0.78	3.53 (+)	7.2e−003	10	hsa-miR-130a
2.6e+002	8.8e+002	0.80	3.35 (+)	3.7e−003	341	hsa-miR-500*
2.6e+002	7.9e+002	0.79	3.06 (+)	7.3e−003	331	hsa-miR-432
9.3e+002	2.7e+003	0.77	2.90 (+)	1.4e−002	20	hsa-miR-17
4.3e+002	1.2e+003	0.86	2.90 (+)	1.0e−003	277	hsa-miR-17*
2.4e+002	6.7e+002	0.83	2.77 (+)	7.0e−003	318	hsa-miR-370
1.6e+003	4.5e+003	0.78	2.75 (+)	1.4e−002	158	hsa-miR-106a
4.3e+002	1.1e+003	0.83	2.67 (+)	3.0e−003	265	hsa-miR-130b
1.0e+003	2.7e+003	0.86	2.63 (+)	7.1e−004	284	hsa-miR-19b
8.6e+002	2.1e+003	0.82	2.43 (+)	8.6e−003	36	hsa-miR-210
6.1e+003	6.8e+002	0.90	8.92 (−)	1.8e−004	183	hsa-miR-199b-5p
1.9e+004	4.5e+003	0.83	4.15 (−)	8.0e−004	40	hsa-miR-222
1.1e+003	3.1e+002	0.90	3.55 (−)	5.6e−005	63	hsa-miR-574-5p
1.1e+004	3.2e+003	0.82	3.52 (−)	2.2e−003	147	hsa-miR-221
5.9e+003	1.8e+003	0.80	3.25 (−)	2.0e−003	43	hsa-miR-29a
5.2e+002	1.6e+002	0.82	3.19 (−)	5.4e−003	289	hsa-miR-22*
5.1e+003	1.7e+003	0.82	3.04 (−)	7.0e−003	52	hsa-miR-34a
8.1e+002	2.9e+002	0.76	2.81 (−)	1.4e−002	190	hsa-miR-29b
1.2e+003	4.5e+002	0.86	2.67 (−)	4.7e−003	4	hsa-miR-10a
3.7e+003	1.5e+003	0.86	2.43 (−)	1.3e−003	5	hsa-miR-10b
7.0e+003	2.9e+003	0.85	2.39 (−)	1.5e−003	39	hsa-miR-22
1.6e+003	6.9e+002	0.78	2.25 (−)	1.5e−002	169	hsa-miR-152
2.9e+003	1.3e+003	0.76	2.19 (−)	2.8e−002	208	hsa-miR-497

(+) the higher expression of this miR is in rhabdomyosarcoma tumors

(−) the higher expression of this miR is in MFH or fibrosarcoma tumors

[0371] FIG. **25** demonstrates binary decisions at node #45 of the decision-tree. Tumors originating in Rhabdomyosarcoma (diamonds) are easily distinguished from tumors of malignant fibrous histiocytoma (MFH) or fibrosarcoma origin (squares) using the expression levels of hsa-miR-206 (SEQ ID NO: 33, y-axis), hsa-miR-22 (SEQ ID NO: 39, x-axis) and hsa-miR-487b (SEQ ID NO: 59, z-axis).

TABLE 47

β values of the decision tree classifier
The classification at node 11 is based on the gender of subject rather than on beta values; accordingly, no data is provided for this node.
P_{TH} = 0.5 for all node

