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(54) **KIT OR DEVICE FOR DETECTING LUNG CANCER, AND LUNG CANCER DETECTION METHOD**

KIT ODER VORRICHTUNG FÜR DEN NACHWEIS VON LUNGENKREBS SOWIE LUNGENKREBSNACHWEISVERFAHREN

KIT OU UN DISPOSITIF POUR LA DÉTECTION D'UN CANCER DU POUMON, ET PROCÉDÉ DE DÉTECTION D'UN CANCER DU POUMON

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Description

Technical Field

[0001] The present invention relates to the use of a kit or a device for the detection of lung cancer, comprising a nucleic acid capable of specifically binding to a particular miRNA, which is used for examining the presence or absence of lung cancer in a subject, and a method for detecting lung cancer, comprising measuring an expression level of the miRNA *in vitro* using the nucleic acid.

Background Art

[0002] The lungs have important functions of supplying oxygen into the body through respiration and eliminating carbon dioxide. Air taken up from the mouth or the nose passes through the trachea and the bronchus, then separately enters the left lung and the right lung, and spreads throughout the lung through the thinner bronchial tubes. Eventually, oxygen is taken up into blood in the alveoli while carbon dioxide is eliminated (Non Patent Literature 1).

[0003] According to the 2012 cancer type-specific statistics in Japan disclosed by the Center for Cancer Control and Information Services, National Cancer Center, the number of individuals affected by lung cancer was 107,241 people. Namely, it is estimated that one out of 10 males and one out of 22 females experience lung cancer. The number of incidences of this cancer among other cancer types takes the 3rd in place. Men are twice as likely as women to develop lung cancer. The number of lung cancer deaths in men and women together climbs to 71,518 people and takes the 1st in place among other cancer types. The estimated number of American individuals affected by lung cancer climbed to 224,210 people in 2014, among which approximately 159,260 people reportedly died (Non Patent Literature 1).

[0004] Lung cancer has multiple histological types. Small-cell lung cancer occupies approximately 15%, while the remaining histological types are called non-small cell lung cancer. The non-small cell lung cancer is further broadly classified into three subtypes; adenocarcinoma, squamous cell carcinoma, and large-cell carcinoma. These histological types differ largely in the site of origin, the manner and rate of progression, symptoms, etc., and therefore differ in treatment methods.

[0005] The stages of lung cancer progression are classified into stages 0 to 4 according to the degrees of tumor spread (T0, Tis, and T1 to T4), lymph node metastasis (N0 to N3), and distant metastasis (M0 and M1). Particularly, as for the tumor spread, T1 denotes tumor of 3 cm or less in greatest diameter; T2 denotes tumor of more than 3 cm but 7 cm or less across; T3 denotes tumor of more than 7 cm across or found to have invaded adjacent sites; and T4 denotes tumor that has invaded adjacent sites more widely regardless of its size.

[0006] The survival rate of lung cancer differs depending on the stages of progression. According to the report of Non Patent Literature 1, the 5-year relative survival rate of non-small cell lung cancer is 45 to 49% for stage 1, 30 to 31% for stage 2, 5 to 14% for stage 3, and 1% for stage 4. Thus, the detection and treatment of lung cancer at an early stage makes a significant contribution to improvement in the survival rate.

[0007] The treatment of lung cancer is mainly performed by surgical resection, radiotherapy, and anticancer drug treatment. Particularly, in early lung cancer, surgery is applicable and the cancer is likely to be completely cured (Non Patent Literature 1). For early lung cancer, there are some therapeutic options, and for example, treatment that places less burden on patients, such as thoracoscopic surgery, stereotactic body radiotherapy (SBRT), photo dynamic therapy, laser treatment, and brachytherapy, which delivers radiation from within the body, can also be applied to such lung cancer (Non Patent Literature 1).

[0008] As described in Non Patent Literature 1, diagnostic tests of lung cancer are medical history check and physical examination as well as chest X-ray examination which is most commonly conducted. When there are findings that suspects lung cancer by the chest X-ray examination, more precise diagnostic imaging such as CT, MRI, or PET is carried out. Alternatively, as tests using samples, sputum cytology, pleural fluid analysis, or pathological examination which involves inserting a needle into a lesion and collecting cells or tissues, which are then examined under a microscope is carried out. Furthermore, CEA and CYFRA21-1 are known as tumor markers for the detection of lung cancer.

[0009] As shown in Patent Literatures 1 and 2, there are reports, albeit at a research stage, on the detection of lung cancer using the expression levels of microRNAs (miRNAs) or combinations of the expression levels of miRNAs and the expression levels of additional protein markers in biological samples including blood.

[0010] Patent Literature 1 discloses a method for detecting lung cancer or other lung diseases using miR-19b (miR-19b-3p) and the like in serum.

[0011] Patent Literature 2 discloses a method for detecting lung cancer using miR-1268 and miR-1228 in serum or plasma.

[0012] Patent Literature 3 discloses a method for detecting lung cancer using miR-1307 and the like in blood cells.

[0013] Patent Literature 4 discloses methods for diagnosing diseases based on the determination of specific miRNAs that have altered expression levels. The miR-6768-5pmarker is not disclosed.

Citation List

Patent Literature

[0014]

Patent Literature 1: JP Patent Publication (Kohyo) No. 2013-502931 A (2013)

Patent Literature 2: International Publication No. WO 2011/146937

Patent Literature 3: U.S. Patent Application Publication No. 13/376281

Patent Literature 4: WO2015/190542

Non Patent Literature

[0015]

Non Patent Literature 1: American Cancer Society, "Lung Cancer (Non-Small Cell)", 2013, p. 2 to 7 and 37 to 56
Non Patent Literature 2: Sobin, L. et al., "TNM Classification of Malignant Tumours, the 7th edition", 2010, p. 129-134
Non Patent Literature 3: Okamura, K. et al, Lung Cancer, 2013, Vol. 80 (1), p. 45-9

Summary of Invention

Technical Problem

[0016] An object of the present invention is to find a novel tumor marker for lung cancer and to provide a method that can effectively detect lung cancer using a nucleic acid capable of specifically binding to the marker. Chest X-ray examination is being commonly practiced as a test of lung cancer. Nonetheless, the number of lung cancer deaths is increasing yearly and takes the first place by cancer type. For these reasons, it is not always true that the X-ray examination works as a deterrent for lung cancer. Although CT and MRI are capable of detecting lung cancer with high performance, these tests are not suitable for widespread use as 1st tests because of the necessity of their special apparatuses and expensive examination cost.

[0017] For example, CEA and CYFRA21-1 are known as tumor markers in blood for the detection of lung cancer (Non Patent Literature 3). The usefulness thereof, however, has not yet been established. The lung cancer guidebook provided by the American Cancer Society makes no mention about these markers (Non Patent Literature 1). According to the report of Non Patent Literature 3, these tumor markers in blood have general lung cancer detection sensitivity of 69% (CEA) and 43% (CYFRA21-1). The tumor markers such as CEA and CYFRA21-1 may elevate for reasons other than lung cancer and therefore allegedly fail to determine the presence or absence of lung cancer. The false diagnosis of other cancers as lung cancer wastes appropriate therapeutic opportunity or places unnecessary economical and physical burdens on patients due to the application of wrong medicine.

[0018] As described below, there are reports, albeit at a research stage, on the determination of lung cancer using the expression levels of microRNAs (miRNAs) in biological samples including blood, none of which, however, have yet been brought into practical use.

[0019] Patent Literature 1 discloses a method for detecting lung cancer or other lung diseases using miR-19b (miR-19b-3p) and the like in serum. However, the number of samples from healthy subjects used as negative controls was as small as a dozen. Therefore, the universality of the marker for the difference among subjects is not insured. Thus, this method has low reliability as a method for detecting lung cancer.

[0020] Patent Literature 2 discloses a method for detecting lung cancer using miR-1268 and miR-1228 in serum or plasma. These markers, however, were validated in only 3 mesothelioma cases as a cancer other than lung cancer. Thus, the possibility that these markers have a high rate of false positives and detect cancers other than lung cancer cannot be excluded.

[0021] Patent Literature 3 discloses a method for detecting lung cancer using miR-1307 and the like in blood cells. However, a marker obtained using one case group was not validated in another independent case group. Thus, this method has low reliability as a method for testing lung cancer.

[0022] As mentioned above, the existing tumor markers exhibit low performance in the detection of lung cancer, or neither performance nor detection methods are specifically shown as to the markers at a research stage. Therefore, use of these markers might lead to carrying out needless extra examination due to the false detection of healthy subjects

as being lung cancer patients, or might waste therapeutic opportunity because of overlooking lung cancer patients. In addition, the measurement of several dozens to several hundreds of miRNAs increases examination cost and is therefore difficult to use in large-scale screening such as medical checkup. Furthermore, the collection of lung tissues for measuring the tumor markers is highly invasive to patients and is not favorable. Hence, there is a demand for a highly accurate lung cancer marker that is detectable from blood, which can be collected with limited invasiveness, and is capable of correctly determining a lung cancer patient as a lung cancer patient and a healthy subject as a healthy subject. Particularly, the early detection of lung cancer can increase the applicability of surgery and drastically improve the survival rates. For early lung cancer, there are multiple therapeutic options. There is a possibility that treatment that places less burden on patients, such as thoracoscopic surgery or stereotactic body radiotherapy, can also be applied to such lung cancer. Therefore, a highly sensitive lung cancer marker that can detect lung cancer even at an early stage of progression is desired.

Solution to Problem

[0023] The present inventors have conducted diligent studies to attain the object and consequently completed the present invention by finding multiple genes usable as markers for the detection of lung cancer from blood, which can be collected with limited invasiveness, and finding that lung cancer can be significantly detected by using a nucleic acid capable of specifically binding to any of these markers.

<Summary of Invention>

[0024] Specifically, the present invention has the following features:
In a first aspect the invention provides the use of a kit in the *in vitro* diagnosis of lung cancer, the kit comprising a nucleic acid capable of specifically binding to lung cancer marker miR-6768-5p.

[0025] In a further aspect the invention provides the use of a device in the *in vitro* diagnosis of lung cancer, comprising a nucleic acid capable of specifically binding to a polynucleotide of lung cancer marker miR-6768-5p.

[0026] In a further aspect the invention provides a method for detecting lung cancer, comprising measuring an expression level of a target nucleic acid in a sample from a subject using the kit defined in any one of claims 1 to 5 or the device defined in any one of claims 6 to 12, and evaluating *in vitro* whether or not the subject has lung cancer using both of the measured expression level and a control expression level of in a sample from a healthy subject measured in the same way.

[0027] In a further aspect the invention provides the use of a marker in the *in vitro* diagnosis of lung cancer, the marker comprising polynucleotide miR-6768-5p.

[0028] Further aspects and embodiments of the invention are set out in the accompanying claims and are described in more detail below.

<Definition of Terms>

[0029] The terms used herein are defined as follows.

[0030] Abbreviations or terms such as nucleotide, polynucleotide, DNA, and RNA abide by "Guidelines for the preparation of specification which contain nucleotide and/or amino acid sequences" (edited by Japan Patent Office) and common use in the art.

[0031] The term "polynucleotide" used herein is used for a nucleic acid including any of RNA, DNA, and RNA/DNA (chimera). The DNA includes any of cDNA, genomic DNA, and synthetic DNA. The RNA includes any of total RNA, mRNA, rRNA, miRNA, siRNA, snoRNA, snRNA, non-coding RNA and synthetic RNA. Here the "synthetic DNA" and the "synthetic RNA" refer to DNA and RNA artificially prepared using, for example, an automatic nucleic acid synthesizer, on the basis of predetermined nucleotide sequences (which may be any of natural and non-natural sequences). The "non-natural sequence" is intended to be used in a broad sense and includes, for example, a sequence comprising substitution, deletion, insertion, and/or addition of one or more nucleotide(s) (i.e., a variant sequence) and a sequence comprising one or more modified nucleotide(s) (i.e., a modified sequence), which are different from the natural sequence. Herein, the term "polynucleotide" is used interchangeably with the term "nucleic acid".

[0032] The term "fragment" used herein is a polynucleotide having a nucleotide sequence that consists of a consecutive portion of a polynucleotide and desirably has a length of 15 or more nucleotides, preferably 17 or more nucleotides, more preferably 19 or more nucleotides.

[0033] The term "gene" used herein is intended to include not only RNA and double-stranded DNA but each single-stranded DNA such as a plus strand (or a sense strand) or a complementary strand (or an antisense strand) constituting the duplex. The gene is not particularly limited by its length.

[0034] Thus, the "gene" used herein includes any of double-stranded DNA including human genomic DNA, single-

stranded DNA (plus strand) including cDNA, single-stranded DNA having a sequence complementary to the plus strand (complementary strand), microRNA (miRNA), and their fragments, and transcripts, unless otherwise specified. The "gene" includes not only a "gene" represented by a particular nucleotide sequence (or SEQ ID NO) but "nucleic acids" encoding RNAs having biological functions equivalent to an RNA encoded by the gene, for example, a congener (i.e., a homolog or an ortholog), a variant (e.g., a genetic polymorph), and a derivative. Specific examples of such a "nucleic acid" encoding a congener, a variant, or a derivative can include a "nucleic acid" having a nucleotide sequence hybridizing under stringent conditions described later to a complementary sequence of a nucleotide sequence represented by any of SEQ ID NOs: 1 to 618, or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t. The "gene" is not particularly limited by its functional region and can contain, for example, an expression regulatory region, a coding region, an exon, or an intron. The "gene" may be contained in a cell or may exist alone after being released into the outside of a cell. Alternatively, the "gene" may be in a state enclosed in a vesicle called exosome.

[0035] The term "exosome" used herein is a vesicle that is encapsulated by a lipid bilayer and secreted from a cell. The exosome is derived from a multivesicular endosome and may incorporate biomaterials such as a "gene" (e.g., RNA or DNA) or a protein when released into an extracellular environment. The exosome is known to be contained in a body fluid such as blood, serum, plasma, or lymph.

[0036] The term "transcript" used herein refers to an RNA synthesized with the DNA sequence of a gene as a template. RNA polymerase binds to a site called a promoter located upstream of the gene and adds ribonucleotides complementary to the nucleotide sequence of the DNA to the 3' end to synthesize RNA. This RNA contains not only the gene itself but also the whole sequence from a transcription initiation site to the end of a polyA sequence, including an expression regulatory region, a coding region, an exon, or an intron.

[0037] The term "microRNA (miRNA)" used herein is intended to mean a 15- to 25-nucleotide non-coding RNA that is involved in the suppression of translation of mRNA, and that transcribed as an RNA precursor having a hairpin-like structure, cleaved by a dsRNA-cleaving enzyme which has RNase III cleavage activity, and integrated into a protein complex called RISC, unless otherwise specified. The term "miRNA" used herein includes not only a "miRNA" represented by a particular nucleotide sequence (or SEQ ID NO) but a precursor of the "miRNA" (pre-miRNA or pri-miRNA), and miRNAs having biological functions equivalent thereto, for example, a congener (i.e., a homolog or an ortholog), a variant (e.g., a genetic polymorph), and a derivative. Such a precursor, a congener, a variant, or a derivative can be specifically identified using miRBase Release 20 (http://www.mirbase.org/), and examples thereof can include a "miRNA" having a nucleotide sequence hybridizing under stringent conditions described later to a complementary sequence of any particular nucleotide sequence represented by any of SEQ ID NOs: 1 to 618. The term "miRNA" used herein may be a gene product of a miR gene. Such a gene product includes a mature miRNA (e.g., a 15- to 25-nucleotide or 19- to 25-nucleotide non-coding RNA involved in the suppression of translation of mRNA as described above) or a miRNA precursor (e.g., pre-miRNA or pri-miRNA as described above).

[0038] The term "probe" used herein includes a polynucleotide that is used for specifically detecting RNA resulting from the expression of a gene or a polynucleotide derived from the RNA, and/or a polynucleotide complementary thereto.

[0039] The term "primer" used herein includes a polynucleotide that specifically recognizes and amplifies RNA resulting from the expression of a gene or a polynucleotide derived from the RNA, and/or a polynucleotide complementary thereto.

[0040] In this context, the complementary polynucleotide (complementary strand or reverse strand) means a polynucleotide in a complementary base relationship of A:T (U) and G:C base pairs with the full-length sequence of a polynucleotide consisting of a nucleotide sequence defined by any of SEQ ID NOs: 1 to 618 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, or a partial sequence thereof (here, this full-length or partial sequence is referred to as a plus strand for the sake of convenience). However, such a complementary strand is not limited to a sequence completely complementary to the nucleotide sequence of the target plus strand and may have a complementary relationship to an extent that permits hybridization under stringent conditions to the target plus strand.

[0041] The term "stringent conditions" used herein refers to conditions under which a nucleic acid probe hybridizes to its target sequence to a larger extent (e.g., a measurement value equal to or larger than a mean of background measurement values + a standard deviation of the background measurement values $\times$ 2) than that for other sequences. The stringent conditions are dependent on a sequence and differ depending on an environment where hybridization is performed. A target sequence that is 100% complementary to the nucleic acid probe can be identified by controlling the stringency of hybridization and/or washing conditions. Specific examples of the "stringent conditions" will be mentioned later.

[0042] The term "Tm value" used herein means a temperature at which the double-stranded moiety of a polynucleotide is denatured into single strands so that the double strands and the single strands exist at a ratio of 1:1.

[0043] The term "variant" used herein means, in the case of a nucleic acid, a natural variant attributed to polymorphism, mutation, or the like; a variant containing the deletion, substitution, addition, or insertion of 1, 2, or 3 or more nucleotides in a nucleotide sequence represented by any of SEQ ID NOs: 1 to 618 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, or a partial sequence thereof; a variant containing the deletion, substitution, addition, or insertion of 1 or 2 or more nucleotides in a nucleotide sequence of a premature miRNA of a

sequence represented by any of SEQ ID NOs: 1 to 618 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, or a partial sequence thereof; a variant that exhibits identity of approximately 90% or higher, approximately 95% or higher, approximately 97% or higher, approximately 98% or higher, approximately 99% or higher to each of these nucleotide sequences or the partial sequence thereof; or a nucleic acid hybridizing under the stringent conditions defined above to a polynucleotide or an oligonucleotide comprising each of these nucleotide sequences or the partial sequence thereof.

[0044] The term "several" used herein means an integer of approximately 10, 9, 8, 7, 6, 5, 4, 3, or 2.

[0045] The variant used herein can be prepared by use of a well-known technique such as sitedirected mutagenesis or PCR-based mutagenesis.

[0046] The term "identity" used herein can be determined with or without an introduced gap, using a protein or gene search system based on BLAST or FASTA described above (Zheng Zhang et al., 2000, J. Comput. Biol., Vol. 7, p. 203-214; Altschul, S.F. et al., 1990, Journal of Molecular Biology, Vol. 215, p. 403-410; and Pearson, W.R. et al., 1988, Proc. Natl. Acad. Sci. U. S. A., Vol. 85, p. 2444-2448).

[0047] The term "derivative" used herein is meant to include a modified nucleic acid, for example, a derivative labeled with a fluorophore or the like, a derivative containing a modified nucleotide (e.g., a nucleotide containing a group such as halogen, alkyl such as methyl, alkoxy such as methoxy, thio, or carboxymethyl, and a nucleotide that has undergone base rearrangement, double bond saturation, deamination, replacement of an oxygen molecule with a sulfur atom, etc.), PNA (peptide nucleic acid; Nielsen, P.E. et al., 1991, Science, Vol. 254, p. 1497-500), and LNA (locked nucleic acid; Obika, S. et al., 1998, Tetrahedron Lett., Vol. 39, p. 5401-5404) without any limitation.

[0048] As used herein, the "nucleic acid" capable of specifically binding to a polynucleotide selected from the lung cancer marker miRNAs described above is a synthesized or prepared nucleic acid and specifically includes a "nucleic acid probe" or a "primer". The "nucleic acid" is utilized directly or indirectly for detecting the presence or absence of lung cancer in a subject, for diagnosing the presence or absence of lung cancer, the severity of lung cancer, the presence or absence of amelioration or the degree of amelioration of lung cancer, or the sensitivity of lung cancer for treatment, or for screening for a candidate substance useful in the prevention, amelioration, or treatment of lung cancer. The "nucleic acid" includes a nucleotide, an oligonucleotide, and a polynucleotide capable of specifically recognizing and binding to a transcript represented by any of SEQ ID NOs: 1 to 618 or a synthetic cDNA nucleic acid thereof *in vivo,* particularly, in a sample such as a body fluid (e.g., blood or urine), in relation to the development of lung cancer. The nucleotide, the oligonucleotide, and the polynucleotide can be effectively used as probes for detecting the aforementioned gene expressed *in vivo,* in tissues, in cells, or the like on the basis of the properties described above, or as primers for amplifying the aforementioned gene expressed *in vivo.*

[0049] The term "detection" used herein is interchangeable with the term "examination", "measurement", "detection", or "decision support". As used herein, the term "evaluation" is meant to include diagnosing or evaluation-supporting on the basis of examination results or measurement results.

[0050] The term "subject" used herein means a mammal such as a primate including a human and a chimpanzee, a pet animal including a dog and a cat, a livestock animal including cattle, a horse, sheep, and a goat, and a rodent including a mouse and a rat. The term "healthy subject" also means such a mammal without the cancer to be detected.

[0051] The term "P" or "P value" used herein refers to a probability at which a more extreme statistic than that actually calculated from data under null hypothesis is observed in a statistical test. Thus, smaller "P" or "P value" means more significant difference between subjects to be compared.

[0052] The term "sensitivity" used herein means a value of (the number of true positives) / (the number of true positives + the number of false negatives). High sensitivity allows lung cancer to be detected early, leading to the complete resection of cancer sites and reduction in the rate of recurrence.

[0053] The term "specificity" used herein means a value of (the number of true negatives) / (the number of true negatives + the number of false positives). High specificity prevents needless extra examination for healthy subjects misjudged as being lung cancer patients, leading to reduction in burden on patients and reduction in medical expense.

[0054] The term "accuracy" used herein means a value of (the number of true positives + the number of true negatives) / (the total number of cases). The accuracy indicates the ratio of samples that correctly identified in the discriminant results to all samples, and serves as a primary index for evaluating detection performance.

[0055] As used herein, the "sample" that is subject to determination, detection, or diagnosis refers to a tissue and a biological material in which the expression of the gene of the present invention varies as lung cancer develops, lung cancer progresses, and therapeutic effects on lung cancer are exerted. Specifically, the "sample" refers to a lung tissue, a peripulmonary vascular channel, lymph node, and organ, an organ suspected of having metastasis, the skin, a body fluid such as blood, urine, saliva, sweat, or tissue exudates, serum or plasma prepared from blood, feces, hair, and the like. The "sample" further refers to a biological sample extracted therefrom, specifically, a gene such as RNA or miRNA.

[0056] The term "hsa-miR-6768-5p gene" or "hsa-miR-6768-5p" used herein includes the hsa-miR-6768-5p gene (miRBase Accession No. MIMAT0027436) described in SEQ ID NO: 1, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6768-5p gene can be obtained by a method described in Ladewig E et al., 2012,

Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6768" (miRBase Accession No. MI0022613, SEQ ID NO: 175) having a hairpin-like structure is known as a precursor of "hsa-miR-6768-5p".

[0057] The term "hsa-miR-6836-3p gene" or "hsa-miR-6836-3p" used herein includes the hsa-miR-6836-3p gene (miRBase Accession No. MIMAT0027575) described in SEQ ID NO: 2, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6836-3p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6836" (miRBase Accession No. MI0022682, SEQ ID NO: 176) having a hairpin-like structure is known as a precursor of "hsa-miR-6836-3p".

[0058] The term "hsa-miR-6782-5p gene" or "hsa-miR-6782-5p" used herein includes the hsa-miR-6782-5p gene (miRBase Accession No. MIMAT0027464) described in SEQ ID NO: 3, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6782-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6782" (miRBase Accession No. MI0022627, SEQ ID NO: 177) having a hairpin-like structure is known as a precursor of "hsa-miR-6782-5p".

[0059] The term "hsa-miR-3663-3p gene" or "hsa-miR-3663-3p" used herein includes the hsa-miR-3663-3p gene (miRBase Accession No. MIMAT0018085) described in SEQ ID NO: 4, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-3663-3p gene can be obtained by a method described in Liao JY et al., 2010, PLoS One, Vol. 5, e10563. Also, "hsa-mir-3663" (miRBase Accession No. MI0016064, SEQ ID NO: 178) having a hairpin-like structure is known as a precursor of "hsa-miR-3663-3p".

[0060] The term "hsa-miR-1908-3p gene" or "hsa-miR-1908-3p" used herein includes the hsa-miR-1908-3p gene (miRBase Accession No. MIMAT0026916) described in SEQ ID NO: 5, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-1908-3p gene can be obtained by a method described in Bar M et al., 2008, Stem Cells, Vol. 26, p. 2496-2505. Also, "hsa-mir-1908" (miRBase Accession No. MI0008329, SEQ ID NO: 179) having a hairpin-like structure is known as a precursor of "hsa-miR-1908-3p".

[0061] The term "hsa-miR-6726-5p gene" or "hsa-miR-6726-5p" used herein includes the hsa-miR-6726-5p gene (miRBase Accession No. MIMAT0027353) described in SEQ ID NO: 6, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6726-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6726" (miRBase Accession No. MI0022571, SEQ ID NO: 180) having a hairpin-like structure is known as a precursor of "hsa-miR-6726-5p".

[0062] The term "hsa-miR-4258 gene" or "hsa-miR-4258" used herein includes the hsa-miR-4258 gene (miRBase Accession No. MIMAT0016879) described in SEQ ID NO: 7, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4258 gene can be obtained by a method described in Goff LA et al., 2009, PLoS One, Vol. 4, e7192. Also, "hsa-mir-4258" (miRBase Accession No. MI0015857, SEQ ID NO: 181) having a hairpin-like structure is known as a precursor of "hsa-miR-4258".

[0063] The term "hsa-miR-1343-3p gene" or "hsa-miR-1343-3p" used herein includes the hsa-miR-1343-3p gene (miRBase Accession No. MIMAT0019776) described in SEQ ID NO: 8, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-1343-3p gene can be obtained by a method described in Persson H et al., 2011, Cancer Res, Vol. 71, p. 78-86. Also, "hsa-mir-1343" (miRBase Accession No. MI0017320, SEQ ID NO: 182) having a hairpin-like structure is known as a precursor of "hsa-miR-1343-3p".

[0064] The term "hsa-miR-4516 gene" or "hsa-miR-4516" used herein includes the hsa-miR-4516 gene (miRBase Accession No. MIMAT0019053) described in SEQ ID NO: 9, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4516 gene can be obtained by a method described in Jima DD et al., 2010, Blood, Vol. 116, e118-e127. Also, "hsa-mir-4516" (miRBase Accession No. MI0016882, SEQ ID NO: 183) having a hairpin-like structure is known as a precursor of "hsa-miR-4516".

[0065] The term "hsa-miR-6875-5p gene" or "hsa-miR-6875-5p" used herein includes the hsa-miR-6875-5p gene (miRBase Accession No. MIMAT0027650) described in SEQ ID NO: 10, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6875-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6875" (miRBase Accession No. MI0022722, SEQ ID NO: 184) having a hairpin-like structure is known as a precursor of "hsa-miR-6875-5p".

[0066] The term "hsa-miR-4651 gene" or "hsa-miR-4651" used herein includes the hsa-miR-4651 gene (miRBase Accession No. MIMAT0019715) described in SEQ ID NO: 11, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4651 gene can be obtained by a method described in Persson H et al., 2011, Cancer Res, Vol. 71, p. 78-86. Also, "hsa-mir-4651" (miRBase Accession No. MI0017279, SEQ ID NO: 185) having a hairpin-like structure is known as a precursor of "hsa-miR-4651".

[0067] The term "hsa-miR-6825-5p gene" or "hsa-miR-6825-5p" used herein includes the hsa-miR-6825-5p gene (miRBase Accession No. MIMAT0027550) described in SEQ ID NO: 12, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6825-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6825" (miRBase Accession No. MI0022670, SEQ ID NO: 186) having a hairpin-like structure is known as a precursor of "hsa-miR-6825-5p".

[0068] The term "hsa-miR-6840-3p gene" or "hsa-miR-6840-3p" used herein includes the hsa-miR-6840-3p gene

(miRBase Accession No. MIMAT0027583) described in SEQ ID NO: 13, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6840-3p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6840" (miRBase Accession No. MI0022686, SEQ ID NO: 187) having a hairpin-like structure is known as a precursor of "hsa-miR-6840-3p".

[0069] The term "hsa-miR-6780b-5p gene" or "hsa-miR-6780b-5p" used herein includes the hsa-miR-6780b-5p gene (miRBase Accession No. MIMAT0027572) described in SEQ ID NO: 14, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6780b-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6780b" (miRBase Accession No. MI0022681, SEQ ID NO: 188) having a hairpin-like structure is known as a precursor of "hsa-miR-6780b-5p".

[0070] The term "hsa-miR-6749-5p gene" or "hsa-miR-6749-5p" used herein includes the hsa-miR-6749-5p gene (miRBase Accession No. MIMAT0027398) described in SEQ ID NO: 15, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6749-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6749" (miRBase Accession No. MI0022594, SEQ ID NO: 189) having a hairpin-like structure is known as a precursor of "hsa-miR-6749-5p".

[0071] The term "hsa-miR-8063 gene" or "hsa-miR-8063" used herein includes the hsa-miR-8063 gene (miRBase Accession No. MIMAT0030990) described in SEQ ID NO: 16, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-8063 gene can be obtained by a method described in Wang HJ et al., 2013, Shock, Vol. 39, p. 480-487. Also, "hsa-mir-8063" (miRBase Accession No. MI0025899, SEQ ID NO: 190) having a hairpin-like structure is known as a precursor of "hsa-miR-8063".

[0072] The term "hsa-miR-6784-5p gene" or "hsa-miR-6784-5p" used herein includes the hsa-miR-6784-5p gene (miRBase Accession No. MIMAT0027468) described in SEQ ID NO: 17, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6784-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6784" (miRBase Accession No. MI0022629, SEQ ID NO: 191) having a hairpin-like structure is known as a precursor of "hsa-miR-6784-5p".

[0073] The term "hsa-miR-3679-5p gene" or "hsa-miR-3679-5p" used herein includes the hsa-miR-3679-5p gene (miRBase Accession No. MIMAT0018104) described in SEQ ID NO: 18, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-3679-5p gene can be obtained by a method described in Creighton CJ et al., 2010, PLoS One, Vol. 5, e9637. Also, "hsa-mir-3679" (miRBase Accession No. MI0016080, SEQ ID NO: 192) having a hairpin-like structure is known as a precursor of "hsa-miR-3679-5p".

[0074] The term "hsa-miR-3184-5p gene" or "hsa-miR-3184-5p" used herein includes the hsa-miR-3184-5p gene (miRBase Accession No. MIMAT0015064) described in SEQ ID NO: 19, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-3184-5p gene can be obtained by a method described in Stark MS et al., 2010, PLoS One, Vol. 5, e9685. Also, "hsa-mir-3184" (miRBase Accession No. MI0014226, SEQ ID NO: 193) having a hairpin-like structure is known as a precursor of "hsa-miR-3184-5p".

[0075] The term "hsa-miR-663b gene" or "hsa-miR-663b" used herein includes the hsa-miR-663b gene (miRBase Accession No. MIMAT0005867) described in SEQ ID NO: 20, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-663b gene can be obtained by a method described in Takada S et al., 2008, Leukemia, Vol. 22, p. 1274-1278. Also, "hsa-mir-663b" (miRBase Accession No. MI0006336, SEQ ID NO: 194) having a hairpin-like structure is known as a precursor of "hsa-miR-663b".

[0076] The term "hsa-miR-6880-5p gene" or "hsa-miR-6880-5p" used herein includes the hsa-miR-6880-5p gene (miRBase Accession No. MIMAT0027660) described in SEQ ID NO: 21, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6880-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6880" (miRBase Accession No. MI0022727, SEQ ID NO: 195) having a hairpin-like structure is known as a precursor of "hsa-miR-6880-5p".

[0077] The term "hsa-miR-1908-5p gene" or "hsa-miR-1908-5p" used herein includes the hsa-miR-1908-5p gene (miRBase Accession No. MIMAT0007881) described in SEQ ID NO: 22, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-1908-5p gene can be obtained by a method described in Bar M et al., 2008, Stem Cells, Vol. 26, p. 2496-2505. Also, "hsa-mir-1908" (miRBase Accession No. MI0008329, SEQ ID NO: 179) having a hairpin-like structure is known as a precursor of "hsa-miR-1908-5p".

[0078] The term "hsa-miR-92a-2-5p gene" or "hsa-miR-92a-2-5p" used herein includes the hsa-miR-92a-2-5p gene (miRBase Accession No. MIMAT0004508) described in SEQ ID NO: 23, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-92a-2-5p gene can be obtained by a method described in Mourelatos Z et al., 2002, Genes Dev, Vol. 16, p. 720-728. Also, "hsa-mir-92a-2" (miRBase Accession No. MI0000094, SEQ ID NO: 196) having a hairpin-like structure is known as a precursor of "hsa-miR-92a-2-5p".

[0079] The term "hsa-miR-7975 gene" or "hsa-miR-7975" used herein includes the hsa-miR-7975 gene (miRBase Accession No. MIMAT0031178) described in SEQ ID NO: 24, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-7975 gene can be obtained by a method described in Velthut-Meikas A et al., 2013, Mol Endocrinol, online. Also, "hsa-mir-7975" (miRBase Accession No. MI0025751, SEQ ID NO: 197) having a hairpin-like

structure is known as a precursor of "hsa-miR-7975".

[0080] The term "hsa-miR-7110-5p gene" or "hsa-miR-7110-5p" used herein includes the hsa-miR-7110-5p gene (miRBase Accession No. MIMAT0028117) described in SEQ ID NO: 25, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-7110-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-7110" (miRBase Accession No. MI0022961, SEQ ID NO: 198) having a hairpin-like structure is known as a precursor of "hsa-miR-7110-5p".

[0081] The term "hsa-miR-6842-5p gene" or "hsa-miR-6842-5p" used herein includes the hsa-miR-6842-5p gene (miRBase Accession No. MIMAT0027586) described in SEQ ID NO: 26, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6842-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6842" (miRBase Accession No. MI0022688, SEQ ID NO: 199) having a hairpin-like structure is known as a precursor of "hsa-miR-6842-5p".

[0082] The term "hsa-miR-6857-5p gene" or "hsa-miR-6857-5p" used herein includes the hsa-miR-6857-5p gene (miRBase Accession No. MIMAT0027614) described in SEQ ID NO: 27, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6857-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6857" (miRBase Accession No. MI0022703, SEQ ID NO: 200) having a hairpin-like structure is known as a precursor of "hsa-miR-6857-5p".

[0083] The term "hsa-miR-5572 gene" or "hsa-miR-5572" used herein includes the hsa-miR-5572 gene (miRBase Accession No. MIMAT0022260) described in SEQ ID NO: 28, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-5572 gene can be obtained by a method described in Tandon M et al., 2012, Oral Dis, Vol. 18, p. 127-131. Also, "hsa-mir-5572" (miRBase Accession No. MI0019117, SEQ ID NO: 201) having a hairpin-like structure is known as a precursor of "hsa-miR-5572".

[0084] The term "hsa-miR-3197 gene" or "hsa-miR-3197" used herein includes the hsa-miR-3197 gene (miRBase Accession No. MIMAT0015082) described in SEQ ID NO: 29, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-3197 gene can be obtained by a method described in Stark MS et al., 2010, PLoS One, Vol. 5, e9685. Also, "hsa-mir-3197" (miRBase Accession No. MI0014245, SEQ ID NO: 202) having a hairpin-like structure is known as a precursor of "hsa-miR-3197".

[0085] The term "hsa-miR-6131 gene" or "hsa-miR-6131" used herein includes the hsa-miR-6131 gene (miRBase Accession No. MIMAT0024615) described in SEQ ID NO: 30, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6131 gene can be obtained by a method described in Dannemann M et al., 2012, Genome Biol Evol, Vol. 4, p. 552-564. Also, "hsa-mir-6131" (miRBase Accession No. MI0021276, SEQ ID NO: 203) having a hairpin-like structure is known as a precursor of "hsa-miR-6131".

[0086] The term "hsa-miR-6889-5p gene" or "hsa-miR-6889-5p" used herein includes the hsa-miR-6889-5p gene (miRBase Accession No. MIMAT0027678) described in SEQ ID NO: 31, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6889-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6889" (miRBase Accession No. MI0022736, SEQ ID NO: 204) having a hairpin-like structure is known as a precursor of "hsa-miR-6889-5p".

[0087] The term "hsa-miR-4454 gene" or "hsa-miR-4454" used herein includes the hsa-miR-4454 gene (miRBase Accession No. MIMAT0018976) described in SEQ ID NO: 32, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4454 gene can be obtained by a method described in Jima DD et al., 2010, Blood, Vol. 116, e118-e127. Also, "hsa-mir-4454" (miRBase Accession No. MI0016800, SEQ ID NO: 205) having a hairpin-like structure is known as a precursor of "hsa-miR-4454".

[0088] The term "hsa-miR-1199-Sp gene" or "hsa-miR-1199-Sp" used herein includes the hsa-miR-1199-5p gene (miRBase Accession No. MIMAT0031119) described in SEQ ID NO: 33, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-1199-5p gene can be obtained by a method described in Salvi A et al., 2013, Int J Oncol, Vol. 42, p. 391-402. Also, "hsa-mir-1199" (miRBase Accession No. MI0020340, SEQ ID NO: 206) having a hairpin-like structure is known as a precursor of "hsa-miR-1199-Sp".

[0089] The term "hsa-miR-1247-3p gene" or "hsa-miR-1247-3p" used herein includes the hsa-miR-1247-3p gene (miRBase Accession No. MIMAT0022721) described in SEQ ID NO: 34, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-1247-3p gene can be obtained by a method described in Morin RD et al., 2008, Genome Res, Vol. 18, p. 610-621. Also, "hsa-mir-1247" (miRBase Accession No. MI0006382, SEQ ID NO: 207) having a hairpin-like structure is known as a precursor of "hsa-miR-1247-3p".

[0090] The term "hsa-miR-6800-5p gene" or "hsa-miR-6800-5p" used herein includes the hsa-miR-6800-5p gene (miRBase Accession No. MIMAT0027500) described in SEQ ID NO: 35, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6800-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6800" (miRBase Accession No. MI0022645, SEQ ID NO: 208) having a hairpin-like structure is known as a precursor of "hsa-miR-6800-5p".

[0091] The term "hsa-miR-6872-3p gene" or "hsa-miR-6872-3p" used herein includes the hsa-miR-6872-3p gene (miRBase Accession No. MIMAT0027645) described in SEQ ID NO: 36, a homolog or an ortholog of a different organism

species, and the like. The hsa-miR-6872-3p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6872" (miRBase Accession No. MI0022719, SEQ ID NO: 209) having a hairpin-like structure is known as a precursor of "hsa-miR-6872-3p".

[0092] The term "hsa-miR-4649-5p gene" or "hsa-miR-4649-5p" used herein includes the hsa-miR-4649-5p gene (miRBase Accession No. MIMAT0019711) described in SEQ ID NO: 37, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4649-5p gene can be obtained by a method described in Persson H et al., 2011, Cancer Res, Vol. 71, p. 78-86. Also, "hsa-mir-4649" (miRBase Accession No. MI0017276, SEQ ID NO: 210) having a hairpin-like structure is known as a precursor of "hsa-miR-4649-5p".

[0093] The term "hsa-miR-6791-5p gene" or "hsa-miR-6791-5p" used herein includes the hsa-miR-6791-5p gene (miRBase Accession No. MIMAT0027482) described in SEQ ID NO: 38, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6791-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6791" (miRBase Accession No. MI0022636, SEQ ID NO: 211) having a hairpin-like structure is known as a precursor of "hsa-miR-6791-5p".

[0094] The term "hsa-miR-4433b-3p gene" or "hsa-miR-4433b-3p" used herein includes the hsa-miR-4433b-3p gene (miRBase Accession No. MIMAT0030414) described in SEQ ID NO: 39, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4433b-3p gene can be obtained by a method described in Ple H et al., 2012, PLoS One, Vol. 7, e50746. Also, "hsa-mir-4433b" (miRBase Accession No. MI0025511, SEQ ID NO: 212) having a hairpin-like structure is known as a precursor of "hsa-miR-4433b-3p".

[0095] The term "hsa-miR-3135b gene" or "hsa-miR-3135b" used herein includes the hsa-miR-3135b gene (miRBase Accession No. MIMAT0018985) described in SEQ ID NO: 40, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-3135b gene can be obtained by a method described in Jima DD et al., 2010, Blood, Vol. 116, e1 18-e127. Also, "hsa-mir-3135b" (miRBase Accession No. MI0016809, SEQ ID NO: 213) having a hairpin-like structure is known as a precursor of "hsa-miR-3135b".

[0096] The term "hsa-miR-128-2-5p gene" or "hsa-miR-128-2-5p" used herein includes the hsa-miR-128-2-5p gene (miRBase Accession No. MIMAT0031095) described in SEQ ID NO: 41, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-128-2-5p gene can be obtained by a method described in Lagos-Quintana M et al., 2002, Curr Biol, Vol. 12, p. 735-739. Also, "hsa-mir-128-2" (miRBase Accession No. MI0000727, SEQ ID NO: 214) having a hairpin-like structure is known as a precursor of "hsa-miR-128-2-Sp".

[0097] The term "hsa-miR-4675 gene" or "hsa-miR-4675" used herein includes the hsa-miR-4675 gene (miRBase Accession No. MIMAT0019757) described in SEQ ID NO: 42, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4675 gene can be obtained by a method described in Persson H et al., 2011, Cancer Res, Vol. 71, p. 78-86. Also, "hsa-mir-4675" (miRBase Accession No. MI0017306, SEQ ID NO: 215) having a hairpin-like structure is known as a precursor of "hsa-miR-4675".

[0098] The term "hsa-miR-4472 gene" or "hsa-miR-4472" used herein includes the hsa-miR-4472 gene (miRBase Accession No. MIMAT0018999) described in SEQ ID NO: 43, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4472 gene can be obtained by a method described in Jima DD et al., 2010, Blood, Vol. 116, e118-e127. Also, "hsa-mir-4472-1 and hsa-mir-4472-2" (miRBase Accession Nos. MI0016823 and MI0016824, SEQ ID NOs: 216 and 217) having a hairpin-like structure are known as precursors of "hsa-miR-4472".

[0099] The term "hsa-miR-6785-5p gene" or "hsa-miR-6785-5p" used herein includes the hsa-miR-6785-5p gene (miRBase Accession No. MIMAT0027470) described in SEQ ID NO: 44, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6785-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6785" (miRBase Accession No. MI0022630, SEQ ID NO: 218) having a hairpin-like structure is known as a precursor of "hsa-miR-6785-5p".

[0100] The term "hsa-miR-6741-5p gene" or "hsa-miR-6741-5p" used herein includes the hsa-miR-6741-5p gene (miRBase Accession No. MIMAT0027383) described in SEQ ID NO: 45, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6741-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6741" (miRBase Accession No. MI0022586, SEQ ID NO: 219) having a hairpin-like structure is known as a precursor of "hsa-miR-6741-5p".

[0101] The term "hsa-miR-7977 gene" or "hsa-miR-7977" used herein includes the hsa-miR-7977 gene (miRBase Accession No. MIMAT0031180) described in SEQ ID NO: 46, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-7977 gene can be obtained by a method described in Velthut-Meikas A et al., 2013, Mol Endocrinol, online. Also, "hsa-mir-7977" (miRBase Accession No. MI0025753, SEQ ID NO: 220) having a hairpin-like structure is known as a precursor of "hsa-miR-7977".

[0102] The term "hsa-miR-3665 gene" or "hsa-miR-3665" used herein includes the hsa-miR-3665 gene (miRBase Accession No. MIMAT0018087) described in SEQ ID NO: 47, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-3665 gene can be obtained by a method described in Xie X et al., 2005, Nature, Vol. 434, p. 338-345. Also, "hsa-mir-3665" (miRBase Accession No. MI0016066, SEQ ID NO: 221) having a hairpin-like structure is known as a precursor of "hsa-miR-3665".