		miR 1			miR 2			miR 3		
Node	β0 intercept	miR hsa-	SEQ ID NO	β1	miR hsa-	SEQ ID NO	β2	miR hsa-	SEQ ID NO	β3
1	−23.3111	miR-372	55	2.3127						
2	−26.9408	miR-122	6	2.3127						
3	−3.8519	miR-200b	29	1.8567	miR-126	9	−1.379			
4	−8.2646	miR-200c	30	1.9582	miR-30a	46	−1.2306			
5	17.4706	miR-146a	16	1.1979	let-7e	2	−1.7697	miR-30a	46	−0.88435
6	−32.5621	miR-9*	66	1.5475	miR-92b	68	1.7188			
7	−9.5521	miR-222	40	−1.1606	miR-497	208	2.0005			
8	−23.053	miR-193a-3p	25	−1.0267	miR-7	65	1.2404	miR-375	56	1.6602
9	−29.3207	miR-194	27	2.0115	miR-21*	35	1.1414			
10	1.244	miR-181a	21	−1.5458	miR-143	14	0.9879			
12	21.3416	miR-200b	29	−1.942	miR-516a-5p	211	−1.256			
13	10.3775	miR-125a-5p	7	−1.1455	miR-205	32	1.1064	miR-345	51	−1.0128
14	−40.666	miR-193a-3p	25	1.9505	miR-342-3p	50	0.93196	miR-375	56	0.82076
15	26.2937	miR-22	39	−1.8153	miR-10a	4	0.61098	miR-205	32	−0.91632
16	9.4008	miR-93	148	−1.3023	miR-138	11	1.5494	miR-10a	4	−1.119
17	42.5529	miR-21	34	−1.801	miR-146b-5p	17	−1.4509			
18	0.52521	miR-193a-3p	25	1.7974	miR-31	49	−0.63021	miR-92a	67	−1.3119
19	−20.7179	miR-138	11	0.9662	miR-378	202	−1.3077	miR-21	34	1.6447
20	15.0039	miR-100	3	1.0814	miR-21	34	−2.0444			
21	−31.6015	miR-191	24	1.5137	miR-29c	191	0.22547	miR-934	69	1.734
22	−44.3141	miR-10b	5	1.41	let-7c	1	0.86212	miR-361-5p	54	1.6178
23	7.6168	miR-138	11	−0.32773	miR-10b	5	1.3275	miR-185	23	−1.8652
24	2.4904	miR-342-3p	50	−1.7146	miR-30d	47	1.5521			
26	−10.0563	miR-17	20	1.9063	miR-29c*	45	−1.3096			
27	−2.3904	miR-222	40	1.5531	miR-92b	68	−1.5907	miR-92a	67	−0.63749
28	−22.027	miR-652	64	1.9688	miR-214	37	−0.65807	miR-34c-5p	53	1.0197
29	−11.4697	miR-21	34	1.8457	miR-148a	18	−1.3936			
30	21.7628	miR-224	42	−1.3059	miR-210	36	−0.79749	1201	146	−0.50909
31	−17.747	miR-17	20	0.95763	miR-29a	43	1.6268	miR-30a	46	−1.3361
32	−2.3716	miR-31	49	1.0661	miR-146a	16	0.62041	miR-345	51	−1.8214
33	−4.226	miR-200b	29	0.48415	miR-149	19	−2.0172	miR-30a	46	1.0224
34	−29.6828	miR-7	65	2.1394	miR-375	56	0.87847			
35	−23.6445	miR-202	31	2.1832	miR-509-3p	61	0.76095	miR-214*	38	0.057027
36	−41.4047	miR-29c*	45	1.2571	miR-143	14	1.9413			
37	−25.1227	miR-221	147	2.2247	miR-210	36	−0.63202			
38	−24.5409	miR-31	49	−0.19797	miR-126	9	2.3043			
39	−20.7495	miR-130a	10	1.014	miR-10b	5	−1.0484	miR-21*	35	1.7948
40	−6.0971	miR-100	3	1.9198	miR-222	40	−1.0289	miR-145	15	−0.77759
41	−38.5059	miR-140-3p	12	1.6462	miR-455-5p	58	1.6244			
42	−10.7873	miR-210	36	−0.84091	miR-193a-5p	26	1.9298			
43	−30.4778	miR-181a	21	2.3127						
44	31.0975	miR-193a-3p	25	−2.0358	miR-31	49	−1.0974			
45	−17.5516	miR-22	39	−0.91078	miR-487b	59	1.0201	miR-206	487	1.8651

TABLE 48

Using fine-needle aspiration (FNA), pleural effusion or bronchial brushing for the identification of cancer tissue of origin

Class identified	Biopsy Site	Histological Type	Sampling Method
lung-small	Lymph Node	Neuroendocrine; Small	percutaneous FNA
UpperSCC	Lung	Non-small; squamous	percutaneous FNA
UpperSCC	Lung	Non-small; adenocarcinoma	percutaneous FNA
lung-small	Lung	Neuroendocrine; Small	percutaneous FNA
lung-adeno	Lung	Non-small; adenocarcinoma	percutaneous FNA
UpperSCC	Lung	Non-small; squamous	percutaneous FNA
lung-small	Lymph Node	Neuroendocrine; Small	transbronchial FNA
lung-small	Lung	Neuroendocrine; Small	transbronchial FNA
lung-adeno	Lung pleura	Non-small; adenocarcinoma	Pleural effusion
lung-adeno	Lung pleura	Non-small; adenocarcinoma	Pleural effusion
Lung, small	Lung	Neuroendocrine; Small	bronchial brushing
Lung, small	Lung	Neuroendocrine; Small	bronchial brushing
Lung, small	Lung	Neuroendocrine; Small	bronchial brushing
Lung, small	Lung	Neuroendocrine; Small	bronchial brushing
Lung, small	Lung	Neuroendocrine; Small	bronchial brushing

[0372] The foregoing description of the specific embodiments so fully reveals the general nature of the invention that others can, by applying current knowledge, readily modify and/or adapt for 5 various applications such specific embodiments without undue experimentation and without departing from the generic concept, and, therefore, such adaptations and modifications should and are intended to be comprehended within the meaning and range of equivalents of the disclosed embodiments. Although the invention has been described in conjunction with specific embodiments thereof, it is evident that many alternatives, modifications and variations will be 10 apparent to those skilled in the art. Accordingly, it is intended to embrace all such alternatives, modifications and variations that fall within the spirit and broad scope of the appended claims.

[0373] It should be understood that the detailed description and specific examples, while indicating preferred embodiments of the invention, are given by way of illustration only, since various changes and modifications within the spirit and scope of the invention will become 15 apparent to those skilled in the art from this detailed description.

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ccuccuagcu uuccccagg 79

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auagguaugu gucuguuagg 80

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cacaaauucg uaucuagggg aauauguagu ugacauaaac acuccgcucu 110

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uagucacaga uucgauucua ggggaauaua uggucgaugc aaaaacuuca 110

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ucacacuaaa uagcuacugc uaggc 85

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ucaggcucuu gggaccuagg cggaggggga 89

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gaguaauaau gcgccgucca cggca 85

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aauguuaaaa gggcauuggc cguguagug 89

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uuucacgaca ccaggguugc auca 84

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cuaccacagg guagaaccac ggacaggaua ccggggcacc 100

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acacugucug guaaagaugg cucccgggug gguuc 95

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ugagaugaag cacuguagcu caggaagaga gaaguuguuc ugcagc 106

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uggaaauacu guucuugagg ucaugguu 88

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ugaaauucag uucuucagcu gggauaucuc ugucaucgu 99

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uuugucuc 68

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gggacggggg cugugcuggg gcagcugga 89

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aggcacuugu agcauuaugg ugac 84

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aaaaccaucg accguugauu guacccuaug gcuaaccauc aucuacucca 110

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uuugggauuu gaaaaaacca cugaccguug acuguaccuu gggguccuua 110

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uuccucuggu ccuucccucc ca 82

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gcgcuuggau uucgcccccu gcucuccugc cu 92

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ccuacaaagu cccaguucuc ggcccccg 88

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ugcuguuacu uuugaugguu accaa 85

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ugcuguuauc uggggcgagg gccag 85

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gucugguaac gauguucaaa ggugacccgc 90

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acugccuggu aaugaugacg gcggagcccu gcacg 95