[0103] The term "hsa-miR-128-1-5p gene" or "hsa-miR-128-1-5p" used herein includes the hsa-miR-128-1-5p gene (miRBase Accession No. MIMAT0026477) described in SEQ ID NO: 48, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-128-1-5p gene can be obtained by a method described in Lagos-Quintana M et al., 2002, Curr Biol, Vol. 12, p. 735-739. Also, "hsa-mir-128-1" (miRBase Accession No. MI0000447, SEQ ID NO: 222) having a hairpin-like structure is known as a precursor of "hsa-miR-128-1-5p".

[0104] The term "hsa-miR-4286 gene" or "hsa-miR-4286" used herein includes the hsa-miR-4286 gene (miRBase Accession No. MIMAT0016916) described in SEQ ID NO: 49, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4286 gene can be obtained by a method described in Goff LA et al., 2009, PLoS One, Vol. 4, e7192. Also, "hsa-mir-4286" (miRBase Accession No. MI0015894, SEQ ID NO: 223) having a hairpin-like structure is known as a precursor of "hsa-miR-4286".

[0105] The term "hsa-miR-6765-3p gene" or "hsa-miR-6765-3p" used herein includes the hsa-miR-6765-3p gene (miRBase Accession No. MIMAT0027431) described in SEQ ID NO: 50, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6765-3p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6765" (miRBase Accession No. MI0022610, SEQ ID NO: 224) having a hairpin-like structure is known as a precursor of "hsa-miR-6765-3p".

[0106] The term "hsa-miR-4632-5p gene" or "hsa-miR-4632-5p" used herein includes the hsa-miR-4632-5p gene (miRBase Accession No. MIMAT0022977) described in SEQ ID NO: 51, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4632-5p gene can be obtained by a method described in Persson H et al., 2011, Cancer Res, Vol. 71, p. 78-86. Also, "hsa-mir-4632" (miRBase Accession No. MI0017259, SEQ ID NO: 225) having a hairpin-like structure is known as a precursor of "hsa-miR-4632-5p".

[0107] The term "hsa-miR-365a-5p gene" or "hsa-miR-365a-5p" used herein includes the hsa-miR-365a-5p gene (miRBase Accession No. MIMAT0009199) described in SEQ ID NO: 52, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-365a-5p gene can be obtained by a method described in Xie X et al., 2005, Nature, Vol. 434, p. 338-345. Also, "hsa-mir-365a" (miRBase Accession No. MI0000767, SEQ ID NO: 226) having a hairpin-like structure is known as a precursor of "hsa-miR-365a-5p".

[0108] The term "hsa-miR-6088 gene" or "hsa-miR-6088" used herein includes the hsa-miR-6088 gene (miRBase Accession No. MIMAT0023713) described in SEQ ID NO: 53, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6088 gene can be obtained by a method described in Yoo JK et al., 2012, Stem Cells Dev, Vol. 21, p. 2049-2057. Also, "hsa-mir-6088" (miRBase Accession No. MI0020365, SEQ ID NO: 227) having a hairpin-like structure is known as a precursor of "hsa-miR-6088".

[0109] The term "hsa-miR-6816-5p gene" or "hsa-miR-6816-5p" used herein includes the hsa-miR-6816-5p gene (miRBase Accession No. MIMAT0027532) described in SEQ ID NO: 54, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6816-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6816" (miRBase Accession No. MI0022661, SEQ ID NO: 228) having a hairpin-like structure is known as a precursor of "hsa-miR-6816-5p".

[0110] The term "hsa-miR-6885-5p gene" or "hsa-miR-6885-5p" used herein includes the hsa-miR-6885-5p gene (miRBase Accession No. MIMAT0027670) described in SEQ ID NO: 55, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6885-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6885" (miRBase Accession No. MI0022732, SEQ ID NO: 229) having a hairpin-like structure is known as a precursor of "hsa-miR-6885-5p".

[0111] The term "hsa-miR-711 gene" or "hsa-miR-711" used herein includes the hsa-miR-711 gene (miRBase Accession No. MIMAT0012734) described in SEQ ID NO: 56, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-711 gene can be obtained by a method described in Artzi S et al., 2008, BMC Bioinformatics, Vol. 9, p. 39. Also, "hsa-mir-711" (miRBase Accession No. MI0012488, SEQ ID NO: 230) having a hairpin-like structure is known as a precursor of "hsa-miR-711".

[0112] The term "hsa-miR-6765-5p gene" or "hsa-miR-6765-5p" used herein includes the hsa-miR-6765-5p gene (miRBase Accession No. MIMAT0027430) described in SEQ ID NO: 57, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6765-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6765" (miRBase Accession No. MI0022610, SEQ ID NO: 224) having a hairpin-like structure is known as a precursor of "hsa-miR-6765-5p".

[0113] The term "hsa-miR-3180 gene" or "hsa-miR-3180" used herein includes the hsa-miR-3180 gene (miRBase Accession No. MIMAT0018178) described in SEQ ID NO: 58, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-3180 gene can be obtained by a method described in Creighton CJ et al., 2010, PLoS One, Vol. 5, e9637. Also, "hsa-mir-3180-4 and hsa-mir-3180-5" (miRBase Accession Nos. MI0016408 and MI0016409, SEQ ID NOs: 231 and 232) having a hairpin-like structure are known as precursors of "hsa-miR-3180".

[0114] The term "hsa-miR-4442 gene" or "hsa-miR-4442" used herein includes the hsa-miR-4442 gene (miRBase Accession No. MIMAT0018960) described in SEQ ID NO: 59, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4442 gene can be obtained by a method described in Jima DD et al., 2010, Blood, Vol. 116,

e118-e127. Also, "hsa-mir-4442" (miRBase Accession No. MI0016785, SEQ ID NO: 233) having a hairpin-like structure is known as a precursor of "hsa-miR-4442".

[0115] The term "hsa-miR-4792 gene" or "hsa-miR-4792" used herein includes the hsa-miR-4792 gene (miRBase Accession No. MIMAT0019964) described in SEQ ID NO: 60, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4792 gene can be obtained by a method described in Persson H et al., 2011, Cancer Res, Vol. 71, p. 78-86. Also, "hsa-mir-4792" (miRBase Accession No. MI0017439, SEQ ID NO: 234) having a hairpin-like structure is known as a precursor of "hsa-miR-4792".

[0116] The term "hsa-miR-6721-5p gene" or "hsa-miR-6721-5p" used herein includes the hsa-miR-6721-5p gene (miRBase Accession No. MIMAT0025852) described in SEQ ID NO: 61, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6721-5p gene can be obtained by a method described in Li Y et al., 2012, Gene, Vol. 497, p. 330-335. Also, "hsa-mir-6721" (miRBase Accession No. MI0022556, SEQ ID NO: 235) having a hairpin-like structure is known as a precursor of "hsa-miR-6721-5p".

[0117] The term "hsa-miR-6798-5p gene" or "hsa-miR-6798-5p" used herein includes the hsa-miR-6798-5p gene (miRBase Accession No. MIMAT0027496) described in SEQ ID NO: 62, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6798-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6798" (miRBase Accession No. MI0022643, SEQ ID NO: 236) having a hairpin-like structure is known as a precursor of "hsa-miR-6798-5p".

[0118] The term "hsa-miR-3162-5p gene" or "hsa-miR-3162-5p" used herein includes the hsa-miR-3162-5p gene (miRBase Accession No. MIMAT0015036) described in SEQ ID NO: 63, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-3162-5p gene can be obtained by a method described in Stark MS et al., 2010, PLoS One, Vol. 5, e9685. Also, "hsa-mir-3162" (miRBase Accession No. MI0014192, SEQ ID NO: 237) having a hairpin-like structure is known as a precursor of "hsa-miR-3162-5p".

[0119] The term "hsa-miR-6126 gene" or "hsa-miR-6126" used herein includes the hsa-miR-6126 gene (miRBase Accession No. MIMAT0024599) described in SEQ ID NO: 64, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6126 gene can be obtained by a method described in Smith JL et al., 2012, J Virol, Vol. 86, p. 5278-5287. Also, "hsa-mir-6126" (miRBase Accession No. MI0021260, SEQ ID NO: 238) having a hairpin-like structure is known as a precursor of "hsa-miR-6126".

[0120] The term "hsa-miR-4758-5p gene" or "hsa-miR-4758-5p" used herein includes the hsa-miR-4758-5p gene (miRBase Accession No. MIMAT0019903) described in SEQ ID NO: 65, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4758-5p gene can be obtained by a method described in Persson H et al., 2011, Cancer Res, Vol. 71, p. 78-86. Also, "hsa-mir-4758" (miRBase Accession No. MI0017399, SEQ ID NO: 239) having a hairpin-like structure is known as a precursor of "hsa-miR-4758-5p".

[0121] The term "hsa-miR-2392 gene" or "hsa-miR-2392" used herein includes the hsa-miR-2392 gene (miRBase Accession No. MIMAT0019043) described in SEQ ID NO: 66, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-2392 gene can be obtained by a method described in Jima DD et al., 2010, Blood, Vol. 116, e118-e127. Also, "hsa-mir-2392" (miRBase Accession No. MI0016870, SEQ ID NO: 240) having a hairpin-like structure is known as a precursor of "hsa-miR-2392".

[0122] The term "hsa-miR-486-3p gene" or "hsa-miR-486-3p" used herein includes the hsa-miR-486-3p gene (miRBase Accession No. MIMAT0004762) described in SEQ ID NO: 67, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-486-3p gene can be obtained by a method described in Fu H et al., 2005, FEBS Lett, Vol. 579, p. 3849-3854. Also, "hsa-mir-486 and hsa-mir-486-2" (miRBase Accession Nos. MI0002470 and MI0023622, SEQ ID NOs: 241 and 242) having a hairpin-like structure are known as precursors of "hsa-miR-486-3p".

[0123] The term "hsa-miR-6727-5p gene" or "hsa-miR-6727-5p" used herein includes the hsa-miR-6727-5p gene (miRBase Accession No. MIMAT0027355) described in SEQ ID NO: 68, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6727-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6727" (miRBase Accession No. MI0022572, SEQ ID NO: 243) having a hairpin-like structure is known as a precursor of "hsa-miR-6727-5p".

[0124] The term "hsa-miR-4728-5p gene" or "hsa-miR-4728-5p" used herein includes the hsa-miR-4728-5p gene (miRBase Accession No. MIMAT0019849) described in SEQ ID NO: 69, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4728-5p gene can be obtained by a method described in Persson H et al., 2011, Cancer Res, Vol. 71, p. 78-86. Also, "hsa-mir-4728" (miRBase Accession No. MI0017365, SEQ ID NO: 244) having a hairpin-like structure is known as a precursor of "hsa-miR-4728-5p".

[0125] The term "hsa-miR-6746-5p gene" or "hsa-miR-6746-5p" used herein includes the hsa-miR-6746-5p gene (miRBase Accession No. MIMAT0027392) described in SEQ ID NO: 70, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6746-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6746" (miRBase Accession No. MI0022591, SEQ ID NO: 245) having a hairpin-like structure is known as a precursor of "hsa-miR-6746-5p".

[0126] The term "hsa-miR-4270 gene" or "hsa-miR-4270" used herein includes the hsa-miR-4270 gene (miRBase

Accession No. MIMAT0016900) described in SEQ ID NO: 71, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4270 gene can be obtained by a method described in Goff LA et al., 2009, PLoS One, Vol. 4, e7192. Also, "hsa-mir-4270" (miRBase Accession No. MI0015878, SEQ ID NO: 246) having a hairpin-like structure is known as a precursor of "hsa-miR-4270".

[0127] The term "hsa-miR-3940-5p gene" or "hsa-miR-3940-5p" used herein includes the hsa-miR-3940-5p gene (miRBase Accession No. MIMAT00 19229) described in SEQ ID NO: 72, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-3940-5p gene can be obtained by a method described in Liao JY et al., 2010, PLoS One, Vol. 5, e10563. Also, "hsa-mir-3940" (miRBase Accession No. MI0016597, SEQ ID NO: 247) having a hairpin-like structure is known as a precursor of "hsa-miR-3940-5p".

[0128] The term "hsa-miR-4725-3p gene" or "hsa-miR-4725-3p" used herein includes the hsa-miR-4725-3p gene (miRBase Accession No. MIMAT0019844) described in SEQ ID NO: 73, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4725-3p gene can be obtained by a method described in Persson H et al., 2011, Cancer Res, Vol. 71, p. 78-86. Also, "hsa-mir-4725" (miRBase Accession No. MI0017362, SEQ ID NO: 248) having a hairpin-like structure is known as a precursor of "hsa-miR-4725-3p".

[0129] The term "hsa-miR-7108-5p gene" or "hsa-miR-7108-5p" used herein includes the hsa-miR-7108-5p gene (miRBase Accession No. MIMAT0028113) described in SEQ ID NO: 74, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-7108-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-7108" (miRBase Accession No. MI0022959, SEQ ID NO: 249) having a hairpin-like structure is known as a precursor of "hsa-miR-7108-5p".

[0130] The term "hsa-miR-3656 gene" or "hsa-miR-3656" used herein includes the hsa-miR-3656 gene (miRBase Accession No. MIMAT0018076) described in SEQ ID NO: 75, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-3656 gene can be obtained by a method described in Meiri E et al., 2010, Nucleic Acids Res, Vol. 38, p. 6234-6246. Also, "hsa-mir-3656" (miRBase Accession No. MI0016056, SEQ ID NO: 250) having a hairpin-like structure is known as a precursor of "hsa-miR-3656".

[0131] The term "hsa-miR-6879-5p gene" or "hsa-miR-6879-5p" used herein includes the hsa-miR-6879-5p gene (miRBase Accession No. MIMAT0027658) described in SEQ ID NO: 76, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6879-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6879" (miRBase Accession No. MI0022726, SEQ ID NO: 251) having a hairpin-like structure is known as a precursor of "hsa-miR-6879-5p".

[0132] The term "hsa-miR-6738-5p gene" or "hsa-miR-6738-5p" used herein includes the hsa-miR-6738-5p gene (miRBase Accession No. MIMAT0027377) described in SEQ ID NO: 77, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6738-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6738" (miRBase Accession No. MI0022583, SEQ ID NO: 252) having a hairpin-like structure is known as a precursor of "hsa-miR-6738-5p".

[0133] The term "hsa-miR-1260a gene" or "hsa-miR-1260a" used herein includes the hsa-miR-1260a gene (miRBase Accession No. MIMAT0005911) described in SEQ ID NO: 78, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-1260a gene can be obtained by a method described in Morin RD et al., 2008, Genome Res, Vol. 18, p. 610-621. Also, "hsa-mir-1260a" (miRBase Accession No. MI0006394, SEQ ID NO: 253) having a hairpin-like structure is known as a precursor of "hsa-miR-1260a".

[0134] The term "hsa-miR-4446-3p gene" or "hsa-miR-4446-3p" used herein includes the hsa-miR-4446-3p gene (miRBase Accession No. MIMAT00 18965) described in SEQ ID NO: 79, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4446-3p gene can be obtained by a method described in Jima DD et al., 2010, Blood, Vol. 116, e118-e127. Also, "hsa-mir-4446" (miRBase Accession No. MI0016789, SEQ ID NO: 254) having a hairpin-like structure is known as a precursor of "hsa-miR-4446-3p".

[0135] The term "hsa-miR-3131 gene" or "hsa-miR-3131" used herein includes the hsa-miR-3131 gene (miRBase Accession No. MIMAT0014996) described in SEQ ID NO: 80, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-3131 gene can be obtained by a method described in Stark MS et al., 2010, PLoS One, Vol. 5, e9685. Also, "hsa-mir-3131" (miRBase Accession No. MI0014151, SEQ ID NO: 255) having a hairpin-like structure is known as a precursor of "hsa-miR-3131".

[0136] The term "hsa-miR-4463 gene" or "hsa-miR-4463" used herein includes the hsa-miR-4463 gene (miRBase Accession No. MIMAT0018987) described in SEQ ID NO: 81, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4463 gene can be obtained by a method described in Jima DD et al., 2010, Blood, Vol. 116, e118-e127. Also, "hsa-mir-4463" (miRBase Accession No. MI0016811, SEQ ID NO: 256) having a hairpin-like structure is known as a precursor of "hsa-miR-4463".

[0137] The term "hsa-miR-3185 gene" or "hsa-miR-3185" used herein includes the hsa-miR-3185 gene (miRBase Accession No. MIMAT0015065) described in SEQ ID NO: 82, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-3185 gene can be obtained by a method described in Stark MS et al., 2010, PLoS One, Vol. 5, e9685. Also, "hsa-mir-3185" (miRBase Accession No. MI0014227, SEQ ID NO: 257) having a hairpin-like structure

is known as a precursor of "hsa-miR-3185".

[0138] The term "hsa-miR-6870-5p gene" or "hsa-miR-6870-5p" used herein includes the hsa-miR-6870-5p gene (miRBase Accession No. MIMAT0027640) described in SEQ ID NO: 83, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6870-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6870" (miRBase Accession No. MI0022717, SEQ ID NO: 258) having a hairpin-like structure is known as a precursor of "hsa-miR-6870-5p".

[0139] The term "hsa-miR-6779-5p gene" or "hsa-miR-6779-5p" used herein includes the hsa-miR-6779-5p gene (miRBase Accession No. MIMAT0027458) described in SEQ ID NO: 84, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6779-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6779" (miRBase Accession No. MI0022624, SEQ ID NO: 259) having a hairpin-like structure is known as a precursor of "hsa-miR-6779-5p".

[0140] The term "hsa-miR-1273g-3p gene" or "hsa-miR-1273g-3p" used herein includes the hsa-miR-1273g-3p gene (miRBase Accession No. MIMAT0022742) described in SEQ ID NO: 85, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-1273g-3p gene can be obtained by a method described in Reshmi G et al., 2011, Genomics, Vol. 97, p. 333-340. Also, "hsa-mir-1273g" (miRBase Accession No. MI0018003, SEQ ID NO: 260) having a hairpin-like structure is known as a precursor of "hsa-miR-1273g-3p".

[0141] The term "hsa-miR-8059 gene" or "hsa-miR-8059" used herein includes the hsa-miR-8059 gene (miRBase Accession No. MIMAT0030986) described in SEQ ID NO: 86, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-8059 gene can be obtained by a method described in Wang HJ et al., 2013, Shock, Vol. 39, p. 480-487. Also, "hsa-mir-8059" (miRBase Accession No. MI0025895, SEQ ID NO: 261) having a hairpin-like structure is known as a precursor of "hsa-miR-8059".

[0142] The term "hsa-miR-4697-5p gene" or "hsa-miR-4697-5p" used herein includes the hsa-miR-4697-5p gene (miRBase Accession No. MIMAT0019791) described in SEQ ID NO: 87, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4697-5p gene can be obtained by a method described in Persson H et al., 2011, Cancer Res, Vol. 71, p. 78-86. Also, "hsa-mir-4697" (miRBase Accession No. MI0017330, SEQ ID NO: 262) having a hairpin-like structure is known as a precursor of "hsa-miR-4697-5p".

[0143] The term "hsa-miR-4674 gene" or "hsa-miR-4674" used herein includes the hsa-miR-4674 gene (miRBase Accession No. MIMAT0019756) described in SEQ ID NO: 88, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4674 gene can be obtained by a method described in Persson H et al., 2011, Cancer Res, Vol. 71, p. 78-86. Also, "hsa-mir-4674" (miRBase Accession No. MI0017305, SEQ ID NO: 263) having a hairpin-like structure is known as a precursor of "hsa-miR-4674".

[0144] The term "hsa-miR-4433-3p gene" or "hsa-miR-4433-3p" used herein includes the hsa-miR-4433-3p gene (miRBase Accession No. MIMAT0018949) described in SEQ ID NO: 89, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4433-3p gene can be obtained by a method described in Jima DD et al., 2010, Blood, Vol. 116, e118-e127. Also, "hsa-mir-4433" (miRBase Accession No. MI0016773, SEQ ID NO: 264) having a hairpin-like structure is known as a precursor of "hsa-miR-4433-3p".

[0145] The term "hsa-miR-4257 gene" or "hsa-miR-4257" used herein includes the hsa-miR-4257 gene (miRBase Accession No. MIMAT0016878) described in SEQ ID NO: 90, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4257 gene can be obtained by a method described in Goff LA et al., 2009, PLoS One, Vol. 4, e7192. Also, "hsa-mir-4257" (miRBase Accession No. MI0015856, SEQ ID NO: 265) having a hairpin-like structure is known as a precursor of "hsa-miR-4257".

[0146] The term "hsa-miR-1915-5p gene" or "hsa-miR-1915-5p" used herein includes the hsa-miR-1915-5p gene (miRBase Accession No. MIMAT0007891) described in SEQ ID NO: 91, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-1915-5p gene can be obtained by a method described in Bar M et al., 2008, Stem Cells, Vol. 26, p. 2496-2505. Also, "hsa-mir-1915" (miRBase Accession No. MI0008336, SEQ ID NO: 266) having a hairpin-like structure is known as a precursor of "hsa-miR-1915-5p".

[0147] The term "hsa-miR-4417 gene" or "hsa-miR-4417" used herein includes the hsa-miR-4417 gene (miRBase Accession No. MIMAT0018929) described in SEQ ID NO: 92, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4417 gene can be obtained by a method described in Jima DD et al., 2010, Blood, Vol. 116, e118-e127. Also, "hsa-mir-4417" (miRBase Accession No. MI0016753, SEQ ID NO: 267) having a hairpin-like structure is known as a precursor of "hsa-miR-4417".

[0148] The term "hsa-miR-1343-5p gene" or "hsa-miR-1343-5p" used herein includes the hsa-miR-1343-5p gene (miRBase Accession No. MIMAT0027038) described in SEQ ID NO: 93, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-1343-5p gene can be obtained by a method described in Persson H et al., 2011, Cancer Res, Vol. 71, p. 78-86. Also, "hsa-mir-1343" (miRBase Accession No. MI0017320, SEQ ID NO: 182) having a hairpin-like structure is known as a precursor of "hsa-miR-1343-5p".

[0149] The term "hsa-miR-6781-5p gene" or "hsa-miR-6781-5p" used herein includes the hsa-miR-6781-5p gene (miRBase Accession No. MIMAT0027462) described in SEQ ID NO: 94, a homolog or an ortholog of a different organism

species, and the like. The hsa-miR-6781-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6781" (miRBase Accession No. MI0022626, SEQ ID NO: 268) having a hairpin-like structure is known as a precursor of "hsa-miR-6781-5p".

[0150] The term "hsa-miR-4695-5p gene" or "hsa-miR-4695-5p" used herein includes the hsa-miR-4695-5p gene (miRBase Accession No. MIMAT00 19788) described in SEQ ID NO: 95, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4695-5p gene can be obtained by a method described in Persson H et al., 2011, Cancer Res, Vol. 71, p. 78-86. Also, "hsa-mir-4695" (miRBase Accession No. MI0017328, SEQ ID NO: 269) having a hairpin-like structure is known as a precursor of "hsa-miR-4695-5p".

[0151] The term "hsa-miR-1237-5p gene" or "hsa-miR-1237-5p" used herein includes the hsa-miR-1237-5p gene (miRBase Accession No. MIMAT0022946) described in SEQ ID NO: 96, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-1237-5p gene can be obtained by a method described in Berezikov E et al., 2007, Mol Cell, Vol. 28, p. 328-336. Also, "hsa-mir-1237" (miRBase Accession No. MI0006327, SEQ ID NO: 270) having a hairpin-like structure is known as a precursor of "hsa-miR-1237-5p".

[0152] The term "hsa-miR-6775-5p gene" or "hsa-miR-6775-5p" used herein includes the hsa-miR-6775-5p gene (miRBase Accession No. MIMAT0027450) described in SEQ ID NO: 97, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6775-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6775" (miRBase Accession No. MI0022620, SEQ ID NO: 271) having a hairpin-like structure is known as a precursor of "hsa-miR-6775-5p".

[0153] The term "hsa-miR-7845-5p gene" or "hsa-miR-7845-5p" used herein includes the hsa-miR-7845-5p gene (miRBase Accession No. MIMAT0030420) described in SEQ ID NO: 98, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-7845-5p gene can be obtained by a method described in Ple H et al., 2012, PLoS One, Vol. 7, e50746. Also, "hsa-mir-7845" (miRBase Accession No. MI0025515, SEQ ID NO: 272) having a hairpin-like structure is known as a precursor of "hsa-miR-7845-5p".

[0154] The term "hsa-miR-4746-3p gene" or "hsa-miR-4746-3p" used herein includes the hsa-miR-4746-3p gene (miRBase Accession No. MIMAT0019881) described in SEQ ID NO: 99, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4746-3p gene can be obtained by a method described in Persson H et al., 2011, Cancer Res, Vol. 71, p. 78-86. Also, "hsa-mir-4746" (miRBase Accession No. MI0017385, SEQ ID NO: 273) having a hairpin-like structure is known as a precursor of "hsa-miR-4746-3p".

[0155] The term "hsa-miR-7641 gene" or "hsa-miR-7641" used herein includes the hsa-miR-7641 gene (miRBase Accession No. MIMAT0029782) described in SEQ ID NO: 100, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-7641 gene can be obtained by a method described in Yoo JK et al., 2013, Arch Pharm Res, Vol. 36, p. 353-358. Also, "hsa-mir-7641-1 and hsa-mir-7641-2" (miRBase Accession Nos. MI0024975 and MI0024976, SEQ ID NOs: 274 and 275) having a hairpin-like structure are known as precursors of "hsa-miR-7641".

[0156] The term "hsa-miR-7847-3p gene" or "hsa-miR-7847-3p" used herein includes the hsa-miR-7847-3p gene (miRBase Accession No. MIMAT0030422) described in SEQ ID NO: 101, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-7847-3p gene can be obtained by a method described in Ple H et al., 2012, PLoS One, Vol. 7, e50746. Also, "hsa-mir-7847" (miRBase Accession No. MI0025517, SEQ ID NO: 276) having a hairpin-like structure is known as a precursor of "hsa-miR-7847-3p".

[0157] The term "hsa-miR-6806-5p gene" or "hsa-miR-6806-5p" used herein includes the hsa-miR-6806-5p gene (miRBase Accession No. MIMAT0027512) described in SEQ ID NO: 102, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6806-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6806" (miRBase Accession No. MI0022651, SEQ ID NO: 277) having a hairpin-like structure is known as a precursor of "hsa-miR-6806-5p".

[0158] The term "hsa-miR-4467 gene" or "hsa-miR-4467" used herein includes the hsa-miR-4467 gene (miRBase Accession No. MIMAT0018994) described in SEQ ID NO: 103, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4467 gene can be obtained by a method described in Jima DD et al., 2010, Blood, Vol. 116, e118-e127. Also, "hsa-mir-4467" (miRBase Accession No. MI0016818, SEQ ID NO: 278) having a hairpin-like structure is known as a precursor of "hsa-miR-4467".

[0159] The term "hsa-miR-4726-5p gene" or "hsa-miR-4726-5p" used herein includes the hsa-miR-4726-5p gene (miRBase Accession No. MIMAT0019845) described in SEQ ID NO: 104, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4726-5p gene can be obtained by a method described in Persson H et al., 2011, Cancer Res, Vol. 71, p. 78-86. Also, "hsa-mir-4726" (miRBase Accession No. MI0017363, SEQ ID NO: 279) having a hairpin-like structure is known as a precursor of "hsa-miR-4726-5p".

[0160] The term "hsa-miR-4648 gene" or "hsa-miR-4648" used herein includes the hsa-miR-4648 gene (miRBase Accession No. MIMAT0019710) described in SEQ ID NO: 105, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4648 gene can be obtained by a method described in Persson H et al., 2011, Cancer Res, Vol. 71, p. 78-86. Also, "hsa-mir-4648" (miRBase Accession No. MI0017275, SEQ ID NO: 280) having a hairpin-like structure is known as a precursor of "hsa-miR-4648".

[0161] The term "hsa-miR-6089 gene" or "hsa-miR-6089" used herein includes the hsa-miR-6089 gene (miRBase Accession No. MIMAT0023714) described in SEQ ID NO: 106, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6089 gene can be obtained by a method described in Yoo JK et al., 2012, Stem Cells Dev, Vol. 21, p. 2049-2057. Also, "hsa-mir-6089-1 and hsa-mir-6089-2" (miRBase Accession Nos. MI0020366 and MI0023563, SEQ ID NOs: 281 and 282) having a hairpin-like structure are known as precursors of "hsa-miR-6089".

[0162] The term "hsa-miR-1260b gene" or "hsa-miR-1260b" used herein includes the hsa-miR-1260b gene (miRBase Accession No. MIMAT0015041) described in SEQ ID NO: 107, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-1260b gene can be obtained by a method described in Stark MS et al., 2010, PLoS One, Vol. 5, e9685. Also, "hsa-mir-1260b" (miRBase Accession No. MI0014197, SEQ ID NO: 283) having a hairpin-like structure is known as a precursor of "hsa-miR-1260b".

[0163] The term "hsa-miR-4532 gene" or "hsa-miR-4532" used herein includes the hsa-miR-4532 gene (miRBase Accession No. MIMAT0019071) described in SEQ ID NO: 108, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4532 gene can be obtained by a method described in Jima DD et al., 2010, Blood, Vol. 116, e118-e127. Also, "hsa-mir-4532" (miRBase Accession No. MI0016899, SEQ ID NO: 284) having a hairpin-like structure is known as a precursor of "hsa-miR-4532".

[0164] The term "hsa-miR-5195-3p gene" or "hsa-miR-5195-3p" used herein includes the hsa-miR-5195-3p gene (miRBase Accession No. MIMAT0021127) described in SEQ ID NO: 109, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-5195-3p gene can be obtained by a method described in Schotte D et al., 2011, Leukemia, Vol. 25, p. 1389-1399. Also, "hsa-mir-5195" (miRBase Accession No. MI0018174, SEQ ID NO: 285) having a hairpin-like structure is known as a precursor of "hsa-miR-5195-3p".

[0165] The term "hsa-miR-3188 gene" or "hsa-miR-3188" used herein includes the hsa-miR-3188 gene (miRBase Accession No. MIMAT0015070) described in SEQ ID NO: 110, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-3188 gene can be obtained by a method described in Stark MS et al., 2010, PLoS One, Vol. 5, e9685. Also, "hsa-mir-3188" (miRBase Accession No. MI0014232, SEQ ID NO: 286) having a hairpin-like structure is known as a precursor of "hsa-miR-3188".

[0166] The term "hsa-miR-6848-5p gene" or "hsa-miR-6848-5p" used herein includes the hsa-miR-6848-5p gene (miRBase Accession No. MIMAT0027596) described in SEQ ID NO: 111, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6848-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6848" (miRBase Accession No. MI0022694, SEQ ID NO: 287) having a hairpin-like structure is known as a precursor of "hsa-miR-6848-5p".

[0167] The term "hsa-miR-1233-5p gene" or "hsa-miR-1233-5p" used herein includes the hsa-miR-1233-5p gene (miRBase Accession No. MIMAT0022943) described in SEQ ID NO: 112, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-1233-5p gene can be obtained by a method described in Berezikov E et al., 2007, Mol Cell, Vol. 28, p. 328-336. Also, "hsa-mir-1233-1 and hsa-mir-1233-2" (miRBase Accession Nos. MI0006323 and MI0015973, SEQ ID NOs: 288 and 289) having a hairpin-like structure are known as precursors of "hsa-miR-1233-5p".

[0168] The term "hsa-miR-6717-5p gene" or "hsa-miR-6717-5p" used herein includes the hsa-miR-6717-5p gene (miRBase Accession No. MIMAT0025846) described in SEQ ID NO: 113, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6717-5p gene can be obtained by a method described in Li Y et al., 2012, Gene, Vol. 497, p. 330-335. Also, "hsa-mir-6717" (miRBase Accession No. MI0022551, SEQ ID NO: 290) having a hairpin-like structure is known as a precursor of "hsa-miR-6717-5p".

[0169] The term "hsa-miR-3195 gene" or "hsa-miR-3195" used herein includes the hsa-miR-3195 gene (miRBase Accession No. MIMAT0015079) described in SEQ ID NO: 114, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-3195 gene can be obtained by a method described in Stark MS et al., 2010, PLoS One, Vol. 5, e9685. Also, "hsa-mir-3195" (miRBase Accession No. MI0014240, SEQ ID NO: 291) having a hairpin-like structure is known as a precursor of "hsa-miR-3195".

[0170] The term "hsa-miR-6757-5p gene" or "hsa-miR-6757-5p" used herein includes the hsa-miR-6757-5p gene (miRBase Accession No. MIMAT0027414) described in SEQ ID NO: 115, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6757-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6757" (miRBase Accession No. MI0022602, SEQ ID NO: 292) having a hairpin-like structure is known as a precursor of "hsa-miR-6757-5p".

[0171] The term "hsa-miR-8072 gene" or "hsa-miR-8072" used herein includes the hsa-miR-8072 gene (miRBase Accession No. MIMAT0030999) described in SEQ ID NO: 116, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-8072 gene can be obtained by a method described in Wang HJ et al., 2013, Shock, Vol. 39, p. 480-487. Also, "hsa-mir-8072" (miRBase Accession No. MI0025908, SEQ ID NO: 293) having a hairpin-like structure is known as a precursor of "hsa-miR-8072".

[0172] The term "hsa-miR-4745-5p gene" or "hsa-miR-4745-5p" used herein includes the hsa-miR-4745-5p gene (miRBase Accession No. MIMAT0019878) described in SEQ ID NO: 117, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4745-5p gene can be obtained by a method described in Persson H et al., 2011,

Cancer Res, Vol. 71, p. 78-86. Also, "hsa-mir-4745" (miRBase Accession No. MI0017384, SEQ ID NO: 294) having a hairpin-like structure is known as a precursor of "hsa-miR-4745-5p".

[0173] The term "hsa-miR-6511a-5p gene" or "hsa-miR-651 1a-5p" used herein includes the hsa-miR-6511a-5p gene (miRBase Accession No. MIMAT0025478) described in SEQ ID NO: 118, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6511 a-5p gene can be obtained by a method described in Joyce CE et al., 2011, Hum Mol Genet, Vol. 20, p. 4025-4040. Also, "hsa-mir-6511a-1, hsa-mir-6511a-2, hsa-mir-6511a-3, and hsa-mir-6511a-4" (miRBase Accession Nos. MI0022223, MI0023564, MI0023565, and MI0023566, SEQ ID NOs: 295,296,297, and 298) having a hairpin-like structure are known as precursors of "hsa-miR-6511a-5p".

[0174] The term "hsa-miR-6776-5p gene" or "hsa-miR-6776-5p" used herein includes the hsa-miR-6776-5p gene (miRBase Accession No. MIMAT0027452) described in SEQ ID NO: 119, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6776-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6776" (miRBase Accession No. MI0022621, SEQ ID NO: 299) having a hairpin-like structure is known as a precursor of "hsa-miR-6776-5p".

[0175] The term "hsa-miR-371a-5p gene" or "hsa-miR-371a-5p" used herein includes the hsa-miR-371a-5p gene (miRBase Accession No. MIMAT0004687) described in SEQ ID NO: 120, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-371a-5p gene can be obtained by a method described in Suh MR et al., 2004, Dev Biol, Vol. 270, p. 488-498. Also, "hsa-mir-371a" (miRBase Accession No. MI0000779, SEQ ID NO: 300) having a hairpin-like structure is known as a precursor of "hsa-miR-371a-5p".

[0176] The term "hsa-miR-1227-5p gene" or "hsa-miR-1227-Sp" used herein includes the hsa-miR-1227-5p gene (miRBase Accession No. MIMAT0022941) described in SEQ ID NO: 121, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-1227-5p gene can be obtained by a method described in Berezikov E et al., 2007, Mol Cell, Vol. 28, p. 328-336. Also, "hsa-mir-1227" (miRBase Accession No. MI0006316, SEQ ID NO: 301) having a hairpin-like structure is known as a precursor of "hsa-miR-1227-5p".

[0177] The term "hsa-miR-7150 gene" or "hsa-miR-7150" used herein includes the hsa-miR-7150 gene (miRBase Accession No. MIMAT0028211) described in SEQ ID NO: 122, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-7150 gene can be obtained by a method described in Oulas A et al., 2009, Nucleic Acids Res, Vol. 37, p. 3276-3287. Also, "hsa-mir-7150" (miRBase Accession No. MI0023610, SEQ ID NO: 302) having a hairpin-like structure is known as a precursor of "hsa-miR-7150".

[0178] The term "hsa-miR-1915-3p gene" or "hsa-miR-1915-3p" used herein includes the hsa-miR-1915-3p gene (miRBase Accession No. MIMAT0007892) described in SEQ ID NO: 123, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-1915-3p gene can be obtained by a method described in Bar M et al., 2008, Stem Cells, Vol. 26, p. 2496-2505. Also, "hsa-mir-1915" (miRBase Accession No. MI0008336, SEQ ID NO: 266) having a hairpin-like structure is known as a precursor of "hsa-miR-1915-3p".

[0179] The term "hsa-miR-187-5p gene" or "hsa-miR-187-5p" used herein includes the hsa-miR-187-5p gene (miRBase Accession No. MIMAT0004561) described in SEQ ID NO: 124, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-187-5p gene can be obtained by a method described in Lim LP et al., 2003, Science, Vol. 299, p. 1540. Also, "hsa-mir-187" (miRBase Accession No. MI0000274, SEQ ID NO: 303) having a hairpin-like structure is known as a precursor of "hsa-miR-187-5p".

[0180] The term "hsa-miR-614 gene" or "hsa-miR-614" used herein includes the hsa-miR-614 gene (miRBase Accession No. MIMAT0003282) described in SEQ ID NO: 125, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-614 gene can be obtained by a method described in Cummins JM et al., 2006, Proc Natl Acad Sci U S A, Vol. 103, p. 3687-3692. Also, "hsa-mir-614" (miRBase Accession No. MI0003627, SEQ ID NO: 304) having a hairpin-like structure is known as a precursor of "hsa-miR-614".

[0181] The term "hsa-miR-19b-3p gene" or "hsa-miR-19b-3p" used herein includes the hsa-miR-19b-3p gene (miRBase Accession No. MIMAT0000074) described in SEQ ID NO: 126, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-19b-3p gene can be obtained by a method described in Lagos-Quintana M et al., 2001, Science, Vol. 294, p. 853-858. Also, "hsa-mir-19b-1 and hsa-mir-19b-2" (miRBase Accession Nos. MI0000074 and MI0000075, SEQ ID NOs: 305 and 306) having a hairpin-like structure are known as precursors of "hsa-miR-19b-3p" .

[0182] The term "hsa-miR-1225-5p gene" or "hsa-miR-1225-5p" used herein includes the hsa-miR-1225-5p gene (miRBase Accession No. MIMAT0005572) described in SEQ ID NO: 127, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-1225-5p gene can be obtained by a method described in Berezikov E et al., 2007, Mol Cell, Vol. 28, p. 328-336. Also, "hsa-mir-1225" (miRBase Accession No. MI0006311, SEQ ID NO: 307) having a hairpin-like structure is known as a precursor of "hsa-miR-1225-5p".

[0183] The term "hsa-miR-451a gene" or "hsa-miR-451a" used herein includes the hsa-miR-451a gene (miRBase Accession No. MIMAT0001631) described in SEQ ID NO: 128, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-451a gene can be obtained by a method described in Altuvia Yet al., 2005, Nucleic Acids Res, Vol. 33, p. 2697-2706. Also, "hsa-mir-451a" (miRBase Accession No. MI0001729, SEQ ID NO: 308) having a hairpin-like structure is known as a precursor of "hsa-miR-451a".

[0184] The term "hsa-miR-939-5p gene" or "hsa-miR-939-5p" used herein includes the hsa-miR-939-5p gene (miRBase Accession No. MIMAT0004982) described in SEQ ID NO: 129, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-939-5p gene can be obtained by a method described in Lui WO et al., 2007, Cancer Res, Vol. 67, p. 6031-6043. Also, "hsa-mir-939" (miRBase Accession No. MI0005761, SEQ ID NO: 309) having a hairpin-like structure is known as a precursor of "hsa-miR-939-5p".

[0185] The term "hsa-miR-223-3p gene" or "hsa-miR-223-3p" used herein includes the hsa-miR-223-3p gene (miRBase Accession No. MIMAT0000280) described in SEQ ID NO: 130, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-223-3p gene can be obtained by a method described in Lim LP et al., 2003, Science, Vol. 299, p. 1540. Also, "hsa-mir-223" (miRBase Accession No. MI0000300, SEQ ID NO: 310) having a hairpin-like structure is known as a precursor of "hsa-miR-223-3p".

[0186] The term "hsa-miR-1228-Sp gene" or "hsa-miR-1228-Sp" used herein includes the hsa-miR-1228-5p gene (miRBase Accession No. MIMAT0005582) described in SEQ ID NO: 131, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-1228-5p gene can be obtained by a method described in Berezikov E et al., 2007, Mol Cell, Vol. 28, p. 328-336. Also, "hsa-mir-1228" (miRBase Accession No. MI0006318, SEQ ID NO: 311) having a hairpin-like structure is known as a precursor of "hsa-miR-1228-5p".

[0187] The term "hsa-miR-125a-3p gene" or "hsa-miR-125a-3p" used herein includes the hsa-miR-125a-3p gene (miRBase Accession No. MIMAT0004602) described in SEQ ID NO: 132, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-125a-3p gene can be obtained by a method described in Lagos-Quintana M et al., 2002, Curr Biol, Vol. 12, p. 735-739. Also, "hsa-mir-125a" (miRBase Accession No. MI0000469, SEQ ID NO: 312) having a hairpin-like structure is known as a precursor of "hsa-miR-125a-3p".

[0188] The term "hsa-miR-92b-5p gene" or "hsa-miR-92b-5p" used herein includes the hsa-miR-92b-5p gene (miRBase Accession No. MIMAT0004792) described in SEQ ID NO: 133, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-92b-5p gene can be obtained by a method described in Cummins JM et al., 2006, Proc Natl Acad Sci U S A, Vol. 103, p. 3687-3692. Also, "hsa-mir-92b" (miRBase Accession No. MI0003560, SEQ ID NO: 313) having a hairpin-like structure is known as a precursor of "hsa-miR-92b-5p".

[0189] The term "hsa-miR-22-3p gene" or "hsa-miR-22-3p" used herein includes the hsa-miR-22-3p gene (miRBase Accession No. MIMAT0000077) described in SEQ ID NO: 134, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-22-3p gene can be obtained by a method described in Lagos-Quintana M et al., 2001, Science, Vol. 294, p. 853-858. Also, "hsa-mir-22" (miRBase Accession No. MI0000078, SEQ ID NO: 314) having a hairpin-like structure is known as a precursor of "hsa-miR-22-3p".

[0190] The term "hsa-miR-4271 gene" or "hsa-miR-4271" used herein includes the hsa-miR-4271 gene (miRBase Accession No. MIMAT0016901) described in SEQ ID NO: 135, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4271 gene can be obtained by a method described in Goff LA et al., 2009, PLoS One, Vol. 4, e7192. Also, "hsa-mir-4271" (miRBase Accession No. MI0015879, SEQ ID NO: 315) having a hairpin-like structure is known as a precursor of "hsa-miR-4271".

[0191] The term "hsa-miR-642b-3p gene" or "hsa-miR-642b-3p" used herein includes the hsa-miR-642b-3p gene (miRBase Accession No. MIMAT0018444) described in SEQ ID NO: 136, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-642b-3p gene can be obtained by a method described in Witten D et al., 2010, BMC Biol, Vol. 8, p. 58. Also, "hsa-mir-642b" (miRBase Accession No. MI0016685, SEQ ID NO: 316) having a hairpin-like structure is known as a precursor of "hsa-miR-642b-3p".

[0192] The term "hsa-miR-6075 gene" or "hsa-miR-6075" used herein includes the hsa-miR-6075 gene (miRBase Accession No. MIMAT0023700) described in SEQ ID NO: 137, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6075 gene can be obtained by a method described in Voellenkle C et al., 2012, RNA, Vol. 18, p. 472-484. Also, "hsa-mir-6075" (miRBase Accession No. MI0020352, SEQ ID NO: 317) having a hairpin-like structure is known as a precursor of "hsa-miR-6075".

[0193] The term "hsa-miR-6125 gene" or "hsa-miR-6125" used herein includes the hsa-miR-6125 gene (miRBase Accession No. MIMAT0024598) described in SEQ ID NO: 138, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6125 gene can be obtained by a method described in Smith JL et al., 2012, J Virol, Vol. 86, p. 5278-5287. Also, "hsa-mir-6125" (miRBase Accession No. MI0021259, SEQ ID NO: 318) having a hairpin-like structure is known as a precursor of "hsa-miR-6125".