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<400> SEQUENCE: 101

cccucgucuu acccagcagu guuugggugc gguugggagu cucuaauacu gccggguaau 60

gauggagg 68

<210> SEQ ID NO 102
<211> LENGTH: 110
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 102

cgccucagag ccgcccgccg uuccuuuuuc cuaugcauau acuucuuuga ggaucuggcc 60

uaaagaggua uagggcaugg gaaaacgggg cggucggguc cuccccagcg 110

<210> SEQ ID NO 103
<211> LENGTH: 110
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 103

aaagauccuc agacaaucca ugugcuucuc uuguccuuca uuccaccgga gucugucuca 60

uacccaacca gauuucagug gagugaaguu caggaggcau ggagcugaca 110

<210> SEQ ID NO 104
<211> LENGTH: 86
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 104

ugcuuccccga ggccacaugc uucuuuauau ccccauaugg auuacuuugc uauggaaugu 60

aaggaagugu gugguuucgg caagug 86

<210> SEQ ID NO 105
<211> LENGTH: 72
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 105

ugucggguag cuuaucagac ugauguugac uguugaaucu cauggcaaca ccagucgaug 60

ggcugucuga ca 72

<210> SEQ ID NO 106
<211> LENGTH: 110
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 106

acccggcagu gccuccaggc gcagggcagc cccugcccac cgcacacugc gcugccccag 60

acccacugug cgugugacag cggcugaucu gugccugggc agcgcgaccc 110

<210> SEQ ID NO 107
<211> LENGTH: 110
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 107

ggccuggcug gacagaguug ucaugugucu gccugucuac acuugcugug cagaacaucc 60

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gcucaccugu acagcaggca cagacaggca gucacaugac aacccagccu 110

<210> SEQ ID NO 108
<211> LENGTH: 85
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 108

ggcugagccg caguaguucu ucaguggcaa gcuuuauguc cugacccagc uaaagcugcc 60

aguugaagaa cuguugcccu cugcc 85

<210> SEQ ID NO 109
<211> LENGTH: 110
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 109

gcugcuggaa gguguaggua cccucaaugg cucaguagcc aguguagauc cugucuuucg 60

uaaucagcag cuacaucugg cuacuggguc ucugauggca ucuucuagcu 110

<210> SEQ ID NO 110
<211> LENGTH: 110
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 110

ccuggccucc ugcagugcca cgcuccgugu auuugacaag cugaguugga cacuccaugu 60

gguagagugu caguuuguca aauaccccaa gugcggcaca ugcuuaccag 110

<210> SEQ ID NO 111
<211> LENGTH: 81
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 111

gggcuuucaa gucacuagug guuccguuua guagaugauu gugcauuguu ucaaaauggu 60

gcccuaguga cuacaaagcc c 81

<210> SEQ ID NO 112
<211> LENGTH: 64
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 112

augacugauu ucuuuuggug uucagaguca auauaauuuu cuagcaccau cugaaaucgg 60

uuau 64

<210> SEQ ID NO 113
<211> LENGTH: 88
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 113

aucucuuaca caggcugacc gauuucuccu gguguucaga gucuguuuuu gucuagcacc 60

auuugaaauc gguuaugaug uaggggga 88

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<210> SEQ ID NO 114
<211> LENGTH: 71
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 114

gcgacuguaa acauccucga cuggaagcug ugaagccaca gaugggcuuu cagucggaug 60

uuugcagcug c 71

<210> SEQ ID NO 115
<211> LENGTH: 70
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 115

guuguuguaa acaucccga cuggaagcug uaagacacag cuaagcuuuc agucagaugu 60

uugcugcuac 70

<210> SEQ ID NO 116
<211> LENGTH: 92
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 116

gggcagucuu ugcuacugua aacauccuug acuggaagcu guaagguguu cagaggagcu 60

uucagucgga uguuuacagc ggcaggcugc ca 92

<210> SEQ ID NO 117
<211> LENGTH: 71
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 117

ggagaggagg caagaugcug gcauagcugu ugaacuggga accugcuaug ccaacauauu 60

gccaucuuuc c 71

<210> SEQ ID NO 118
<211> LENGTH: 99
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 118

gaaacugggc ucaaggugag gggugcuauc ugugauugag ggacaugguu aauggaauug 60

ucucacacag aaaucgcacc cgucaccuug gccuacuua 99

<210> SEQ ID NO 119
<211> LENGTH: 98
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 119

acccaaaccc uaggucugcu gacuccuagu ccagggcucg ugauggcugg ugggcccuga 60

acgagggguc uggaggccug gguuugaaua ucgacagc 98

<210> SEQ ID NO 120
<211> LENGTH: 110
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