[0194] The term "hsa-miR-887-3p gene" or "hsa-miR-887-3p" used herein includes the hsa-miR-887-3p gene (miRBase Accession No. MIMAT0004951) described in SEQ ID NO: 139, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-887-3p gene can be obtained by a method described in Berezikov E et al., 2006, Genome Res, Vol. 16, p. 1289-1298. Also, "hsa-mir-887" (miRBase Accession No. MI0005562, SEQ ID NO: 319) having a hairpin-like structure is known as a precursor of "hsa-miR-887-3p".

[0195] The term "hsa-miR-6851-5p gene" or "hsa-miR-6851-5p" used herein includes the hsa-miR-6851-5p gene (miRBase Accession No. MIMAT0027602) described in SEQ ID NO: 140, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6851-5p gene can be obtained by a method described in Ladewig E et al., 2012,

Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6851" (miRBase Accession No. MI0022697, SEQ ID NO: 320) having a hairpin-like structure is known as a precursor of "hsa-miR-6851-5p".

[0196] The term "hsa-miR-6763-5p gene" or "hsa-miR-6763-5p" used herein includes the hsa-miR-6763-5p gene (miRBase Accession No. MIMAT0027426) described in SEQ ID NO: 141, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6763-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6763" (miRBase Accession No. MI0022608, SEQ ID NO: 321) having a hairpin-like structure is known as a precursor of "hsa-miR-6763-5p".

[0197] The term "hsa-miR-3928-3p gene" or "hsa-miR-3928-3p" used herein includes the hsa-miR-3928-3p gene (miRBase Accession No. MIMAT0018205) described in SEQ ID NO: 142, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-3928-3p gene can be obtained by a method described in Creighton CJ et al., 2010, PLoS One, Vol. 5, e9637. Also, "hsa-mir-3928" (miRBase Accession No. MI0016438, SEQ ID NO: 322) having a hairpin-like structure is known as a precursor of "hsa-miR-3928-3p".

[0198] The term "hsa-miR-4443 gene" or "hsa-miR-4443" used herein includes the hsa-miR-4443 gene (miRBase Accession No. MIMAT0018961) described in SEQ ID NO: 143, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4443 gene can be obtained by a method described in Jima DD et al., 2010, Blood, Vol. 116, e118-e127. Also, "hsa-mir-4443" (miRBase Accession No. MI0016786, SEQ ID NO: 323) having a hairpin-like structure is known as a precursor of "hsa-miR-4443".

[0199] The term "hsa-miR-3648 gene" or "hsa-miR-3648" used herein includes the hsa-miR-3648 gene (miRBase Accession No. MIMAT0018068) described in SEQ ID NO: 144, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-3648 gene can be obtained by a method described in Meiri E et al., 2010, Nucleic Acids Res, Vol. 38, p. 6234-6246. Also, "hsa-mir-3648" (miRBase Accession No. MI0016048, SEQ ID NO: 324) having a hairpin-like structure is known as a precursor of "hsa-miR-3648".

[0200] The term "hsa-miR-149-3p gene" or "hsa-miR-149-3p" used herein includes the hsa-miR-149-3p gene (miRBase Accession No. MIMAT0004609) described in SEQ ID NO: 145, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-149-3p gene can be obtained by a method described in Lagos-Quintana M et al., 2002, Curr Biol, Vol. 12, p. 735-739. Also, "hsa-mir-149" (miRBase Accession No. MI0000478, SEQ ID NO: 325) having a hairpin-like structure is known as a precursor of "hsa-miR-149-3p".

[0201] The term "hsa-miR-4689 gene" or "hsa-miR-4689" used herein includes the hsa-miR-4689 gene (miRBase Accession No. MIMAT0019778) described in SEQ ID NO: 146, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4689 gene can be obtained by a method described in Persson H et al., 2011, Cancer Res, Vol. 71, p. 78-86. Also, "hsa-mir-4689" (miRBase Accession No. MI0017322, SEQ ID NO: 326) having a hairpin-like structure is known as a precursor of "hsa-miR-4689".

[0202] The term "hsa-miR-4763-3p gene" or "hsa-miR-4763-3p" used herein includes the hsa-miR-4763-3p gene (miRBase Accession No. MIMAT0019913) described in SEQ ID NO: 147, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4763-3p gene can be obtained by a method described in Persson H et al., 2011, Cancer Res, Vol. 71, p. 78-86. Also, "hsa-mir-4763" (miRBase Accession No. MI0017404, SEQ ID NO: 327) having a hairpin-like structure is known as a precursor of "hsa-miR-4763-3p".

[0203] The term "hsa-miR-6729-5p gene" or "hsa-miR-6729-5p" used herein includes the hsa-miR-6729-5p gene (miRBase Accession No. MIMAT0027359) described in SEQ ID NO: 148, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6729-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6729" (miRBase Accession No. MI0022574, SEQ ID NO: 328) having a hairpin-like structure is known as a precursor of "hsa-miR-6729-5p".

[0204] The term "hsa-miR-3196 gene" or "hsa-miR-3196" used herein includes the hsa-miR-3196 gene (miRBase Accession No. MIMAT0015080) described in SEQ ID NO: 149, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-3196 gene can be obtained by a method described in Stark MS et al., 2010, PLoS One, Vol. 5, e9685. Also, "hsa-mir-3196" (miRBase Accession No. MI0014241, SEQ ID NO: 329) having a hairpin-like structure is known as a precursor of "hsa-miR-3196".

[0205] The term "hsa-miR-8069 gene" or "hsa-miR-8069" used herein includes the hsa-miR-8069 gene (miRBase Accession No. MIMAT0030996) described in SEQ ID NO: 150, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-8069 gene can be obtained by a method described in Wang HJ et al., 2013, Shock, Vol. 39, p. 480-487. Also, "hsa-mir-8069" (miRBase Accession No. MI0025905, SEQ ID NO: 330) having a hairpin-like structure is known as a precursor of "hsa-miR-8069".

[0206] The term "hsa-miR-1268a gene" or "hsa-miR-1268a" used herein includes the hsa-miR-1268a gene (miRBase Accession No. MIMAT0005922) described in SEQ ID NO: 151, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-1268a gene can be obtained by a method described in Morin RD et al., 2008, Genome Res, Vol. 18, p. 610-621. Also, "hsa-mir-1268a" (miRBase Accession No. MI0006405, SEQ ID NO: 331) having a hairpin-like structure is known as a precursor of "hsa-miR-1268a".

[0207] The term "hsa-miR-4739 gene" or "hsa-miR-4739" used herein includes the hsa-miR-4739 gene (miRBase

Accession No. MIMAT0019868) described in SEQ ID NO: 152, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4739 gene can be obtained by a method described in Persson H et al., 2011, Cancer Res, Vol. 71, p. 78-86. Also, "hsa-mir-4739" (miRBase Accession No. MI0017377, SEQ ID NO: 332) having a hairpin-like structure is known as a precursor of "hsa-miR-4739".

[0208] The term "hsa-miR-1268b gene" or "hsa-miR-1268b" used herein includes the hsa-miR-1268b gene (miRBase Accession No. MIMAT0018925) described in SEQ ID NO: 153, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-1268b gene can be obtained by a method described in Jima DD et al., 2010, Blood, Vol. 116, e118-e127. Also, "hsa-mir-1268b" (miRBase Accession No. MI0016748, SEQ ID NO: 333) having a hairpin-like structure is known as a precursor of "hsa-miR-1268b".

[0209] The term "hsa-miR-5698 gene" or "hsa-miR-5698" used herein includes the hsa-miR-5698 gene (miRBase Accession No. MIMAT0022491) described in SEQ ID NO: 154, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-5698 gene can be obtained by a method described in Watahiki A et al., 2011, PLoS One, Vol. 6, e24950. Also, "hsa-mir-5698" (miRBase Accession No. MI0019305, SEQ ID NO: 334) having a hairpin-like structure is known as a precursor of "hsa-miR-5698".

[0210] The term "hsa-miR-6752-5p gene" or "hsa-miR-6752-5p" used herein includes the hsa-miR-6752-5p gene (miRBase Accession No. MIMAT0027404) described in SEQ ID NO: 155, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6752-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6752" (miRBase Accession No. MI0022597, SEQ ID NO: 335) having a hairpin-like structure is known as a precursor of "hsa-miR-6752-5p".

[0211] The term "hsa-miR-4507 gene" or "hsa-miR-4507" used herein includes the hsa-miR-4507 gene (miRBase Accession No. MIMAT0019044) described in SEQ ID NO: 156, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4507 gene can be obtained by a method described in Jima DD et al., 2010, Blood, Vol. 116, e118-e127. Also, "hsa-mir-4507" (miRBase Accession No. MI0016871, SEQ ID NO: 336) having a hairpin-like structure is known as a precursor of "hsa-miR-4507".

[0212] The term "hsa-miR-564 gene" or "hsa-miR-564" used herein includes the hsa-miR-564 gene (miRBase Accession No. MIMAT0003228) described in SEQ ID NO: 157, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-564 gene can be obtained by a method described in Cummins JM et al., 2006, Proc Natl Acad Sci U S A, Vol. 103, p. 3687-3692. Also, "hsa-mir-564" (miRBase Accession No. MI0003570, SEQ ID NO: 337) having a hairpin-like structure is known as a precursor of "hsa-miR-564".

[0213] The term "hsa-miR-4497 gene" or "hsa-miR-4497" used herein includes the hsa-miR-4497 gene (miRBase Accession No. MIMAT0019032) described in SEQ ID NO: 158, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4497 gene can be obtained by a method described in Jima DD et al., 2010, Blood, Vol. 116, e118-e127. Also, "hsa-mir-4497" (miRBase Accession No. MI0016859, SEQ ID NO: 338) having a hairpin-like structure is known as a precursor of "hsa-miR-4497".

[0214] The term "hsa-miR-6877-5p gene" or "hsa-miR-6877-5p" used herein includes the hsa-miR-6877-5p gene (miRBase Accession No. MIMAT0027654) described in SEQ ID NO: 159, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6877-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6877" (miRBase Accession No. MI0022724, SEQ ID NO: 339) having a hairpin-like structure is known as a precursor of "hsa-miR-6877-5p".

[0215] The term "hsa-miR-6087 gene" or "hsa-miR-6087" used herein includes the hsa-miR-6087 gene (miRBase Accession No. MIMAT0023712) described in SEQ ID NO: 160, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6087 gene can be obtained by a method described in Yoo JK et al., 2012, Stem Cells Dev, Vol. 21, p. 2049-2057. Also, "hsa-mir-6087" (miRBase Accession No. MI0020364, SEQ ID NO: 340) having a hairpin-like structure is known as a precursor of "hsa-miR-6087".

[0216] The term "hsa-miR-4731-5p gene" or "hsa-miR-4731-5p" used herein includes the hsa-miR-4731-5p gene (miRBase Accession No. MIMAT0019853) described in SEQ ID NO: 161, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4731-5p gene can be obtained by a method described in Persson H et al., 2011, Cancer Res, Vol. 71, p. 78-86. Also, "hsa-mir-4731" (miRBase Accession No. MI0017368, SEQ ID NO: 341) having a hairpin-like structure is known as a precursor of "hsa-miR-4731-5p".

[0217] The term "hsa-miR-615-5p gene" or "hsa-miR-615-5p" used herein includes the hsa-miR-615-5p gene (miRBase Accession No. MIMAT0004804) described in SEQ ID NO: 162, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-615-5p gene can be obtained by a method described in Cummins JM et al., 2006, Proc Natl Acad Sci U S A, Vol. 103, p. 3687-3692. Also, "hsa-mir-615" (miRBase Accession No. MI0003628, SEQ ID NO: 342) having a hairpin-like structure is known as a precursor of "hsa-miR-615-5p".

[0218] The term "hsa-miR-760 gene" or "hsa-miR-760" used herein includes the hsa-miR-760 gene (miRBase Accession No. MIMAT0004957) described in SEQ ID NO: 163, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-760 gene can be obtained by a method described in Berezikov E et al., 2006, Genome Res, Vol. 16, p. 1289-1298. Also, "hsa-mir-760" (miRBase Accession No. MI0005567, SEQ ID NO: 343) having a hairpin-like

structure is known as a precursor of "hsa-miR-760".

[0219] The term "hsa-miR-6891-5p gene" or "hsa-miR-6891-5p" used herein includes the hsa-miR-6891-5p gene (miRBase Accession No. MIMAT0027682) described in SEQ ID NO: 164, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6891-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6891" (miRBase Accession No. MI0022738, SEQ ID NO: 344) having a hairpin-like structure is known as a precursor of "hsa-miR-6891-5p".

[0220] The term "hsa-miR-6887-5p gene" or "hsa-miR-6887-5p" used herein includes the hsa-miR-6887-5p gene (miRBase Accession No. MIMAT0027674) described in SEQ ID NO: 165, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6887-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6887" (miRBase Accession No. MI0022734, SEQ ID NO: 345) having a hairpin-like structure is known as a precursor of "hsa-miR-6887-5p".

[0221] The term "hsa-miR-4525 gene" or "hsa-miR-4525" used herein includes the hsa-miR-4525 gene (miRBase Accession No. MIMAT0019064) described in SEQ ID NO: 166, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4525 gene can be obtained by a method described in Jima DD et al., 2010, Blood, Vol. 116, e118-e127. Also, "hsa-mir-4525" (miRBase Accession No. MI0016892, SEQ ID NO: 346) having a hairpin-like structure is known as a precursor of "hsa-miR-4525".

[0222] The term "hsa-miR-1914-3p gene" or "hsa-miR-1914-3p" used herein includes the hsa-miR-1914-3p gene (miRBase Accession No. MIMAT0007890) described in SEQ ID NO: 167, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-1914-3p gene can be obtained by a method described in Bar M et al., 2008, Stem Cells, Vol. 26, p. 2496-2505. Also, "hsa-mir-1914" (miRBase Accession No. MI0008335, SEQ ID NO: 347) having a hairpin-like structure is known as a precursor of "hsa-miR-1914-3p".

[0223] The term "hsa-miR-619-5p gene" or "hsa-miR-619-5p" used herein includes the hsa-miR-619-5p gene (miRBase Accession No. MIMAT0026622) described in SEQ ID NO: 168, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-619-5p gene can be obtained by a method described in Cummins JM et al., 2006, Proc Natl Acad Sci U S A, Vol. 103, p. 3687-3692. Also, "hsa-mir-619" (miRBase Accession No. MI0003633, SEQ ID NO: 348) having a hairpin-like structure is known as a precursor of "hsa-miR-619-5p".

[0224] The term "hsa-miR-5001-5p gene" or "hsa-miR-5001-5p" used herein includes the hsa-miR-5001-5p gene (miRBase Accession No. MIMAT0021021) described in SEQ ID NO: 169, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-5001-5p gene can be obtained by a method described in Hansen TB et al., 2011, RNA Biol, Vol. 8, p. 378-383. Also, "hsa-mir-5001" (miRBase Accession No. MI0017867, SEQ ID NO: 349) having a hairpin-like structure is known as a precursor of "hsa-miR-5001-5p".

[0225] The term "hsa-miR-6722-3p gene" or "hsa-miR-6722-3p" used herein includes the hsa-miR-6722-3p gene (miRBase Accession No. MIMAT0025854) described in SEQ ID NO: 170, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6722-3p gene can be obtained by a method described in Li Y et al., 2012, Gene, Vol. 497, p. 330-335. Also, "hsa-mir-6722" (miRBase Accession No. MI0022557, SEQ ID NO: 350) having a hairpin-like structure is known as a precursor of "hsa-miR-6722-3p".

[0226] The term "hsa-miR-3621 gene" or "hsa-miR-3621" used herein includes the hsa-miR-3621 gene (miRBase Accession No. MIMAT0018002) described in SEQ ID NO: 171, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-3621 gene can be obtained by a method described in Witten D et al., 2010, BMC Biol, Vol. 8, p. 58. Also, "hsa-mir-3621" (miRBase Accession No. MI0016012, SEQ ID NO: 351) having a hairpin-like structure is known as a precursor of "hsa-miR-3621".

[0227] The term "hsa-miR-4298 gene" or "hsa-miR-4298" used herein includes the hsa-miR-4298 gene (miRBase Accession No. MIMAT0016852) described in SEQ ID NO: 172, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4298 gene can be obtained by a method described in Goff LA et al., 2009, PLoS One, Vol. 4, e7192. Also, "hsa-mir-4298" (miRBase Accession No. MI0015830, SEQ ID NO: 352) having a hairpin-like structure is known as a precursor of "hsa-miR-4298".

[0228] The term "hsa-miR-675-5p gene" or "hsa-miR-675-5p" used herein includes the hsa-miR-675-5p gene (miRBase Accession No. MIMAT0004284) described in SEQ ID NO: 173, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-675-5p gene can be obtained by a method described in Cai X et al., 2007, RNA, Vol. 13, p. 313-316. Also, "hsa-mir-675" (miRBase Accession No. MI0005416, SEQ ID NO: 353) having a hairpin-like structure is known as a precursor of "hsa-miR-675-5p".

[0229] The term "hsa-miR-4655-5p gene" or "hsa-miR-4655-5p" used herein includes the hsa-miR-4655-5p gene (miRBase Accession No. MIMAT0019721) described in SEQ ID NO: 174, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4655-5p gene can be obtained by a method described in Persson H et al., 2011, Cancer Res, Vol. 71, p. 78-86. Also, "hsa-mir-4655" (miRBase Accession No. MI0017283, SEQ ID NO: 354) having a hairpin-like structure is known as a precursor of "hsa-miR-4655-5p".

[0230] The term "hsa-miR-6073 gene" or "hsa-miR-6073" used herein includes the hsa-miR-6073 gene (miRBase Accession No. MIMAT0023698) described in SEQ ID NO: 561, a homolog or an ortholog of a different organism species,

and the like. The hsa-miR-6073 gene can be obtained by a method described in Voellenkle C et al., 2012, RNA, Vol. 18, p. 472-484. Also, "hsa-mir-6073" (miRBase Accession No. MI0020350, SEQ ID NO: 580) having a hairpin-like structure is known as a precursor of "hsa-miR-6073".

[0231] The term "hsa-miR-6845-5p gene" or "hsa-miR-6845-5p" used herein includes the hsa-miR-6845-5p gene (miRBase Accession No. MIMAT0027590) described in SEQ ID NO: 562, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6845-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6845" (miRBase Accession No. MI0022691, SEQ ID NO: 581) having a hairpin-like structure is known as a precursor of "hsa-miR-6845-5p".

[0232] The term "hsa-miR-6769b-5p gene" or "hsa-miR-6769b-5p" used herein includes the hsa-miR-6769b-5p gene (miRBase Accession No. MIMAT0027620) described in SEQ ID NO: 563, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6769b-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6769b" (miRBase Accession No. MI0022706, SEQ ID NO: 582) having a hairpin-like structure is known as a precursor of "hsa-miR-6769b-5p".

[0233] The term "hsa-miR-4665-3p gene" or "hsa-miR-4665-3p" used herein includes the hsa-miR-4665-3p gene (miRBase Accession No. MIMAT0019740) described in SEQ ID NO: 564, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4665-3p gene can be obtained by a method described in Persson H et al., 2011, Cancer Res, Vol. 71, p. 78-86. Also, "hsa-mir-4665" (miRBase Accession No. MI0017295, SEQ ID NO: 583) having a hairpin-like structure is known as a precursor of "hsa-miR-4665-3p".

[0234] The term "hsa-miR-1913 gene" or "hsa-miR-1913" used herein includes the hsa-miR-1913 gene (miRBase Accession No. MIMAT0007888) described in SEQ ID NO: 565, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-1913 gene can be obtained by a method described in Bar M et al., 2008, Stem Cells, Vol. 26, p. 2496-2505. Also, "hsa-mir-1913" (miRBase Accession No. MI0008334, SEQ ID NO: 584) having a hairpin-like structure is known as a precursor of "hsa-miR-1913".

[0235] The term "hsa-miR-1228-3p gene" or "hsa-miR-1228-3p" used herein includes the hsa-miR-1228-3p gene (miRBase Accession No. MIMAT0005583) described in SEQ ID NO: 566, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-1228-3p gene can be obtained by a method described in Berezikov E et al., 2007, Mol Cell, Vol. 28, p. 328-336. Also, "hsa-mir-1228" (miRBase Accession No. MI0006318, SEQ ID NO: 311) having a hairpin-like structure is known as a precursor of "hsa-miR-1228-3p".

[0236] The term "hsa-miR-940 gene" or "hsa-miR-940" used herein includes the hsa-miR-940 gene (miRBase Accession No. MIMAT0004983) described in SEQ ID NO: 567, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-940 gene can be obtained by a method described in Lui WO et al., 2007, Cancer Res, Vol. 67, p. 6031-6043. Also, "hsa-mir-940" (miRBase Accession No. MI0005762, SEQ ID NO: 585) having a hairpin-like structure is known as a precursor of "hsa-miR-940".

[0237] The term "hsa-miR-296-3p gene" or "hsa-miR-296-3p" used herein includes the hsa-miR-296-3p gene (miRBase Accession No. MIMAT0004679) described in SEQ ID NO: 568, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-296-3p gene can be obtained by a method described in Houbaviy HB et al., 2003, Dev Cell, Vol. 5, p. 351-358. Also, "hsa-mir-296" (miRBase Accession No. MI0000747, SEQ ID NO: 586) having a hairpin-like structure is known as a precursor of "hsa-miR-296-3p".

[0238] The term "hsa-miR-4690-5p gene" or "hsa-miR-4690-5p" used herein includes the hsa-miR-4690-5p gene (miRBase Accession No. MIMAT0019779) described in SEQ ID NO: 569, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4690-5p gene can be obtained by a method described in Persson H et al., 2011, Cancer Res, Vol. 71, p. 78-86. Also, "hsa-mir-4690" (miRBase Accession No. MI0017323, SEQ ID NO: 587) having a hairpin-like structure is known as a precursor of "hsa-miR-4690-5p".

[0239] The term "hsa-miR-548q gene" or "hsa-miR-548q" used herein includes the hsa-miR-548q gene (miRBase Accession No. MIMAT0011163) described in SEQ ID NO: 570, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-548q gene can be obtained by a method described in Wyman SK et al., 2009, PLoS One., Vol. 4, e5311. Also, "hsa-mir-548q" (miRBase Accession No. MI0010637, SEQ ID NO: 588) having a hairpin-like structure is known as a precursor of "hsa-miR-548q".

[0240] The term "hsa-miR-663a gene" or "hsa-miR-663a" used herein includes the hsa-miR-663a gene (miRBase Accession No. MIMAT0003326) described in SEQ ID NO: 571, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-663a gene can be obtained by a method described in Cummins JM et al., 2006, Proc Natl Acad Sci USA, Vol. 103, p. 3687-3692. Also, "hsa-mir-663a" (miRBase Accession No. MI0003672, SEQ ID NO: 589) having a hairpin-like structure is known as a precursor of "hsa-miR-663a".

[0241] The term "hsa-miR-1249 gene" or "hsa-miR-1249" used herein includes the hsa-miR-1249 gene (miRBase Accession No. MIMAT0005901) described in SEQ ID NO: 572, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-1249 gene can be obtained by a method described in Morin RD et al., 2008, Genome Res, Vol. 18, p. 610-621. Also, "hsa-mir-1249" (miRBase Accession No. MI0006384, SEQ ID NO: 590) having a hairpin-like structure is known as a precursor of "hsa-miR-1249".

[0242] The term "hsa-miR-1202 gene" or "hsa-miR-1202" used herein includes the hsa-miR-1202 gene (miRBase Accession No. MIMAT0005865) described in SEQ ID NO: 573, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-1202 gene can be obtained by a method described in Marton S et al., 2008, Leukemia, Vol. 22, p. 330-338. Also, "hsa-mir-1202" (miRBase Accession No. MI0006334, SEQ ID NO: 591) having a hairpin-like structure is known as a precursor of "hsa-miR-1202".

[0243] The term "hsa-miR-7113-3p gene" or "hsa-miR-7113-3p" used herein includes the hsa-miR-7113-3p gene (miRBase Accession No. MIMAT0028124) described in SEQ ID NO: 574, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-7113-3p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-7113" (miRBase Accession No. MI0022964, SEQ ID NO: 592) having a hairpin-like structure is known as a precursor of "hsa-miR-7113-3p".

[0244] The term "hsa-miR-1225-3p gene" or "hsa-miR-1225-3p" used herein includes the hsa-miR-1225-3p gene (miRBase Accession No. MIMAT0005573) described in SEQ ID NO: 575, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-1225-3p gene can be obtained by a method described in Berezikov E et al., 2007, Mol Cell, Vol. 28, p. 328-336. Also, "hsa-mir-1225" (miRBase Accession No. MI0006311, SEQ ID NO: 307) having a hairpin-like structure is known as a precursor of "hsa-miR-1225-3p".

[0245] The term "hsa-miR-4783-3p gene" or "hsa-miR-4783-3p" used herein includes the hsa-miR-4783-3p gene (miRBase Accession No. MIMAT0019947) described in SEQ ID NO: 576, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4783-3p gene can be obtained by a method described in Persson H et al., 2011, Cancer Res, Vol. 71, p. 78-86. Also, "hsa-mir-4783" (miRBase Accession No. MI0017428, SEQ ID NO: 593) having a hairpin-like structure is known as a precursor of "hsa-miR-4783-3p".

[0246] The term "hsa-miR-4448 gene" or "hsa-miR-4448" used herein includes the hsa-miR-4448 gene (miRBase Accession No. MIMAT0018967) described in SEQ ID NO: 577, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4448 gene can be obtained by a method described in Jima DD et al., 2010, Blood, Vol. 116, e118-e127. Also, "hsa-mir-4448" (miRBase Accession No. MI0016791, SEQ ID NO: 594) having a hairpin-like structure is known as a precursor of "hsa-miR-4448".

[0247] The term "hsa-miR-4534 gene" or "hsa-miR-4534" used herein includes the hsa-miR-4534 gene (miRBase Accession No. MIMAT0019073) described in SEQ ID NO: 578, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4534 gene can be obtained by a method described in Jima DD et al., 2010, Blood, Vol. 116, e118-e127. Also, "hsa-mir-4534" (miRBase Accession No. MI0016901, SEQ ID NO: 595) having a hairpin-like structure is known as a precursor of "hsa-miR-4534".

[0248] The term "hsa-miR-1307-3p gene" or "hsa-miR-1307-3p" used herein includes the hsa-miR-1307-3p gene (miRBase Accession No. MIMAT0005951) described in SEQ ID NO: 579, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-1307-3p gene can be obtained by a method described in Morin RD et al., 2008, Genome Res, Vol. 18, p. 610-621. Also, "hsa-mir-1307" (miRBase Accession No. MI0006444, SEQ ID NO: 596) having a hairpin-like structure is known as a precursor of "hsa-miR-1307-3p".

[0249] A mature miRNA may become a variant due to the sequence cleaved shorter or longer by one to several upstream or downstream nucleotides or nucleotide substitution when cut out as the mature miRNA from its RNA precursor having a hairpin-like structure. This variant is called isomiR (Morin RD. et al., 2008, Genome Res., Vol. 18, p. 610-621). The miRBase Release 20 shows the nucleotide sequences represented by SEQ ID NOs: 1 to 174 and 561 to 579 as well as a large number of the nucleotide sequence variants and fragments represented by SEQ ID NOs: 355 to 560 and 597 to 618, called isomiRs. These variants can also be obtained as miRNAs having a nucleotide sequence represented by any of SEQ ID NOs: 1 to 174 and 561 to 579. Specifically, among the variants of polynucleotides consisting of the nucleotide sequence represented by any of SEQ ID NOs: 5, 8, 9, 11, 18, 20, 22, 23, 24, 28, 29, 30, 32, 34, 37, 40, 41, 47, 48, 49, 51, 52, 53, 56, 58, 59, 60, 61, 63, 64, 65, 66, 67, 69, 72, 73, 75, 78, 79, 80, 81, 82, 85, 88, 89, 91, 92, 95, 96, 103, 104, 105, 106, 107, 108, 109, 110, 112, 113, 114, 117, 118, 120, 123, 124, 125, 126, 128, 129, 130, 131, 132, 133, 134, 135, 136, 138, 139, 142, 143, 144, 145, 146, 147, 149, 151, 152, 153, 154, 156, 157, 158, 160, 161, 162, 163, 166, 167, 168, 169, 172, 173, 174, 565, 566, 567, 568, 569, 571, 572, 573, 576, 577, 579, or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t in the nucleotide sequence, examples of the longest variants registered in the miRBase Release 20 include polynucleotides represented by SEQ ID NOs: 355, 357, 359, 361, 363, 365, 367, 369, 371, 373, 375, 377, 379, 381, 383, 385, 387, 389, 391, 393, 395, 397, 399, 401, 403, 405, 407, 409, 411, 413, 415, 417, 419, 421, 423, 425, 427, 429, 431, 433, 435, 437, 439, 441, 443, 445, 447, 449, 451, 453, 455, 457, 459, 461, 463, 465, 467, 469, 471, 473, 475, 477, 479, 481, 483, 485, 487, 489, 491, 493, 495, 497, 499, 501, 503, 505, 507, 509, 511, 513, 515, 517, 519, 521, 523, 525, 527, 529, 531, 533, 535, 537, 539, 541, 543, 545, 547, 549, 551, 553, 555, 557, 559, 597, 599, 601, 603, 605, 607, 609, 611, 613, 615 and 617, respectively.

[0250] Also, among the variants of polynucleotides consisting of a nucleotide sequence represented by any of SEQ ID NOs: 5, 8, 9, 11, 18, 20, 22, 23, 24, 28, 29, 30, 32, 34, 37, 40, 41, 47, 48, 49, 51, 52, 53, 56, 58, 59, 60, 61, 63, 64, 65, 66, 67, 69, 72, 73, 75, 78, 79, 80, 81, 82, 85, 88, 89, 91, 92, 95, 96, 103, 104, 105, 106, 107, 108, 109, 110, 112, 113, 114, 117, 118, 120, 123, 124, 125, 126, 128, 129, 130, 131, 132, 133, 134, 135, 136, 138, 139, 142, 143, 144, 145,

146, 147, 149, 151, 152, 153, 154, 156, 157, 158, 160, 161, 162, 163, 166, 167, 168, 169, 172, 173, 174, 565, 566, 567, 568, 569, 571, 572, 573, 576, 577, 579 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t in the nucleotide sequence, examples of the shortest variants registered in the miRBase Release 20 include polynucleotides having sequences represented by SEQ ID NOs: 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392, 394, 396, 398, 400, 402, 404, 406, 408, 410, 412, 414, 416, 418, 420, 422, 424, 426, 428, 430, 432, 434, 436, 438, 440, 442, 444, 446, 448, 450, 452, 454, 456, 458, 460, 462, 464, 466, 468, 470, 472, 474, 476, 478, 480, 482, 484, 486, 488, 490, 492, 494, 496, 498, 500, 502, 504, 506, 508, 510, 512, 514, 516, 518, 520, 522, 524, 526, 528, 530, 532, 534, 536, 538, 540, 542, 544, 546, 548, 550, 552, 554, 556, 558, 560, 598, 600, 602, 604, 606, 608, 610, 612, 614, 616 and 618, respectively.

[0251] In addition to these variants and fragments, examples thereof include a large number of isomiR polynucleotides of SEQ ID NOs: 1 to 174 and 561 to 579 registered in miRBase.

[0252] Examples of the polynucleotide comprising a nucleotide sequence represented by any of SEQ ID NOs: 1 to 174 and 561 to 579 include a polynucleotide represented by any of SEQ ID NOs: 175 to 354 and 579 to 596, which are their respective precursors.

[0253] The names and miRBase Accession Nos. (registration numbers) of the genes represented by SEQ ID NOs: 1 to 618 are shown in Table 1.

[0254] As used herein, the term "capable of specifically binding" means that the nucleic acid probe or the primer used in the present invention binds to a particular target nucleic acid and cannot substantially bind to other nucleic acids.

[Table 1]

SEQ ID NO:	Gene name	miRBase registration No.
1	hsa-miR-6768-5p	MIMAT0027436
2	hsa-miR-6836-3p	MIMAT0027575
3	hsa-miR-6782-5p	MIMAT0027464
4	hsa-miR-3663-3p	MIMAT0018085
5	hsa-miR-1908-3p	MIMA T0026916
6	hsa-miR-6726-5p	MIMAT0027353
7	hsa-miR-4258	MIMAT0016879
8	hsa-miR-1343-3p	MIMAT0019776
9	hsa-miR-4516	MIMAT0019053
10	hsa-miR-6875-5p	MIMAT0027650
11	hsa-miR-4651	MIMAT0019715
12	hsa-miR-6825-5p	MIMAT0027550
13	hsa-miR-6840-3p	MIMAT0027583
14	hsa-miR-6780b-5p	MIMAT0027572
15	hsa-miR-6749-5p	MIMAT0027398
16	hsa-miR-8063	MIMAT0030990
17	hsa-miR-6784-5p	MIMAT0027468
18	hsa-miR-3679-5p	MIMAT0018104
19	hsa-miR-3184-5p	MIMAT0015064
20	hsa-miR-663b	MIMAT0005867
21	hsa-miR-6880-5p	MIMAT0027660
22	hsa-miR-1908-5p	MIMAT0007881
23	hsa-miR-92a-2-5p	MIMAT0004508
24	hsa-miR-7975	MIMAT0031178
25	hsa-miR-7110-5p	MIMAT0028117

(continued)

SEQ ID NO:	Gene name	miRBase registration No.
26	hsa-miR-6842-5p	MIMAT0027586
27	hsa-miR-6857-5p	MIMAT0027614
28	hsa-miR-5572	MIMA T0022260
29	hsa-miR-3197	MIMAT0015082
30	hsa-miR-6131	MIMAT0024615
31	hsa-miR-6889-5p	MIMAT0027678
32	hsa-miR-4454	MIMAT0018976
33	hsa-miR-1199-5p	MIMAT0031119
34	hsa-miR-1247-3p	MIMAT0022721
35	hsa-miR-6800-5p	MIMAT0027500
36	hsa-miR-6872-3p	MIMAT0027645
37	hsa-miR-4649-5p	MIMAT0019711
38	hsa-miR-6791-5p	MIMAT0027482
39	hsa-miR-4433b-3p	MIMA T0030414
40	hsa-miR-3135b	MIMAT0018985
41	hsa-miR-128-2-5p	MIMAT0031095
42	hsa-miR-4675	MIMAT0019757
43	hsa-miR-4472	MIMAT0018999
44	hsa-miR-6785-5p	MIMAT0027470
45	hsa-miR-6741-5p	MIMAT0027383
46	hsa-miR-7977	MIMA T0031180
47	hsa-miR-3665	MIMAT0018087
48	hsa-miR-128-1-5p	MIMAT0026477
49	hsa-miR-4286	MIMAT0016916
50	hsa-miR-6765-3p	MIMAT0027431
51	hsa-miR-4632-5p	MIMAT0022977
52	hsa-miR-365a-5p	MIMA T0009199
53	hsa-miR-6088	MIMAT0023713
54	hsa-miR-6816-5p	MIMAT0027532
55	hsa-miR-6885-5p	MIMAT0027670
56	hsa-miR-711	MIMAT0012734
57	hsa-miR-6765-5p	MIMAT0027430
58	hsa-miR-3180	MIMAT0018178
59	hsa-miR-4442	MIMAT0018960
60	hsa-miR-4792	MIMAT0019964
61	hsa-miR-6721-5p	MIMAT0025852
62	hsa-miR-6798-5p	MIMAT0027496
63	hsa-miR-3162-5p	MIMAT0015036

(continued)

SEQ ID NO:	Gene name	miRBase registration No.
64	hsa-miR-6126	MIMAT0024599
65	hsa-miR-4758-5p	MIMAT0019903
66	hsa-miR-2392	MIMAT0019043
67	hsa-miR-486-3p	MIMAT0004762
68	hsa-miR-6727-5p	MIMAT0027355
69	hsa-miR-4728-5p	MIMAT0019849
70	hsa-miR-6746-5p	MIMAT0027392
71	hsa-miR-4270	MIMAT0016900
72	hsa-miR-3 940-5p	MIMAT0019229
73	hsa-miR-4725-3p	MIMAT0019844
74	hsa-miR-7108-5p	MIMAT0028113
75	hsa-miR-3656	MIMAT0018076
76	hsa-miR-6879-5p	MIMAT0027658
77	hsa-miR-6738-5p	MIMAT0027377
78	hsa-miR-1260a	MIMAT0005911
79	hsa-miR-4446-3p	MIMAT0018965
80	hsa-miR-3131	MIMAT0014996
81	hsa-miR-4463	MIMAT0018987
82	hsa-miR-3185	MIMAT0015065
83	hsa-miR-6870-5p	MIMAT0027640
84	hsa-miR-6779-5p	MIMAT0027458
85	hsa-miR-1273g-3p	MIMAT0022742
86	hsa-miR-8059	MIMAT0030986
87	hsa-miR-4697-5p	MIMAT0019791
88	hsa-miR-4674	MIMAT0019756
89	hsa-miR-4433-3p	MIMAT0018949
90	hsa-miR-4257	MIMAT0016878
91	hsa-miR-1915-5p	MIMAT0007891
92	hsa-miR-4417	MIMAT0018929
93	hsa-miR- 1343-5p	MIMAT0027038
94	hsa-miR-6781-5p	MIMAT0027462
95	hsa-miR-4695-5p	MIMAT0019788
96	hsa-miR-1237-5p	MIMAT0022946
97	hsa-miR-6775-5p	MIMAT0027450
98	hsa-miR-7845-5p	MIMAT0030420
99	hsa-miR-4746-3p	MIMAT0019881
100	hsa-miR-7641	MIMAT0029782
101	hsa-miR-7847-3p	MIMAT0030422

(continued)

SEQ ID NO:	Gene name	miRBase registration No.
102	hsa-miR-6806-5p	MIMAT0027512
103	hsa-miR-4467	MIMAT0018994
104	hsa-miR-4726-5p	MIMAT0019845
105	hsa-miR-4648	MIMAT0019710
106	hsa-miR-6089	MIMAT0023714
107	hsa-miR-1260b	MIMAT0015041
108	hsa-miR-4532	MIMAT0019071
109	hsa-miR-5195-3p	MIMAT0021127
110	hsa-miR-3188	MIMAT0015070
111	hsa-miR-6848-5p	MIMAT0027596
112	hsa-miR-1233-5p	MIMAT0022943
113	hsa-miR-6717-5p	MIMAT0025846
114	hsa-miR-3195	MIMAT0015079
115	hsa-miR-6757-5p	MIMAT0027414
116	hsa-miR-8072	MIMAT0030999
117	hsa-miR-4745-5p	MIMAT0019878
118	hsa-miR-6511a-5p	MIMAT0025478
119	hsa-miR-6776-5p	MIMAT0027452
120	hsa-miR-371a-5p	MIMAT0004687
121	hsa-miR-1227-5p	MIMAT0022941
122	hsa-miR-7150	MIMAT0028211
123	hsa-miR-1915-3p	MIMAT0007892
124	hsa-miR-187-5p	MIMAT0004561
125	hsa-miR-614	MIMAT0003282
126	hsa-miR-19b-3p	MIMAT0000074
127	hsa-miR-1225-5p	MIMAT0005572
128	hsa-miR-451a	MIMAT0001631
129	hsa-miR-939-5p	MIMAT0004982
130	hsa-miR-223-3p	MIMAT0000280
131	hsa-miR-1228-5p	MIMAT0005582
132	hsa-miR-125a-3p	MIMAT0004602
133	hsa-miR-92b-5p	MIMAT0004792
134	hsa-miR-22-3p	MIMAT0000077
135	hsa-miR-4271	MIMAT0016901
136	hsa-miR-642b-3p	MIMAT0018444
137	hsa-miR-6075	MIMAT0023700
138	hsa-miR-6125	MIMAT0024598
139	hsa-miR-887-3p	MIMAT0004951

(continued)

SEQ ID NO:	Gene name	miRBase registration No.
140	hsa-miR-6851-5p	MIMAT0027602
141	hsa-miR-6763-5p	MIMAT0027426
142	hsa-miR-3928-3p	MIMAT0018205
143	hsa-miR-4443	MIMAT0018961
144	hsa-miR-3648	MIMAT0018068
145	hsa-miR-149-3p	MIMAT0004609
146	hsa-miR-4689	MIMAT0019778
147	hsa-miR-4763-3p	MIMAT0019913
148	hsa-miR-6729-5p	MIMAT0027359
149	hsa-miR-3196	MIMAT0015080
150	hsa-miR-8069	MIMAT0030996
151	hsa-miR-1268a	MIMAT0005922
152	hsa-miR-4739	MIMAT0019868
153	hsa-miR-1268b	MIMAT0018925
154	hsa-miR-5698	MIMAT0022491
155	hsa-miR-6752-5p	MIMAT0027404
156	hsa-miR-4507	MIMAT0019044
157	hsa-miR-564	MIMAT0003228
158	hsa-miR-4497	MIMAT0019032
159	hsa-miR-6877-5p	MIMAT0027654
160	hsa-miR-6087	MIMAT0023712
161	hsa-miR-4731-5p	MIMAT0019853
162	hsa-miR-615-5p	MIMAT0004804
163	hsa-miR-760	MIMAT0004957
164	hsa-miR-6891-5p	MIMAT0027682
165	hsa-miR-6887-5p	MIMAT0027674
166	hsa-miR-4525	MIMAT0019064
167	hsa-miR-1914-3p	MIMAT0007890
168	hsa-miR-619-5p	MIMAT0026622
169	hsa-miR-5001-5p	MIMAT0021021
170	hsa-miR-6722-3p	MIMAT0025854
171	hsa-miR-3621	MIMAT0018002
172	hsa-miR-4298	MIMAT0016852
173	hsa-miR-675-5p	MIMAT0004284
174	hsa-miR-4655-5p	MIMAT0019721
175	hsa-mir-6768	MI0022613
176	hsa-mir-6836	MI0022682
177	hsa-mir-6782	MI0022627

(continued)

SEQ ID NO:	Gene name	miRBase registration No.
178	hsa-mir-3663	M10016064
179	hsa-mir-1908	MI0008329
180	hsa-mir-6726	MI0022571
181	hsa-mir-4258	MI0015857
182	hsa-mir-1343	MI0017320
183	hsa-mir-4516	MI0016882
184	hsa-mir-6875	MI0022722
185	hsa-mir-4651	MI0017279
186	hsa-mir-6825	MI0022670
187	hsa-mir-6840	MI0022686
188	hsa-mir-6780b	MI0022681
189	hsa-mir-6749	MI0022594
190	hsa-mir-8063	MI0025899
191	hsa-mir-6784	MI0022629
192	hsa-mir-3679	MI0016080
193	hsa-mir-3184	MI0014226
194	hsa-mir-663b	MI0006336
195	hsa-mir-6880	MI0022727
196	hsa-mir-92a-2	MI0000094
197	hsa-mir-7975	MI0025751
198	hsa-mir-7110	MI0022961
199	hsa-mir-6842	MI0022688
200	hsa-mir-6857	MI0022703
201	hsa-mir-5572	MI0019117
202	hsa-mir-3197	MI0014245
203	hsa-mir-6131	MI0021276
204	hsa-mir-6889	MI0022736
205	hsa-mir-4454	MI0016800
206	hsa-mir-1199	MI0020340
207	hsa-mir-1247	MI0006382
208	hsa-mir-6800	MI0022645
209	hsa-mir-6872	MI0022719
210	hsa-mir-4649	MI0017276
211	hsa-mir-6791	MI0022636
212	hsa-mir-4433b	MI0025511
213	hsa-mir-3135b	MI0016809
214	hsa-mir-128-2	MI0000727
215	hsa-mir-4675	MI0017306

(continued)