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<400> SEQUENCE: 120

ggccagcugu gaguguuucu uuggcagugu cuuagcuggu uguugugagc aauaguaagg 60

aagcaaucag caaguauacu gcccuagaag ugcugcacgu uguggggccc 110

<210> SEQ ID NO 121
<211> LENGTH: 77
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 121

agucuaguua cuaggcagug uaguuagcug auugcuaaua guaccaauca cuaaccacac 60

ggccagguaa aaagauu 77

<210> SEQ ID NO 122
<211> LENGTH: 72
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 122

ggagcuuauc agaaucucca gggguacuuu auaauuucaa aaagucccc aggugugauu 60

cugauuugcu uc 72

<210> SEQ ID NO 123
<211> LENGTH: 67
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 123

gugggccuca aauguggagc acuauucuga uguccaagug gaaagugcug cgacauuuga 60

gcgucac 67

<210> SEQ ID NO 124
<211> LENGTH: 64
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 124

ccccgcgacg agccccucgc acaaaccgga ccugagcguu uuguucguuc ggcucgcgug 60

aggc 64

<210> SEQ ID NO 125
<211> LENGTH: 66
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 125

agggcuccug acuccagguc cuguguguua ccuagaaaua gcacuggacu uggagucaga 60

aggccu 66

<210> SEQ ID NO 126
<211> LENGTH: 96
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 126

ucccuggcgu gaggguaugu gccuuuggac uacaucgugg aagccagcac caugcagucc 60

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augggcauau acacuugccu caaggccuau gucauc 96

<210> SEQ ID NO 127
<211> LENGTH: 84
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 127

uugguacuug gagagugguu aucccugucc uguucguuuu gcucaugucg aaucguacag 60

ggucauccac uuuuucagua ucaa 84

<210> SEQ ID NO 128
<211> LENGTH: 112
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 128

ccaccccggu ccugcucccg ccccagcagc acacuguggu uuguacggca cuguggccac 60

guccaaacca cacuguggug uuagagcgag gguggggggag gcaccgccga gg 112

<210> SEQ ID NO 129
<211> LENGTH: 94
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 129

caugcugugu gugguacccu acugcagaca guggcaauca uguauaauua aaaaugauug 60

guacgucugu ggguagagua cugcaugaca caug 94

<210> SEQ ID NO 130
<211> LENGTH: 91
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 130

caugcugugu gugguacccu acugcagaca guggcaauca uguauaauua aaaaugauug 60

guacgucugu ggguagagua cugcaugaca c 91

<210> SEQ ID NO 131
<211> LENGTH: 75
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 131

gugguacccu acugcagacg uggcaaucau guauaauuaa aaaugauugg uacgucugug 60

gguagaguac ugcau 75

<210> SEQ ID NO 132
<211> LENGTH: 90
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 132

ucucaggcug ugaccuucuc gaggaaagaa gcacuuucug uugucugaaa gaaaagaaag 60

ugcuuccuuu cagaggguua cgguuugaga 90

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<210> SEQ ID NO 133
<211> LENGTH: 90
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 133

ucucagguug ugaccuucuc gaggaaagaa gcacuuucug uugucugaaa gaaaagaaag 60

ugcuuccuuu cagaggguua cgguuugaga 90

<210> SEQ ID NO 134
<211> LENGTH: 96
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 134

gggaccugcg ugggugcggg cgugugagug ugugugugug aguguguguc gcuccggguc 60

cacgcucaug cacacaccca cacgcccaca cucagg 96

<210> SEQ ID NO 135
<211> LENGTH: 98
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 135

acgaauggcu augcacugca caacccuagg agagggugcc auucacauag acuauaauug 60

aauggcgcca cuaggguugu gcagugcaca accuacac 98

<210> SEQ ID NO 136
<211> LENGTH: 110
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 136