SEQ ID NO:	Gene name	miRBase registration No.
216	hsa-mir-4472-1	MI0016823
217	hsa-mir-4472-2	MI0016824
218	hsa-mir-6785	MI0022630
219	hsa-mir-6741	MI0022586
220	hsa-mir-7977	MI0025753
221	hsa-mir-3665	MI0016066
222	hsa-mir-128-1	MI0000447
223	hsa-mir-4286	MI0015894
224	hsa-mir-6765	MI0022610
225	hsa-mir-4632	M10017259
226	hsa-mir-365a	MI0000767
227	hsa-mir-6088	MI0020365
228	hsa-mir-6816	MI0022661
229	hsa-mir-6885	MI0022732
230	hsa-mir-711	MI0012488
231	hsa-mir-3180-4	MI0016408
232	hsa-mir-3180-5	MI0016409
233	hsa-mir-4442	MI0016785
234	hsa-mir-4792	MI0017439
235	hsa-mir-6721	MI0022556
236	hsa-mir-6798	MI0022643
237	hsa-mir-3162	MI0014192
238	hsa-mir-6126	MI0021260
239	hsa-mir-4758	MI0017399
240	hsa-mir-2392	MI0016870
241	hsa-mir-486	MI0002470
242	hsa-mir-486-2	MI0023622
243	hsa-mir-6727	MI0022572
244	hsa-mir-4728	MI0017365
245	hsa-mir-6746	MI0022591
246	hsa-mir-4270	MI0015878
247	hsa-mir-3940	MI0016597
248	hsa-mir-4725	MI0017362
249	hsa-mir-7108	MI0022959
250	hsa-mir-3656	MI0016056
251	hsa-mir-6879	MI0022726
252	hsa-mir-6738	MI0022583
253	hsa-mir-1260a	MI0006394

(continued)

SEQ ID NO:	Gene name	miRBase registration No.
254	hsa-mir-4446	MI0016789
255	hsa-mir-3131	MI0014151
256	hsa-mir-4463	MI0016811
257	hsa-mir-3185	MI0014227
258	hsa-mir-6870	MI0022717
259	hsa-mir-6779	MI0022624
260	hsa-mir-1273g	MI0018003
261	hsa-mir-8059	MI0025895
262	hsa-mir-4697	MI0017330
263	hsa-mir-4674	MI0017305
264	hsa-mir-4433	MI0016773
265	hsa-mir-4257	MI0015856
266	hsa-mir-1915	MI0008336
267	hsa-mir-4417	MI0016753
268	hsa-mir-6781	MI0022626
269	hsa-mir-4695	MI0017328
270	hsa-mir-1237	MI0006327
271	hsa-mir-6775	MI0022620
272	hsa-mir-7845	MI0025515
273	hsa-mir-4746	MI0017385
274	hsa-mir-7641-1	MI0024975
275	hsa-mir-7641-2	MI0024976
276	hsa-mir-7847	MI0025517
277	hsa-mir-6806	MI0022651
278	hsa-mir-4467	MI0016818
279	hsa-mir-4726	MI0017363
280	hsa-mir-4648	MI00I7275
281	hsa-mir-6089-1	MI0020366
282	hsa-mir-6089-2	MI0023563
283	hsa-mir-1260b	MI0014197
284	hsa-mir-4532	MI0016899
285	hsa-mir-5195	MI0018174
286	hsa-mir-3188	MI0014232
287	hsa-mir-6848	MI0022694
288	hsa-mir-1233-1	MI0006323
289	hsa-mir-1233-2	MI0015973
290	hsa-mir-6717	MI0022551
291	hsa-mir-3195	MI0014240

(continued)

SEQ ID NO:	Gene name	miRBase registration No.
292	hsa-mir-6757	M10022602
293	hsa-mir-8072	MI0025908
294	hsa-mir-4745	MI0017384
295	hsa-mir-6511a-1	MI0022223
296	hsa-mir-6511a-2	MI0023564
297	hsa-mir-6511a-3	MI0023565
298	hsa-mir-6511a-4	MI0023566
299	hsa-mir-6776	MI0022621
300	hsa-mir-371a	MI0000779
301	hsa-mir-1227	MI0006316
302	hsa-mir-7150	MI0023610
303	hsa-mir-187	MI0000274
304	hsa-mir-614	MI0003627
305	hsa-mir-19b-1	MI0000074
306	hsa-mir-19b-2	MI0000075
307	hsa-mir-1225	MI0006311
308	hsa-mir-451a	MI0001729
309	hsa-mir-939	MI0005761
310	hsa-mir-223	MI0000300
311	hsa-mir-1228	MI0006318
312	hsa-mir-125a	MI0000469
313	hsa-mir-92b	MI0003560
314	hsa-mir-22	MI0000078
315	hsa-mir-4271	MI0015879
316	hsa-mir-642b	MI0016685
317	hsa-mir-6075	MI0020352
318	hsa-mir-6125	MI0021259
319	hsa-mir-887	MI0005562
320	hsa-mir-6851	MI0022697
321	hsa-mir-6763	MI0022608
322	hsa-mir-3928	MI0016438
323	hsa-mir-4443	MI0016786
324	hsa-mir-3648	MI0016048
325	hsa-mir-149	MI0000478
326	hsa-mir-4689	MI0017322
327	hsa-mir-4763	MI0017404
328	hsa-mir-6729	MI0022574
329	hsa-mir-3196	MI0014241

(continued)

SEQ ID NO:	Gene name	miRBase registration No.
330	hsa-mir-8069	MI0025905
331	hsa-mir-1268a	MI0006405
332	hsa-mir-4739	MI0017377
333	hsa-mir-1268b	MI0016748
334	hsa-mir-5698	MI0019305
335	hsa-mir-6752	MI0022597
336	hsa-mir-4507	MI0016871
337	hsa-mir-564	MI0003570
338	hsa-mir-4497	MI0016859
339	hsa-mir-6877	MI0022724
340	hsa-mir-6087	MI0020364
341	hsa-mir-4731	MI0017368
342	hsa-mir-615	MI0003628
343	hsa-mir-760	MI0005567
344	hsa-mir-6891	MI0022738
345	hsa-mir-6887	MI0022734
346	hsa-mir-4525	MI0016892
347	hsa-mir-1914	MI0008335
348	hsa-mir-619	MI0003633
349	hsa-mir-5001	MI0017867
350	hsa-mir-6722	MI0022557
351	hsa-mir-3621	MI0016012
352	hsa-mir-4298	MI0015830
353	hsa-mir-675	MI0005416
354	hsa-mir-4655	MI0017283
355	isomiR example 1 of SEQ ID NO: 5	-
356	isomiR example 2 of SEQ ID NO: 5	-
357	isomiR example 1 of SEQ ID NO: 8	-
358	isomiR example 2 of SEQ ID NO: 8	-
359	isomiR example 1 of SEQ ID NO: 9	-
360	isomiR example 2 of SEQ ID NO: 9	-
361	isomiR example 1 of SEQ ID NO: 11	-
362	isomiR example 2 of SEQ ID NO: 11	-
363	isomiR example 1 of SEQ ID NO: 18	-
364	isomiR example 2 of SEQ ID NO: 18	-
365	isomiR example 1 of SEQ ID NO: 20	-
366	isomiR example 2 of SEQ ID NO: 20	-
367	isomiR example 1 of SEQ ID NO: 22	-

(continued)

SEQ ID NO:	Gene name	miRBase registration No.
368	isomiR example 2 of SEQ ID NO: 22	-
369	isomiR example 1 of SEQ ID NO: 23	-
370	isomiR example 2 of SEQ ID NO: 23	-
371	isomiR example 1 of SEQ ID NO: 24	-
372	isomiR example 2 of SEQ ID NO: 24	-
373	isomiR example 1 of SEQ ID NO: 28	-
374	isomiR example 2 of SEQ ID NO: 28	-
375	isomiR example 1 of SEQ ID NO: 29	-
376	isomiR example 2 of SEQ ID NO: 29	-
377	isomiR example 1 of SEQ ID NO: 30	-
378	isomiR example 2 of SEQ ID NO: 30	-
379	isomiR example 1 of SEQ ID NO: 32	-
380	isomiR example 2 of SEQ ID NO: 32	-
381	isomiR example 1 of SEQ ID NO: 34	-
382	isomiR example 2 of SEQ ID NO: 34	-
383	isomiR example 1 of SEQ ID NO: 37	-
384	isomiR example 2 of SEQ ID NO: 37	-
385	isomiR example 1 of SEQ ID NO: 40	-
386	isomiR example 2 of SEQ ID NO: 40	-
387	isomiR example 1 of SEQ ID NO: 41	-
388	isomiR example 2 of SEQ ID NO: 41	-
389	isomiR example 1 of SEQ ID NO: 47	-
390	isomiR example 2 of SEQ ID NO: 47	-
391	isomiR example 1 of SEQ ID NO: 48	-
392	isomiR example 2 of SEQ ID NO: 48	-
393	isomiR example 1 of SEQ ID NO: 49	-
394	isomiR example 2 of SEQ ID NO: 49	-
395	isomiR example 1 of SEQ ID NO: 51	-
396	isomiR example 2 of SEQ ID NO: 51	-
397	isomiR example 1 of SEQ ID NO: 52	-
398	isomiR example 2 of SEQ ID NO: 52	-
399	isomiR example 1 of SEQ ID NO: 53	-
400	isomiR example 2 of SEQ ID NO: 53	-
401	isomiR example 1 of SEQ ID NO: 56	-
402	isomiR example 2 of SEQ ID NO: 56	-
403	isomiR example 1 of SEQ ID NO: 58	-
404	isomiR example 2 of SEQ ID NO: 58	-
405	isomiR example 1 of SEQ ID NO: 59	-

(continued)

SEQ ID NO:	Gene name	miRBase registration No.
406	isomiR example 2 of SEQ ID NO: 59	-
407	isomiR example 1 of SEQ ID NO: 60	-
408	isomiR example 2 of SEQ ID NO: 60	-
409	isomiR example 1 of SEQ ID NO: 61	-
410	isomiR example 2 of SEQ ID NO: 61	-
411	isomiR example 1 of SEQ ID NO: 63	-
412	isomiR example 2 of SEQ ID NO: 63	-
413	isomiR example 1 of SEQ ID NO: 64	-
414	isomiR example 2 of SEQ ID NO: 64	-
415	isomiR example 1 of SEQ ID NO: 65	-
416	isomiR example 2 of SEQ ID NO: 65	-
417	isomiR example 1 of SEQ ID NO: 66	-
418	isomiR example 2 of SEQ ID NO: 66	-
419	isomiR example 1 of SEQ ID NO: 67	-
420	isomiR example 2 of SEQ ID NO: 67	-
421	isomiR example 1 of SEQ ID NO: 69	-
422	isomiR example 2 of SEQ ID NO: 69	-
423	isomiR example 1 of SEQ ID NO: 72	-
424	isomiR example 2 of SEQ ID NO: 72	-
425	isomiR example 1 of SEQ ID NO: 73	-
426	isomiR example 2 of SEQ ID NO: 73	-
427	isomiR example 1 of SEQ ID NO: 75	-
428	isomiR example 2 of SEQ ID NO: 75	-
429	isomiR example 1 of SEQ ID NO: 78	-
430	isomiR example 2 of SEQ ID NO: 78	-
431	isomiR example 1 of SEQ ID NO: 79	-
432	isomiR example 2 of SEQ ID NO: 79	-
433	isomiR example 1 of SEQ ID NO: 80	-
434	isomiR example 2 of SEQ ID NO: 80	-
435	isomiR example 1 of SEQ ID NO: 81	-
436	isomiR example 2 of SEQ ID NO: 81	-
437	isomiR example 1 of SEQ ID NO: 82	-
438	isomiR example 2 of SEQ ID NO: 82	-
439	isomiR example 1 of SEQ ID NO: 85	-
440	isomiR example 2 of SEQ ID NO: 85	-
441	isomiR example 1 of SEQ ID NO: 88	-
442	isomiR example 2 of SEQ ID NO: 88	-
443	isomiR example 1 of SEQ ID NO: 89	-

(continued)

SEQ ID NO:	Gene name	miRBase registration No.
444	isomiR example 2 of SEQ ID NO: 89	-
445	isomiR example 1 of SEQ ID NO: 91	-
446	isomiR example 2 of SEQ ID NO: 91	-
447	isomiR example 1 of SEQ ID NO: 92	-
448	isomiR example 2 of SEQ ID NO: 92	-
449	isomiR example 1 of SEQ ID NO: 95	-
450	isomiR example 2 of SEQ ID NO: 95	-
451	isomiR example 1 of SEQ ID NO: 96	-
452	isomiR example 2 of SEQ ID NO: 96	-
453	isomiR example 1 of SEQ ID NO: 103	-
454	isomiR example 2 of SEQ ID NO: 103	-
455	isomiR example 1 of SEQ ID NO: 104	-
456	isomiR example 2 of SEQ ID NO: 104	-
457	isomiR example 1 of SEQ ID NO: 105	-
458	isomiR example 2 of SEQ ID NO: 105	-
459	isomiR example 1 of SEQ ID NO: 106	-
460	isomiR example 2 of SEQ ID NO: 106	-
461	isomiR example 1 of SEQ ID NO: 107	-
462	isomiR example 2 of SEQ ID NO: 107	-
463	isomiR example 1 of SEQ ID NO: 108	-
464	isomiR example 2 of SEQ ID NO: 108	-
465	isomiR example 1 of SEQ ID NO: 109	-
466	isomiR example 2 of SEQ ID NO: 109	-
467	isomiR example 1 of SEQ ID NO: 110	-
468	isomiR example 2 of SEQ ID NO: 110	-
469	isomiR example 1 of SEQ ID NO: 112	-
470	isomiR example 2 of SEQ ID NO: 112	-
471	isomiR example 1 of SEQ ID NO: 113	-
472	isomiR example 2 of SEQ ID NO: 113	-
473	isomiR example 1 of SEQ ID NO: 114	-
474	isomiR example 2 of SEQ ID NO: 114	-
475	isomiR example 1 of SEQ ID NO: 117	-
476	isomiR example 2 of SEQ ID NO: 117	-
477	isomiR example 1 of SEQ ID NO: 118	-
478	isomiR example 2 of SEQ ID NO: 118	-
479	isomiR example 1 of SEQ ID NO: 120	-
480	isomiR example 2 of SEQ ID NO: 120	-
481	isomiR example 1 of SEQ ID NO: 123	-

(continued)

SEQ ID NO:	Gene name	miRBase registration No.
482	isomiR example 2 of SEQ ID NO: 123	-
483	isomiR example 1 of SEQ ID NO: 124	-
484	isomiR example 2 of SEQ ID NO: 124	-
485	isomiR example 1 of SEQ ID NO: 125	-
486	isomiR example 2 of SEQ ID NO: 125	-
487	isomiR example 1 of SEQ ID NO: 126	-
488	isomiR example 2 of SEQ ID NO: 126	-
489	isomiR example 1 of SEQ ID NO: 128	-
490	isomiR example 2 of SEQ ID NO: 128	-
491	isomiR example 1 of SEQ ID NO: 129	-
492	isomiR example 2 of SEQ ID NO: 129	-
493	isomiR example 1 of SEQ ID NO: 130	-
494	isomiR example 2 of SEQ ID NO: 130	-
495	isomiR example 1 of SEQ ID NO: 131	-
496	isomiR example 2 of SEQ ID NO: 131	-
497	isomiR example 1 of SEQ ID NO: 132	-
498	isomiR example 2 of SEQ ID NO: 132	-
499	isomiR example 1 of SEQ ID NO: 133	-
500	isomiR example 2 of SEQ ID NO: 133	-
501	isomiR example 1 of SEQ ID NO: 134	-
502	isomiR example 2 of SEQ ID NO: 134	-
503	isomiR example 1 of SEQ ID NO: 135	-
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506	isomiR example 2 of SEQ ID NO: 136	-
507	isomiR example 1 of SEQ ID NO: 138	-
508	isomiR example 2 of SEQ ID NO: 138	-
509	isomiR example 1 of SEQ ID NO: 139	-
510	isomiR example 2 of SEQ ID NO: 139	-
511	isomiR example 1 of SEQ ID NO: 142	-
512	isomiR example 2 of SEQ ID NO: 142	-
513	isomiR example 1 of SEQ ID NO: 143	-
514	isomiR example 2 of SEQ ID NO: 143	-
515	isomiR example 1 of SEQ ID NO: 144	-
516	isomiR example 2 of SEQ ID NO: 144	-
517	isomiR example 1 of SEQ ID NO: 145	-
518	isomiR example 2 of SEQ ID NO: 145	-
519	isomiR example 1 of SEQ ID NO: 146	-

(continued)

SEQ ID NO:	Gene name	miRBase registration No.
520	isomiR example 2 of SEQ ID NO: 146	-
521	isomiR example 1 of SEQ ID NO: 147	-
522	isomiR example 2 of SEQ ID NO: 147	-
523	isomiR example 1 of SEQ ID NO: 149	-
524	isomiR example 2 of SEQ ID NO: 149	-
525	isomiR example 1 of SEQ ID NO: 151	-
526	isomiR example 2 of SEQ ID NO: 151	-
527	isomiR example 1 of SEQ ID NO: 152	-
528	isomiR example 2 of SEQ ID NO: 152	-
529	isomiR example 1 of SEQ ID NO: 153	-
530	isomiR example 2 of SEQ ID NO: 153	-
531	isomiR example 1 of SEQ ID NO: 154	-
532	isomiR example 2 of SEQ ID NO: 154	-
533	isomiR example 1 of SEQ ID NO: 156	-
534	isomiR example 2 of SEQ ID NO: 156	-
535	isomiR example 1 of SEQ ID NO: 157	-
536	isomiR example 2 of SEQ ID NO: 157	-
537	isomiR example 1 of SEQ ID NO: 158	-
538	isomiR example 2 of SEQ ID NO: 158	-
539	isomiR example 1 of SEQ ID NO: 160	-
540	isomiR example 2 of SEQ ID NO: 160	-
541	isomiR example 1 of SEQ ID NO: 161	-
542	isomiR example 2 of SEQ ID NO: 161	-
543	isomiR example 1 of SEQ ID NO: 162	-
544	isomiR example 2 of SEQ ID NO: 162	-
545	isomiR example 1 of SEQ ID NO: 163	-
546	isomiR example 2 of SEQ ID NO: 163	-
547	isomiR example 1 of SEQ ID NO: 166	-
548	isomiR example 2 of SEQ ID NO: 166	-
549	isomiR example 1 of SEQ ID NO: 167	-
550	isomiR example 2 of SEQ ID NO: 167	-
551	isomiR example 1 of SEQ ID NO: 168	-
552	isomiR example 2 of SEQ ID NO: 168	-
553	isomiR example 1 of SEQ ID NO: 169	-
554	isomiR example 2 of SEQ ID NO: 169	-
555	isomiR example 1 of SEQ ID NO: 172	-
556	isomiR example 2 of SEQ ID NO: 172	-
557	isomiR example 1 of SEQ ID NO: 173	-

(continued)

SEQ ID NO:	Gene name	miRBase registration No.
558	isomiR example 2 of SEQ ID NO: 173	-
559	isomiR example 1 of SEQ ID NO: 174	-
560	isomiR example 2 of SEQ ID NO: 174	-
561	hsa-miR-6073	MIMAT0023698
562	hsa-miR-6845-5p	MIMAT0027590
563	hsa-miR-6769b-5p	MIMAT0027620
564	hsa-miR-4665-3p	MIMAT0019740
565	hsa-miR-1913	MIMAT0007888
566	hsa-miR-1228-3p	MIMAT0005583
567	hsa-miR-940	MIMAT0004983
568	hsa-miR-296-3p	MIMAT0004679
569	hsa-miR-4690-5p	MIMAT0019779
570	hsa-miR-548q	MIMAT0011163
571	hsa-miR-663a	MIMAT0003326
572	hsa-miR-1249	MIMAT0005901
573	hsa-miR-1202	MIMAT0005865
574	hsa-miR-7113-3p	MIMAT0028124
575	hsa-miR-1225-3p	MIMAT0005573
576	hsa-miR-4783-3p	MIMAT0019947
577	hsa-miR-4448	MIMAT0018967
578	hsa-miR-4534	MIMAT0019073
579	hsa-miR-1307-3p	MIMAT0005951
580	hsa-mir-6073	MI0020350
581	hsa-mir-6845	MI0022691
582	hsa-mir-6769b	MI0022706
583	hsa-mir-4665	M10017295
584	hsa-mir-1913	MI0008334
585	hsa-mir-940	MI0005762
586	hsa-mir-296	MI0000747
587	hsa-mir-4690	MI0017323
588	hsa-mir-548q	MI0010637
589	hsa-mir-663a	MI0003672
590	hsa-mir-1249	MI0006384
591	hsa-mir-1202	MI0006334
592	hsa-mir-7113	MI0022964
593	hsa-mir-4783	MI0017428
594	hsa-mir-4448	MI0016791
595	hsa-mir-4534	MI0016901

(continued)

SEQ ID NO:	Gene name	miRBase registration No.
596	hsa-mir-1307	MI0006444
597	isomiR example 1 of SEQ ID NO: 565	-
598	isomiR example 2 of SEQ ID NO: 565	-
599	isomiR example 1 of SEQ ID NO: 566	-
600	isomiR example 2 of SEQ ID NO: 566	-
601	isomiR example 1 of SEQ ID NO: 567	-
602	isomiR example 2 of SEQ ID NO: 567	-
603	isomiR example 1 of SEQ ID NO: 568	-
604	isomiR example 2 of SEQ ID NO: 568	-
605	isomiR example 1 of SEQ ID NO: 569	-
606	isomiR example 2 of SEQ ID NO: 569	-
607	isomiR example 1 of SEQ ID NO: 571	-
608	isomiR example 2 of SEQ ID NO: 571	-
609	isomiR example 1 of SEQ ID NO: 572	-
610	isomiR example 2 of SEQ ID NO: 572	-
611	isomiR example 1 of SEQ ID NO: 573	-
612	isomiR example 2 of SEQ ID NO: 573	-
613	isomiR example 1 of SEQ ID NO: 576	-
614	isomiR example 2 of SEQ ID NO: 576	-
615	isomiR example 1 of SEQ ID NO: 577	-
616	isomiR example 2 of SEQ ID NO: 577	-
617	isomiR example 1 of SEQ ID NO: 579	-
618	isomiR example 2 of SEQ ID NO: 579	-

[0255] The present application claims priority from Japanese Patent Application No. 2014-125561

Advantageous Effects of Invention

[0256] According to the present invention, lung cancer can be detected easily and in high accuracy.

[0257] For example, the presence or absence of lung cancer in a patient can be easily detected by using, as an index, the expression level measurement values of several miRNAs in blood, serum, and/or plasma of the patient, which can be collected with limited invasiveness.

Brief Description of Drawings

[0258]

[Figure 1] This figure shows the relationship between the nucleotide sequences of hsa-miR-1908-5p represented by SEQ ID NO: 22 and hsa-miR-1908-3p represented by SEQ ID NO: 5, which are produced from a precursor hsa-mir-1908 represented by SEQ ID NO: 179.

[Figure 2] Left diagram: the expression level measurement values of hsa-miR-6768-5p (SEQ ID NO: 1) in healthy subjects (100 persons) and lung cancer patients (17 persons) selected as a training cohort were each plotted on the ordinate. The horizontal line in the diagram depicts a threshold (10.08) that was optimized by Fisher's discriminant analysis and discriminated between the two groups. Right diagram: the expression level measurement values of

hsa-miR-6768-5p (SEQ ID NO: 1) in healthy subjects (50 persons) and lung cancer patients (8 persons) selected as a validation cohort were each plotted on the ordinate. The horizontal line in the diagram depicts the threshold (10.08) that was set in the training cohort and discriminated between the two groups.

[Figure 3] Left diagram: the expression level measurement values of hsa-miR-6768-5p (SEQ ID NO: 1) in healthy subjects (100 persons, circles) and lung cancer patients (17 persons, triangles) selected as a training cohort were each plotted on the abscissa against their expression level measurement values of hsa-miR-6836-3p (SEQ ID NO: 2) on the ordinate. The line in the diagram depicts a discriminant function (0 = -1.42x + y + 4.7) that was optimized by Fisher's discriminant analysis and discriminated between the two groups. Right diagram: the expression level measurement values of hsa-miR-6768-5p (SEQ ID NO: 1) in healthy subjects (50 persons, circles) and lung cancer patients (8 persons, triangles) selected as a validation cohort were each plotted on the abscissa against their expression level measurement values of hsa-miR-6836-3p (SEQ ID NO: 2) on the ordinate. The line in the diagram depicts the threshold (0 = -1.42x + y + 4.7) that was set in the training cohort and discriminated between the two groups.

[Figure 4] Figure 4A: a discriminant (-1.86 x hsa-miR-6768-5p - 0.68 x hsa-miR-19b-3p + 0.43 x hsa-miR-6073 - 0.87 x hsa-miR-6717-5p + 25.68) was prepared by use of Fisher's discriminant analysis from the expression level measurement values of hsa-miR-6768-5p (SEQ ID NO: 1), hsa-miR-6717-5p (SEQ ID NO: 113), hsa-miR-19b-3p (SEQ ID NO: 126), and hsa-miR-6073 (SEQ IDNO: 561) in 17 lung cancer patients, 99 healthy subjects, 75 pancreatic cancer patients, 62 biliary tract cancer patients, 32 colorectal cancer patients, 35 stomach cancer patients, 32 esophageal cancer patients, 33 liver cancer patients, and 13 benign pancreaticobiliary disease patients selected as a training cohort, and discriminant scores obtained from the discriminant were plotted on the ordinate against the sample groups on the abscissa. The dotted line in the diagram depicts a discriminant boundary that offered a discriminant score of 0 and discriminated between the two groups. Figure 4B: discriminant scores obtained from the discriminant prepared in the training cohort as to the expression level measurement values of hsa-miR-6768-5p (SEQ ID NO: 1), hsa-miR-6717-5p (SEQ ID NO: 113), hsa-miR-19b-3p (SEQ ID NO: 126), and hsa-miR-6073 (SEQ ID NO: 561) in 8 lung cancer patients, 51 healthy subjects, 23 pancreatic cancer patients, 38 biliary tract cancer patients, 18 colorectal cancer patients, 15 stomach cancer patients, 18 esophageal cancer patients, 19 liver cancer patients, and 8 benign pancreaticobiliary disease patients selected as a validation cohort were plotted on the ordinate against the sample groups on the abscissa. The dotted line in the diagram depicts the discriminant boundary that offered a discriminant score of 0 and discriminated between the two groups.

Description of Embodiments

[0259] Hereinafter, the present invention will be described further specifically.

1. Target nucleic acid for lung cancer

[0260] A primary target nucleic acid used as a lung cancer marker for detecting the presence and/or absence of lung cancer or lung cancer cells using the nucleic acid probe or the primer for the detection of lung cancer defined above according to the present invention can be hsa-miR-6768-5p, optionally together with one or more miRNA(s) selected from the group consisting of hsa-miR-6836-3p, hsa-miR-6782-5p, hsa-miR-3663-3p, hsa-miR-1908-3p, hsa-miR-6726-5p, hsa-miR-4258, hsa-miR-1343-3p, hsa-miR-4516, hsa-miR-6875-5p, hsa-miR-4651, hsa-miR-6825-5p, hsa-miR-6840-3p, hsa-miR-6780b-5p, hsa-miR-6749-5p, hsa-miR-8063, hsa-miR-6784-5p, hsa-miR-3679-5p, hsa-miR-3184-5p, hsa-miR-663b, hsa-miR-6880-5p, hsa-miR-1908-5p, hsa-miR-92a-2-5p, hsa-miR-7975, hsa-miR-7110-5p, hsa-miR-6842-5p, hsa-miR-6857-5p, hsa-miR-5572, hsa-miR-3197, hsa-miR-6131, hsa-miR-6889-5p, hsa-miR-4454, hsa-miR-1199-5p, hsa-miR-1247-3p, hsa-miR-6800-5p, hsa-miR-6872-3p, hsa-miR-4649-5p, hsa-miR-6791-5p, hsa-miR-4433b-3p, hsa-miR-3135b, hsa-miR-128-2-5p, hsa-miR-4675, hsa-miR-4472, hsa-miR-6785-5p, hsa-miR-6741-5p, hsa-miR-7977, hsa-miR-3665, hsa-miR-128-1-5p, hsa-miR-4286, hsa-miR-6765-3p, hsa-miR-4632-5p, hsa-miR-365a-5p, hsa-miR-6088, hsa-miR-6816-5p, hsa-miR-6885-5p, hsa-miR-711, hsa-miR-6765-5p, hsa-miR-3180, hsa-miR-4442, hsa-miR-4792, hsa-miR-6721-5p, hsa-miR-6798-5p, hsa-miR-3162-5p, hsa-miR-6126, hsa-miR-4758-5p, hsa-miR-2392, hsa-miR-486-3p, hsa-miR-6727-5p, hsa-miR-4728-5p, hsa-miR-6746-5p, hsa-miR-4270, hsa-miR-3940-5p, hsa-miR-4725-3p, hsa-miR-7108-5p, hsa-miR-3656, hsa-miR-6879-5p, hsa-miR-6738-5p, hsa-miR-1260a, hsa-miR-4446-3p, hsa-miR-3131, hsa-miR-4463, hsa-miR-3185, hsa-miR-6870-5p, hsa-miR-6779-5p, hsa-miR-1273g-3p, hsa-miR-8059, hsa-miR-4697-5p, hsa-miR-4674, hsa-miR-4433-3p, hsa-miR-4257, hsa-miR-1915-5p, hsa-miR-4417, hsa-miR-1343-5p, hsa-miR-6781-5p, hsa-miR-4695-5p, hsa-miR-1237-5p, hsa-miR-6775-5p, hsa-miR-7845-5p, hsa-miR-4746-3p, hsa-miR-7641, hsa-miR-7847-3p, hsa-miR-6806-5p, hsa-miR-4467, hsa-miR-4726-5p, hsa-miR-4648, hsa-miR-6089, hsa-miR-1260b, hsa-miR-4532, hsa-miR-5195-3p, hsa-miR-3188, hsa-miR-6848-5p, hsa-miR-1233-5p, hsa-miR-6717-5p, hsa-miR-3195, hsa-miR-6757-5p, hsa-miR-8072, hsa-miR-4745-5p, hsa-miR-6511a-5p, hsa-miR-6776-5p, hsa-miR-371a-5p, hsa-miR-1227-5p, hsa-miR-7150, hsa-miR-1915-3p, hsa-miR-187-5p, hsa-miR-614, hsa-miR-1225-5p, hsa-miR-451a, hsa-miR-939-5p, hsa-miR-223-3p, hsa-miR-125a-3p, hsa-miR-92b-5p, hsa-miR-22-3p,

hsa-miR-6073, hsa-miR-6845-5p, hsa-miR-6769b-5p, hsa-miR-4665-3p, hsa-miR-1913, hsa-miR-1228-3p, hsa-miR-940, hsa-miR-296-3p, hsa-miR-4690-5p, hsa-miR-548q, hsa-miR-663a, hsa-miR-1249, hsa-miR-1202, hsa-miR-7113-3p, hsa-miR-1225-3p, hsa-miR-4783-3p, hsa-miR-4448 and hsa-miR-4534. Furthermore, at least one or more miRNA(s) selected from the group consisting of other lung cancer markers that can be combined with these miRNAs, i.e., hsa-miR-19b-3p, hsa-miR-1228-5p, and hsa-miR-1307-3p, can also be preferably used as a target nucleic acid. Moreover, at least one or more miRNA(s) selected from the group consisting of other lung cancer markers that can be combined with these miRNAs, i.e., hsa-miR-4271, hsa-miR-642b-3p, hsa-miR-6075, hsa-miR-6125, hsa-miR-887-3p, hsa-miR-6851-5p, hsa-miR-6763-5p, hsa-miR-3928-3p, hsa-miR-4443, hsa-miR-3648, hsa-miR-149-3p, hsa-miR-4689, hsa-miR-4763-3p, hsa-miR-6729-5p, hsa-miR-3196, hsa-miR-8069, hsa-miR-1268a, hsa-miR-4739, hsa-miR-1268b, hsa-miR-5698, hsa-miR-6752-5p, hsa-miR-4507, hsa-miR-564, hsa-miR-4497, hsa-miR-6877-5p, hsa-miR-6087, hsa-miR-4731-5p, hsa-miR-615-5p, hsa-miR-760, hsa-miR-6891-5p, hsa-miR-6887-5p, hsa-miR-4525, hsa-miR-1914-3p, hsa-miR-619-5p, hsa-miR-5001-5p, hsa-miR-6722-3p, hsa-miR-3621, hsa-miR-4298, hsa-miR-675-5p and hsa-miR-4655-5p can also be preferably used as a target nucleic acid.

[0261] These miRNAs include, for example, a human gene comprising a nucleotide sequence represented by SEQ ID NO: 1 optionally together with any of SEQ ID NOs 2 to 174 and 561 to 579 (i.e., hsa-miR-6768-5p, hsa-miR-6836-3p, hsa-miR-6782-5p, hsa-miR-3663-3p, hsa-miR-1908-3p, hsa-miR-6726-5p, hsa-miR-4258, hsa-miR-1343-3p, hsa-miR-4516, hsa-miR-6875-5p, hsa-miR-4651, hsa-miR-6825-5p, hsa-miR-6840-3p, hsa-miR-6780b-5p, hsa-miR-6749-5p, hsa-miR-8063, hsa-miR-6784-5p, hsa-miR-3679-5p, hsa-miR-3184-5p, hsa-miR-663b, hsa-miR-6880-5p, hsa-miR-1908-5p, hsa-miR-92a-2-5p, hsa-miR-7975, hsa-miR-7110-5p, hsa-miR-6842-5p, hsa-miR-6857-5p, hsa-miR-5572, hsa-miR-3197, hsa-miR-6131, hsa-miR-6889-5p, hsa-miR-4454, hsa-miR-1199-5p, hsa-miR-1247-3p, hsa-miR-6800-5p, hsa-miR-6872-3p, hsa-miR-4649-5p, hsa-miR-6791-5p, hsa-miR-4433b-3p, hsa-miR-3135b, hsa-miR-128-2-5p, hsa-miR-4675, hsa-miR-4472, hsa-miR-6785-5p, hsa-miR-6741-5p, hsa-miR-7977, hsa-miR-3665, hsa-miR-128-1-5p, hsa-miR-4286, hsa-miR-6765-3p, hsa-miR-4632-5p, hsa-miR-365a-5p, hsa-miR-6088, hsa-miR-6816-5p, hsa-miR-6885-5p, hsa-miR-711, hsa-miR-6765-5p, hsa-miR-3180, hsa-miR-4442, hsa-miR-4792, hsa-miR-6721-5p, hsa-miR-6798-5p, hsa-miR-3162-5p, hsa-miR-6126, hsa-miR-4758-5p, hsa-miR-2392, hsa-miR-486-3p, hsa-miR-6727-5p, hsa-miR-4728-5p, hsa-miR-6746-5p, hsa-miR-4270, hsa-miR-3940-5p, hsa-miR-4725-3p, hsa-miR-7108-5p, hsa-miR-3656, hsa-miR-6879-5p, hsa-miR-6738-5p, hsa-miR-1260a, hsa-miR-4446-3p, hsa-miR-3131, hsa-miR-4463, hsa-miR-3185, hsa-miR-6870-5p, hsa-miR-6779-5p, hsa-miR-1273g-3p, hsa-miR-8059, hsa-miR-4697-5p, hsa-miR-4674, hsa-miR-4433-3p, hsa-miR-4257, hsa-miR-1915-5p, hsa-miR-4417, hsa-miR-1343-5p, hsa-miR-6781-5p, hsa-miR-4695-5p, hsa-miR-1237-5p, hsa-miR-6775-5p, hsa-miR-7845-5p, hsa-miR-4746-3p, hsa-miR-7641, hsa-miR-7847-3p, hsa-miR-6806-5p, hsa-miR-4467, hsa-miR-4726-5p, hsa-miR-4648, hsa-miR-6089, hsa-miR-1260b, hsa-miR-4532, hsa-miR-5195-3p, hsa-miR-3188, hsa-miR-6848-5p, hsa-miR-1233-5p, hsa-miR-6717-5p, hsa-miR-3195, hsa-miR-6757-5p, hsa-miR-8072, hsa-miR-4745-5p, hsa-miR-6511a-5p, hsa-miR-6776-5p, hsa-miR-371a-5p, hsa-miR-1227-5p, hsa-miR-7150, hsa-miR-1915-3p, hsa-miR-187-5p, hsa-miR-614, hsa-miR-19b-3p, hsa-miR-1225-5p, hsa-miR-451a, hsa-miR-939-5p, hsa-miR-223-3p, hsa-miR-1228-5p, hsa-miR-125a-3p, hsa-miR-92b-5p, hsa-miR-22-3p, hsa-miR-6073, hsa-miR-6845-5p, hsa-miR-6769b-5p, hsa-miR-4665-3p, hsa-miR-1913, hsa-miR-1228-3p, hsa-miR-940, hsa-miR-296-3p, hsa-miR-4690-5p, hsa-miR-548q, hsa-miR-663a, hsa-miR-1249, hsa-miR-1202, hsa-miR-7113-3p, hsa-miR-1225-3p, hsa-miR-4783-3p, hsa-miR-4448 and hsa-miR-4534, hsa-miR-1307-3p, hsa-miR-4271, hsa-miR-642b-3p, hsa-miR-6075, hsa-miR-6125, hsa-miR-887-3p, hsa-miR-6851-5p, hsa-miR-6763-5p, hsa-miR-3928-3p, hsa-miR-4443, hsa-miR-3648, hsa-miR-149-3p, hsa-miR-4689, hsa-miR-4763-3p, hsa-miR-6729-5p, hsa-miR-3196, hsa-miR-8069, hsa-miR-1268a, hsa-miR-4739, hsa-miR-1268b, hsa-miR-5698, hsa-miR-6752-5p, hsa-miR-4507, hsa-miR-564, hsa-miR-4497, hsa-miR-6877-5p, hsa-miR-6087, hsa-miR-4731-5p, hsa-miR-615-5p, hsa-miR-760, hsa-miR-6891-5p, hsa-miR-6887-5p, hsa-miR-4525, hsa-miR-1914-3p, hsa-miR-619-5p, hsa-miR-5001-5p, hsa-miR-6722-3p, hsa-miR-3621, hsa-miR-4298, hsa-miR-675-5p and hsa-miR-4655-5p, respectively), a congener thereof, a transcript thereof, and a variant or a derivative thereof. In this context, the gene, the congener, the transcript, the variant, and the derivative are as defined above.

[0262] The target nucleic acid is preferably a human gene comprising a nucleotide sequence represented by SEQ ID NOs: 1 optionally together with any of SEQ ID NOs: 2 to 618 or a transcript thereof, more preferably the transcript, i.e., a miRNA or its precursor RNA (pri-miRNA or pre-miRNA).

[0263] The first target gene is the hsa-miR-6768-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0264] The second target gene is the hsa-miR-6836-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0265] The third target gene is the hsa-miR-6782-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0266] The fourth target gene is the hsa-miR-3663-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0267] The fifth target gene is the hsa-miR-1908-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0268] The sixth target gene is the hsa-miR-6726-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0269] The seventh target gene is the hsa-miR-4258 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0270] The eighth target gene is the hsa-miR-1343-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0271] The ninth target gene is the hsa-miR-4516 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0272] The 10th target gene is the hsa-miR-6875-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0273] The 11th target gene is the hsa-miR-4651 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0274] The 12th target gene is the hsa-miR-6825-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0275] The 13th target gene is the hsa-miR-6840-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0276] The 14th target gene is the hsa-miR-6780b-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0277] The 15th target gene is the hsa-miR-6749-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0278] The 16th target gene is the hsa-miR-8063 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0279] The 17th target gene is the hsa-miR-6784-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0280] The 18th target gene is the hsa-miR-3679-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0281] The 19th target gene is the hsa-miR-3184-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0282] The 20th target gene is the hsa-miR-663b gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0283] The 21st target gene is the hsa-miR-6880-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0284] The 22nd target gene is the hsa-miR-1908-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0285] The 23rd target gene is the hsa-miR-92a-2-5p gene, a congener thereof, a transcript thereof, or a variant or a

derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0286] The 24th target gene is the hsa-miR-7975 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0287] The 25th target gene is the hsa-miR-7110-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0288] The 26th target gene is the hsa-miR-6842-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0289] The 27th target gene is the hsa-miR-6857-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0290] The 28th target gene is the hsa-miR-5572 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0291] The 29th target gene is the hsa-miR-3197 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0292] The 30th target gene is the hsa-miR-6131 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0293] The 31st target gene is the hsa-miR-6889-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0294] The 32nd target gene is the hsa-miR-4454 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0295] The 33rd target gene is the hsa-miR-1199-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0296] The 34th target gene is the hsa-miR-1247-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0297] The 35th target gene is the hsa-miR-6800-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0298] The 36th target gene is the hsa-miR-6872-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0299] The 37th target gene is the hsa-miR-4649-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0300] The 38th target gene is the hsa-miR-6791-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0301] The 39th target gene is the hsa-miR-4433b-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0302] The 40th target gene is the hsa-miR-3135b gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0303] The 41st target gene is the hsa-miR-128-2-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0304] The 42nd target gene is the hsa-miR-4675 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript

thereof can serve as a marker for lung cancer.

[0305] The 43rd target gene is the hsa-miR-4472 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0306] The 44th target gene is the hsa-miR-6785-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0307] The 45th target gene is the hsa-miR-6741-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0308] The 46th target gene is the hsa-miR-7977 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0309] The 47th target gene is the hsa-miR-3665 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0310] The 48th target gene is the hsa-miR-128-1-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0311] The 49th target gene is the hsa-miR-4286 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0312] The 50th target gene is the hsa-miR-6765-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0313] The 51st target gene is the hsa-miR-4632-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0314] The 52nd target gene is the hsa-miR-365a-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0315] The 53rd target gene is the hsa-miR-6088 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0316] The 54th target gene is the hsa-miR-6816-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0317] The 55th target gene is the hsa-miR-6885-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0318] The 56th target gene is the hsa-miR-711 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0319] The 57th target gene is the hsa-miR-6765-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0320] The 58th target gene is the hsa-miR-3180 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0321] The 59th target gene is the hsa-miR-4442 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0322] The 60th target gene is the hsa-miR-4792 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0323] The 61st target gene is the hsa-miR-6721-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0324] The 62nd target gene is the hsa-miR-6798-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0325] The 63rd target gene is the hsa-miR-3162-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0326] The 64th target gene is the hsa-miR-6126 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0327] The 65th target gene is the hsa-miR-4758-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0328] The 66th target gene is the hsa-miR-2392 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0329] The 67th target gene is the hsa-miR-486-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0330] The 68th target gene is the hsa-miR-6727-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0331] The 69th target gene is the hsa-miR-4728-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0332] The 70th target gene is the hsa-miR-6746-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0333] The 71st target gene is the hsa-miR-4270 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0334] The 72nd target gene is the hsa-miR-3940-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0335] The 73rd target gene is the hsa-miR-4725-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0336] The 74th target gene is the hsa-miR-7108-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0337] The 75th target gene is the hsa-miR-3656 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0338] The 76th target gene is the hsa-miR-6879-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0339] The 77th target gene is the hsa-miR-6738-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0340] The 78th target gene is the hsa-miR-1260a gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0341] The 79th target gene is the hsa-miR-4446-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0342] The 80th target gene is the hsa-miR-3131 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0343] The 81st target gene is the hsa-miR-4463 gene, a congener thereof, a transcript thereof, or a variant or a

derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0344] The 82nd target gene is the hsa-miR-3185 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0345] The 83rd target gene is the hsa-miR-6870-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0346] The 84th target gene is the hsa-miR-6779-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0347] The 85th target gene is the hsa-miR-1273g-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0348] The 86th target gene is the hsa-miR-8059 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0349] The 87th target gene is the hsa-miR-4697-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0350] The 88th target gene is the hsa-miR-4674 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0351] The 89th target gene is the hsa-miR-4433-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0352] The 90th target gene is the hsa-miR-4257 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0353] The 91st target gene is the hsa-miR-1915-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0354] The 92nd target gene is the hsa-miR-4417 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0355] The 93rd target gene is the hsa-miR-1343-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0356] The 94th target gene is the hsa-miR-6781-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0357] The 95th target gene is the hsa-miR-4695-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0358] The 96th target gene is the hsa-miR-1237-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0359] The 97th target gene is the hsa-miR-6775-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0360] The 98th target gene is the hsa-miR-7845-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0361] The 99th target gene is the hsa-miR-4746-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0362] The 100th target gene is the hsa-miR-7641 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript

thereof can serve as a marker for lung cancer.

[0363] The 101st target gene is the hsa-miR-7847-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0364] The 102nd target gene is the hsa-miR-6806-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0365] The 103rd target gene is the hsa-miR-4467 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0366] The 104th target gene is the hsa-miR-4726-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0367] The 105th target gene is the hsa-miR-4648 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0368] The 106th target gene is the hsa-miR-6089 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0369] The 107th target gene is the hsa-miR-1260b gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0370] The 108th target gene is the hsa-miR-4532 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0371] The 109th target gene is the hsa-miR-5195-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0372] The 110th target gene is the hsa-miR-3188 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0373] The 111st target gene is the hsa-miR-6848-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0374] The 112nd target gene is the hsa-miR-1233-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0375] The 113rd target gene is the hsa-miR-6717-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0376] The 114th target gene is the hsa-miR-3195 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0377] The 115th target gene is the hsa-miR-6757-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0378] The 116th target gene is the hsa-miR-8072 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0379] The 117th target gene is the hsa-miR-4745-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0380] The 118th target gene is the hsa-miR-6511a-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0381] The 119th target gene is the hsa-miR-6776-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0382] The 120th target gene is the hsa-miR-371a-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0383] The 121st target gene is the hsa-miR-1227-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0384] The 122nd target gene is the hsa-miR-7150 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0385] The 123rd target gene is the hsa-miR-1915-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0386] The 124th target gene is the hsa-miR-187-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0387] The 125th target gene is the hsa-miR-614 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0388] The 126th target gene is the hsa-miR-19b-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. The previously known report shows that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer (Patent Literature 1).

[0389] The 127th target gene is the hsa-miR-1225-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0390] The 128th target gene is the hsa-miR-451a gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0391] The 129th target gene is the hsa-miR-939-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0392] The 130th target gene is the hsa-miR-223-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0393] The 131st target gene is the hsa-miR-1228-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. The previously known report shows that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer (Patent Literature 2).

[0394] The 132nd target gene is the hsa-miR-125a-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0395] The 133rd target gene is the hsa-miR-92b-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0396] The 134th target gene is the hsa-miR-22-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0397] The 135th target gene is the hsa-miR-4271 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0398] The 136th target gene is the hsa-miR-642b-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0399] The 137th target gene is the hsa-miR-6075 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0400] The 138th target gene is the hsa-miR-6125 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0401] The 139th target gene is the hsa-miR-887-3p gene, a congener thereof, a transcript thereof, or a variant or a

derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0402] The 140th target gene is the hsa-miR-6851-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0403] The 141st target gene is the hsa-miR-6763-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0404] The 142nd target gene is the hsa-miR-3928-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0405] The 143rd target gene is the hsa-miR-4443 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0406] The 144th target gene is the hsa-miR-3648 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0407] The 145th target gene is the hsa-miR-149-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0408] The 146th target gene is the hsa-miR-4689 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0409] The 147th target gene is the hsa-miR-4763-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0410] The 148th target gene is the hsa-miR-6729-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0411] The 149th target gene is the hsa-miR-3196 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0412] The 150th target gene is the hsa-miR-8069 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0413] The 151st target gene is the hsa-miR-1268a gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer (Patent Literature 2).

[0414] The 152nd target gene is the hsa-miR-4739 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0415] The 153rd target gene is the hsa-miR-1268b gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0416] The 154th target gene is the hsa-miR-5698 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0417] The 155th target gene is the hsa-miR-6752-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0418] The 156th target gene is the hsa-miR-4507 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0419] The 157th target gene is the hsa-miR-564 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0420] The 158th target gene is the hsa-miR-4497 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript

thereof can serve as a marker for lung cancer.

[0421] The 159th target gene is the hsa-miR-6877-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0422] The 160th target gene is the hsa-miR-6087 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0423] The 161st target gene is the hsa-miR-4731-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0424] The 162nd target gene is the hsa-miR-615-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0425] The 163rd target gene is the hsa-miR-760 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0426] The 164th target gene is the hsa-miR-6891-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0427] The 165th target gene is the hsa-miR-6887-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0428] The 166th target gene is the hsa-miR-4525 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0429] The 167th target gene is the hsa-miR-1914-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0430] The 168th target gene is the hsa-miR-619-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0431] The 169th target gene is the hsa-miR-5001-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0432] The 170th target gene is the hsa-miR-6722-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0433] The 171st target gene is the hsa-miR-3621 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0434] The 172nd target gene is the hsa-miR-4298 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0435] The 173rd target gene is the hsa-miR-675-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0436] The 174th target gene is the hsa-miR-4655-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0437] The 175th target gene is the hsa-miR-6073 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0438] The 176th target gene is the hsa-miR-6845-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0439] The 177th target gene is the hsa-miR-6769b-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0440] The 178th target gene is the hsa-miR-4665-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0441] The 179th target gene is the hsa-miR-1913 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0442] The 180th target gene is the hsa-miR-1228-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0443] The 181st target gene is the hsa-miR-940 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0444] The 182nd target gene is the hsa-miR-296-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0445] The 183rd target gene is the hsa-miR-4690-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0446] The 184th target gene is the hsa-miR-548q gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0447] The 185th target gene is the hsa-miR-663a gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0448] The 186th target gene is the hsa-miR-1249 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0449] The 187th target gene is the hsa-miR-1202 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0450] The 188th target gene is the hsa-miR-7113-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0451] The 189th target gene is the hsa-miR-1225-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0452] The 190th target gene is the hsa-miR-4783-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0453] The 191st target gene is the hsa-miR-4448 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0454] The 192nd target gene is the hsa-miR-4534 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer.

[0455] The 193rd target gene is the hsa-miR-1307-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. The previously known report shows that change in the expression of the gene or the transcript thereof can serve as a marker for lung cancer (Patent Literature 3).

2. Nucleic acid probe or primer for detection of lung cancer

[0456] In the present invention, a nucleic acid capable of specifically binding to any of the target nucleic acids as the lung cancer markers described above can be used as a nucleic acid, for example, a nucleic acid probe or a primer, for the detection or diagnosis of lung cancer.

[0457] In the present invention, the nucleic acid probe or the primer that can be used for detecting lung cancer or for diagnosing lung cancer permits qualitative and/or quantitative measurement of the presence, expression level, or abundance of human-derived hsa-miR-6768-5p, optionally in combination with any of hsa-miR-6836-3p, hsa-miR-6782-5p, hsa-miR-3663-3p, hsa-miR-1908-3p, hsa-miR-6726-5p, hsa-miR-4258, hsa-miR-1343-3p, hsa-miR-4516, hsa-miR-

6875-5p, hsa-miR-4651, hsa-miR-6825-5p, hsa-miR-6840-3p, hsa-miR-6780b-5p, hsa-miR-6749-5p, hsa-miR-8063, hsa-miR-6784-5p, hsa-miR-3679-5p, hsa-miR-3184-5p, hsa-miR-663b, hsa-miR-6880-5p, hsa-miR-1908-5p, hsa-miR-92a-2-5p, hsa-miR-7975, hsa-miR-7110-5p, hsa-miR-6842-5p, hsa-miR-6857-5p, hsa-miR-5572, hsa-miR-3197, hsa-miR-6131, hsa-miR-6889-5p, hsa-miR-4454, hsa-miR-1199-5p, hsa-miR-1247-3p, hsa-miR-6800-5p, hsa-miR-6872-3p, hsa-miR-4649-5p, hsa-miR-6791-5p, hsa-miR-4433b-3p, hsa-miR-3135b, hsa-miR-128-2-5p, hsa-miR-4675, hsa-miR-4472, hsa-miR-6785-5p, hsa-miR-6741-5p, hsa-miR-7977, hsa-miR-3665, hsa-miR-128-1-5p, hsa-miR-4286, hsa-miR-6765-3p, hsa-miR-4632-5p, hsa-miR-365a-5p, hsa-miR-6088, hsa-miR-6816-5p, hsa-miR-6885-5p, hsa-miR-711, hsa-miR-6765-5p, hsa-miR-3180, hsa-miR-4442, hsa-miR-4792, hsa-miR-6721-5p, hsa-miR-6798-5p, hsa-miR-3162-5p, hsa-miR-6126, hsa-miR-4758-5p, hsa-miR-2392, hsa-miR-486-3p, hsa-miR-6727-5p, hsa-miR-4728-5p, hsa-miR-6746-5p, hsa-miR-4270, hsa-miR-3940-5p, hsa-miR-4725-3p, hsa-miR-7108-5p, hsa-miR-3656, hsa-miR-6879-5p, hsa-miR-6738-5p, hsa-miR-1260a, hsa-miR-4446-3p, hsa-miR-3131, hsa-miR-4463, hsa-miR-3185, hsa-miR-6870-5p, hsa-miR-6779-5p, hsa-miR-1273g-3p, hsa-miR-8059, hsa-miR-4697-5p, hsa-miR-4674, hsa-miR-4433-3p, hsa-miR-4257, hsa-miR-1915-5p, hsa-miR-4417, hsa-miR-1343-5p, hsa-miR-6781-5p, hsa-miR-4695-5p, hsa-miR-1237-5p, hsa-miR-6775-5p, hsa-miR-7845-5p, hsa-miR-4746-3p, hsa-miR-7641, hsa-miR-7847-3p, hsa-miR-6806-5p, hsa-miR-4467, hsa-miR-4726-5p, hsa-miR-4648, hsa-miR-6089, hsa-miR-1260b, hsa-miR-4532, hsa-miR-5195-3p, hsa-miR-3188, hsa-miR-6848-5p, hsa-miR-1233-5p, hsa-miR-6717-5p, hsa-miR-3195, hsa-miR-6757-5p, hsa-miR-8072, hsa-miR-4745-5p, hsa-miR-6511a-5p, hsa-miR-6776-5p, hsa-miR-371a-5p, hsa-miR-1227-5p, hsa-miR-7150, hsa-miR-1915-3p, hsa-miR-187-5p, hsa-miR-614, hsa-miR-1225-5p, hsa-miR-451a, hsa-miR-939-5p, hsa-miR-223-3p, hsa-miR-125a-3p, hsa-miR-92b-5p, hsa-miR-22-3p, hsa-miR-6073, hsa-miR-6845-5p, hsa-miR-6769b-5p, hsa-miR-4665-3p, hsa-miR-1913, hsa-miR-1228-3p, hsa-miR-940, hsa-miR-296-3p, hsa-miR-4690-5p, hsa-miR-548q, hsa-miR-663a, hsa-miR-1249, hsa-miR-1202, hsa-miR-7113-3p, hsa-miR-1225-3p, hsa-miR-4783-3p, hsa-miR-4448, and hsa-miR-4534 or a combination thereof, congeners thereof, transcripts thereof, or variants or derivatives thereof, optionally in combination therewith, hsa-miR-19b-3p, hsa-miR-1228-5p, and hsa-miR-1307-3p or a combination thereof, congeners thereof, transcripts thereof, or variants or derivatives thereof, and, optionally in combination therewith, hsa-miR-4271, hsa-miR-642b-3p, hsa-miR-6075, hsa-miR-6125, hsa-miR-887-3p, hsa-miR-6851-5p, hsa-miR-6763-5p, hsa-miR-3928-3p, hsa-miR-4443, hsa-miR-3648, hsa-miR-149-3p, hsa-miR-4689, hsa-miR-4763-3p, hsa-miR-6729-5p, hsa-miR-3196, hsa-miR-8069, hsa-miR-1268a, hsa-miR-4739, hsa-miR-1268b, hsa-miR-5698, hsa-miR-6752-5p, hsa-miR-4507, hsa-miR-564, hsa-miR-4497, hsa-miR-6877-5p, hsa-miR-6087, hsa-miR-4731-5p, hsa-miR-615-5p, hsa-miR-760, hsa-miR-6891-5p, hsa-miR-6887-5p, hsa-miR-4525, hsa-miR-1914-3p, hsa-miR-619-5p, hsa-miR-5001-5p, hsa-miR-6722-3p, hsa-miR-3621, hsa-miR-4298, hsa-miR-675-5p and hsa-miR-4655-5p or a combination thereof, congeners thereof, transcripts thereof, or variants or derivatives thereof.

[0458] The expression level of each target nucleic acid described above is increased or decreased (hereinafter, referred to as "increased/decreased") according to the type of the target nucleic acid in a subject who has lung cancer as compared with a healthy subject. Hence, the nucleic acid of the present invention can be effectively used for measuring the expression level of the target nucleic acid in a body fluid derived from a subject (e.g., a human) who is suspected of having lung cancer and a body fluid derived from a healthy subject, and detecting lung cancer by the comparison thereof.

[0459] The nucleic acid probe or the primer that can be used in the present invention is a nucleic acid probe capable of specifically binding to a polynucleotide consisting of a nucleotide sequence represented by SEQ ID NO: 1 optionally in combination with at lesat one of SEQ ID NOs 2 to 125, 127 to 130, 132 to 134, and 561 to 578, or a primer for amplifying a polynucleotide consisting of a nucleotide sequence represented by at least one of SEQ ID NOs: 1 to 125, 127 to 130, 132 to 134, and 561 to 578.

[0460] The nucleic acid probe or the primer that can be further used in the present invention can comprise a nucleic acid probe capable of specifically binding to a polynucleotide consisting of a nucleotide sequence represented by at least one of SEQ ID NOs: 126, 131, and 579, or a primer for amplifying a polynucleotide consisting of a nucleotide sequence represented by at least one of SEQ ID NOs: 126, 131, and 579.

[0461] The nucleic acid probe or the primer that can be further used in the present invention can comprise a nucleic acid probe capable of specifically binding to a polynucleotide consisting of a nucleotide sequence represented by at least one of SEQ ID NOs: 135 to 174, or a primer for amplifying a polynucleotide consisting of a nucleotide sequence represented by at least one of SEQ ID NOs: 135 to 174.

[0462] Specifically, these nucleic acid probes or primers comprise a combination of one or more polynucleotides selected from a polynucleotide group comprising nucleotide sequences represented SEQ ID NO: 1 optionally in combination with any of SEQ ID NOs 2 to 618, or nucleotide sequences derived from the nucleotide sequences by the replacement of u with t, and a complementary polynucleotide group thereof, a polynucleotide group respectively hybridizing under stringent conditions (mentioned later) to DNAs consisting of nucleotide sequences complementary to these nucleotide sequences, and a complementary polynucleotide group thereof, and a polynucleotide group comprising 15 or more, preferably 17 or more consecutive nucleotides in the nucleotide sequences of these polynucleotide groups. These polynucleotides can be used as nucleic acid probes and primers for detecting the lung cancer markers as target nucleic acids.

[0463] More specifically, examples of the nucleic acid probe or the primer that can be used in the present invention include one or more polynucleotide(s) selected from the group consisting of the following polynucleotides (a) to (e):

(a) a polynucleotide consisting of a nucleotide sequence represented by SEQ ID NO: 1 optionally in combination with any of SEQ ID NOs 125, 127 to 130, 132 to 134, and 561 to 578 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, a variant thereof, a derivative thereof, or a fragment thereof comprising 15 or more consecutive nucleotides,
(b) a polynucleotide comprising a nucleotide sequence represented by SEQ ID NO: 1 optionally in combination with any of SEQ ID NO 125, 127 to 130, 132 to 134, and 561 to 578,
(c) a polynucleotide consisting of a nucleotide sequence complementary to a nucleotide sequence represented by SEQ ID NO: 1 optionally in combination with any of SEQ ID NOs 125, 127 to 130, 132 to 134, and 561 to 578 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, a variant thereof, a derivative thereof, or a fragment thereof comprising 15 or more consecutive nucleotides,
(d) a polynucleotide comprising a nucleotide sequence complementary to a nucleotide sequence represented by SEQ ID NO: 1 optionally in combination with any of SEQ ID NOs 125, 127 to 130, 132 to 134, and 561 to 578 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, and
(e) a polynucleotide hybridizing under stringent conditions to any of the polynucleotides (a) to (d).

[0464] In addition to at least one or more polynucleotide(s) selected from the polynucleotides (a) to (e), the nucleic acid probe or the primer that can be further used in the present invention can comprise the polynucleotides selected from the group consisting of the following polynucleotides (f) to (j):

(f) a polynucleotide consisting of a nucleotide sequence represented by any of SEQ ID NOs: 126, 131, and 579 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, a variant thereof, a derivative thereof, or a fragment thereof comprising 15 or more consecutive nucleotides,
(g) a polynucleotide comprising a nucleotide sequence represented by any of SEQ ID NOs: 126, 131, and 579,
(h) a polynucleotide consisting of a nucleotide sequence complementary to a nucleotide sequence represented by any of SEQ ID NOs: 126, 131, and 579 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, a variant thereof, a derivative thereof, or a fragment thereof comprising 15 or more consecutive nucleotides,
(i) a polynucleotide comprising a nucleotide sequence complementary to a nucleotide sequence represented by any of SEQ ID NOs: 126, 131, and 579 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, and
(j) a polynucleotide hybridizing under stringent conditions to any of the polynucleotides (f) to (i).

[0465] In addition to at least one or more polynucleotide(s) selected from the polynucleotides (a) to (j), the nucleic acid probe or the primer that can be further used in the present invention can comprise the polynucleotides selected from the group consisting of the following polynucleotides (k) to (o):

(k) a polynucleotide consisting of a nucleotide sequence represented by any of SEQ ID NOs: 135 to 174 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, a variant thereof, a derivative thereof, or a fragment thereof comprising 15 or more consecutive nucleotides,
(l) a polynucleotide comprising a nucleotide sequence represented by any of SEQ ID NOs: 135 to 174,
(m) a polynucleotide consisting of a nucleotide sequence complementary to a nucleotide sequence represented by any of SEQ ID NOs: 135 to 174 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, a variant thereof, a derivative thereof, or a fragment thereof comprising 15 or more consecutive nucleotides,
(n) a polynucleotide comprising a nucleotide sequence complementary to a nucleotide sequence represented by any of SEQ ID NOs: 135 to 174 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, and
(o) a polynucleotide hybridizing under stringent conditions to any of the polynucleotides (k) to (n).

[0466] For these polynucleotides, the "fragment thereof comprising 15 or more consecutive nucleotides" can contain the number of nucleotides in the range from, for example, 15 consecutive nucleotides to less than the total number of nucleotides of the sequence, from 17 consecutive nucleotides to less than the total number of nucleotides of the sequence, or from 19 consecutive nucleotides to less than the total number of nucleotides of the sequence, in the nucleotide sequence of each polynucleotide, though the fragment is not limited thereto.

[0467] These polynucleotides or the fragments thereof used in the present invention may each be DNA or may each be RNA.

[0468] The polynucleotides that can be used in the present invention can each be prepared by use of a general technique such as a DNA recombination technique, PCR, or a method using an automatic DNA/RNA synthesizer.

[0469] The DNA recombination technique and the PCR can employ a technique described in, for example, Ausubel et al., Current Protocols in Molecular Biology, John Willey & Sons, US (1993); and Sambrook et al., Molecular Cloning - A Laboratory Manual, Cold Spring Harbor Laboratory Press, US (1989).

[0470] The human-derived hsa-miR-6768-5p, hsa-miR-6836-3p, hsa-miR-6782-5p, hsa-miR-3663-3p, hsa-miR-1908-3p, hsa-miR-6726-5p, hsa-miR-4258, hsa-miR-1343-3p, hsa-miR-4516, hsa-miR-6875-5p, hsa-miR-4651, hsa-miR-6825-5p, hsa-miR-6840-3p, hsa-miR-6780b-5p, hsa-miR-6749-5p, hsa-miR-8063, hsa-miR-6784-5p, hsa-miR-3679-5p, hsa-miR-3184-5p, hsa-miR-663b, hsa-miR-6880-5p, hsa-miR-1908-5p, hsa-miR-92a-2-5p, hsa-miR-7975, hsa-miR-7110-5p, hsa-miR-6842-5p, hsa-miR-6857-5p, hsa-miR-5572, hsa-miR-3197, hsa-miR-6131, hsa-miR-6889-5p, hsa-miR-4454, hsa-miR-1199-5p, hsa-miR-1247-3p, hsa-miR-6800-5p, hsa-miR-6872-3p, hsa-miR-4649-5p, hsa-miR-6791-5p, hsa-miR-4433b-3p, hsa-miR-3135b, hsa-miR-128-2-5p, hsa-miR-4675, hsa-miR-4472, hsa-miR-6785-5p, hsa-miR-6741-5p, hsa-miR-7977, hsa-miR-3665, hsa-miR-128-1-5p, hsa-miR-4286, hsa-miR-6765-3p, hsa-miR-4632-5p, hsa-miR-365a-5p, hsa-miR-6088, hsa-miR-6816-5p, hsa-miR-6885-5p, hsa-miR-711, hsa-miR-6765-5p, hsa-miR-3180, hsa-miR-4442, hsa-miR-4792, hsa-miR-6721-5p, hsa-miR-6798-5p, hsa-miR-3162-5p, hsa-miR-6126, hsa-miR-4758-5p, hsa-miR-2392, hsa-miR-486-3p, hsa-miR-6727-5p, hsa-miR-4728-5p, hsa-miR-6746-5p, hsa-miR-4270, hsa-miR-3940-5p, hsa-miR-4725-3p, hsa-miR-7108-5p, hsa-miR-3656, hsa-miR-6879-5p, hsa-miR-6738-5p, hsa-miR-1260a, hsa-miR-4446-3p, hsa-miR-3131, hsa-miR-4463, hsa-miR-3185, hsa-miR-6870-5p, hsa-miR-6779-5p, hsa-miR-1273g-3p, hsa-miR-8059, hsa-miR-4697-5p, hsa-miR-4674, hsa-miR-4433-3p, hsa-miR-4257, hsa-miR-1915-5p, hsa-miR-4417, hsa-miR-1343-5p, hsa-miR-6781-5p, hsa-miR-4695-5p, hsa-miR-1237-5p, hsa-miR-6775-5p, hsa-miR-7845-5p, hsa-miR-4746-3p, hsa-miR-7641, hsa-miR-7847-3p, hsa-miR-6806-5p, hsa-miR-4467, hsa-miR-4726-5p, hsa-miR-4648, hsa-miR-6089, hsa-miR-1260b, hsa-miR-4532, hsa-miR-5195-3p, hsa-miR-3188, hsa-miR-6848-5p, hsa-miR-1233-5p, hsa-miR-6717-5p, hsa-miR-3195, hsa-miR-6757-5p, hsa-miR-8072, hsa-miR-4745-5p, hsa-miR-6511a-5p, hsa-miR-6776-5p, hsa-miR-371a-5p, hsa-miR-1227-5p, hsa-miR-7150, hsa-miR-1915-3p, hsa-miR-187-5p, hsa-miR-614, hsa-miR-19b-3p, hsa-miR-1225-5p, hsa-miR-451a, hsa-miR-939-5p, hsa-miR-223-3p, hsa-miR-1228-5p, hsa-miR-125a-3p, hsa-miR-92b-5p, hsa-miR-22-3p, hsa-miR-6073, hsa-miR-6845-5p, hsa-miR-6769b-5p, hsa-miR-4665-3p, hsa-miR-1913, hsa-miR-1228-3p, hsa-miR-940, hsa-miR-296-3p, hsa-miR-4690-5p, hsa-miR-548q, hsa-miR-663a, hsa-miR-1249, hsa-miR-1202, hsa-miR-7113-3p, hsa-miR-1225-3p, hsa-miR-4783-3p, hsa-miR-4448 and hsa-miR-4534, hsa-miR-1307-3p, hsa-miR-4271, hsa-miR-642b-3p, hsa-miR-6075, hsa-miR-6125, hsa-miR-887-3p, hsa-miR-6851-5p, hsa-miR-6763-5p, hsa-miR-3928-3p, hsa-miR-4443, hsa-miR-3648, hsa-miR-149-3p, hsa-miR-4689, hsa-miR-4763-3p, hsa-miR-6729-5p, hsa-miR-3196, hsa-miR-8069, hsa-miR-1268a, hsa-miR-4739, hsa-miR-1268b, hsa-miR-5698, hsa-miR-6752-5p, hsa-miR-4507, hsa-miR-564, hsa-miR-4497, hsa-miR-6877-5p, hsa-miR-6087, hsa-miR-4731-5p, hsa-miR-615-5p, hsa-miR-760, hsa-miR-6891-5p, hsa-miR-6887-5p, hsa-miR-4525, hsa-miR-1914-3p, hsa-miR-619-5p, hsa-miR-5001-5p, hsa-miR-6722-3p, hsa-miR-3621, hsa-miR-4298, hsa-miR-675-5p and hsa-miR-4655-5p represented by SEQ ID NOs: 1 to 174, and 561 to 579 are known in the art, and their acquisition methods are also known as mentioned above. Therefore, each polynucleotide that can be used as a nucleic acid probe or a primer in the present invention can be prepared by cloning the gene.

[0471] Such a nucleic acid probe or a primer can be chemically synthesized using an automatic DNA synthesis apparatus. In general, a phosphoramidite method is used in this synthesis, and single-stranded DNA up to approximately 100 nucleotides can be automatically synthesized by this method. The automatic DNA synthesis apparatus is commercially available from, for example, Polygen GmbH, ABI, or Applied Biosystems, Inc.

[0472] Alternatively, the polynucleotide of the present invention can also be prepared by a cDNA cloning method. The cDNA cloning technique can employ, for example, microRNA Cloning Kit Wako.

[0473] In this context, the sequences of the nucleic acid probe and the primer for detecting the polynucleotide consisting of a nucleotide sequence represented by any of SEQ ID NOs: 1 to 174, and 561 to 579 do not exist as miRNAs or precursors thereof *in vivo*. For example, the nucleotide sequences represented by SEQ ID NO: 5 and SEQ ID NO: 22 are produced from the precursor represented by SEQ ID NO: 179. This precursor has a hairpin-like structure as shown in Figure 1, and the nucleotide sequences represented by SEQ ID NO: 5 and SEQ ID NO: 22 have mismatch sequences with each other. Likewise, a nucleotide sequence completely complementary to the nucleotide sequence represented by SEQ ID NO: 5 or SEQ ID NO: 22 is not naturally produced *in vivo*. Therefore, the nucleic acid probe and the primer for detecting the nucleotide sequence represented by any of SEQ ID NOs: 1 to 174, and 561 to 579 each have an artificial nucleotide sequence that does not exist *in vivo*.

3. Kit or device for detection of lung cancer

[0474] The present invention also provides the use of a kit or a device for the detection of lung cancer, comprising one or more polynucleotide(s) (which can include a variant, a fragment, and a derivative; hereinafter, also referred to as a polynucleotide for detection) that can be used as a nucleic acid probe or a primer in the present invention for

measuring a target nucleic acid as a lung cancer marker.

[0475] The target nucleic acid as a lung cancer marker according to the present invention is hsa-miR-6768-5p, optionally in combination with any of the following group hsa-miR-6836-3p, hsa-miR-6782-5p, hsa-miR-3663-3p, hsa-miR-1908-3p, hsa-miR-6726-5p, hsa-miR-4258, hsa-miR-1343-3p, hsa-miR-4516, hsa-miR-6875-5p, hsa-miR-4651, hsa-miR-6825-5p, hsa-miR-6840-3p, hsa-miR-6780b-5p, hsa-miR-6749-5p, hsa-miR-8063, hsa-miR-6784-5p, hsa-miR-3679-5p, hsa-miR-3184-5p, hsa-miR-663b, hsa-miR-6880-5p, hsa-miR-1908-5p, hsa-miR-92a-2-5p, hsa-miR-7975, hsa-miR-7110-5p, hsa-miR-6842-5p, hsa-miR-6857-5p, hsa-miR-5572, hsa-miR-3197, hsa-miR-6131, hsa-miR-6889-5p, hsa-miR-4454, hsa-miR-1199-5p, hsa-miR-1247-3p, hsa-miR-6800-5p, hsa-miR-6872-3p, hsa-miR-4649-5p, hsa-miR-6791-5p, hsa-miR-4433b-3p, hsa-miR-3135b, hsa-miR-128-2-5p, hsa-miR-4675, hsa-miR-4472, hsa-miR-6785-5p, hsa-miR-6741-5p, hsa-miR-7977, hsa-miR-3665, hsa-miR-128-1-5p, hsa-miR-4286, hsa-miR-6765-3p, hsa-miR-4632-5p, hsa-miR-365a-5p, hsa-miR-6088, hsa-miR-6816-5p, hsa-miR-6885-5p, hsa-miR-711, hsa-miR-6765-5p, hsa-miR-3180, hsa-miR-4442, hsa-miR-4792, hsa-miR-6721-5p, hsa-miR-6798-5p, hsa-miR-3162-5p, hsa-miR-6126, hsa-miR-4758-5p, hsa-miR-2392, hsa-miR-486-3p, hsa-miR-6727-5p, hsa-miR-4728-5p, hsa-miR-6746-5p, hsa-miR-4270, hsa-miR-3940-5p, hsa-miR-4725-3p, hsa-miR-7108-5p, hsa-miR-3656, hsa-miR-6879-5p, hsa-miR-6738-5p, hsa-miR-1260a, hsa-miR-4446-3p, hsa-miR-3131, hsa-miR-4463, hsa-miR-3185, hsa-miR-6870-5p, hsa-miR-6779-5p, hsa-miR-1273g-3p, hsa-miR-8059, hsa-miR-4697-5p, hsa-miR-4674, hsa-miR-4433-3p, hsa-miR-4257, hsa-miR-1915-5p, hsa-miR-4417, hsa-miR-1343-5p, hsa-miR-6781-5p, hsa-miR-4695-5p, hsa-miR-1237-5p, hsa-miR-6775-5p, hsa-miR-7845-5p, hsa-miR-4746-3p, hsa-miR-7641, hsa-miR-7847-3p, hsa-miR-6806-5p, hsa-miR-4467, hsa-miR-4726-5p, hsa-miR-4648, hsa-miR-6089, hsa-miR-1260b, hsa-miR-4532, hsa-miR-5195-3p, hsa-miR-3188, hsa-miR-6848-5p, hsa-miR-1233-5p, hsa-miR-6717-5p, hsa-miR-3195, hsa-miR-6757-5p, hsa-miR-8072, hsa-miR-4745-5p, hsa-miR-6511a-5p, hsa-miR-6776-5p, hsa-miR-371a-5p, hsa-miR-1227-5p, hsa-miR-7150, hsa-miR-1915-3p, hsa-miR-187-5p, hsa-miR-614, hsa-miR-1225-5p, hsa-miR-451a, hsa-miR-939-5p, hsa-miR-223-3p, hsa-miR-125a-3p, hsa-miR-92b-5p, hsa-miR-22-3p, hsa-miR-6073, hsa-miR-6845-5p, hsa-miR-6769b-5p, hsa-miR-4665-3p, hsa-miR-1913, hsa-miR-1228-3p, hsa-miR-940, hsa-miR-296-3p, hsa-miR-4690-5p, hsa-miR-548q, hsa-miR-663a, hsa-miR-1249, hsa-miR-1202, hsa-miR-7113-3p, hsa-miR-1225-3p, hsa-miR-4783-3p, hsa-miR-4448 and hsa-miR-4534.

[0476] An additional target nucleic acid that can be optionally used in the measurement is selected from the following group 2: hsa-miR-19b-3p, hsa-miR-1228-5p and hsa-miR-1307-3p.

[0477] An additional target nucleic acid that can be optionally further used in the measurement is selected from the following group 3: hsa-miR-4271, hsa-miR-642b-3p, hsa-miR-6075, hsa-miR-6125, hsa-miR-887-3p, hsa-miR-6851-5p, hsa-miR-6763-5p, hsa-miR-3928-3p, hsa-miR-4443, hsa-miR-3648, hsa-miR-149-3p, hsa-miR-4689, hsa-miR-4763-3p, hsa-miR-6729-5p, hsa-miR-3196, hsa-miR-8069, hsa-miR-1268a, hsa-miR-4739, hsa-miR-1268b, hsa-miR-5698, hsa-miR-6752-5p, hsa-miR-4507, hsa-miR-564, hsa-miR-4497, hsa-miR-6877-5p, hsa-miR-6087, hsa-miR-4731-5p, hsa-miR-615-5p, hsa-miR-760, hsa-miR-6891-5p, hsa-miR-6887-5p, hsa-miR-4525, hsa-miR-1914-3p, hsa-miR-619-5p, hsa-miR-5001-5p, hsa-miR-6722-3p, hsa-miR-3621, hsa-miR-4298, hsa-miR-675-5p and hsa-miR-4655-5p.

[0478] The kit or the device of the present invention comprises a nucleic acid capable of specifically binding to any of the target nucleic acids as the lung cancer markers described above, preferably one or more polynucleotide(s) selected from the nucleic acid probes or the primers described in the preceding Section 2, specifically, the polynucleotides described in the preceding paragraph 2, or variant(s) thereof.

[0479] Specifically, the kit or the device of the present invention can comprise at least one or more polynucleotide(s) comprising (or consisting of) a nucleotide sequence represented by SEQ ID NO: 1 optionally together with any of SEQ ID NOs 2 to 125, 127 to 130, 132 to 134, and 561 to 578 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, polynucleotide(s) comprising (or consisting of) a complementary sequence thereof, polynucleotide(s) hybridizing under stringent conditions to any of these polynucleotides, or variant(s) or fragment(s) comprising 15 or more consecutive nucleotides of any of these polynucleotide sequences.

[0480] The kit or the device of the present invention can further comprise one or more polynucleotide(s) comprising (or consisting of) a nucleotide sequence represented by any of SEQ ID NOs: 126 and 131 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, polynucleotide(s) comprising (or consisting of) a complementary sequence thereof, polynucleotide(s) hybridizing under stringent conditions to any of these polynucleotides, variant(s) or fragment(s) comprising 15 or more consecutive nucleotides of any of these polynucleotide sequences.

[0481] The kit or the device of the present invention can further comprise one or more polynucleotide(s) comprising (or consisting of) a nucleotide sequence represented by any of SEQ ID NOs: 135 to 174 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, polynucleotide(s) comprising (or consisting of) a complementary sequence thereof, polynucleotide(s) hybridizing under stringent conditions to any of these polynucleotides, variant(s) or fragment(s) comprising 15 or more consecutive nucleotides of any of these polynucleotide sequences.

[0482] The fragment that can be contained in the kit or the device of the present invention is, for example, one or more, preferably two or more polynucleotides selected from the group consisting of the following polynucleotides:

(1) a polynucleotide comprising 15 or more consecutive nucleotides in a nucleotide sequence derived from a nu-

cleotide sequence represented by any of SEQ ID NO: 1 optionally in combination with any of SEQ ID NOs 2 to 125, 127 to 130, 132 to 134, and 561 to 578 by the replacement of u with t, or a complementary sequence thereof; and optionally in combination with

(2) a polynucleotide comprising 15 or more consecutive nucleotides in a nucleotide sequence derived from a nucleotide sequence represented by any of SEQ ID NOs: 126, 131 and 579 by the replacement of u with t, or a complementary sequence thereof; and

(3) a polynucleotide comprising 15 or more consecutive nucleotides in a nucleotide sequence derived from a nucleotide sequence represented by any of SEQ ID NOs: 135 to 174 by the replacement of u with t, or a complementary sequence thereof.

[0483] The polynucleotide is a polynucleotide consisting of a nucleotide sequence represented by SEQ ID NO: 1 optionally in combination with any of SEQ ID NOs 2 to 125, 127 to 130, 132 to 134, and 561 to 578, or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, a polynucleotide consisting of a complementary sequence thereof, a polynucleotide hybridizing under stringent conditions to any of these polynucleotides, or a variant thereof comprising 15 or more, preferably 17 or more, more preferably 19 or more consecutive nucleotides.

[0484] In a preferred embodiment, the polynucleotide is a polynucleotide consisting of a nucleotide sequence represented by any of SEQ ID NOs: 126, 134 and 579 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, a polynucleotide consisting of a complementary sequence thereof, a polynucleotide hybridizing under stringent conditions to any of these polynucleotides, or a variant thereof comprising 15 or more, preferably 17 or more, more preferably 19 or more consecutive nucleotides.

[0485] In a preferred embodiment, the polynucleotide is a polynucleotide consisting of a nucleotide sequence represented by any of SEQ ID NOs: 135 to 174 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, a polynucleotide consisting of a complementary sequence thereof, a polynucleotide hybridizing under stringent conditions to any of these polynucleotides, or a variant thereof comprising 15 or more, preferably 17 or more, more preferably 19 or more consecutive nucleotides.

[0486] In a preferred embodiment, the fragment can be a polynucleotide comprising 15 or more, preferably 17 or more, more preferably 19 or more consecutive nucleotides.

[0487] In the present invention, the size of the polynucleotide fragment is the number of bases in the range from, for example, 15 consecutive nucleotides to less than the total number of bases of the sequence, from 17 consecutive nucleotides to less than the total number of bases of the sequence, or from 19 consecutive nucleotides to less than the total number of nucleotides of the sequence, in the nucleotide sequence of each polynucleotide.

[0488] Specific examples of the aforementioned combination of the polynucleotides constituting the kit or the device of the present invention can include the polynucleotides as to combinations of SEQ ID NOs shown in Table 1 (SEQ ID NOs: 2 to 174, and 561 to 579 corresponding to the miRNA markers in Table 1 in combination with SEQ ID NO: 1.). However, these are given merely for illustrative purposes, and various other possible combinations are included in the present invention.

[0489] The aforementioned combination constituting the kit or the device for discriminating a lung cancer patient from a healthy subject according to the present invention is desirably, for example, a combination of two or more of the aforementioned polynucleotides consisting of nucleotide sequences represented by SEQ ID NOs shown in Table 1. Usually, a combination of two of these polynucleotides can produce adequate performance.

[0490] The combination of two polynucleotides consisting of the nucleotide sequences or the complementary sequences thereof for specifically discriminating a lung cancer patient from a healthy subject is preferably a combination comprising SEQ ID NO: 1 optionally in combination with any of SEQ ID NOs 2 to 125, 127 to 130, 132 to 174, and 561 to 578, among the combinations constituted by two of the polynucleotides consisting of the nucleotide sequences represented by SEQ ID NOs: 1 to 174, and 561 to 579.

[0491] The combination of polynucleotides with cancer type specificity capable of discriminating a lung cancer patient not only from a healthy subject but also from other cancer patients is preferably, for example, a combination of multiple polynucleotides comprising at least SEQ ID NO: 1, optionally together with at least one polynucleotide selected from the group consisting of polynucleotides of SEQ ID NOs 2, 3, 4, 5, 7, 9, 10, 11, 19, 21, 26, 29, 31, 52, 53, 63, 65, 69, 72, 87, 90, 113, 124, 125, 126, 128, 130, 143, 148, 160, 162, 561, 562, 563, 564, 565, 566, 567, 568, 569, 570, 571, 572, 573, 574, 575, 576, 577, 578 and 579 (hereinafter, this group is referred to as "cancer type-specific polynucleotide group 1"), with any of the polynucleotides of the other SEQ ID NOs.

[0492] The combination of polynucleotides with cancer type specificity capable of discriminating a lung cancer patient not only from a healthy subject but also from other cancer patients is more preferably a combination of multiple polynucleotides selected from the cancer type-specific polynucleotide group 1.

[0493] The combination of polynucleotides with cancer type specificity capable of discriminating a lung cancer patient not only from a healthy subject but also from other cancer patients is more preferably a combination comprising SEQ ID NO: 1, optionally together with at least one or more polynucleotide(s) selected from the group consisting of polynu-

cleotides of SEQ ID NOs 2, 3, 10, 63, 113, 124, 125, 126, 128, 130, 143, 160, 561, 568, 573 and 578 (hereinafter, this group is referred to as "cancer type-specific polynucleotide group 2") included in the cancer type-specific polynucleotide group 1, among the combinations of multiple polynucleotides selected from the cancer type-specific polynucleotide group 1.

[0494] The number of the polynucleotides with cancer type specificity in the aforementioned combination can be 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or more for the combination and is more preferably 4 or more for the combination. Usually, the combination of 4 of these polynucleotides can produce adequate performance.

[0495] Non-limiting examples of the combination of the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 1 or a complementary sequence thereof with polynucleotides consisting of nucleotide sequences represented by SEQ ID NOs of five polynucleotides selected from the cancer type-specific polynucleotide group 1 or complementary sequences thereof will be listed below.

(1) a combination of SEQ ID NOs: 1, 53, 113, and 125 (markers: hsa-miR-6768-5p, hsa-miR-6088, hsa-miR-6717-5p, and hsa-miR-614);
(2) a combination of SEQ ID NOs: 1, 10, 63, and 113 (markers: hsa-miR-6768-5p, hsa-miR-6875-5p, hsa-miR-3162-5p, and hsa-miR-6717-5p);
(3) a combination of SEQ ID NOs: 1, 19, 113, and 143 (markers: hsa-miR-6768-5p, hsa-miR-3184-5p, hsa-miR-6717-5p, and hsa-miR-4443);
(4) a combination of SEQ ID NOs: 1, 10, 113, and 126 (markers: hsa-miR-6768-5p, hsa-miR-6875-5p, hsa-miR-6717-5p, and hsa-miR-19b-3p); and
(5) a combination of SEQ ID NOs: 1, 2, 10, and 113 (markers: hsa-miR-6768-5p, hsa-miR-6836-3p, hsa-miR-6875-5p, and hsa-miR-6717-5p).

[0496] Non-limiting examples of the combination of the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 2 or a complementary sequence thereof with polynucleotides consisting of nucleotide sequences represented by SEQ ID NOs of five polynucleotides selected from the cancer type-specific polynucleotide group 1 or complementary sequences thereof will be further listed below.

(1) a combination of SEQ ID NOs: 2, 19, 53, and 113 (markers: hsa-miR-6836-3p, hsa-miR-3184-5p, hsa-miR-6088, and hsa-miR-6717-5p);
(2) a combination of SEQ ID NOs: 2, 72, 113, and 125 (markers: hsa-miR-6836-3p, hsa-miR-3940-5p, hsa-miR-6717-5p, and hsa-miR-614);
(3) a combination of SEQ ID NOs: 2,19, 72, and 113 (markers: hsa-miR-6836-3p, hsa-miR-3184-5p, hsa-miR-3940-5p, and hsa-miR-6717-5p);
(4) a combination of SEQ ID NOs: 2, 19, 113, and 579 (markers: hsa-miR-6836-3p, hsa-miR-3184-5p, hsa-miR-6717-5p, and hsa-miR-1307-3p); and
(5) a combination of SEQ ID NOs: 1, 2, 19, and 113 (markers: hsa-miR-6768-5p, hsa-miR-6836-3p, hsa-miR-3184-5p, and hsa-miR-6717-5p).

[0497] Non-limiting examples of the combination of the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 3 or a complementary sequence thereof with polynucleotides consisting of nucleotide sequences represented by SEQ ID NOs of five polynucleotides selected from the cancer type-specific polynucleotide group 1 or complementary sequences thereof will be further listed below.

(1) a combination of SEQ ID NOs: 3, 125, 128, and 568 (markers: hsa-miR-6782-5p, hsa-miR-614, hsa-miR-451a, and hsa-miR-296-3p);
(2) a combination of SEQ ID NOs: 1, 3, 10, and 113 (markers: hsa-miR-6768-5p, hsa-miR-6782-5p, hsa-miR-6875-5p, and hsa-miR-6717-5p);
(3) a combination of SEQ ID NOs: 3, 113, 125, and 126 (markers: hsa-miR-6782-5p, hsa-miR-6717-5p, hsa-miR-614, and hsa-miR-19b-3p);
(4) a combination of SEQ ID NOs: 1, 3, 126, and 573 (markers: hsa-miR-6768-5p, hsa-miR-6782-5p, hsa-miR-19b-3p, and hsa-miR-1202); and
(5) a combination of SEQ ID NOs: 3, 126, 130, and 561 (markers: hsa-miR-6782-5p, hsa-miR-19b-3p, hsa-miR-223-3p, and hsa-miR-6073).

[0498] Non-limiting examples of the combination of the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 10 or a complementary sequence thereof with polynucleotides consisting of nucleotide sequences represented by SEQ ID NOs of five polynucleotides selected from the cancer type-specific polynucleotide group 1 or

complementary sequences thereof will be further listed below.

(1) a combination of SEQ ID NOs: 1, 10, 113, and 143 (markers: hsa-miR-6768-5p, hsa-miR-6875-5p, hsa-miR-6717-5p, and hsa-miR-4443);
(2) a combination of SEQ ID NOs: 1, 10, 113, and 569 (markers: hsa-miR-6768-5p, hsa-miR-6875-5p, hsa-miR-6717-5p, and hsa-miR-4690-5p);
(3) a combination of SEQ ID NOs: 1, 10, 113, and 562 (markers: hsa-miR-6768-5p, hsa-miR-6875-5p, hsa-miR-6717-5p, and hsa-miR-6845-5p);
(4) a combination of SEQ ID NOs: 1, 10, 113, and 578 (markers: hsa-miR-6768-5p, hsa-miR-6875-5p, hsa-miR-6717-5p, hsa-miR-4534); and
(5) a combination of SEQ ID NOs: 1, 7, 10, and 113 (markers: hsa-miR-6768-5p, hsa-miR-4258, hsa-miR-6875-5p, and hsa-miR-6717-5p).