uuggauguug gccuaguucu guguggaaga cuagugauuu uguuguuuuu agauaacuaa 60

aucgacaaca aaucacaguc ugccauaugg cacaggccau gccucuacag 110

<210> SEQ ID NO 137
<211> LENGTH: 110
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 137

cuggauacag aguggaccgg cuggccccau cuggaagacu agugauuuug uuguugucuu 60

acugcgcuca acaacaaauc ccagucuacc uaauggugcc agccaucgca 110

<210> SEQ ID NO 138
<211> LENGTH: 110
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 138

agauuagagu ggcugugguc uagugcugug uggaagacua gugauuuugu uguucugaug 60

uacuacgaca acaagucaca gccggccuca uagcgcagac ucccuucgac 110

<210> SEQ ID NO 139
<211> LENGTH: 89
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

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<400> SEQUENCE: 139

cgggguuggu uguuaucuuu gguuaucuag cuguaugagu gguguggagu cuucauaaag 60

cuagauaacc gaaaguaaaa auaacccca 89

<210> SEQ ID NO 140
<211> LENGTH: 87
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 140

ggaagcgagu uguuaucuuu gguuaucuag cuguaugagu guauuggucu ucauaaagcu 60

agauaaccga aaguaaaaac uccuuca 87

<210> SEQ ID NO 141
<211> LENGTH: 90
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 141

ggaggcccgu uucucucuuu gguuaucuag cuguaugagu gccacagagc cgucauaaag 60

cuagauaacc gaaaguagaa augauucuca 90

<210> SEQ ID NO 142
<211> LENGTH: 78
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 142

cuuucuacac agguuugggau cgguugcaau gcuguguuuc uguaugguau ugcacuuguc 60

ccggccuguu gaguuugg 78

<210> SEQ ID NO 143
<211> LENGTH: 75
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 143

ucaucccugg gugggguuu guugcauuac uuguguucua uauaaaguau ugcacuuguc 60

ccggccugug gaaga 75

<210> SEQ ID NO 144
<211> LENGTH: 96
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 144

cgggccccgg gcgggcggga gggacgggac gcggugcagu guuguuuuuu cccccgccaa 60

uauugcacuc gucccggccu ccggcccccc cggccc 96

<210> SEQ ID NO 145
<211> LENGTH: 83
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 145

agaaauaagg cuucugucua cuacuggaga cacugguagu auaaaaccca gagucuccag 60

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uaauggacgg gagccuuauu ucu 83

<210> SEQ ID NO 146
<211> LENGTH: 24
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 146

agccugauua aacacaugcu cuga 24

<210> SEQ ID NO 147
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 147

agcuacauug ucugcugggu uuc 23

<210> SEQ ID NO 148
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 148

caaagugcug uucgugcagg uag 23

<210> SEQ ID NO 149
<211> LENGTH: 85
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 149

uuuacaguuu gccaugauga aaugcauguu aaguccgugu uucagcugau cagccugauu 60

aaacacaugc ucugagcaga cuaaa 85

<210> SEQ ID NO 150
<211> LENGTH: 110
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 150

ugaacaucca ggucuggggc augaaccugg cauacaaugu agauuucugu guucguuagg 60

caacagcuac auugucugcu ggguuucagg cuaccuggaa acauguucuc 110

<210> SEQ ID NO 151
<211> LENGTH: 80
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 151

cuggggcuc caaagugcug uucgugcagg uagugugauu acccaaccua cugcugagcu 60

agcacuuccc gagccccccgg 80

<210> SEQ ID NO 152
<211> LENGTH: 24
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 152

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uuuggcaaug guagaacuca cacu 24

<210> SEQ ID NO 153
<211> LENGTH: 22
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 153

agagguagua gguugcauag uu 22

<210> SEQ ID NO 154
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 154

aacauucauu gcugucggug ggu 23

<210> SEQ ID NO 155
<211> LENGTH: 22
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 155

ucggauccgu cugagcuugg cu 22

<210> SEQ ID NO 156
<211> LENGTH: 22
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 156

ugagguagga gguuguauag uu 22

<210> SEQ ID NO 157
<211> LENGTH: 22
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 157

ugagguagua guuugugcug uu 22

<210> SEQ ID NO 158
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 158

aaaagugcuu acagugcagg uag 23

<210> SEQ ID NO 159
<211> LENGTH: 20
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 159

uaaggcacgc ggugaaugcc 20

<210> SEQ ID NO 160
<211> LENGTH: 27

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<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 160

accuucuugu auaagcacug ugcuaaa 27

<210> SEQ ID NO 161
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 161

ucacagugaa ccggucucuu u 21

<210> SEQ ID NO 162
<211> LENGTH: 22
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 162

aagcccuuac cccaaaaagc au 22

<210> SEQ ID NO 163
<211> LENGTH: 22
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 163

ucaaaacuga ggggcauuuu cu 22

<210> SEQ ID NO 164
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 164

cauaaaguag aaagcacuac u 21

<210> SEQ ID NO 165
<211> LENGTH: 22
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 165

ggugcagugc ugcaucucug gu 22

<210> SEQ ID NO 166
<211> LENGTH: 22
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 166

ugcccugugg acucaguucu gg 22

<210> SEQ ID NO 167
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 167

agggagggac gggggcugug c 21

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<210> SEQ ID NO 168
<211> LENGTH: 22
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 168

ucucccaacc cuuguaccag ug 22

<210> SEQ ID NO 169
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 169

ucagugcaug acagaacuug g 21

<210> SEQ ID NO 170
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 170

uuaaugcuaa ucgugauagg ggu 23

<210> SEQ ID NO 171
<211> LENGTH: 22
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 171

uagcagcaca uaaugguuug ug 22

<210> SEQ ID NO 172
<211> LENGTH: 22
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 172

uagcagcaca ucaugguuua ca 22

<210> SEQ ID NO 173
<211> LENGTH: 22
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 173

aacauucaac cugucgguga gu 22

<210> SEQ ID NO 174
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 174

aacauucauu guugucggug ggu 23

<210> SEQ ID NO 175
<211> LENGTH: 22
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

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<400> SEQUENCE: 175

uauggcacug guagaauuca cu 22

<210> SEQ ID NO 176
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 176

uaaggugcau cuagugcaga uag 23

<210> SEQ ID NO 177
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 177

cugaccuaug aauugacagc c 21

<210> SEQ ID NO 178
<211> LENGTH: 22
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 178

aacuggcccu caaagucccg cu 22

<210> SEQ ID NO 179
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 179

uagcagcaca gaaauauugg c 21

<210> SEQ ID NO 180
<211> LENGTH: 19
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 180

accgugcaaa gguagcaua 19

<210> SEQ ID NO 181
<211> LENGTH: 22
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 181

acaguagucu gcacauuggu ua 22

<210> SEQ ID NO 182
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 182

cccaguguuc agacuaccug uuc 23

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<210> SEQ ID NO 183
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 183

cccaguguuu agacuaucug uuc 23

<210> SEQ ID NO 184
<211> LENGTH: 22
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 184

gugaaauguu uaggaccacu ag 22

<210> SEQ ID NO 185
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 185

gauuucagug gagugaaguu c 21

<210> SEQ ID NO 186
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 186

uaaagugcuu auagugcagg uag 23

<210> SEQ ID NO 187
<211> LENGTH: 22
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 187

agaauugugg cuggacaucu gu 22

<210> SEQ ID NO 188
<211> LENGTH: 22
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 188

cauugcacuu gucucggucu ga 22

<210> SEQ ID NO 189
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 189

uucacagugg cuaaguucug c 21

<210> SEQ ID NO 190
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 190

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uagcaccauu ugaaaucagu guu 23