[0499] Non-limiting examples of the combination of the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 63 or a complementary sequence thereof with polynucleotides consisting of nucleotide sequences represented by SEQ ID NOs of five polynucleotides selected from the cancer type-specific polynucleotide group 1 or complementary sequences thereof will be further listed below.

(1) a combination of SEQ ID NOs: 1, 63, 567, and 578 (markers: hsa-miR-6768-5p, hsa-miR-3162-5p, hsa-miR-940, and hsa-miR-4534);
(2) a combination of SEQ ID NOs: 1, 53, 63, and 578 (markers: hsa-miR-6768-5p, hsa-miR-6088, hsa-miR-3162-5p, and hsa-miR-4534);
(3) a combination of SEQ ID NOs: 1, 63, 162, and 573 (markers: hsa-miR-6768-5p, hsa-miR-3162-5p, hsa-miR-615-5p, and hsa-miR-1202);
(4) a combination of SEQ ID NOs: 1, 63, 162, and 578 (markers: hsa-miR-6768-5p, hsa-miR-3162-5p, hsa-miR-615-5p, and hsa-miR-4534); and
(5) a combination of SEQ ID NOs: 1, 63, 576, and 578 (markers: hsa-miR-6768-5p, hsa-miR-3162-5p, hsa-miR-4783-3p, and hsa-miR-4534).

[0500] Non-limiting examples of the combination of the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 113 or a complementary sequence thereof with polynucleotides consisting of nucleotide sequences represented by SEQ ID NOs of five polynucleotides selected from the cancer type-specific polynucleotide group 1 or complementary sequences thereof will be further listed below.

(1) a combination of SEQ ID NOs: 1, 10, 113, and 567 (markers: hsa-miR-6768-5p, hsa-miR-6875-5p, hsa-miR-6717-5p, and hsa-miR-940);
(2) a combination of SEQ ID NOs: 1, 53, 63, and 113 (markers: hsa-miR-6768-5p, hsa-miR-6088, hsa-miR-3162-5p, and hsa-miR-6717-5p);
(3) a combination of SEQ ID NOs: 1, 53, 113, and 143 (markers: hsa-miR-6768-5p, hsa-miR-6088, hsa-miR-6717-5p, and hsa-miR-4443);
(4) a combination of SEQ ID NOs: 2, 19, 113, and 125 (markers: hsa-miR-6836-3p, hsa-miR-3184-5p, hsa-miR-6717-5p, and hsa-miR-614); and
(5) a combination of SEQ ID NOs: 2, 10, 113, and 130 (markers: hsa-miR-6836-3p, hsa-miR-6875-5p, hsa-miR-6717-5p, and hsa-miR-223-3p).

[0501] Non-limiting examples of the combination of the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 124 or a complementary sequence thereof with polynucleotides consisting of nucleotide sequences represented by SEQ ID NOs of five polynucleotides selected from the cancer type-specific polynucleotide group 1 or complementary sequences thereof will be further listed below.

(1) a combination of SEQ ID NOs: 113, 124, 125, and 126 (markers: hsa-miR-6717-5p, hsa-miR-187-5p, hsa-miR-614, and hsa-miR-19b-3p);
(2) a combination of SEQ ID NOs: 124, 125, 128, and 568 (markers: hsa-miR-187-5p, hsa-miR-614, hsa-miR-451a, and hsa-miR-296-3p);
(3) a combination of SEQ ID NOs: 113, 124, 125, and 162 (markers: hsa-miR-6717-5p, hsa-miR-187-5p, hsa-miR-614, and hsa-miR-615-5p);
(4) a combination of SEQ ID NOs: 52, 124, 126, and 561 (markers: hsa-miR-365a-5p, hsa-miR-187-5p, hsa-miR-19b-3p, and hsa-miR-6073); and

(5) a combination of SEQ ID NOs: 19, 113, 124, and 126 (markers: hsa-miR-3184-5p, hsa-miR-6717-5p, hsa-miR-187-5p, and hsa-miR-19b-3p).

[0502] Non-limiting examples of the combination of the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 125 or a complementary sequence thereof with polynucleotides consisting of nucleotide sequences represented by SEQ ID NOs of five polynucleotides selected from the cancer type-specific polynucleotide group 1 or complementary sequences thereof will be further listed below.

(1) a combination of SEQ ID NOs: 1, 113, 125, and 160 (markers: hsa-miR-6768-5p, hsa-miR-6717-5p, hsa-miR-614, and hsa-miR-6087);
(2) a combination of SEQ ID NOs: 31, 113, 125, and 568 (markers: hsa-miR-6889-5p, hsa-miR-6717-5p, hsa-miR-614, and hsa-miR-296-3p);
(3) a combination of SEQ ID NOs: 2, 53, 113, and 125 (markers: hsa-miR-6836-3p, hsa-miR-6088, hsa-miR-6717-5p, and hsa-miR-614);
(4) a combination of SEQ ID NOs: 1, 10, 113, and 125 (markers: hsa-miR-6768-5p, hsa-miR-6875-5p, hsa-miR-6717-5p, and hsa-miR-614); and
(5) a combination of SEQ ID NOs: 1, 113, 125, and 143 (markers: hsa-miR-6768-5p, hsa-miR-6717-5p, hsa-miR-614, and hsa-miR-4443).

[0503] Non-limiting examples of the combination of the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 126 or a complementary sequence thereof with polynucleotides consisting of nucleotide sequences represented by SEQ ID NOs of five polynucleotides selected from the cancer type-specific polynucleotide group 1 or complementary sequences thereof will be further listed below.

(1) a combination of SEQ ID NOs: 1, 126, 561, and 573 (markers: hsa-miR-6768-5p, hsa-miR-19b-3p, hsa-miR-6073, and hsa-miR-1202);
(2) a combination of SEQ ID NOs: 113, 125, 126, and 568 (markers: hsa-miR-6717-5p, hsa-miR-614, hsa-miR-19b-3p, and hsa-miR-296-3p);
(3) a combination of SEQ ID NO: 113,125, 126, and 561 (markers: hsa-miR-6717-5p, hsa-miR-614, hsa-miR-19b-3p, and hsa-miR-6073);
(4) a combination of SEQ ID NOs: 1, 113, 125, and 126 (markers: hsa-miR-6768-5p, hsa-miR-6717-5p, hsa-miR-614, and hsa-miR-19b-3p); and
(5) a combination of SEQ ID NOs: 1, 52, 126, and 561 (markers: hsa-miR-6768-5p, hsa-miR-365a-5p, hsa-miR-19b-3p, and hsa-miR-6073).

[0504] Non-limiting examples of the combination of the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 128 or a complementary sequence thereof with polynucleotides consisting of nucleotide sequences represented by SEQ ID NOs of five polynucleotides selected from the cancer type-specific polynucleotide group 1 or complementary sequences thereof will be further listed below.

(1) a combination of SEQ ID NOs: 26, 113, 125, and 128 (markers: hsa-miR-6842-5p, hsa-miR-6717-5p, hsa-miR-614, and hsa-miR-451a);
(2) a combination of SEQ ID NOs: 1, 113, 125, and 128 (markers: hsa-miR-6768-5p, hsa-miR-6717-5p, hsa-miR-614, and hsa-miR-451a);
(3) a combination of SEQ ID NOs: 1, 10, 113, and 128 (markers: hsa-miR-6768-5p, hsa-miR-6875-5p, hsa-miR-6717-5p, and hsa-miR-451a);
(4) a combination of SEQ ID NOs: 31, 113, 125, and 128 (markers: hsa-miR-6889-5p, hsa-miR-6717-5p, hsa-miR-614, and hsa-miR-451a); and
(5) a combination of SEQ ID NOs: 2, 19, 113, and 128 (markers: hsa-miR-6836-3p, hsa-miR-3184-5p, hsa-miR-6717-5p, and hsa-miR-451a).

[0505] Non-limiting examples of the combination of the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 130 or a complementary sequence thereof with polynucleotides consisting of nucleotide sequences represented by SEQ ID NOs of five polynucleotides selected from the cancer type-specific polynucleotide group 1 or complementary sequences thereof will be further listed below.

(1) a combination of SEQ ID NOs: 1, 3, 130, and 143 (markers: hsa-miR-6768-5p, hsa-miR-6782-5p, hsa-miR-223-3p, and hsa-miR-4443);

(2) a combination of SEQ ID NOs: 1, 10, 113, and 130 (markers: hsa-miR-6768-5p, hsa-miR-6875-5p, hsa-miR-6717-5p, and hsa-miR-223-3p);
(3) a combination of SEQ ID NOs: 1, 63, 130, and 578 (markers: hsa-miR-6768-5p, hsa-miR-3162-5p, hsa-miR-223-3p, and hsa-miR-4534);
(4) a combination of SEQ ID NOs: 124, 125, 130, and 568 (markers: hsa-miR-187-5p, hsa-miR-614, hsa-miR-223-3p, and hsa-miR-296-3p); and
(5) a combination of SEQ ID NOs: 2, 19, 113, and 130 (markers: hsa-miR-6836-3p, hsa-miR-3184-5p, hsa-miR-6717-5p, and hsa-miR-223-3p).

[0506] Non-limiting examples of the combination of the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 143 or a complementary sequence thereof with polynucleotides consisting of nucleotide sequences represented by SEQ ID NOs of five polynucleotides selected from the cancer type-specific polynucleotide group 1 or complementary sequences thereof will be further listed below.

(1) a combination of SEQ ID NOs: 1, 3, 126, andl43 (markers: hsa-miR-6768-5p, hsa-miR-6782-5p, hsa-miR-19b-3p, and hsa-miR-4443);
(2) a combination of SEQ ID NOs: 1, 63, 130, and 143 (markers: hsa-miR-6768-5p, hsa-miR-3162-5p, hsa-miR-223-3p, and hsa-miR-4443);
(3) a combination of SEQ ID NOs: 1, 10, 52, and 143 (markers: hsa-miR-6768-5p, hsa-miR-6875-5p, hsa-miR-365a-5p, and hsa-miR-4443);
(4) a combination of SEQ ID NOs: 2, 19, 113, and 143 (markers: hsa-miR-6836-3p, hsa-miR-3184-5p, hsa-miR-6717-5p, and hsa-miR-4443); and
(5) a combination of SEQ ID NOs: 63, 124, 130, and 143 (markers: hsa-miR-3162-5p, hsa-miR-187-5p, hsa-miR-223-3p, and hsa-miR-4443).

[0507] Non-limiting examples of the combination of the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 160 or a complementary sequence thereof with polynucleotides consisting of nucleotide sequences represented by SEQ ID NOs of five polynucleotides selected from the cancer type-specific polynucleotide group 1 or complementary sequences thereof will be further listed below.

(1) a combination of SEQ ID NOs: 1, 10, 113, and 160 (markers: hsa-miR-6768-5p, hsa-miR-6875-5p, hsa-miR-6717-5p, and hsa-miR-6087);
(2) a combination of SEQ ID NOs: 7, 113, 125, and 160 (markers: hsa-miR-4258, hsa-miR-6717-5p, hsa-miR-614, and hsa-miR-6087);
(3) a combination of SEQ ID NOs: 1, 113, 160, and 567 (markers: hsa-miR-6768-5p, hsa-miR-6717-5p, hsa-miR-6087, and hsa-miR-940);
(4) a combination of SEQ ID NOs: 1, 113, 160, and 578 (markers: hsa-miR-6768-5p, hsa-miR-6717-5p, hsa-miR-6087, and hsa-miR-4534); and
(5) a combination of SEQ ID NOs: 2, 19, 113, and 160 (markers: hsa-miR-6836-3p, hsa-miR-3184-5p, hsa-miR-6717-5p, and hsa-miR-6087).

[0508] Non-limiting examples of the combination of the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 561 or a complementary sequence thereof with polynucleotides consisting of nucleotide sequences represented by SEQ ID NOs of five polynucleotides selected from the cancer type-specific polynucleotide group 1 or complementary sequences thereof will be further listed below.

(1) a combination of SEQ ID NOs: 113,125, 130, and 561 (markers: hsa-miR-6717-5p, hsa-miR-614, hsa-miR-223-3p, and hsa-miR-6073);
(2) a combination of SEQ ID NOs: 7, 126, 143, and 561 (markers: hsa-miR-4258, hsa-miR-19b-3p, hsa-miR-4443, and hsa-miR-6073);
(3) a combination of SEQ ID NOs: 1, 113, and 126, 561 (markers: hsa-miR-6768-5p, hsa-miR-6717-5p, hsa-miR-19b-3p, and hsa-miR-6073);
(4) a combination of SEQ ID NOs: 1, 126, 561, and 568 (markers: hsa-miR-6768-5p, hsa-miR-19b-3p, hsa-miR-6073, and hsa-miR-296-3p); and
(5) a combination of SEQ ID NOs: 7, 113, 126, and 561 (markers: hsa-miR-4258, hsa-miR-6717-5p, hsa-miR-19b-3p, and hsa-miR-6073).

[0509] Non-limiting examples of the combination of the polynucleotide consisting of the nucleotide sequence repre-

sented by SEQ ID NO: 568 or a complementary sequence thereof with polynucleotides consisting of nucleotide sequences represented by SEQ ID NOs of five polynucleotides selected from the cancer type-specific polynucleotide group 1 or complementary sequences thereof will be further listed below.

(1) a combination of SEQ ID NOs: 7, 125, 126, and 568 (markers: hsa-miR-4258, hsa-miR-614, hsa-miR-19b-3p, and hsa-miR-296-3p);
(2) a combination of SEQ ID NOs: 124, 125, 126, and 568 (markers: hsa-miR-187-5p, hsa-miR-614, hsa-miR-19b-3p, and hsa-miR-296-3p);
(3) a combination of SEQ ID NOs: 7, 113, 125, and 568 (markers: hsa-miR-4258, hsa-miR-6717-5p, hsa-miR-614, and hsa-miR-296-3p);
(4) a combination of SEQ ID NOs: 1, 113, 125, and 568 (markers: hsa-miR-6768-5p, hsa-miR-6717-5p, hsa-miR-614, and hsa-miR-296-3p); and
(5) a combination of SEQ ID NOs: 113,125, 128, and 568 (markers: hsa-miR-6717-5p, hsa-miR-614, hsa-miR-451a, and hsa-miR-296-3p).

[0510] Non-limiting examples of the combination of the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 573 or a complementary sequence thereof with polynucleotides consisting of nucleotide sequences represented by SEQ ID NOs of five polynucleotides selected from the cancer type-specific polynucleotide group 1 or complementary sequences thereof will be further listed below.

(1) a combination of SEQ ID NOs: 113,125, 126, and 573 (markers: hsa-miR-6717-5p, hsa-miR-614, hsa-miR-19b-3p, and hsa-miR-1202);
(2) a combination of SEQ ID NOs: 1, 113, 125, and 573 (markers: hsa-miR-6768-5p, hsa-miR-6717-5p, hsa-miR-614, and hsa-miR-1202);
(3) a combination of SEQ ID NOs: 1, 53, 113, and 573 (markers: hsa-miR-6768-5p, hsa-miR-6088, hsa-miR-6717-5p, and hsa-miR-1202);
(4) a combination of SEQ ID NOs: 1, 124, 126, and 573 (markers: hsa-miR-6768-5p, hsa-miR-187-5p, hsa-miR-19b-3p, and hsa-miR-1202); and
(5) a combination of SEQ ID NOs: 1, 63, 130, and 573 (markers: hsa-miR-6768-5p, hsa-miR-3162-5p, hsa-miR-223-3p, and hsa-miR-1202).

[0511] Non-limiting examples of the combination of the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 578 or a complementary sequence thereof with polynucleotides consisting of nucleotide sequences represented by SEQ ID NOs of five polynucleotides selected from the cancer type-specific polynucleotide group 1 or complementary sequences thereof will be further listed below.

(1) a combination of SEQ ID NOs: 1, 126, 567, and 578 (markers: hsa-miR-6768-5p, hsa-miR-19b-3p, hsa-miR-940, and hsa-miR-4534);
(2) a combination of SEQ ID NOs: 1, 19, 113, and 578 (markers: hsa-miR-6768-5p, hsa-miR-3184-5p, hsa-miR-6717-5p, and hsa-miR-4534);
(3) a combination of SEQ ID NOs: 31, 126, 561, and 578 (markers: hsa-miR-6889-5p, hsa-miR-19b-3p, hsa-miR-6073, and hsa-miR-4534);
(4) a combination of SEQ ID NOs: 1, 126, 160, and 578 (markers: hsa-miR-6768-5p, hsa-miR-19b-3p, hsa-miR-6087, and hsa-miR-4534); and
(5) a combination of SEQ ID NOs: 1, 113, 125, 578 (markers: hsa-miR-6768-5p, hsa-miR-6717-5p, hsa-miR-614, and hsa-miR-4534).

[0512] The kit or the device of the present invention can also contain a polynucleotide that is already known or that will be found in the future, to enable detection of lung cancer, in addition to the polynucleotide(s) (which can include the variant(s), the fragment(s), and the derivative(s)) according to the present invention described above.

[0513] The kit of the present invention can also contain an antibody for measuring a marker for lung cancer examination known in the art, such as CEA, or CYFRA21-1, in addition to the polynucleotide(s) according to the present invention described above.

[0514] These polynucleotides contained in the kit of the present invention can be packaged in different containers either individually or in any combination.

[0515] The kit of the present invention can contain a kit for extracting a nucleic acid (e.g., total RNA) from body fluids, cells, or tissues, a fluorescent material for labeling, an enzyme and a medium for nucleic acid amplification, an instruction manual, etc.

[0516] The device of the present invention is a device for cancer marker measurement in which nucleic acids such as the polynucleotides according to the present invention described above are bonded or attached to, for example, a solid phase. Examples of the material for the solid phase include plastics, paper, glass, and silicon. The material for the solid phase is preferably a plastic from the viewpoint of easy processability. The solid phase has any shape and is, for example, square, round, reed-shaped, or film-shaped. The device of the present invention includes, for example, a device for measurement by a hybridization technique. Specific examples thereof include blotting devices and nucleic acid arrays (e.g., microarrays, DNA chips, and RNA chips).

[0517] The nucleic acid array technique is a technique which involves bonding or attaching the nucleic acids one by one by use of a method [e.g., a method of spotting the nucleic acids using a high-density dispenser called spotter or arrayer onto the surface of the solid phase surface-treated, if necessary, by coating with L-lysine or the introduction of a functional group such as an amino group or a carboxyl group, a method of spraying the nucleic acids onto the solid phase using an inkjet which injects very small liquid droplets by a piezoelectric element or the like from a nozzle, or a method of sequentially synthesizing nucleotides on the solid phase] to prepare an array such as a chip and measuring a target nucleic acid through the use of hybridization using this array.

[0518] The kit or the device of the present invention comprises nucleic acids capable of specifically binding to the polynucleotides of at least one or more, preferably at least two or more, more preferably at least three or more, most preferably at least five or more to all of the lung cancer marker miRNAs, respectively, of the group 1 described above. The kit or the device of the present invention can optionally further comprise nucleic acids capable of specifically binding to the polynucleotides of at least one or more, preferably at least two or more, more preferably at least three or more, most preferably at least five or more to all of the lung cancer marker miRNAs, respectively, of the group 2 described above. The kit or the device of the present invention can optionally further comprise nucleic acids capable of specifically binding to the polynucleotides of at least one or more, preferably at least two or more, more preferably at least three or more, most preferably at least five or more to all of the lung cancer marker miRNAs, respectively, of the group 3 described above.

[0519] The kit or the device of the present invention can be used for detecting lung cancer as described in Section 4 below.

4. Method for detecting lung cancer

[0520] The present invention further provides a method for detecting lung cancer, comprising using the kit or the device of the present invention (including the aforementioned nucleic acid(s) that can be used in the present invention) described in Section 3 above to measure an expression level(s) of one or more lung cancer-derived gene(s) represented by an expression level(s) of lung cancer-derived gene(s) selected from hsa-miR-6768-5p, optionally in combination with any from the following group hsa-miR-6836-3p, hsa-miR-6782-5p, hsa-miR-3663-3p, hsa-miR-1908-3p, hsa-miR-6726-5p, hsa-miR-4258, hsa-miR-1343-3p, hsa-miR-4516, hsa-miR-6875-5p, hsa-miR-4651, hsa-miR-6825-5p, hsa-miR-6840-3p, hsa-miR-6780b-5p, hsa-miR-6749-5p, hsa-miR-8063, hsa-miR-6784-5p, hsa-miR-3679-5p, hsa-miR-3184-5p, hsa-miR-663b, hsa-miR-6880-5p, hsa-miR-1908-5p, hsa-miR-92a-2-5p, hsa-miR-7975, hsa-miR-7110-5p, hsa-miR-6842-5p, hsa-miR-6857-5p, hsa-miR-5572, hsa-miR-3197, hsa-miR-6131, hsa-miR-6889-5p, hsa-miR-4454, hsa-miR-1199-5p, hsa-miR-1247-3p, hsa-miR-6800-5p, hsa-miR-6872-3p, hsa-miR-4649-5p, hsa-miR-6791-5p, hsa-miR-4433b-3p, hsa-miR-3135b, hsa-miR-128-2-5p, hsa-miR-4675, hsa-miR-4472, hsa-miR-6785-5p, hsa-miR-6741-5p, hsa-miR-7977, hsa-miR-3665, hsa-miR-128-1-5p, hsa-miR-4286, hsa-miR-6765-3p, hsa-miR-4632-5p, hsa-miR-365a-5p, hsa-miR-6088, hsa-miR-6816-5p, hsa-miR-6885-5p, hsa-miR-711, hsa-miR-6765-5p, hsa-miR-3180, hsa-miR-4442, hsa-miR-4792, hsa-miR-6721-5p, hsa-miR-6798-5p, hsa-miR-3162-5p, hsa-miR-6126, hsa-miR-4758-5p, hsa-miR-2392, hsa-miR-486-3p, hsa-miR-6727-5p, hsa-miR-4728-5p, hsa-miR-6746-5p, hsa-miR-4270, hsa-miR-3940-5p, hsa-miR-4725-3p, hsa-miR-7108-5p, hsa-miR-3656, hsa-miR-6879-5p, hsa-miR-6738-5p, hsa-miR-1260a, hsa-miR-4446-3p, hsa-miR-3131, hsa-miR-4463, hsa-miR-3185, hsa-miR-6870-5p, hsa-miR-6779-5p, hsa-miR-1273g-3p, hsa-miR-8059, hsa-miR-4697-5p, hsa-miR-4674, hsa-miR-4433-3p, hsa-miR-4257, hsa-miR-1915-5p, hsa-miR-4417, hsa-miR-1343-5p, hsa-miR-6781-5p, hsa-miR-4695-5p, hsa-miR-1237-5p, hsa-miR-6775-5p, hsa-miR-7845-5p, hsa-miR-4746-3p, hsa-miR-7641, hsa-miR-7847-3p, hsa-miR-6806-5p, hsa-miR-4467, hsa-miR-4726-5p, hsa-miR-4648, hsa-miR-6089, hsa-miR-1260b, hsa-miR-4532, hsa-miR-5195-3p, hsa-miR-3188, hsa-miR-6848-5p, hsa-miR-1233-5p, hsa-miR-6717-5p, hsa-miR-3195, hsa-miR-6757-5p, hsa-miR-8072, hsa-miR-4745-5p, hsa-miR-6511a-5p, hsa-miR-6776-5p, hsa-miR-371a-5p, hsa-miR-1227-5p, hsa-miR-7150, hsa-miR-1915-3p, hsa-miR-187-5p, hsa-miR-614, hsa-miR-1225-5p, hsa-miR-451a, hsa-miR-939-5p, hsa-miR-223-3p, hsa-miR-125a-3p, hsa-miR-92b-5p, hsa-miR-22-3p, hsa-miR-6073, hsa-miR-6845-5p, hsa-miR-6769b-5p, hsa-miR-4665-3p, hsa-miR-1913, hsa-miR-1228-3p, hsa-miR-940, hsa-miR-296-3p, hsa-miR-4690-5p, hsa-miR-548q, hsa-miR-663a, hsa-miR-1249, hsa-miR-1202, hsa-miR-7113-3p, hsa-miR-1225-3p, hsa-miR-4783-3p, hsa-miR-4448 and hsa-miR-4534, optionally an expression level of lung cancer-derived gene(s) selected from the following group B: hsa-miR-19b-3p, hsa-miR-1228-5p, and hsa-miR-1307-3p, and optionally an expression level of lung cancer-derived gene(s) selected from the following group C: hsa-miR-4271,

hsa-miR-642b-3p, hsa-miR-6075, hsa-miR-6125, hsa-miR-887-3p, hsa-miR-6851-5p, hsa-miR-6763-5p, hsa-miR-3928-3p, hsa-miR-4443, hsa-miR-3648, hsa-miR-149-3p, hsa-miR-4689, hsa-miR-4763-3p, hsa-miR-6729-5p, hsa-miR-3196, hsa-miR-8069, hsa-miR-1268a, hsa-miR-4739, hsa-miR-1268b, hsa-miR-5698, hsa-miR-6752-5p, hsa-miR-4507, hsa-miR-564, hsa-miR-4497, hsa-miR-6877-5p, hsa-miR-6087, hsa-miR-4731-5p, hsa-miR-615-5p, hsa-miR-760, hsa-miR-6891-5p, hsa-miR-6887-5p, hsa-miR-4525, hsa-miR-1914-3p, hsa-miR-619-5p, hsa-miR-5001-5p, hsa-miR-6722-3p, hsa-miR-3621, hsa-miR-4298, hsa-miR-675-5p and hsa-miR-4655-5p in a sample *in vitro,* further comparing, for example, the expression level(s) of the aforementioned gene(s) in the sample (e.g., blood, serum, or plasma) collected from a subject who is suspected of having lung cancer with a control expression level in the sample collected from a healthy subject (including a non-lung cancer patient), and evaluating the subject as having lung cancer when the expression level(s) of the target nucleic acid(s) is statistically significantly different between the samples.

[0521] This method of the present invention permits limitedly-invasive early diagnosis of cancer with high sensitivity and specificity, and thereby brings about early treatment and improved prognosis. In addition, exacerbation of the disease or the effectiveness of surgical, radiotherapeutic, and chemotherapeutic treatments can be monitored.

[0522] The method for extracting the lung cancer-derived gene from the sample such as blood, serum, or plasma according to the present invention is particularly preferably prepared by the addition of a reagent for RNA extraction in 3D-Gene(™) RNA extraction reagent from liquid sample kit (Toray Industries, Inc.). A general acidic phenol method (acid guanidinium-phenolchloroform (AGPC)) may be used, or Trizol(™) (Life Technologies Corp.) may be used. The lung cancer-derived gene may be prepared by the addition of a reagent for RNA extraction containing acidic phenol, such as Trizol (Life Technologies Corp.) or Isogen (Nippon Gene Co., Ltd.). Alternatively, a kit such as miRNeasy(™) Mini Kit (Qiagen N.V.) can be used, though the method is not limited thereto.

[0523] The present invention also provides use of the kit or the device of the present invention for detecting *in vitro* an expression product of a lung cancer-derived miRNA gene in a sample derived from a subject.

[0524] In the method of the present invention, a kit or a device comprising, each alone or in every possible composition, the polynucleotides that can be used in the present invention as described above is used as the kit or the device.

[0525] In the detection or (genetic) diagnosis of lung cancer according to the present invention, each polynucleotide contained in the kit or the device of the present invention can be used as a probe or a primer. In the case of using the polynucleotide as a primer, TaqMan(™) MicroRNA Assays from Life Technologies Corp., miScript PCR System from Qiagen N.V., or the like can be used, though the method is not limited thereto.

[0526] The polynucleotide contained in the kit or the device of the present invention can be used as a primer or a probe according to a routine method in a method known in the art for specifically detecting the particular gene, for example, a hybridization technique such as Northern blot, Southern blot, *in situ* hybridization, Northern hybridization, or Southern hybridization, or a quantitative amplification technique such as quantitative RT-PCR. A body fluid such as blood, serum, plasma, or urine from a subject is collected as a sample to be assayed according to the type of the detection method used. Alternatively, total RNA prepared from such a body fluid by the method described above may be used, and various polynucleotides including cDNA prepared on the basis of the RNA may be used.

[0527] The kit or the device of the present invention is useful for the diagnosis of lung cancer or the detection of the presence or absence of lung cancer. Specifically, the detection of lung cancer using the kit or the device can be performed by detecting *in vitro* an expression level of a gene using the nucleic acid probe or the primer contained in the kit or the device in a sample such as blood, serum, plasma, or urine from a subject suspected of having lung cancer. The subject suspected of having lung cancer can be evaluated as having lung cancer when the expression level of a target miRNA marker measured using polynucleotide(s) (including a variant(s), a fragment(s), and a derivative(s) thereof) consisting of a nucleotide sequence represented by SEQ ID NO: 1 optionally in combination with one or more of SEQ ID NOs 2 to 125, 127 to 130, 132 to 134 and 561 to 578 or a complementary sequence thereof, optionally a nucleotide sequence represented by one or more of SEQ ID NOs: 126 and 131 or a complementary sequence thereof, and optionally a nucleotide sequence represented by one or more of SEQ ID NOs: 135 to 174 or a complementary sequence thereof in the sample such as blood, serum, plasma, or urine of the subject is statistically significantly different from the expression level thereof in the sample such as blood, serum, or plasma, or urine of a healthy subject.

[0528] The method of the present invention can be combined with chest X-ray examination as well as a diagnostic imaging method such as CT, MRI, or PET. The method of the present invention is capable of specifically detecting lung cancer and can substantially discriminate lung cancer from the other cancers.

[0529] The method for detecting the absence of an expression product of a lung cancer-derived gene or the presence of the expression product of a lung cancer-derived gene in a sample using the kit or the device of the present invention comprises collecting a body fluid such as blood, serum, plasma, or urine from a subject, and measuring the expression level of the target gene contained therein using one or more polynucleotide(s) (including a variant(s), a fragment(s), and a derivative(s)) selected from the polynucleotide group of the present invention, to evaluate the presence or absence of lung cancer or to detect lung cancer. Using the method for detecting lung cancer according to the present invention, for example, the presence or absence of amelioration of the disease or the degree of amelioration thereof in a lung cancer patient given a therapeutic drug for the amelioration of the disease can be also evaluated or diagnosed.

[0530] The method of the present invention can comprise, for example, the following steps (a), (b), and (c):

(a) a step of contacting a sample derived from a subject with a polynucleotide in the kit or the device of the present invention *in vitro;*
(b) a step of measuring an expression level of the target nucleic acid in the sample using the polynucleotide as a nucleic acid probe or a primer; and
(c) a step of evaluating the presence or absence of lung cancer (cells) in the subject on the basis of the step (b).

[0531] Specifically, the present invention provides a method for detecting lung cancer, comprising measuring an expression level of a target nucleic acid in a sample of a subject using a nucleic acid capable of specifically binding to at least one or more (preferably at least two or more) polynucleotide(s) selected from miR-6768-5p, optionally in combination with any of the group consisting of miR-6836-3p, miR-6782-5p, miR-3663-3p, miR-1908-3p, miR-6726-5p, miR-4258, miR-1343-3p, miR-4516, miR-6875-5p, miR-4651, miR-6825-5p, miR-6840-3p, miR-6780b-5p, miR-6749-5p, miR-8063, miR-6784-5p, miR-3679-5p, miR-3184-5p, miR-663b, miR-6880-5p, miR-1908-5p, miR-92a-2-5p, miR-7975, miR-7110-5p, miR-6842-5p, miR-6857-5p, miR-5572, miR-3197, miR-6131, miR-6889-5p, miR-4454, miR-1199-5p, miR-1247-3p, miR-6800-5p, miR-6872-3p, miR-4649-5p, miR-6791-5p, miR-4433b-3p, miR-3135b, miR-128-2-5p, miR-4675, miR-4472, miR-6785-5p, miR-6741-5p, miR-7977, miR-3665, miR-128-1-5p, miR-4286, miR-6765-3p, miR-4632-5p, miR-365a-5p, miR-6088, miR-6816-5p, miR-6885-5p, miR-711, miR-6765-5p, miR-3180, miR-4442, miR-4792, miR-6721-5p, miR-6798-5p, miR-3162-5p, miR-6126, miR-4758-5p, miR-2392, miR-486-3p, miR-6727-5p, miR-4728-5p, miR-6746-5p, miR-4270, miR-3940-5p, miR-4725-3p, miR-7108-5p, miR-3656, miR-6879-5p, miR-6738-5p, miR-1260a, miR-4446-3p, miR-3131, miR-4463, miR-3185, miR-6870-5p, miR-6779-5p, miR-1273g-3p, miR-8059, miR-4697-5p, miR-4674, miR-4433-3p, miR-4257, miR-1915-5p, miR-4417, miR-1343-5p, miR-6781-5p, miR-4695-5p, miR-1237-5p, miR-6775-5p, miR-7845-5p, miR-4746-3p, miR-7641, miR-7847-3p, miR-6806-5p, miR-4467, miR-4726-5p, miR-4648, miR-6089, miR-1260b, miR-4532, miR-5195-3p, miR-3188, miR-6848-5p, miR-1233-5p, miR-6717-5p, miR-3195, miR-6757-5p, miR-8072, miR-4745-5p, miR-6511a-5p, miR-6776-5p, miR-371a-5p, miR-1227-5p, miR-7150, miR-1915-3p, miR-187-5p, miR-614, miR-1225-5p, miR-451a, miR-939-5p, miR-223-3p, miR-125a-3p, miR-92b-5p, miR-22-3p, miR-6073, miR-6845-5p, miR-6769b-5p, miR-4665-3p, miR-1913, miR-1228-3p, miR-940, miR-296-3p, miR-4690-5p, miR-548q, miR-663a, miR-1249, miR-1202, miR-7113-3p, miR-1225-3p, miR-4783-3p, miR-4448 and miR-4534, and evaluating *in vitro* whether or not the subject has lung cancer using the measured expression level and a control expression level of a healthy subject measured in the same way as above.

[0532] As used herein, the term "evaluation" is evaluation support based on results of *in vitro* examination, not physician's judgment.

[0533] As described above, as for the target nucleic acids in a preferred embodiment of the method of the present invention, specifically, miR-6768-5p is hsa-miR-6768-5p, miR-6836-3p is hsa-miR-6836-3p, miR-6782-5p is hsa-miR-6782-5p, miR-3663-3p is hsa-miR-3663-3p, miR-1908-3p is hsa-miR-1908-3p, miR-6726-5p is hsa-miR-6726-5p, miR-4258 is hsa-miR-4258, miR-1343-3p is hsa-miR-1343-3p, miR-4516 is hsa-miR-4516, miR-6875-5p is hsa-miR-6875-5p, miR-4651 is hsa-miR-4651, miR-6825-5p is hsa-miR-6825-5p, miR-6840-3p is hsa-miR-6840-3p, miR-6780b-5p is hsa-miR-6780b-5p, miR-6749-5p is hsa-miR-6749-5p, miR-8063 is hsa-miR-8063, miR-6784-5p is hsa-miR-6784-5p, miR-3679-5p is hsa-miR-3679-5p, miR-3184-5p is hsa-miR-3184-5p, miR-663b is hsa-miR-663b, miR-6880-5p is hsa-miR-6880-5p, miR-1908-5p is hsa-miR-1908-5p, miR-92a-2-5p is hsa-miR-92a-2-5p, miR-7975 is hsa-miR-7975, miR-7110-5p is hsa-miR-7110-5p, miR-6842-5p is hsa-miR-6842-5p, miR-6857-5p is hsa-miR-6857-5p, miR-5572 is hsa-miR-5572, miR-3197 is hsa-miR-3197, miR-6131 is hsa-miR-6131, miR-6889-5p is hsa-miR-6889-5p, miR-4454 is hsa-miR-4454, miR-1199-5p is hsa-miR-1199-5p, miR-1247-3p is hsa-miR-1247-3p, miR-6800-5p is hsa-miR-6800-5p, miR-6872-3p is hsa-miR-6872-3p, miR-4649-5p is hsa-miR-4649-5p, miR-6791-5p is hsa-miR-6791-5p, miR-4433b-3p is hsa-miR-4433b-3p, miR-3135b is hsa-miR-3135b, miR-128-2-5p is hsa-miR-128-2-5p, miR-4675 is hsa-miR-4675, miR-4472 is hsa-miR-4472, miR-6785-5p is hsa-miR-6785-5p, miR-6741-5p is hsa-miR-6741-5p, miR-7977 is hsa-miR-7977, miR-3665 is hsa-miR-3665, miR-128-1-5p is hsa-miR-128-1-5p, miR-4286 is hsa-miR-4286, miR-6765-3p is hsa-miR-6765-3p, miR-4632-5p is hsa-miR-4632-5p, miR-365a-5p is hsa-miR-365a-5p, miR-6088 is hsa-miR-6088, miR-6816-5p is hsa-miR-6816-5p, miR-6885-5p is hsa-miR-6885-5p, miR-711 is hsa-miR-711, miR-6765-5p is hsa-miR-6765-5p, miR-3180 is hsa-miR-3180, miR-4442 is hsa-miR-4442, miR-4792 is hsa-miR-4792, miR-6721-5p is hsa-miR-6721-5p, miR-6798-5p is hsa-miR-6798-5p, miR-3162-5p is hsa-miR-3162-5p, miR-6126 is hsa-miR-6126, miR-4758-5p is hsa-miR-4758-5p, miR-2392 is hsa-miR-2392, miR-486-3p is hsa-miR-486-3p, miR-6727-5p is hsa-miR-6727-5p, miR-4728-5p is hsa-miR-4728-5p, miR-6746-5p is hsa-miR-6746-5p, miR-4270 is hsa-miR-4270, miR-3940-5p is hsa-miR-3940-5p, miR-4725-3p is hsa-miR-4725-3p, miR-7108-5p is hsa-miR-7108-5p, miR-3656 is hsa-miR-3656, miR-6879-5p is hsa-miR-6879-5p, miR-6738-5p is hsa-miR-6738-5p, miR-1260a is hsa-miR-1260a, miR-4446-3p is hsa-miR-4446-3p, miR-3131 is hsa-miR-3131, miR-4463 is hsa-miR-4463, miR-3185 is hsa-miR-3185, miR-6870-5p is hsa-miR-6870-5p, miR-6779-5p is hsa-miR-6779-5p, miR-1273g-3p is hsa-miR-1273g-3p, miR-8059 is hsa-miR-8059, miR-4697-5p is hsa-miR-4697-5p, miR-4674 is hsa-miR-4674, miR-4433-3p is hsa-miR-4433-3p, miR-4257 is hsa-miR-4257, miR-

1915-5p is hsa-miR-1915-5p, miR-4417 is hsa-miR-4417, miR-1343-5p is hsa-miR-1343-5p, miR-6781-5p is hsa-miR-6781-5p, miR-4695-5p is hsa-miR-4695-5p, miR-1237-5p is hsa-miR-1237-5p, miR-6775-5p is hsa-miR-6775-5p, miR-7845-5p is hsa-miR-7845-5p, miR-4746-3p is hsa-miR-4746-3p, miR-7641 is hsa-miR-7641, miR-7847-3p is hsa-miR-7847-3p, miR-6806-5p is hsa-miR-6806-5p, miR-4467 is hsa-miR-4467, miR-4726-5p is hsa-miR-4726-5p, miR-4648 is hsa-miR-4648, miR-6089 is hsa-miR-6089, miR-1260b is hsa-miR-1260b, miR-4532 is hsa-miR-4532, miR-5195-3p is hsa-miR-5195-3p, miR-3188 is hsa-miR-3188, miR-6848-5p is hsa-miR-6848-5p, miR-1233-5p is hsa-miR-1233-5p, miR-6717-5p is hsa-miR-6717-5p, miR-3195 is hsa-miR-3195, miR-6757-5p is hsa-miR-6757-5p, miR-8072 is hsa-miR-8072, miR-4745-5p is hsa-miR-4745-5p, miR-6511a-5p is hsa-miR-6511a-5p, miR-6776-5p is hsa-miR-6776-5p, miR-371a-5p is hsa-miR-371a-5p, miR-1227-5p is hsa-miR-1227-5p, miR-7150 is hsa-miR-7150, miR-1915-3p is hsa-miR-1915-3p, miR-187-5p is hsa-miR-187-5p, miR-614 is hsa-miR-614, miR-1225-5p is hsa-miR-1225-5p, miR-451a is hsa-miR-451a, miR-939-5p is hsa-miR-939-5p, miR-223-3p is hsa-miR-223-3p, miR-125a-3p is hsa-miR-125a-3p, miR-92b-5p is hsa-miR-92b-5p, miR-22-3p is hsa-miR-22-3p, miR-6073 is hsa-miR-6073, miR-6845-5p is hsa-miR-6845-5p, miR-6769b-5p is hsa-miR-6769b-5p, miR-4665-3p is hsa-miR-4665-3p, miR-1913 is hsa-miR-1913, miR-1228-3p is hsa-miR-1228-3p, miR-940 is hsa-miR-940, miR-296-3p is hsa-miR-296-3p, miR-4690-5p is hsa-miR-4690-5p, miR-548q is hsa-miR-548q, miR-663a is hsa-miR-663a, miR-1249 is hsa-miR-1249, miR-1202 is hsa-miR-1202, miR-7113-3p is hsa-miR-7113-3p, miR-1225-3p is hsa-miR-1225-3p, miR-4783-3p is hsa-miR-4783-3p, miR-4448 is hsa-miR-4448, and miR-4534 is hsa-miR-4534.

[0534] In a preferred embodiment of the method of the present invention, specifically, the nucleic acid (specifically, probe or primer) is selected from the group consisting of the following polynucleotides (a) to (e):

(a) a polynucleotide consisting of a nucleotide sequence represented by SEQ ID NO: 1 optionally in combination with any of SEQ ID NOs 2 to 125, 127 to 130, 132 to 134, and 561 to 578 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, a variant thereof, a derivative thereof, or a fragment thereof comprising 15 or more consecutive nucleotides,
(b) a polynucleotide comprising a nucleotide sequence represented by SEQ ID NO: 1 optionally in combination with any of SEQ ID NOs 2 to 125, 127 to 130, 132 to 134, and 561 to 578,
(c) a polynucleotide consisting of a nucleotide sequence complementary to a nucleotide sequence represented by SEQ ID NO: 1 optionally in combination with any of SEQ ID NOs 2 to 125, 127 to 130, 132 to 134, and 561 to 578 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, a variant thereof, a derivative thereof, or a fragment thereof comprising 15 or more consecutive nucleotides,
(d) a polynucleotide comprising a nucleotide sequence complementary to a nucleotide sequence represented by SEQ ID NO: 1 optionally in combination with any of SEQ ID NOs 2 to 125, 127 to 130, 132 to 134, and 561 to 578 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, and
(e) a polynucleotide hybridizing under stringent conditions to any of the polynucleotides (a) to (d).

[0535] The method of the present invention can further employ a nucleic acid capable of specifically binding to at least one or more polynucleotide(s) selected from the group consisting of miR-19b-3p, miR-1228-5p, and miR-1307-3p.

[0536] As for such a nucleic acid, specifically, miR-19b-3p is hsa-miR-19b-3p, miR-1228-5p is hsa-miR-1228-5p, and miR-1307-3p is hsa-miR-1307-3p.

[0537] In a preferred embodiment, such a nucleic acid is specifically selected from the group consisting of the following polynucleotides (f) to (j):

(f) a polynucleotide consisting of a nucleotide sequence represented by any of SEQ ID NOs: 126, 131, and 579 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, a variant thereof, a derivative thereof, or a fragment thereof comprising 15 or more consecutive nucleotides,
(g) a polynucleotide comprising a nucleotide sequence represented by any of SEQ ID NOs: 126, 131, and 579,
(h) a polynucleotide consisting of a nucleotide sequence complementary to a nucleotide sequence represented by any of SEQ ID NOs: 126, 131, and 579 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, a variant thereof, a derivative thereof, or a fragment thereof comprising 15 or more consecutive nucleotides,
(i) a polynucleotide comprising a nucleotide sequence complementary to a nucleotide sequence represented by any of SEQ ID NOs: 126, 131, and 579 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, and
(j) a polynucleotide hybridizing under stringent conditions to any of the polynucleotides (f) to (i).

[0538] The nucleic acid further used in the method of the present invention can comprise a nucleic acid capable of specifically binding to at least one or more polynucleotide(s) selected from the group consisting of miR-4271, miR-642b-3p, miR-6075, miR-6125, miR-887-3p, miR-6851-5p, miR-6763-5p, miR-3928-3p, miR-4443, miR-3648, miR-149-3p,

miR-4689, miR-4763-3p, miR-6729-5p, miR-3196, miR-8069, miR-1268a, miR-4739, miR-1268b, miR-5698, miR-6752-5p, miR-4507, miR-564, miR-4497, miR-6877-5p, miR-6087, miR-4731-5p, miR-615-5p, miR-760, miR-6891-5p, miR-6887-5p, miR-4525, miR-1914-3p, miR-619-5p, miR-5001-5p, miR-6722-3p, miR-3621, miR-4298, miR-675-5p and miR-4655-5p.

[0539] As for such a nucleic acid, specifically, miR-4271 is hsa-miR-4271, miR-642b-3p is hsa-miR-642b-3p, miR-6075 is hsa-miR-6075, miR-6125 is hsa-miR-6125, miR-887-3p is hsa-miR-887-3p, miR-6851-5p is hsa-miR-6851-5p, miR-6763-5p is hsa-miR-6763-5p, miR-3928-3p is hsa-miR-3928-3p, miR-4443 is hsa-miR-4443, miR-3648 is hsa-miR-3648, miR-149-3p is hsa-miR-149-3p, miR-4689 is hsa-miR-4689, miR-4763-3p is hsa-miR-4763-3p, miR-6729-5p is hsa-miR-6729-5p, miR-3196 is hsa-miR-3196, miR-8069 is hsa-miR-8069, miR-1268a is hsa-miR-1268a, miR-4739 is hsa-miR-4739, miR-1268b is hsa-miR-1268b, miR-5698 is hsa-miR-5698, miR-6752-5p is hsa-miR-6752-5p, miR-4507 is hsa-miR-4507, miR-564 is hsa-miR-564, miR-4497 is hsa-miR-4497, miR-6877-5p is hsa-miR-6877-5p, miR-6087 is hsa-miR-6087, miR-4731-5p is hsa-miR-4731-5p, miR-615-5p is hsa-miR-615-5p, miR-760 is hsa-miR-760, miR-6891-5p is hsa-miR-6891-5p, miR-6887-5p is hsa-miR-6887-5p, miR-4525 is hsa-miR-4525, miR-1914-3p is hsa-miR-1914-3p, miR-619-5p is hsa-miR-619-5p, miR-5001-5p is hsa-miR-5001-5p, miR-6722-3p is hsa-miR-6722-3p, miR-3621 is hsa-miR-3621, miR-4298 is hsa-miR-4298, miR-675-5p is hsa-miR-675-5p, and miR-4655-5p is hsa-miR-4655-5p.

[0540] In a preferred embodiment, such a nucleic acid is specifically a polynucleotide selected from the group consisting of the following polynucleotides (k) to (o):

(k) a polynucleotide consisting of a nucleotide sequence represented by any of SEQ ID NOs: 135 to 174 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, a variant thereof, a derivative thereof, or a fragment thereof comprising 15 or more consecutive nucleotides,
(l) a polynucleotide comprising a nucleotide sequence represented by any of SEQ ID NOs: 135 to 174,
(m) a polynucleotide consisting of a nucleotide sequence complementary to a nucleotide sequence represented by any of SEQ ID NOs: 135 to 174 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, a variant thereof, a derivative thereof, or a fragment thereof comprising 15 or more consecutive nucleotides,
(n) a polynucleotide comprising a nucleotide sequence complementary to a nucleotide sequence represented by any of SEQ ID NOs: 135 to 174 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, and
(o) a polynucleotide hybridizing under stringent conditions to any of the polynucleotides (k) to (n).

[0541] Examples of the sample used in the method of the present invention can include samples prepared from a living tissue (preferably a lung tissue) or a body fluid such as blood, serum, plasma, or urine from the subject. Specifically, for example, an RNA-containing sample prepared from the tissue, a polynucleotide-containing sample further prepared therefrom, a body fluid such as blood, serum, plasma, or urine, a portion or the whole of a living tissue collected from the subject by biopsy or the like, or a living tissue excised by surgery can be used, and the sample for measurement can be prepared therefrom.

[0542] As used herein, the subject refers to a mammal, for example, a human, a monkey, a mouse and a rat, without any limitation, and is preferably a human.

[0543] The steps of the method of the present invention can be changed according to the type of the sample to be assayed.

[0544] In the case of using RNA as an analyte, the detection of lung cancer (cells) can comprise, for example, the following steps (a), (b), and (c):

(a) a step of binding RNA prepared from the sample of the subject or a complementary polynucleotide (cDNA) transcribed therefrom to a polynucleotide in the kit or the device of the present invention;
(b) a step of measuring the sample-derived RNA or the cDNA synthesized from the RNA, bound with the polynucleotide by hybridization using the polynucleotide as a nucleic acid probe or by quantitative RT-PCR using the polynucleotide as a primer; and
(c) a step of evaluating the presence or absence of lung cancer (or lung cancer-derived gene expression) on the basis of the measurement results of the step (b).

[0545] For example, various hybridization methods can be used for detecting, examining, evaluating, or diagnosing lung cancer (or lung cancer-derived gene expression) *in vitro* according to the present invention. For example, Northern blot, Southern blot, RT-PCR, DNA chip analysis, *in situ* hybridization, Northern hybridization, or Southern hybridization can be used as such a hybridization method.

[0546] In the case of using the Northern blot, the presence or absence of expression of each gene or the expression level thereof in the RNA can be detected or measured by use of the nucleic acid probe that can be used in the present

invention. Specific examples thereof can include a method which involves labeling the nucleic acid probe (or its complementary strand) with a radioisotope (^{32}P, ^{33}P, ^{35}S, etc.), a fluorescent material, or the like, hybridizing the labeled product with the living tissue-derived RNA from a subject transferred to a nylon membrane or the like according to a routine method, and then detecting and measuring a signal derived from the label (radioisotope or fluorescent material) on the formed DNA/RNA duplex using a radiation detector (examples thereof can include BAS-1800 II (Fujifilm Corp.)) or a fluorescence detector (examples thereof can include STORM 865 (GE Healthcare Japan Corp.)).

[0547] In the case of using the quantitative RT-PCR, the presence or absence of expression of each gene or the expression level thereof in the RNA can be detected or measured by use of the primer that can be used in the present invention. Specific examples thereof can include a method which involves preparing cDNA from the living tissue-derived RNA of a subject according to a routine method, hybridizing a pair of primers (consisting of a plus strand and a reverse strand binding to the cDNA) of the present invention with the cDNA such that the region of each target gene can be amplified with the cDNA as a template, and performing PCR according to a routine method to detect the obtained double-stranded DNA. The method for detecting the double-stranded DNA can include a method of performing the PCR using the primers labeled in advance with a radioisotope or a fluorescent material, a method of electrophoresing the PCR product on an agarose gel and staining the double-stranded DNA with ethidium bromide or the like for detection, and a method of transferring the produced double-stranded DNA to a nylon membrane or the like according to a routine method and hybridizing the double-stranded DNA to a labeled nucleic acid probe for detection.

[0548] In the case of using the nucleic acid array analysis, an RNA chip or a DNA chip in which the nucleic acid probes (single-stranded or double-stranded) of the present invention is attached to a substrate (solid phase) is used. Regions having the attached nucleic acid probes are referred to as probe spots, and regions having no attached nucleic acid probe are referred to as blank spots. A gene group immobilized on a solid-phase substrate is generally called a nucleic acid chip, a nucleic acid array, a microarray, or the like. The DNA or RNA array includes a DNA or RNA macroarray and a DNA or RNA microarray. The term "chip" used herein includes all of them. 3D-Gene(™) Human miRNA Oligo chip (Toray Industries, Inc.) can be used as the DNA chip, though the DNA chip is not limited thereto.

[0549] Examples of the measurement using the DNA chip can include, but are not limited to, a method of detecting and measuring a signal derived from the label on the nucleic acid probes using an image detector (examples thereof can include Typhoon 9410 (GE Healthcare Japan Corp.) and 3D-Gene(™) scanner (Toray Industries, Inc.)).

[0550] The "stringent conditions" used herein are, as mentioned above, conditions under which a nucleic acid probe hybridizes to its target sequence to a larger extent (e.g., a measurement value equal to or larger than a mean of background measurement values + a standard deviation of the background measurement values × 2) than that for other sequences.

[0551] The stringent conditions are defined by hybridization and subsequent washing conditions. The hybridization conditions are not limited and are conditions involving, for example, 30°C to 60°C for 1 to 24 hours in a solution containing SSC, a surfactant, formamide, dextran sulfate, a blocking agent, etc. In this context, 1 × SSC is an aqueous solution (pH 7.0) containing 150 mM sodium chloride and 15 mM sodium citrate. The surfactant includes, for example, SDS (sodium dodecyl sulfate), Triton, or Tween. The hybridization conditions more preferably involve 3 to 10 × SSC and 0.1 to 1% SDS. Examples of the conditions of the washing, following the hybridization, which is another condition to define the stringent conditions, can include conditions involving continuous washing at 30°C in a solution containing 0.5 × SSC and 0.1% SDS, at 30°C in a solution containing 0.2 × SSC and 0.1% SDS, and at 30°C in a 0.05 × SSC solution. It is desirable that the complementary strand should maintain its hybridized state with a target plus strand even by washing under such conditions. Specifically, examples of such a complementary strand can include a strand consisting of a nucleotide sequence in a completely complementary relationship with the nucleotide sequence of the target plus strand, and a strand consisting of a nucleotide sequence having at least 80%, preferably at least 85%, more preferably at least 90% or at least 95%, for example, at least 98% or at least 99% identity to the strand.

[0552] Other examples of the "stringent conditions" for the hybridization are described in, for example, Sambrook, J. & Russel, D., Molecular Cloning, A LABORATORY MANUAL, Cold Spring Harbor Laboratory Press, published on January 15, 2001, Vol. 1, 7.42 to 7.45 and Vol. 2, 8.9 to 8.17, and can be used in the present invention.

[0553] Examples of the conditions for carrying out PCR using a polynucleotide fragment in the kit of the present invention as a primer include treatment for approximately 15 seconds to 1 minute at 5 to 10°C plus a Tm value calculated from the sequence of the primer, using a PCR buffer with composition such as 10 mM Tris-HCL (pH 8.3), 50 mM KCL, and 1 to 2 mM $MgCl_2$. Examples of the method for calculating such a Tm value include Tm value = 2 × (the number of adenine residues + the number of thymine residues) + 4 × (the number of guanine residues + the number of cytosine residues).

[0554] In the case of using the quantitative RT-PCR, a commercially available kit for measurement specially designed for quantitatively measuring miRNA, such as TaqMan(™) MicroRNA Assays (Life Technologies Corp.), LNA(™)-based MicroRNA PCR (Exiqon), or Ncode(™) miRNA qRT-PCT kit (Invitrogen Corp.) may be used.

[0555] For the calculation of gene expression levels, statistical treatment described in, for example, Statistical analysis of gene expression microarray data (Speed T., Chapman and Hall/CRC), and A beginner's guide Microarray gene

expression data analysis (Causton H.C. et al., Blackwell publishing) can be used in the present invention, though the calculation method is not limited thereto. For example, twice, preferably 3 times, more preferably 6 times the standard deviation of the measurement values of the blank spots are added to the average measurement value of the blank spots on the DNA chip, and probe spots having a signal value equal to or larger than the resulting value can be regarded as detection spots. Alternatively, the average measurement value of the blank spots is regarded as a background and can be subtracted from the measurement values of the probe spots to determine gene expression levels. A missing value for a gene expression level can be excluded from the analyte, preferably replaced with the smallest value of the gene expression level in each DNA chip, or more preferably replaced with a value obtained by subtracting 0.1 from a logarithmic value of the smallest value of the gene expression level. In order to eliminate low-signal genes, only a gene having a gene expression level of 2^6, preferably 2^8, more preferably 2^{10} or larger in 20% or more, preferably 50%, more preferably 80% or more of the number of measurement samples can be selected as the analyte. Examples of the normalization of the gene expression level include, but are not limited to, global normalization and quantile normalization (Bolstad, B. M. et al., 2003, Bioinformatics, Vol. 19, p. 185-193).

[0556] The present invention also provides a method comprising measuring a target gene or gene expression level in a sample derived from a subject using the polynucleotide, the kit, or the device (e.g., chip) for detection of the present invention, or a combination thereof, preparing a discriminant (discriminant function) with gene expression levels in a sample derived from a lung cancer patient and a sample derived from a healthy subject as supervising samples, and determining or evaluating the presence and/or absence of the lung cancer-derived gene in the sample.

[0557] Specifically, the present invention further provides the method comprising: a first step of measuring *in vitro* an expression level of a target gene in multiple samples that were known to be able to determine or evaluate the presence and/or absence of the lung cancer-derived gene in the samples, using the polynucleotide, the kit, or the device (e.g., chip) for detection of the present invention, or a combination thereof; a second step of constructing a discriminant with the measurement values of the expression level of the target gene (target nucleic acids) that was obtained in the first step as supervising samples; a third step of measuring *in vitro* an expression level of the target gene in a sample derived from a subject in the same way as in the first step; and a fourth step of assigning the measurement value of the expression level of the target gene obtained in the third step into the discriminant obtained in the second step, and determining or evaluating the presence and/or absence of the lung cancer-derived gene in the sample on the basis of the results obtained from the discriminant, wherein the target gene can be detected using a polynucleotide for the detection, that was contained in the polynucleotide, the kit or the device (e.g., chip). In this context, the discriminant can be prepared by use of Fisher's discriminant analysis, nonlinear discriminant analysis based on Mahalanobis' distance, neural network, Support Vector Machine (SVM), or the like, though the method is not limited thereto.

[0558] When a clustering boundary is a straight line or a hyperplane, the linear discriminant analysis is a method for determining the association of a cluster using Formula 1 as a discriminant. In Formula 1, x represents an explanatory variable, w represents a coefficient of the explanatory variable, and w0 represents a constant term.

$$f(x) = w_0 + \sum_{i=1}^{n} w_i x_i \qquad \text{Formula 1}$$

[0559] Values obtained from the discriminant are referred to as discriminant scores. The measurement values of a newly offered data set can be assigned as explanatory variables to the discriminant to determine clusters by the signs of the discriminant scores.

[0560] The Fisher's discriminant analysis, one type of linear discriminant analysis, is a dimensionality reduction method for selecting a dimension suitable for discriminating classes, and constructs a highly discriminating synthetic variable by focusing on the variance of synthetic variables and minimizing the variance of data having the same label (Venables, W.N. et al., Modern Applied Statistics with S. Fourth edition. Springer., 2002). In the Fisher's linear discriminant analysis, direction w of projection is determined so as to maximize Formula 2. In this Formula, μ represents an average input, ng represents the number of data associate with class g, and μg represents an average input of the data associated with class g. The numerator and the denominator are the inter-classe variance and the intra-classe variance, respectively, when each data is projected in the direction of the vector w. Discriminant coefficient wi is determined by maximizing this ratio (Takafumi Kanamori et al., "Pattern Recognition", Kyoritsu Shuppan Co., Ltd. (2009); and Richard O. et al., Pattern Classification Second Edition., Wiley-Interscience, 2000).

$$J(w)=\frac{\sum_{g=1}^{G} n_g \left(w^T \mu_g - w^T \mu\right)\left(w^T \mu_g - w^T \mu\right)^T}{\sum_{g=1}^{G} \sum_{i:y_i=g} \left(w^T x_i - w^T \mu_g\right)\left(w^T x_i - w^T \mu_g\right)} \qquad \text{Formula 2}$$

$$\mu=\sum_{i=1}^{n} \frac{x_i}{n}, \quad \mu_g = \sum_{i:u_i=g}^{n} \frac{x_i}{n_g}$$

subjectto

[0561] The Mahalanobis' distance is calculated according to Formula 3 in consideration of data correlation and can be used as nonlinear discriminant analysis for determining an associated cluster that shows a closer Mahalanobis' distance from each cluster. In this Formula 3, μ represents a central vector of each cluster, and S-1 represents an inverse matrix of the variance-covariance matrix of the cluster. The central vector is calculated from explanatory variable x, and an average vector, a median value vector, or the like can be used.

$$D(x,\mu)=\left\{(x-\mu)^t S^{-1}(x-\mu)\right\}^{\frac{1}{2}} \qquad \text{Formula 3}$$

[0562] SVM is a discriminant analysis method devised by V. Vapnik (The Nature of Statistical Leaning Theory, Springer, 1995). Particular data points of a data set having known classes are defined as explanatory variables, and classes are defined as objective variables. A boundary plane called hyperplane for correctly classifying the data set into the known classes is determined, and a discriminant for data classification is determined using the boundary plane. Then, the measurement values of a newly offered data set can be assigned as explanatory variables to the discriminant to determine classes. In this respect, the results of the discriminant analysis may be classes, may be a probability of data to be classified into correct classes, or may be the distance from the hyperplane. In SVM, a method of nonlinearly converting a feature vector to a high dimension and performing linear discriminant in the space is known as a method for tackling nonlinear problems. An expression in which an inner product of two factors in a nonlinearly mapped space is expressed only by inputs in their original spaces is called kernel. Examples of the kernel can include a linear kernel, a RBF (Radial Basis Function) kernel, and a Gaussian kernel. While highly dimensional mapping is performed according to the kernel, the optimum discriminant, i.e., a discriminant, can be actually constructed by mere calculation according to the kernel, which avoids calculating features in the mapped space (e.g., Hideki Aso et al., Frontier of Statistical Science 6 "Statistics of pattern recognition and learning - New concepts and approaches", Iwanami Shoten, Publishers (2004); Nello Cristianini et al., Introduction to SVM, Kyoritsu Shuppan Co., Ltd. (2008)).

[0563] C-support vector classification (C-SVC), one type of SVM, involves preparing a hyperplane by supervising with the explanatory variables of two groups and classifying an unknown data set into either of the groups (C. Cortes et al., 1995, Machine Learning, Vol. 20, p. 273-297).

[0564] Exemplary calculation of the C-SVC discriminant that can be used in the method of the present invention will be given below. First, all subjects are divided into two groups, i.e., a lung cancer patient group and a healthy subject group. For example, lung tissue examination can be used for a reference under which each subject is confirmed either as a lung cancer patient or as a healthy subject.

[0565] Next, a data set consisting of comprehensive gene expression levels of serum-derived samples of the two divided groups (hereinafter, this data set is referred to as a training cohort) is prepared, and a C-SVC discriminant is determined by using genes that were found to differ clearly in their gene expression levels between the two groups as explanatory variables, and using this grouping as objective variables (e.g., -1 and +1). An optimizing objective function is represented by Formula 4 wherein e represents all input vectors, y represents an objective variable, a represents a Lagrange's undetermined multiplier vector, Q represents a positive definite matrix, and C represents a parameter for adjusting constrained conditions.

$$\min_a \quad \frac{1}{2} a^T Q a - e^T a \qquad \text{Formula 4}$$

subject to $y^T a = 0$, $0 \le a_i \le C$, $i = 1,\ldots, l$,

[0566] Formula 5 is a finally obtained discriminant, and an associated group can be determined on the basis of the sign of a value obtained according to the discriminant. In this Formula, x represents a support vector, y represents a

label indicating the association of a group, a represents the corresponding coefficient, b represents a constant term, and K represents a kernel function.

$$f(x) = \mathrm{sgn}\left(\sum_{i=1}^{l} y_i a_i K(x_i, x) + b \right) \qquad \text{Formula 5}$$

[0567] For example, a RBF kernel defined by Formula 6 can be used as the kernel function. In this Formula, x represents a support vector, and y represents a kernel parameter for adjusting the complexity of the hyperplane.

$$K(x_i, x_j) = \exp\left(-r\left\|x_i - x_j\right\|^2\right), \quad r < 0 \qquad \text{Formula 6}$$

[0568] In addition, an approach such as neural network, k-nearest neighbor algorithms, decision trees, or logistic regression analysis can be selected as a method for determining or evaluating the presence and/or absence of expression of a lung cancer-derived target gene in a sample derived from a subject, or for evaluating the expression level thereof by comparison with a control derived from a healthy subject.

[0569] The method of the present invention can comprise, for example, the following steps (a), (b), and (c):

(a) a step of measuring an expression level of a target gene in tissues containing lung cancer-derived genes derived from lung cancer patients and/or samples that are already known to contain no lung cancer-derived gene derived from healthy subjects, using the polynucleotide, the kit, or the device (e.g., DNA chip) for detection according to the present invention;
(b) a step of preparing the discriminants of Formulas 1 to 3, 5, and 6 described above from the measurement values of the expression level measured in the step (a); and
(c) a step of measuring an expression level of the target gene in a sample derived from a subject using the polynucleotide, the kit, or the device (e.g., DNA chip) for detection according to the present invention, assigning the obtained measurement value to the discriminants prepared in the step (b), and determining or evaluating the presence and/or absence of expression of the lung cancer-derived target gene in the sample, or evaluating the expression level thereof by comparison with a healthy subject-derived control, on the basis of the obtained results. In this context, in the discriminants of Formulas 1 to 3, 5, and 6, x represents an explanatory variable and includes a value obtained by measuring a polynucleotide selected from the polynucleotides described in Section 2 above, or a fragment thereof, etc. Specifically, the explanatory variable for discriminating a lung cancer patient from a healthy subject according to the present invention is a gene expression level selected from, for example,

(1) a gene expression level in the serum of a lung cancer patient or a healthy subject measured by any DNA comprising 15 or more consecutive nucleotides in a nucleotide sequence represented by SEQ ID NO: 1 optionally in combination with any of SEQ ID NOs 2 to 125, 127 to 130, 132 to 134 and 561 to 578 or a complementary sequence thereof,

[0570] As described above, for the method for determining or evaluating the presence and/or absence of a lung cancer-derived gene in a sample derived from a subject, the preparation of a discriminant requires a discriminant prepared in a training cohort. For enhancing the discriminant accuracy of the discriminant, it is necessary for the discriminant to use genes that show clear difference between two groups in the training cohort.

[0571] Each gene that is used for an explanatory variable in a discriminant is preferably determined as follows. First, comprehensive gene expression levels of a lung cancer patient group and comprehensive gene expression levels of a healthy subject group in a training cohort are used as a data set, the degree of difference in the expression level of each gene between the two groups is determined through the use of, for example, the P value of t test, which is parametric analysis, or the P value of Mann-Whitney's U test or Wilcoxon test, which is nonparametric analysis.

[0572] The gene can be regarded as being statistically significant when the critical rate (significance level) of the P value obtained by the test is smaller than, for example, 5%, 1%, or 0.01%.

[0573] In order to correct an increased probability of type I error attributed to the repetition of a test, a method known in the art, for example, Bonferroni or Holm method, can be used for the correction (e.g., Yasushi Nagata et al., "Basics of statistical multiple comparison methods", Scientist Press Co., Ltd. (2007)). As an example of the Bonferroni correction, for example, the P value obtained by a test is multiplied by the number of repetitions of the test, i.e., the number of genes used in the analysis, and the obtained value can be compared with a desired significance level to suppress a probability

of causing type I error in the whole test.

[0574] Instead of the statistical test, the absolute value (fold change) of an expression ratio of a median value of each gene expression level between gene expression levels of a lung cancer patient group and gene expression levels of a healthy subject group may be calculated to select a gene that is used for an explanatory variable in a discriminant. Alternatively, ROC curves may be prepared using gene expression levels of a lung cancer patient group and a healthy subject group, and a gene that is used for an explanatory variable in a discriminant can be selected on the basis of an AUROC value.

[0575] Next, a discriminant that can be calculated by various methods described above is prepared using any number of genes having large difference in their gene expression levels determined here. Examples of the method for constructing a discriminant that produces the largest discriminant accuracy include a method of constructing a discriminant in every combination of genes that satisfy the significance level of P value, and a method of repetitively evaluating a discriminant while increasing the number of genes for use one by one in a descending order of difference in gene expression level (Furey TS. et al., 2000, Bioinformatics., Vol. 16, p. 906-14). A gene expression level of another independent lung cancer patient or healthy subject is assigned as an explanatory variable to this discriminant to calculate discriminant results of the group to which this independent lung cancer patient or healthy subject associates. Specifically, the found gene set for diagnosis and the discriminant constructed using the gene set for diagnosis can be evaluated in an independent sample group to find a more universal gene set for diagnosis capable of detecting lung cancer and a more universal method for discriminating lung cancer.

[0576] Split-sample method is preferably used for evaluating the discriminant performance (generality) of the discriminant. Specifically, a data set is divided into a training cohort and a validation cohort, and gene selection by a statistical test and discriminant preparation are performed in the training cohort. Accuracy, sensitivity, and specificity are calculated using results of discriminating a validation cohort according to the discriminant and a true group to which the validation cohort associates, to evaluate the discriminant performance. On the other hand, instead of dividing a data set, gene selection by a statistical test and discriminant preparation may be performed using all of samples, and accuracy, sensitivity, and specificity can be calculated by the discriminant of newly prepared samples according to the discriminant to evaluate the discriminant performance.

[0577] The present invention provides a polynucleotide for detection and for disease diagnosis useful in the diagnosis and treatment of lung cancer, a method for detecting lung cancer using the polynucleotide, and a kit and a device for the detection of lung cancer, comprising the polynucleotide. Particularly, in order to select a gene for diagnosis and prepare a discriminant so as to exhibit accuracy beyond a lung cancer diagnosis method using existing tumor markers CEA, a gene set for diagnosis and a discriminant for the method of the present invention, that exhibit accuracy beyond CEA, can be constructed, for example, by comparing genes expressed in serum derived from a patient confirmed to be negative using CEA but finally found to have lung cancer by detailed examination such as computed tomography using a contrast medium, with genes expressed in serum derived from a patient having no lung cancer.

[0578] For example, the gene set for diagnosis is set to any combination selected from one or two or more of the polynucleotides based on a nucleotide sequence represented by SEQ ID NO: 1 optionally together with any of SEQ ID NOs 2 to 125, 127 to 130, 132 to 134, and 561 to 578, or a complementary sequence thereof as described above, optionally one or two or more of the polynucleotides based on a nucleotide sequence represented by any of SEQ ID NOs: 126, 131 and 579, or a complementary sequence thereof, and optionally one or two or more of the polynucleotides based on a nucleotide sequence represented by any of SEQ ID NOs: 135 to 174, or a complementary sequence thereof. Further, a discriminant is constructed using expression levels of the gene set for diagnosis in samples derived from class I lung cancer patients and samples derived from class II healthy subjects as a result of tissue diagnosis. As a result, the presence or absence of lung cancer-derived genes in an unknown sample can be determined with 100% accuracy at the maximum by measuring expression levels of the gene set for diagnosis in the unknown sample.

Examples

[0579] Hereinafter, the present invention will be described further specifically with reference to Examples below. However, the scope of the present invention is not intended to be limited by these Examples.

[Reference Example 1]

<Collection of samples from lung cancer patients and healthy subjects>

[0580] Serum was collected using VENOJECT II vacuum blood collecting tube VP-AS109K60 (Terumo Corp.) from each of 100 healthy subjects and 17 lung cancer patients (8 lung adenocarcinoma cases involving 6 cases with T2N0M0, 1 case with T2N1M0, and 1 case with T2N2M0; and 8 squamous cell cancer cases involving 5 cases with T2N0M0, 1 case with T4N0M0, 1 case with T2N1M0, and 1 case with T4N2M0) confirmed to have no primary cancer other than

lung cancer after acquisition of informed consent, and used as a training cohort. Likewise, serum was collected using VENOJECT II vacuum blood collecting tube VP-AS109K60 (Terumo Corp.) from each of 50 healthy subjects and 8 lung cancer patients (5 adenocarcinoma cases involving 3 cases with T2N0M0, 1 case with T3N0M0, and 1 case with T4N2M0; and 3 squamous cell cancer cases involving 1 case with T2N0M0, 1 case with T4N0M0, and 1 case with T2N1M0) confirmed to have no primary cancer other than lung cancer after acquisition of informed consent, and used as a validation cohort. The histological types and stages of these lung cancer samples are summarized in Tables 2-1 and 2-2.

<Extraction of total RNA>

[0581] Total RNA was obtained from 300 μL of the serum sample obtained from each of 175 persons in total of 150 healthy subjects and 25 lung cancer patients included in the training cohort and the validation cohort, using a reagent for RNA extraction in 3D-Gene(™) RNA extraction reagent from liquid sample kit (Toray Industries, Inc.) according to the protocol provided by the manufacturer.

<Measurement of gene expression level>

[0582] miRNAs in the total RNA obtained from the serum sample of each of 175 persons in total of 150 healthy subjects and 25 lung cancer patients included in the training cohort and the validation cohort were fluorescently labeled using 3D-Gene(™) miRNA Labeling kit (Toray Industries, Inc.) according to the protocol (ver 2.20) provided by the manufacturer. The oligo DNA chip used was 3D-Gene(™) Human miRNA Oligo chip (Toray Industries, Inc.) with attached probes having sequences complementary to 2,555 miRNAs among the miRNAs registered in miRBase Release 20. Hybridization between the miRNAs in the total RNA and the probes on the DNA chip under stringent conditions and washing following the hybridization were performed according to the protocol provided by the manufacturer. The DNA chip was scanned using 3D-Gene(™) scanner (Toray Industries, Inc.) to obtain images. Fluorescence intensity was digitized using 3D-Gene(™) Extraction (Toray Industries, Inc.). The digitized fluorescence intensity was converted to a logarithmic value having a base of 2 and used as a gene expression level, from which a blank value was subtracted. A missing value was replaced with a value obtained by subtracting 0.1 from a logarithmic value of the smallest value of the gene expression level in each DNA chip. As a result, the comprehensive gene expression levels of the miRNAs in the serum were obtained for the 25 lung cancer patients and the 150 healthy subjects. Calculation and statistical analysis using the digitized gene expression levels of the miRNAs were carried out using R language 3.0.2 (R Development Core Team (2013). R: A language and environment for statistical computing. R Foundation for Statistical Computing, URL http://www.R-project.org/) and MASS package 7.3-30 (Venables, W. N. & Ripley, B. D. (2002) Modern Applied Statistics with S. Fourth Edition. Springer, New York. ISBN 0-387-95457-0).

[Reference Example 2]

<Collection of samples from patients with cancers other than lung cancer>

[0583] Serum was collected using VENOJECT II vacuum blood collecting tube VP-AS109K60 (Terumo Corp.) from each of 75 pancreatic cancer patients, 62 biliary tract cancer patients, 32 colorectal cancer patients, 35 stomach cancer patients, 32 esophageal cancer patients, 33 liver cancer patients, and 13 benign pancreaticobiliary disease patients confirmed to have no cancer in other organs after acquisition of informed consent, and used as a training cohort together with the samples of 17 lung cancer patients and 99 healthy subjects of Reference Example 1. Likewise, serum was collected using VENOJECT II vacuum blood collecting tube VP-AS109K60 (Terumo Corp.) from each of 28 pancreatic cancer patients, 38 biliary tract cancer patients, 18 colorectal cancer patients, 15 stomach cancer patients, 18 esophageal cancer patients, 19 liver cancer patients, and 8 benign pancreaticobiliary disease patients confirmed to have no cancer in other organs after acquisition of informed consent, and used as a validation cohort together with the samples of 8 lung cancer patients confirmed to have no cancer in organs except for lung cancer and 51 healthy subjects of Reference Example 1. Subsequent operations were conducted in the same way as in Reference Example 1.

[Table 2-1]

Training cohort		
	Sample name	Cancer stage
Lung adenocarcinoma	LC01	T2N0M0
	LC02	T2N0M0
	LC03	T2N0M0
	LC05	T2N0M0
	LC07	T2N0M0
	LC08	T2N2M0
	LC11	T2N0M0
	LC12	T2N1M0
	LC14	T2N0M0
Squamous cell cancer	LC15	T2N0M0
	LC18	T2N0M0
	LC20	T2N0M0
	LC21	T2N0M0
	LC22	T4N2M0
	LC23	T2N1M0
	LC24	T2N0M0
	LC25	T4N0M0

[Table 2-2]

Validation cohort		
	Sample name	Cancer stage
Lung adenocarcinoma	LC04	T2N0M0
	LC06	T2N0M0
	LC09	T3N0M0
	LC10	T4N2M0
	LC13	T2N0M0
Squamous cell cancer	LC16	T2N1M0
	LC17	T2N0M0
	LC19	T4N0M0

[Example 1]

<Selection of gene marker using samples in the training cohort, and method for evaluating lung cancer discriminant performance of single gene marker using samples in the validation cohort>

[0584] In this Example, a gene marker for discriminating a lung cancer patient from a healthy subject was selected from the training cohort and studied in samples of the validation cohort independent of the training cohort, for a method for evaluating the lung cancer discriminant performance of each selected gene marker alone.

[0585] Specifically, first, the miRNA expression levels in the training cohort and the validation cohort obtained in the preceding Reference Examples were combined and normalized by quantile normalization.

[0586] Next, genes for diagnosis were selected in the training cohort. Here, in order to acquire diagnostic markers

with higher reliability, only genes having a gene expression level of 2^6 or higher in 50% or more of the samples in either of the lung cancer patient group in the training cohort or the healthy subject group in the training cohort were selected. In order to further acquire statistically significant genes for discriminating a lung cancer patient group from a healthy subject group, the P value obtained by two-sample t-test assuming equal variance as to each gene expression level was corrected by the Bonferroni method, and genes that satisfied $p < 0.01$ were acquired as gene markers for use in explanatory variables of a discriminant. The result is described in Table 3.

[0587] In this way, hsa-miR-6768-5p, hsa-miR-6836-3p, hsa-miR-6782-5p, hsa-miR-3663-3p, hsa-miR-1908-3p, hsa-miR-6726-5p, hsa-miR-4258, hsa-miR-1343-3p, hsa-miR-4516, hsa-miR-6875-5p, hsa-miR-4651, hsa-miR-6825-5p, hsa-miR-6840-3p, hsa-miR-6780b-5p, hsa-miR-6749-5p, hsa-miR-8063, hsa-miR-6784-5p, hsa-miR-3679-5p, hsa-miR-3184-5p, hsa-miR-663b, hsa-miR-6880-5p, hsa-miR-1908-5p, hsa-miR-92a-2-5p, hsa-miR-7975, hsa-miR-7110-5p, hsa-miR-6842-5p, hsa-miR-6857-5p, hsa-miR-5572, hsa-miR-3197, hsa-miR-6131, hsa-miR-6889-5p, hsa-miR-4454, hsa-miR-1199-5p, hsa-miR-1247-3p, hsa-miR-6800-5p, hsa-miR-6872-3p, hsa-miR-4649-5p, hsa-miR-6791-5p, hsa-miR-4433b-3p, hsa-miR-3135b, hsa-miR-128-2-5p, hsa-miR-4675, hsa-miR-4472, hsa-miR-6785-5p, hsa-miR-6741-5p, hsa-miR-7977, hsa-miR-3665, hsa-miR-128-1-5p, hsa-miR-4286, hsa-miR-6765-3p, hsa-miR-4632-5p, hsa-miR-365a-5p, hsa-miR-6088, hsa-miR-6816-5p, hsa-miR-6885-5p, hsa-miR-711, hsa-miR-6765-5p, hsa-miR-3180, hsa-miR-4442, hsa-miR-4792, hsa-miR-6721-5p, hsa-miR-6798-5p, hsa-miR-3162-5p, hsa-miR-6126, hsa-miR-4758-5p, hsa-miR-2392, hsa-miR-486-3p, hsa-miR-6727-5p, hsa-miR-4728-5p, hsa-miR-6746-5p, hsa-miR-4270, hsa-miR-3940-5p, hsa-miR-4725-3p, hsa-miR-7108-5p, hsa-miR-3656, hsa-miR-6879-5p, hsa-miR-6738-5p, hsa-miR-1260a, hsa-miR-4446-3p, hsa-miR-3131, hsa-miR-4463, hsa-miR-3185, hsa-miR-6870-5p, hsa-miR-6779-5p, hsa-miR-1273g-3p, hsa-miR-8059, hsa-miR-4697-5p, hsa-miR-4674, hsa-miR-4433-3p, hsa-miR-4257, hsa-miR-1915-5p, hsa-miR-4417, hsa-miR-1343-5p, hsa-miR-6781-5p, hsa-miR-4695-5p, hsa-miR-1237-5p, hsa-miR-6775-5p, hsa-miR-7845-5p, hsa-miR-4746-3p, hsa-miR-7641, hsa-miR-7847-3p, hsa-miR-6806-5p, hsa-miR-4467, hsa-miR-4726-5p, hsa-miR-4648, hsa-miR-6089, hsa-miR-1260b, hsa-miR-4532, hsa-miR-5195-3p, hsa-miR-3188, hsa-miR-6848-5p, hsa-miR-1233-5p, hsa-miR-6717-5p, hsa-miR-3195, hsa-miR-6757-5p, hsa-miR-8072, hsa-miR-4745-5p, hsa-miR-6511a-5p, hsa-miR-6776-5p, hsa-miR-371a-5p, hsa-miR-1227-5p, hsa-miR-7150, hsa-miR-1915-3p, hsa-miR-187-5p, hsa-miR-614, hsa-miR-19b-3p, hsa-miR-1225-5p, hsa-miR-451a, hsa-miR-939-5p, hsa-miR-223-3p, hsa-miR-1228-5p, hsa-miR-125a-3p, hsa-miR-92b-5p, and hsa-miR-22-3p genes, and polynucleotides consisting of the nucleotide sequences of SEQ ID NOs: 1 to 134 related thereto were found.

[0588] Among them, genes newly found as markers for examining the presence or absence of lung cancer are polynucleotides consisting of the nucleotide sequences represented by SEQ ID NOs: 1 to 125, 127 to 130, and 132 to 134.

[0589] A discriminant for determining the presence or absence of lung cancer was further prepared by Fisher's discriminant analysis with the expression levels of these genes as an index. Specifically, any newly found polynucleotide consisting of a nucleotide sequence represented by any of SEQ ID NOs: 1 to 134 in the training cohort was apply for Formula 2 above to construct a discriminant. Calculated accuracy, sensitivity, and specificity are shown in Table 4. In this respect, a discriminant coefficient and a constant term are shown in Table 5.

[0590] Accuracy, sensitivity, and specificity in the validation cohort were calculated using the discriminant thus prepared, and the discriminant performance of the selected polynucleotides was validated using independent samples (Table 4). For example, the expression level measurement value of the nucleotide sequence represented by SEQ ID NO: 1 was compared between the healthy subjects (100 persons) and the lung cancer patients (17 persons) in the training cohort. As a result, the gene expression level measurement values were found to be significantly lower in the lung cancer patient group than in the healthy subject group (see the left diagram of Figure 2). These results were also reproducible for the healthy subjects (50 persons) and the lung cancer patients (8 persons) in the validation cohort (see the right diagram of Figure 2). Likewise, the results obtained about the other polynucleotides shown in SEQ ID NOs: 2 to 134 showed that the gene expression level measurement values were significantly lower (-) or higher (+) in the lung cancer patient group than in the healthy subject group (Table 3). These results were able to be validated in the validation cohort. For example, as for this nucleotide sequence represented by SEQ ID NO: 1, the number of samples that were correctly identified in the detection of lung cancer was calculated using the threshold (10.08) that was set in the training cohort and discriminated between the two groups. As a result, 7 true positives, 50 true negatives, 0 false positives, and 1 false negative were obtained. From these values, 98.3% accuracy, 87.5% sensitivity, and 100% specificity were obtained as detection performance. In this way, the detection performance was calculated as to all of the polynucleotides shown in SEQ ID NOs: 1 to 134, and described in Table 4.

[0591] For example, 33 polynucleotides consisting of the nucleotide sequences represented by SEQ ID NOs: 1, 2, 3, 5, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 22, 26, 27, 28, 29, 33, 34, 38, 41, 42, 44, 65, 124, 125, and 133 exhibited sensitivity of 87.5%, 100%, 100%, 75%, 75%, 75%, 87.5%, 87.5%, 87.5%, 87.5%, 87.5%, 87.5%, 87.5%, 87.5%, 87.5%, 100%, 75%, 87.5%, 87.5%, 87.5%, 87.5%, 87.5%, 87.5%, 87.5%, 75%, 87.5%, 75%, 75%, 75%, 75%, 75%, 75% and 75% respectively, in the validation cohort (Table 4). In this context, the tumor markers CEA and CYFRA21-1 in blood for lung cancer reportedly have general lung cancer detection sensitivity of 69% and 43%, respectively (Non Patent Literature 3). These results demonstrated that the 33 polynucleotides consisting of the nucleotide sequences

represented by SEQ ID NOs: 1, 2, 3, 5, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 22, 26, 27, 28, 29, 33, 34, 38, 41, 42, 44, 65, 124, 125, and 133 can discriminate, each alone, lung cancer in the validation cohort with sensitivity beyond the existing markers CEA and CYFRA21-1.

[0592] For example, 10 polynucleotides consisting of the nucleotide sequences represented by SEQ ID NOs: 2, 3, 11, 13, 20, 21, 22, 30, 31, and 37 were able to correctly determine lung cancer as to all of 4 samples from lung adenocarcinoma or squamous cell cancer having a tumor size of less than 7 cm and having no lymph node metastasis, contained in the validation cohort. Thus, these polynucleotides can detect even relatively early lung cancer and contributes to the early diagnosis of lung cancer.