<210> SEQ ID NO 191
<211> LENGTH: 22
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 191

uagcaccauu ugaaaucggu ua 22

<210> SEQ ID NO 192
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 192

uaagugcuuc cauguuuugg uga 23

<210> SEQ ID NO 193
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 193

acuuaaacgu ggauguacuu gcu 23

<210> SEQ ID NO 194
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 194

uaagugcuuc cauguuugag ugu 23

<210> SEQ ID NO 195
<211> LENGTH: 22
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 195

cuuucagucg gauguuugca gc 22

<210> SEQ ID NO 196
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uucccggcca augcauua 18

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uucaaguaau ccaggauagg cu 22

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aacacaccug guuaaccucu uu 22

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gaacggcuuc auacaggagu u 21

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uccagcauca gugauuuugu ug 22

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aauccuugga accuaggugu gagu 24

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aacauagagg aaauuccacg u 21

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gaaguuguuc gugguggauu cg 22

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<400> SEQUENCE: 327

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ucacuccucu ccucccgucu u 21

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aaucauacag ggacauccag uu 22

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aaacaaacau ggugcacuuc uu 22

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<400> SEQUENCE: 345

uaaggcaccc uucugaguag a 21

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uucacaggga ggugucau 18

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ccucccacac ccaaggcuug ca 22

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ggagaaauua uccuuggugu gu 22

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aaacauucgc ggugcacuuc uu 22

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uacgucaucg uugucaucgu ca 22

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gcugggcagg gcuucugagc uccuu 25

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uaugucugcu gaccaucacc uu 22

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ggcggaggga aguagguccg uuggu 25

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uacccauugc auaucggagu ug 22

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accaggaggc ugaggccccu 20

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aaggagcuua caaucuagcu ggg 23

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gcaggaacuu gugagucucc u 21

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cugcccuggc ccgagggacc ga 22

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cacccguaga accgaccuug cg 22

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aagugauugg aggugggugg gg 22

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agaagcugaa gggagagaga ca 22

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aaucugcagg gggagccugg gu 22

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agcgagguug cccuuuguau auu 23

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agggcugggg acagagaug 19

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agugaagcau uggacugua 19

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aucccacucc ugacacca 18

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cauccuagcc cuaagucugg c 21

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cccaggcugg aguguagugg cgugaucu 28

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cgccugugaa uagucacugc ac 22

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gaaucccacu ucugacacca 20

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guuccuguug gccgagugga gac 23

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uggggccucc cacagcuguu uc 22

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ugguggucua gugguua 17

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uguccaaagu aaacgcccug acgca 25

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uucaugggga agcagauuug 20

<210> SEQ ID NO 388
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<212> TYPE: RNA
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<400> SEQUENCE: 388

ugaggggcag agagcgagac uuu 23

<210> SEQ ID NO 389
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cauagcccgg ucgcugguac auga 24

<210> SEQ ID NO 390
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<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 390

gccgagacua gagucacauc cug 23

1. A method of identifying a tissue of origin of a cancer, said method comprising:

(a) obtaining a biological sample from a subject;

(b) measuring the relative abundance in said sample of nucleic acid sequences selected from the group consisting of SEQ ID NOS: 1-390 or a sequence having at least about 80% identity thereto; and

(c) comparing said measurement to a reference abundance of said nucleic acid by using a classifier algorithm;

wherein the relative abundance of said nucleic acid sequences allows for the identification of the tissue of origin of said sample.

2.-**41**. (canceled)

42. A method of distinguishing between cancers of different origins, said method comprising:

(a) obtaining a biological sample from a subject;

(b) measuring the relative abundance in said sample of nucleic acid sequences selected from the group consisting of SEQ ID NOS: 1-390 or a sequence having at least about 80% identity thereto; and

(c) comparing said measurement to a reference abundance of said nucleic acid by using a classifier algorithm;

wherein the relative abundance of said nucleic acid sequence in said sample allows for distinguishing between cancers of different origins.

43.-**94**. (canceled)

95. A kit for cancer origin identification, said kit comprising a probe comprising a sequence selected from the group consisting of a sequence that is complementary to a sequence selected from SEQ ID NOS: 1-390; a fragment thereof and a sequence having at least about 80% identity thereto.

* * * * *