[Table 3]

SEQ ID NO:	Gene name	P value after Bonferroni correction	Expression level in lung cancer patient with respect to healthy subject
1	hsa-miR-6768-5p	6.71E-24	+
2	hsa-miR-6836-3p	1.44E-20	-
3	hsa-miR-6782-5p	2.89E-20	+
4	hsa-miR-3663-3p	2.77E-18	-
5	hsa-miR-1908-3p	3.58E-18	-
6	hsa-miR-6726-5p	1.02E-17	-
7	hsa-miR-4258	3.38E-17	-
8	hsa-miR-1343-3p	7.45E-17	-
9	hsa-miR-4516	7.91E-17	-
10	hsa-miR-6875-5p	3.69E-16	+
11	hsa-miR-4651	5.14E-16	-
12	hsa-miR-6825-5p	1.28E-14	+
13	hsa-miR-6840-3p	2.69E-14	-
14	hsa-miR-6780b-5p	3.47E-14	+
15	hsa-miR-6749-5p	3.82E-14	-
16	hsa-miR-8063	3.58E-13	-
17	hsa-miR-6784-5p	7.06E-13	+
18	hsa-miR-3679-5p	7.64E-13	+
19	hsa-miR-3184-5p	1.78E-12	+
20	hsa-miR-663b	5.72E-12	-
21	hsa-miR-6880-5p	9.41E-12	+
22	hsa-miR-1908-5p	1.84E-11	+
23	hsa-miR-92a-2-5p	1.85E-11	+
24	hsa-miR-7975	2.06E-11	-
25	hsa-miR-7110-5p	2.64E-11	+
26	hsa-miR-6842-5p	2.66E-11	+
27	hsa-miR-6857-5p	5.09E-11	+
28	hsa-miR-5572	7.39E-11	+
29	hsa-miR-3197	8.45E-11	+
30	hsa-miR-6131	1.51E-10	-

(continued)

SEQ ID NO:	Gene name	P value after Bonferroni correction	Expression level in lung cancer patient with respect to healthy subject
31	hsa-miR-6889-5p	2.73E-10	+
32	hsa-miR-4454	2.92E-10	-
33	hsa-miR-1199-5p	6.01E-10	-
34	hsa-miR-1247-3p	7.10E-10	+
35	hsa-miR-6800-5p	8.76E-10	+
36	hsa-miR-6872-3p	1.18E-09	-
37	hsa-miR-4649-5p	1.37E-09	-
38	hsa-miR-6791-5p	1.51E-09	+
39	hsa-miR-4433b-3p	1.57E-09	+
40	hsa-miR-3135b	1.78E-09	-
41	hsa-miR-128-2-5p	2.59E-09	-
42	hsa-miR-4675	2.65E-09	-
43	hsa-miR-4472	3.21E-09	+
44	hsa-miR-6785-5p	3.84E-09	-
45	hsa-miR-6741-5p	6.85E-09	-
46	hsa-miR -7977	8.90E-09	-
47	hsa-miR-3665	2.49E-08	-
48	hsa-miR-128-1-5p	3.03E-08	+
49	hsa-miR-4286	3.07E-08	-
50	hsa-miR-6765-3p	3.14E-08	-
51	hsa-miR-4632-5p	4.02E-08	+
52	hsa-miR-365a-5p	4.58E-08	+
53	hsa-miR-6088	7.80E-08	-
54	hsa-miR-6816-5p	1.19E-07	+
55	hsa-miR -6885-5p	1.59E-07	-
56	hsa-miR-711	1.93E-07	+
57	hsa-miR-6765-5p	2.99E-07	+
58	hsa-miR-3180	3.65E-07	+
59	hsa-miR-4442	3.89E-07	-
60	hsa-miR-4792	3.97E-07	+
61	hsa-miR-6721-5p	6.66E-07	+
62	hsa-miR-6798-5p	8.81E-07	+
63	hsa-miR-3162-5p	1.07E-06	+
64	hsa-miR-6126	1.26E-06	+
65	hsa-miR-4758-5p	1.35E-06	-
66	hsa-miR-2392	1.58E-06	+

(continued)

SEQ ID NO:	Gene name	P value after Bonferroni correction	Expression level in lung cancer patient with respect to healthy subject
67	hsa-miR-486-3p	3.01E-06	-
68	hsa-miR-6727-5p	3.06E-06	-
69	hsa-miR-4728-5p	3.61E-06	-
70	hsa-miR-6746-5p	5.00E-06	-
71	hsa-miR-4270	5.64E-06	-
72	hsa-miR-3940-5p	6.33E-06	+
73	hsa-miR-4725-3p	6.79E-06	+
74	hsa-miR-7108-5p	7.35E-06	+
75	hsa-miR-3656	1.20E-05	+
76	hsa-miR-6879-5p	1.22E-05	+
77	hsa-miR-6738-5p	1.25E-05	-
78	hsa-miR-1260a	1.51E-05	-
79	hsa-miR-4446-3p	1.67E-05	-
80	hsa-miR-3131	1.91E-05	-
81	hsa-miR-4463	2.63E-05	+
82	hsa-miR-3185	3.31E-05	+
83	hsa-miR-6870-5p	3.95E-05	+
84	hsa-miR-6779-5p	4.61E-05	-
85	hsa-miR-1273g-3p	4.73E-05	-
86	hsa-miR-8059	5.08E-05	-
87	hsa-miR-4697-5p	5.16E-05	-
88	hsa-miR-4674	7.31E-05	-
89	hsa-miR-4433-3p	8.12E-05	+
90	hsa-miR-4257	9.79E-05	-
91	hsa-miR-1915-5p	1.18E-04	-
92	hsa-miR-4417	1.36E-04	+
93	hsa-miR-1343-5p	1.45E-04	+
94	hsa-miR-6781-5p	1.54E-04	+
95	hsa-miR-4695-5p	1.57E-04	+
96	hsa-miR-1237-5p	1.80E-04	+
97	hsa-miR-6775-5p	2.34E-04	-
98	hsa-miR-7845-5p	2.40E-04	+
99	hsa-miR-4746-3p	2.62E-04	+
100	hsa-miR-7641	4.57E-04	-
101	hsa-miR-7847-3p	5.01E-04	-
102	hsa-miR-6806-5p	5.86E-04	-

(continued)

SEQ ID NO:	Gene name	P value after Bonferroni correction	Expression level in lung cancer patient with respect to healthy subject
103	hsa-miR-4467	6.28E-04	+
104	hsa-miR-4726-5p	6.35E-04	-
105	hsa-miR-4648	6.87E-04	+
106	hsa-miR-6089	8.08E-04	+
107	hsa-miR-1260b	8.29E-04	-
108	hsa-miR-4532	8.69E-04	-
109	hsa-miR-5195-3p	1.02E-03	-
110	hsa-miR-3188	1.12E-03	+
111	hsa-miR-6848-5p	1.36E-03	+
112	hsa-miR-1233-5p	1.41E-03	-
113	hsa-miR-6717-5p	1.63E-03	+
114	hsa-miR-3195	1.95E-03	+
115	hsa-miR-6757-5p	2.65E-03	-
116	hsa-miR-8072	3.49E-03	+
117	hsa-miR-4745-5p	4.17E-03	-
118	hsa-miR-6511a-5p	4.77E-03	-
119	hsa-miR-6776-5p	5.08E-03	+
120	hsa-miR-371a-5p	6.92E-03	-
121	hsa-miR-1227-5p	7.47E-03	+
122	hsa-miR-7150	8.50E-03	+
123	hsa-miR-1915-3p	9.50E-03	+
124	hsa-miR-187-5p	1.56E-18	-
125	hsa-miR-614	2.22E-14	-
126	hsa-miR-19b-3p	1.77E-13	+
127	hsa-miR-1225-5p	2.30E-08	+
128	hsa-miR-451a	5.96E-08	+
129	hsa-miR-939-5p	1.29E-07	+
130	hsa-miR-223-3p	4.79E-06	+
131	hsa-miR-1228-5p	5.66E-06	+
132	hsa-miR-125a-3p	1.47E-04	-
133	hsa-miR-92b-5p	2.51E-04	+
134	hsa-miR-22-3p	6.49E-04	+

[Example 2]

<Method for evaluating lung cancer discriminant performance by combination of multiple gene markers using samples in the validation cohort>

[0593] In this Example, a method for evaluating lung cancer discriminant performance by a combination of the gene markers selected in Example 1 was studied. Specifically, Fisher's discriminant analysis was conducted as to 8,910 combinations of two polynucleotides comprising at least one or more of the expression level measurement values of any of the newly found polynucleotides consisting of the nucleotide sequences represented by SEQ ID NOs: 1 to 125, 127 to 130, and 132 to 134 among the polynucleotides consisting of the nucleotide sequences represented by SEQ ID NOs: 1 to 134 selected in Example 1, to construct a discriminant for determining the presence or absence of lung cancer. Next, accuracy, sensitivity, and specificity in the validation cohort were calculated using the discriminant thus prepared, and the discriminant performance of the selected polynucleotides was validated using the independent samples.

[0594] For example, the expression level measurement values of the nucleotide sequences represented by SEQ ID NO: 1 and SEQ ID NO: 2 were compared between the healthy subjects (100 persons) and the lung cancer patients (17 persons) in the training cohort. As a result, a scatter diagram that significantly separated the gene expression level measurement values of the lung cancer patient group from those of the healthy subject group was obtained (see the left diagram of Figure 3). These results were also reproducible for the healthy subjects (50 persons) and the lung cancer patients (8 persons) in the validation cohort (see the right diagram of Figure 3). Likewise, a scatter diagram that significantly separated the gene expression level measurement values of the lung cancer patient group from those of the healthy subject group was also obtained as to the other combinations of two expression level measurement values comprising at least one or more of the expression level measurement values of any of the newly found polynucleotides consisting of the nucleotide sequences represented by SEQ ID NOs: 1 to 125, 127 to 130, and 132 to 134 among the polynucleotides consisting of the nucleotide sequences represented by SEQ ID NOs: 1 to 134. These results were able to be validated in the validation cohort. For example, as for these nucleotide sequences represented by SEQ ID NO: 1 and SEQ ID NO: 2, the number of samples that correctly identified in the detection of lung cancer was calculated using the function (0 = - 1.42x + y + 4.7) that was set in the training cohort and discriminated between the two groups. As a result, 7 true positives, 50 true negatives, 0 false positives, and 1 false negative were obtained. From these values, 98.3% accuracy, 87.5% sensitivity, and 100% specificity were obtained as detection performance. In this way, the detection performance was calculated as to all of the combinations of two expression level measurement values comprising at least one or more of the expression level measurement values of any of the newly found polynucleotides consisting of the nucleotide sequences represented by SEQ ID NOs: 1 to 125, 127 to 130, and 132 to 134 among the polynucleotides consisting of the nucleotide sequences represented by SEQ ID NOs: 1 to 134. Among them, 133 combinations comprising the expression level measurement value of the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 1 and the detection performance thereof were described in Table 6 as an example. For example, all of 9 combinations of the expression level measurement values of the polynucleotides consisting of the nucleotide sequences represented by SEQ ID NOs: 1 and 6, SEQ ID NOs: 1 and 11, SEQ ID NOs: 1 and 19, SEQ ID NOs: 1 and 34, SEQ ID NOs: 1 and 38, SEQ ID NOs: 1 and 52, SEQ ID NOs: 1 and 53, SEQ ID NOs: 1 and 56, and SEQ ID NOs: 1 and 113 exhibited sensitivity of 100% in the validation cohort. Likewise, all of the 133 combinations of two polynucleotides consisting of the nucleotide sequence represented by SEQ ID NO: 1 and a nucleotide sequence represented by any of SEQ ID NOs: 2 to 134 exhibited sensitivity of 75% or higher. These values of sensitivity were higher than the sensitivity of the existing tumor markers CEA (69%) and CYFRA21-1 (43%) in blood (Non Patent Literature 3). Likewise, 5,742 combinations of the measurement values of the polynucleotides having sensitivity beyond the existing markers CEA and CYFRA21-1 were obtained in the validation cohort. All of the nucleotide sequences 1 to 134 described in Table 3 obtained in Example 1 were employed at least once in these combinations. Thus, the combinations of two of the polynucleotides that consist of the nucleotide sequences represented by SEQ ID NOs: 1 to 134 also produced excellent lung cancer detection sensitivity.

[0595] Markers for the detection of lung cancer with better sensitivity are obtained by further combining 3, 4, 5, 6, 7, 8, 9, 10 or more of the expression level measurement values of the polynucleotides consisting of the nucleotide sequences represented by SEQ ID NOs: 1 to 134. For example, the polynucleotides consisting of the nucleotide sequences represented by SEQ ID NOs: 1 to 134 selected in Example 1 were measured to obtain their expression levels between the healthy subject group and the lung cancer group in the validation cohort. All of the polynucleotides were ranked in the descending order of their P values based on the Student's t-test which indicates statistical significance of difference between groups (i.e., one having the lowest P value was ranked in the first place), and lung cancer detection sensitivity was evaluated using combinations of one or more polynucleotides to which the polynucleotides were added one by one from the top to the bottom according to the rank. In short, the order in which the polynucleotides were combined in this evaluation is in reverse in terms of SEQ ID NOs from SEQ ID NO: 134 to SEQ ID NOs: 133, 132, ... shown in Table 3. As a result, the sensitivity in the validation cohort was 62.5% for 1 polynucleotide (SEQ ID NO: 134), 75% for 3 polynu-

cleotides (SEQ ID NOs: 132 to 134), 87.5% for 5 polynucleotides (SEQ ID NOs: 130 to 134), 100% for 6 polynucleotides (SEQ ID NOs: 129 to 134), 100% for 10 polynucleotides (SEQ ID NOs: 125 to 134), 100% for 20 polynucleotides (SEQ ID NOs: 115 to 134), 100% for 30 polynucleotides (SEQ ID NOs: 105 to 134), 100% for 50 polynucleotides (SEQ ID NOs: 85 to 134), 100% for 80 polynucleotides (SEQ ID NOs: 55 to 134), 100% for 120 polynucleotides (SEQ ID NOs: 15 to 134), and 100% for 134 polynucleotides (SEQ ID NOs: 1 to 134).

[0596] These results demonstrated that a combination of multiple polynucleotides can produce higher lung cancer discriminant performance than that of each polynucleotide alone or a combination of a fewer number of polynucleotides. In this context, the combinations of multiple polynucleotides are not limited to the combinations of the polynucleotides added in the order of statistically significant difference as described above, and any combination of multiple polynucleotides can be used in the detection of lung cancer.

[0597] From these results, it can be concluded that all of the polynucleotides consisting of the nucleotide sequences represented by SEQ ID NOs: 1 to 134 serve as excellent markers for the detection of lung cancer.

[Table 4]

	Training cohort			Validation cohort		
SEQ ID NO:	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
1	97.4	94.1	98	98.3	87.5	100
2	94.9	82.4	97	100	100	100
3	97.4	82.4	100	96.6	100	96
4	94	70.6	98	93.1	62.5	98
5	95.7	76.5	99	96.6	75	100
6	92.3	64.7	97	93.1	62.5	98
7	94.9	76.5	98	94.8	75	98
8	94.9	94.1	95	94.8	75	98
9	97.4	82.4	100	98.3	87.5	100
10	96.6	82.4	99	91.4	87.5	92
11	94.9	76.5	98	96.6	87.5	98
12	96.6	88.2	98	93.1	87.5	94
13	92.3	64.7	97	94.8	87.5	96
14	92.3	70.6	96	98.3	87.5	100
15	95.7	82.4	98	98.3	87.5	100
16	91.5	76.5	94	94.8	87.5	96
17	94	82.4	96	93.1	87.5	94
18	94.9	70.6	99	100	100	100
19	89.7	64.7	94	93.1	75	96
20	93.2	58.8	99	98.3	87.5	100
21	93.2	64.7	98	93.1	62.5	98
22	91.5	64.7	96	94.8	87.5	96
23	94	70.6	98	87.9	37.5	96
24	93.2	58.8	99	91.4	50	98
25	89.7	64.7	94	91.4	62.5	96
26	93.2	64.7	98	94.8	87.5	96
27	93.2	76.5	96	94.8	87.5	96
28	92.3	82.4	94	93.1	87.5	94

(continued)

	Training cohort			Validation cohort		
SEQ ID NO:	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
29	89.7	52.9	96	96.6	87.5	98
30	89.7	35.3	99	93.1	62.5	98
31	90.6	47.1	98	94.8	62.5	100
32	93.2	58.8	99	91.4	50	98
33	92.3	64.7	97	96.6	87.5	98
34	89.7	41.2	98	93.1	75	96
35	89.7	52.9	96	93.1	50	100
36	92.3	64.7	97	89.7	50	96
37	88.9	41.2	97	93.1	50	100
38	87.2	47.1	94	96.6	87.5	98
39	90.6	58.8	96	84.5	50	90
40	91.5	47.1	99	91.4	37.5	100
41	91.5	52.9	98	96.6	75	100
42	90.6	47.1	98	96.6	75	100
43	94	64.7	99	91.4	50	98
44	88	47.1	95	93.1	75	96
45	91.5	47.1	99	87.9	37.5	96
46	89.7	47.1	97	87.9	50	94
47	92.3	52.9	99	93.1	50	100
48	88	41.2	96	87.9	62.5	92
49	87.2	41.2	95	89.7	62.5	94
50	88.9	47.1	96	87.9	37.5	96
51	92.3	47.1	100	94.8	62.5	100
52	91.5	47.1	99	94.8	62.5	100
53	91.5	47.1	99	91.4	62.5	96
54	86.3	41.2	94	94.8	62.5	100
55	90.6	41.2	99	94.8	62.5	100
56	90.6	58.8	96	94.8	62.5	100
57	91.5	52.9	98	93.1	62.5	98
58	88.9	35.3	98	93.1	62.5	98
59	86.3	41.2	94	87.9	50	94
60	89.7	47.1	97	89.7	37.5	98
61	90.6	52.9	97	86.2	37.5	94
62	87.2	29.4	97	87.9	62.5	92
63	88.9	41.2	97	82.8	0	96
64	89.7	35.3	99	93.1	50	100
65	89.7	41.2	98	94.8	75	98

(continued)

	Training cohort			Validation cohort		
SEQ ID NO:	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
66	89.7	29.4	100	91.4	37.5	100
67	90.6	41.2	99	94.8	62.5	100
68	88	47.1	95	87.9	25	98
69	88	35.3	97	91.4	50	98
70	87.2	41.2	95	86.2	25	96
71	88	35.3	97	84.5	25	94
72	88	23.5	99	89.7	37.5	98
73	88	35.3	97	86.2	12.5	98
74	89.7	35.3	99	87.9	37.5	96
75	88	41.2	96	93.1	62.5	98
76	89.7	35.3	99	94.8	62.5	100
77	88.9	35.3	98	87.9	37.5	96
78	88	35.3	97	87.9	50	94
79	88.9	29.4	99	93.1	50	100
80	88.9	29.4	99	87.9	25	98
81	88	23.5	99	87.9	12.5	100
82	83.8	11.8	96	87.9	37.5	96
83	88.9	23.5	100	87.9	12.5	100
84	87.2	23.5	98	87.9	12.5	100
85	89.7	47.1	97	94.8	62.5	100
86	87.2	29.4	97	86.2	12.5	98
87	88	23.5	99	86.2	37.5	94
88	85.5	29.4	95	91.4	37.5	100
89	87.2	29.4	97	86.2	25	96
90	88.9	35.3	98	87.9	50	94
91	89.7	41.2	98	91.4	62.5	96
92	86.3	23.5	97	84.5	12.5	96
93	89.7	41.2	98	94.8	62.5	100
94	87.2	17.6	99	81	0	94
95	89.7	41.2	98	94.8	62.5	100
96	87.2	29.4	97	89.7	37.5	98
97	86.3	17.6	98	81	0	94
98	89.7	35.3	99	87.9	37.5	96
99	87.2	17.6	99	94.8	62.5	100
100	84.5	18.8	95	86.2	25	96
101	83.8	11.8	96	84.5	0	98
102	86.3	5.9	100	91.4	37.5	100

(continued)

	Training cohort			Validation cohort		
SEQ ID NO:	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
103	83.8	11.8	96	86.2	12.5	98
104	84.6	17.6	96	86.2	25	96
105	85.5	11.8	98	89.7	25	100
106	89.7	41.2	98	89.7	37.5	98
107	87.2	23.5	98	91.4	50	98
108	88	23.5	99	91.4	37.5	100
109	87.2	17.6	99	87.9	25	98
110	86.3	23.5	97	89.7	25	100
111	85.5	11.8	98	86.2	25	96
112	86.3	17.6	98	86.2	0	100
113	84.6	23.5	95	89.7	25	100
114	86.3	23.5	97	84.5	25	94
115	82.9	0	97	89.7	25	100
116	88	23.5	99	89.7	25	100
117	88	17.6	100	89.7	25	100
118	84.6	11.8	97	86.2	0	100
119	85.5	5.9	99	89.7	25	100
120	84.6	0	99	84.5	0	98
121	88.9	23.5	100	87.9	12.5	100
122	88	17.6	100	89.7	25	100
123	84.6	5.9	98	94.8	62.5	100
124	99.1	94.1	100	96.6	75	100
125	94	76.5	97	93.1	75	96
126	95.7	82.4	98	93.1	62.5	98
127	89.7	52.9	96	93.1	50	100
128	93.2	58.8	99	89.7	37.5	98
129	91.5	58.8	97	86.2	50	92
130	94	58.8	100	94.8	62.5	100
131	84.6	17.6	96	87.9	25	98
132	89.7	35.3	99	89.7	25	100
133	89.7	35.3	99	96.6	75	100
134	87.2	23.5	98	86.2	12.5	98

[Table 5]

SEQ ID NO:	Discriminant coefficient	Constant term
1	3.665	36.958

(continued)

SEQ ID NO:	Discriminant coefficient	Constant term
2	3.482	28.279
3	3.305	21.564
4	3.967	46.907
5	2.921	18.418
6	3.258	31.351
7	2.321	19.901
8	2.482	17.979
9	5.340	69.250
10	3.780	34.781
11	6.053	65.389
12	2.169	14.787
13	3.363	28.960
14	3.278	29.867
15	4.768	47.106
16	2.668	21.511
17	3.933	49.822
18	2.781	19.688
19	2.340	19.400
20	3.173	27.138
21	2.395	19.027
22	4.481	51.987
23	1.923	18.732
24	2.221	21.483
25	1.879	15.097
26	3.449	21.201
27	1.940	10.546
28	2.467	16.896
29	3.381	32.369
30	1.883	19.278
31	2.995	22.556
32	2.257	25.609
33	2.593	16.685
34	4.054	25.898
35	4.316	37.567
36	2.347	13.660
37	2.787	28.233
38	4.929	45.747
39	3.956	32.281

(continued)

SEQ ID NO:	Discriminant coefficient	Constant term
40	2.822	21.631
41	2.892	30.757
42	3.016	22.359
43	2.179	11.954
44	2.956	26.296
45	4.228	28.830
46	2.347	22.562
47	7.619	102.957
48	2.849	21.598
49	2.506	18.167
50	1.885	16.130
51	4.534	36.471
52	3.307	19.440
53	3.370	33.776
54	4.473	45.416
55	3.058	33.429
56	4.044	33.691
57	4.924	52.340
58	4.740	41.821
59	3.556	33.458
60	2.051	13.913
61	4.118	31.479
62	2.848	30.006
63	2.967	23.118
64	3.094	33.898
65	6.747	57.639
66	3.115	18.546
67	2.952	23.150
68	6.267	79.386
69	5.244	36.656
70	3.634	23.502
71	5.682	45.289
72	4.756	58.458
73	3.941	38.866
74	4.639	42.673
75	4.686	54.180
76	3.379	28.223
77	3.897	27.668

(continued)

SEQ ID NO:	Discriminant coefficient	Constant term
78	2.497	17.033
79	2.622	18.728
80	2.639	18.344
81	4.764	52.837
82	2.582	18.301
83	3.517	26.318
84	6.525	46.333
85	2.880	21.133
86	3.254	24.541
87	4.996	39.036
88	3.508	36.118
89	3.944	29.161
90	3.193	21.619
91	1.406	8.631
92	5.754	47.280
93	3.850	40.213
94	5.850	61.192
95	4.464	33.686
96	4.601	58.630
97	6.817	56.624
98	3.273	21.990
99	2.934	19.283
100	1.405	10.220
101	3.974	25.352
102	3.294	21.365
103	2.273	22.405
104	4.014	26.327
105	1.371	8.370
106	5.947	79.958
107	2.441	20.646
108	3.287	38.733
109	3.026	20.705
110	3.417	20.796
111	5.205	38.779
112	2.897	32.216
113	2.584	17.226
114	3.934	32.685
115	3.076	22.309

(continued)

SEQ ID NO:	Discriminant coefficient	Constant term
116	5.228	64.304
117	2.180	25.963
118	2.566	14.847
119	3.282	19.125
120	3.663	26.980
121	6.563	62.775
122	4.018	31.312
123	4.220	46.687
124	2.174	20.711
125	1.889	11.995
126	1.102	5.734
127	3.626	27.002
128	0.979	9.798
129	2.534	19.444
130	1.051	6.668
131	3.974	47.286
132	1.456	9.155
133	3.272	26.342
134	1.514	8.925

[Table 6]

	Training set			Validation set		
SEQ ID NO:	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
1_2	98.3	94.1	99	98.3	87.5	100
1_3	100	100	100	98.3	87.5	100
1_4	97.4	88.2	99	98.3	87.5	100
1_5	99.1	100	99	98.3	87.5	100
1_6	99.1	100	99	100	100	100
1_7	99.1	100	99	98.3	87.5	100
1_8	98.3	94.1	99	98.3	87.5	100
1_9	99.1	100	99	98.3	87.5	100
1_10	100	100	100	98.3	87.5	100
1_11	98.3	100	98	100	100	100
1_12	98.3	100	98	98.3	87.5	100
1_13	98.3	100	98	98.3	87.5	100
1_14	100	100	100	98.3	87.5	100
1_15	98.3	100	98	98.3	87.5	100

(continued)

	Training set			Validation set		
SEQ ID NO:	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
1_16	99.1	100	99	98.3	87.5	100
1_17	98.3	100	98	98.3	87.5	100
1_18	99.1	100	99	98.3	87.5	100
1_19	99.1	100	99	100	100	100
1_20	98.3	94.1	99	98.3	87.5	100
1_21	98.3	94.1	99	96.6	87.5	98
1_22	98.3	100	98	98.3	87.5	100
1_23	97.4	94.1	98	98.3	87.5	100
1_24	97.4	94.1	98	98.3	87.5	100
1_25	98.3	100	98	98.3	87.5	100
1_26	99.1	100	99	96.6	87.5	98
1_27	98.3	100	98	98.3	87.5	100
1_28	98.3	100	98	98.3	87.5	100
1_29	98.3	94.1	99	98.3	87.5	100
1_30	97.4	94.1	98	98.3	87.5	100
1_31	98.3	100	98	98.3	87.5	100
1_32	97.4	94.1	98	96.6	75	100
1_33	98.3	94.1	99	98.3	87.5	100
1_34	99.1	100	99	100	100	100
1_35	98.3	100	98	98.3	87.5	100
1_36	97.4	94.1	98	96.6	75	100
1_37	98.3	100	98	98.3	87.5	100
1_38	98.3	100	98	100	100	100
1_39	97.4	94.1	98	98.3	87.5	100
1_40	98.3	100	98	96.6	75	100
1_41	98.3	100	98	98.3	87.5	100
1_42	98.3	100	98	98.3	87.5	100
1_43	97.4	94.1	98	98.3	87.5	100
1_44	97.4	94.1	98	98.3	87.5	100
1_45	97.4	94.1	98	98.3	87.5	100
1_46	96.6	88.2	98	96.6	75	100
1_47	98.3	100	98	98.3	87.5	100
1_48	99.1	100	99	98.3	87.5	100
1_49	97.4	94.1	98	96.6	75	100
1_50	97.4	94.1	98	96.6	75	100
1_51	99.1	100	99	98.3	87.5	100
1_52	99.1	100	99	100	100	100

(continued)

	Training set			Validation set		
SEQ ID NO:	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
1_53	99.1	100	99	100	100	100
1_54	98.3	100	98	98.3	87.5	100
1_55	98.3	100	98	98.3	87.5	100
1_56	100	100	100	100	100	100
1_57	98.3	100	98	98.3	87.5	100
1_58	98.3	100	98	98.3	87.5	100
1_59	98.3	100	98	98.3	87.5	100
1_60	97.4	94.1	98	98.3	87.5	100
1_61	98.3	100	98	98.3	87.5	100
1_62	97.4	94.1	98	98.3	87.5	100
1_63	98.3	100	98	98.3	87.5	100
1_64	98.3	100	98	98.3	87.5	100
1_65	97.4	94.1	98	98.3	87.5	100
1_66	98.3	100	98	98.3	87.5	100
1_67	98.3	100	98	98.3	87.5	100
1_68	98.3	100	98	98.3	87.5	100
1_69	97.4	94.1	98	98.3	87.5	100
1_70	97.4	94.1	98	98.3	87.5	100
1_71	97.4	94.1	98	98.3	87.5	100
1_72	97.4	94.1	98	98.3	87.5	100
1_73	98.3	94.1	99	98.3	87.5	100
1_74	98.3	100	98	98.3	87.5	100
1_75	97.4	100	97	98.3	87.5	100
1_76	99.1	94.1	100	98.3	87.5	100
1_77	97.4	94.1	98	98.3	87.5	100
1_78	97.4	94.1	98	98.3	87.5	100
1_79	97.4	94.1	98	98.3	87.5	100
1_80	98.3	94.1	99	98.3	87.5	100
1_81	97.4	94.1	98	98.3	87.5	100
1_82	99.1	100	99	98.3	87.5	100
1_83	98.3	100	98	98.3	87.5	100
1_84	98.3	100	98	98.3	87.5	100
1_85	97.4	88.2	99	98.3	87.5	100
1_86	97.4	94.1	98	98.3	87.5	100
1_87	98.3	100	98	98.3	87.5	100
1_88	98.3	100	98	98.3	87.5	100
1_89	97.4	94.1	98	98.3	87.5	100

(continued)

	Training set			Validation set		
SEQ ID NO:	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
1_90	97.4	94.1	98	98.3	87.5	100
1_91	98.3	94.1	99	98.3	87.5	100
1_92	97.4	94.1	98	98.3	87.5	100
1_93	98.3	100	98	98.3	87.5	100
1_94	98.3	100	98	98.3	87.5	100
1_95	98.3	94.1	99	98.3	87.5	100
1_96	98.3	100	98	98.3	87.5	100
1_97	97.4	94.1	98	98.3	87.5	100
1_98	98.3	94.1	99	98.3	87.5	100
1_99	98.3	100	98	98.3	87.5	100
1_100	99.1	100	99	98.3	87.5	100
1_101	97.4	94.1	98	98.3	87.5	100
1_102	97.4	94.1	98	98.3	87.5	100
1_103	99.1	100	99	98.3	87.5	100
1_104	97.4	94.1	98	98.3	87.5	100
1_105	97.4	94.1	98	98.3	87.5	100
1_106	98.3	94.1	99	98.3	87.5	100
1_107	96.6	88.2	98	96.6	75	100
1_108	98.3	100	98	98.3	87.5	100
1_109	99.1	100	99	98.3	87.5	100
1_110	97.4	94.1	98	98.3	87.5	100
1_111	97.4	94.1	98	98.3	87.5	100
1_112	97.4	94.1	98	98.3	87.5	100
1_113	99.1	100	99	100	100	100
1_114	98.3	100	98	98.3	87.5	100
1_115	97.4	94.1	98	98.3	87.5	100
1_116	98.3	100	98	98.3	87.5	100
1_117	97.4	94.1	98	98.3	87.5	100
1_118	97.4	94.1	98	98.3	87.5	100
1_119	97.4	94.1	98	98.3	87.5	100
1_120	98.3	100	98	98.3	87.5	100
1_121	98.3	94.1	99	98.3	87.5	100
1_122	98.3	100	98	98.3	87.5	100
1_123	98.3	100	98	98.3	87.5	100
1_124	98.3	100	98	98.3	87.5	100
1_125	97.4	94.1	98	98.3	87.5	100
1_126	99.1	100	99	98.3	87.5	100

(continued)

	Training set			Validation set		
SEQ ID NO:	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
1_127	98.3	100	98	98.3	87.5	100
1_128	98.3	100	98	98.3	87.5	100
1_129	98.3	100	98	98.3	87.5	100
1_130	98.3	100	98	98.3	87.5	100
1_131	97.4	94.1	98	98.3	87.5	100
1_132	98.3	88.2	100	98.3	87.5	100
1_133	97.4	94.1	98	98.3	87.5	100
1_134	98.3	100	98	98.3	87.5	100

[Example 3]

<Selection of gene marker using all samples and method for evaluating lung cancer discriminant performance of acquired gene marker>

[0598] In this Example, the samples in the training cohort and the validation cohort used in Examples 1 and 2 were integrated, and selection of a gene marker and evaluation of its lung cancer discriminant performance were conducted using all of the samples.

[0599] Specifically, the miRNA expression levels in the serum of the 25 lung cancer patients and the 150 healthy subjects obtained in the preceding Reference Examples were normalized by quantile normalization. In order to acquire diagnostic markers with higher reliability, only genes having a gene expression level of 2^6 or higher in 50% or more of the samples in either of the lung cancer patient group or the healthy subject group were selected in the gene marker selection. In order to further acquire statistical significance for discriminating a lung cancer patient group from a healthy subject group, the P value obtained by two-sample t-test assuming equal variance as to each gene expression level was corrected by the Bonferroni method, and genes that satisfied $p < 0.01$ were selected as gene markers for use in explanatory variables of a discriminant. The acquired genes are described in Table 7. In this way, hsa-miR-4271, hsa-miR-642b-3p, hsa-miR-6075, hsa-miR-6125, hsa-miR-887-3p, hsa-miR-6851-5p, hsa-miR-6763-5p, hsa-miR-3928-3p, hsa-miR-4443, hsa-miR-3648, hsa-miR-149-3p, hsa-miR-4689, hsa-miR-4763-3p, hsa-miR-6729-5p, hsa-miR-3196, hsa-miR-8069, hsa-miR-1268a, hsa-miR-4739, hsa-miR-1268b, hsa-miR-5698, hsa-miR-6752-5p, hsa-miR-4507, hsa-miR-564, hsa-miR-4497, hsa-miR-6877-5p, hsa-miR-6087, hsa-miR-4731-5p, hsa-miR-615-5p, hsa-miR-760, hsa-miR-6891-5p, hsa-miR-6887-5p, hsa-miR-4525, hsa-miR-1914-3p, hsa-miR-619-5p, hsa-miR-5001-5p, hsa-miR-6722-3p, hsa-miR-3621, hsa-miR-4298, hsa-miR-675-5p, and hsa-miR-4655-5p genes, and the nucleotide sequences of SEQ ID NOs: 135 to 174 related thereto were found in addition to the genes described in Table 3. As with the nucleotide sequences of SEQ ID NOs: 1 to 134, the results obtained about the polynucleotides shown in SEQ ID NOs: 135 to 174 also showed that the measurement values were significantly lower (-) or higher (+) in the lung cancer patient group than in the healthy subject group (Table 7). These results were able to be validated in the validation cohort. Thus, the presence or absence of lung cancer in the newly obtained samples can be determined by the methods described in Examples 1 and 2 by using the gene expression level measurement values described in Table 7 either alone or in combination with the gene expression level measurement values described in Table 3.

[Table 7]

SEQ ID NO:	Gene name	P value after Bonferroni correction	Expression level in lung cancer patient with respect to healthy subject
1	hsa-miR-6768-5p	6.12E-37	+
2	hsa-miR-6836-3p	4.68E-36	-
3	hsa-miR-6782-5p	7.67E-29	-
4	hsa-miR-3663-3p	4.91E-29	-

(continued)

SEQ ID NO:	Gene name	P value after Bonferroni correction	Expression level in lung cancer patient with respect to healthy subject
5	hsa-miR-1908-3p	2.76E-30	-
6	hsa-miR-6726-5p	1.23E-26	+
7	hsa-miR-4258	6.12E-28	-
8	hsa-miR-1343-3p	7.70E-26	-
9	hsa-miR-4516	1.71E-29	-
10	hsa-miR-6875-5p	1.59E-18	-
11	hsa-miR-4651	6.58E-26	+
12	hsa-miR-6825-5p	2.30E-22	-
13	hsa-miR-6840-3p	4.47E-24	+
14	hsa-miR-6780b-5p	7.12E-26	-
15	hsa-miR-6749-5p	3.83E-25	-
16	hsa-miR-8063	7.83E-21	-
17	hsa-miR-6784-5p	1.37E-17	+
18	hsa-miR-3679-5p	2.70E-25	-
19	hsa-miR-3184-5p	5.58E-19	+
20	hsa-miR-663b	2.07E-22	-
21	hsa-miR-6880-5p	4.49E-19	+
22	hsa-miR-1908-5p	7.91E-21	+
23	hsa-miR-92a-2-5p	6.69E-15	+
24	hsa-miR-7975	3.32E-17	+
25	hsa-miR-7110-5p	2.07E-16	+
26	hsa-miR-6842-5p	3.25E-19	-
27	hsa-miR-6857-5p	7.70E-16	+
28	hsa-miR-5572	1.14E-17	+
29	hsa-miR-3197	7.43E-21	+
30	hsa-miR-6131	8.81E-19	+
31	hsa-miR-6889-5p	7.76E-18	+
32	hsa-miR-4454	6.20E-15	-
33	hsa-miR-1199-5p	1.10E-16	-
34	hsa-miR-1247-3p	2.61E-15	-
35	hsa-miR-6800-5p	1.65E-14	-
36	hsa-miR-6872-3p	3.40E-13	+
37	hsa-miR-4649-5p	2.50E-16	-
38	hsa-miR-6791-5p	2.29E-18	-
39	hsa-miR-4433b-3p	1.12E-12	+
40	hsa-miR-3135b	7.14E-09	+

(continued)

SEQ ID NO:	Gene name	P value after Bonferroni correction	Expression level in lung cancer patient with respect to healthy subject
41	hsa-miR-128-2-5p	3.95E-17	+
42	hsa-miR-4675	3.41E-17	-
43	hsa-miR-4472	1.34E-15	-
44	hsa-miR-6785-5p	7.27E-16	+
45	hsa-miR-6741-5p	1.57E-11	+
46	hsa-miR-7977	4.98E-13	+
47	hsa-miR-3665	1.23E-11	+
48	hsa-miR-128-1-5p	6.12E-11	+
49	hsa-miR-4286	8.20E-12	+
50	hsa-miR-6765-3p	3.54E-12	+
51	hsa-miR-4632-5p	1.23E-14	-
52	hsa-miR-365a-5p	3.37E-12	-
53	hsa-miR-6088	2.65E-13	-
54	hsa-miR-6816-5p	3.35E-14	+
55	hsa-miR-6885-5p	1.83E-13	-
56	hsa-miR-711	2.81E-14	+
57	hsa-miR-6765-5p	1.37E-11	+
58	hsa-miR-3180	1.69E-14	+
59	hsa-miR-4442	2.64E-12	-
60	hsa-miR-4792	2.35E-11	+
61	hsa-miR-6721-5p	1.63E-09	+
62	hsa-miR-6798-5p	9.64E-11	-
63	hsa-miR-3162-5p	1.05E-08	-
64	hsa-miR-6126	3.64E-14	+
65	hsa-miR-4758-5p	3.51E-15	-
66	hsa-miR-2392	2.75E-12	+
67	hsa-miR-486-3p	2.02E-11	-
68	hsa-miR-6727-5p	3.30E-09	+
69	hsa-miR-4728-5p	9.06E-11	-
70	hsa-miR-6746-5p	1.45E-08	+
71	hsa-miR-4270	1.52E-08	+
72	hsa-miR-3940-5p	3.98E-09	+
73	hsa-miR-4725-3p	2.40E-08	-
74	hsa-miR-7108-5p	5.64E-10	+
75	hsa-miR-3656	6.69E-13	+
76	hsa-miR-6879-5p	3.97E-13	+

(continued)

SEQ ID NO:	Gene name	P value after Bonferroni correction	Expression level in lung cancer patient with respect to healthy subject
77	hsa-miR-6738-5p	1.60E-09	+
78	hsa-miR-1260a	1.22E-08	+
79	hsa-miR-4446-3p	3.23E-10	-
80	hsa-miR-3131	2.40E-09	+
81	hsa-miR-4463	1.54E-08	-
82	hsa-miR-3185	5.62E-10	-
83	hsa-miR-6870-5p	3.81E-08	+
84	hsa-miR-6779-5p	3.02E-07	+
85	hsa-miR-1273g-3p	2.06E-09	+
86	hsa-miR-8059	2.01E-06	-
87	hsa-miR-4697-5p	1.86E-08	+
88	hsa-miR-4674	4.38E-10	-
89	hsa-miR-4433-3p	2.20E-07	-
90	hsa-miR-4257	1.87E-08	+
91	hsa-miR-1915-5p	4.76E-10	-
92	hsa-miR-4417	2.14E-07	-
93	hsa-miR-1343-5p	1.06E-10	+
94	hsa-miR-6781-5p	4.10E-05	-
95	hsa-miR-4695-5p	3.31E-11	-
96	hsa-miR-1237-5p	3.95E-10	+
97	hsa-miR-6775-5p	4.09E-05	+
98	hsa-miR-7845-5p	2.84E-07	-
99	hsa-miR-4746-3p	9.11E-11	-
100	hsa-miR-7641	1.14E-06	-
101	hsa-miR-7847-3p	5.71E-05	+
102	hsa-miR-6806-5p	1.87E-09	-
103	hsa-miR-4467	2.48E-08	-
104	hsa-miR-4726-5p	8.08E-07	+
105	hsa-miR-4648	1.15E-08	+
106	hsa-miR-6089	1.19E-07	+
107	hsa-miR-1260b	1.62E-05	+
108	hsa-miR-4532	8.30E-09	+
109	hsa-miR-5195-3p	2.03E-07	+
110	hsa-miR-3188	4.84E-08	-
111	hsa-miR-6848-5p	6.01E-07	+
112	hsa-miR-1233-5p	3.76E-06	+

(continued)

SEQ ID NO:	Gene name	P value after Bonferroni correction	Expression level in lung cancer patient with respect to healthy subject
113	hsa-miR-6717-5p	2.38E-05	+
114	hsa-miR-3195	7.67E-06	-
115	hsa-miR-6757-5p	1.58E-06	-
116	hsa-miR-8072	1.17E-05	-
117	hsa-miR-4745-5p	5.89E-07	+
119	hsa-miR-6776-5p	1.26E-07	-
120	hsa-miR-371a-5p	9.22E-05	+
121	hsa-miR-1227-5p	9.64E-05	-
122	hsa-miR-7150	0.000252	-
123	hsa-miR-1915-3p	2.18E-09	-
124	hsa-miR-187-5p	2.81E-27	-
125	hsa-miR-614	1.65E-21	-
126	hsa-miR-19b-3p	1.33E-19	+
127	hsa-miR-1225-5p	6.67E-13	-
128	hsa-miR-451a	2.23E-10	-
129	hsa-miR-939-5p	1.89E-11	+
130	hsa-miR-223-3p	9.32E-11	-
131	hsa-miR-1228-5p	1.49E-09	+
132	hsa-miR-125a-3p	1.07E-05	+
133	hsa-miR-92b-5p	1.09E-11	+
134	hsa-miR-22-3p	9.71E-07	+
135	hsa-miR-4271	5.64E-07	+
136	hsa-miR-642b-3p	6.99E-06	-
137	hsa-miR-6075	1.17E-05	+
138	hsa-miR-6125	1.63E-05	+
139	hsa-miR-887-3p	1.68E-05	+
140	hsa-miR-6851-5p	1.97E-05	-
141	hsa-miR-6763-5p	3.54E-05	-
142	hsa-miR-3928-3p	4.67E-05	-
143	hsa-miR-4443	5.36E-05	+
144	hsa-miR-3648	6.01E-05	+
145	hsa-miR-149-3p	9.80E-05	-
146	hsa-miR-4689	1.01E-04	+
147	hsa-miR-4763-3p	1.20E-04	+
148	hsa-miR-6729-5p	1.28E-04	+
149	hsa-miR-3196	1.31E-04	+

(continued)

SEQ ID NO:	Gene name	P value after Bonferroni correction	Expression level in lung cancer patient with respect to healthy subject
150	hsa-miR-8069	1.84E-04	+
151	hsa-miR-1268a	2.58E-04	+
152	hsa-miR-4739	2.68E-04	+
153	hsa-miR-1268b	3.37E-04	+
154	hsa-miR-5698	4.34E-04	-
155	hsa-miR-6752-5p	5.63E-04	+
156	hsa-miR-4507	6.34E-04	+
157	hsa-miR-564	6.68E-04	-
158	hsa-miR-4497	8.11E-04	-
159	hsa-miR-6877-5p	8.21E-04	-
160	hsa-miR-6087	8.91E-04	-
161	hsa-miR-4731-5p	1.15E-03	-
162	hsa-miR-615-5p	1.25E-03	-
163	hsa-miR-760	1.42E-03	-
164	hsa-miR-6891-5p	1.71E-03	+
165	hsa-miR-6887-5p	1.82E-03	-
166	hsa-miR-4525	2.09E-03	-
167	hsa-miR-1914-3p	2.11E-03	-
168	hsa-miR-619-5p	2.61E-03	-
169	hsa-miR-5001-5p	3.01E-03	-
170	hsa-miR-6722-3p	3.88E-03	+
171	hsa-miR-3621	4.02E-03	-
172	hsa-miR-4298	7.88E-03	-
173	hsa-miR-675-5p	8.33E-03	-
174	hsa-miR-4655-5p	9.06E-03	+

[Example 4]

<Method for evaluating lung cancer-specific discriminant performance by combination of multiple gene markers using samples in the validation cohort>

[0600] In this Example, gene markers for diagnosis were selected by comparing gene expression levels of miRNAs in serum of lung cancer patients with that of a control group consisting of healthy subjects, pancreatic cancer patients, biliary tract cancer patients, colorectal cancer patients, stomach cancer patients, liver cancer patients, and benign pancreaticobiliary disease patients, in the same way as the method described in Example 1, using the gene markers selected in Example 1, and targeting the training cohort as the sample group described in Reference Example 2. The polynucleotides consisting of the nucleotide sequences represented by SEQ ID NOs: 561 to 579 thus selected were further combined therewith to study a method for evaluating lung cancer-specific discriminant performance.

[0601] Specifically, first, the miRNA expression levels in the training cohort and the validation cohort obtained in Reference Example 2 mentioned above were combined and normalized by quantile normalization. Next, Fisher's discriminant analysis was conducted as to combinations of 1 to 4 expression level measurement values comprising at least

one or more of the expression level measurement values of the polynucleotides consisting of the nucleotide sequences represented by SEQ ID NOs: 1 to 174, and 561 to 579, to construct a discriminant for determining the presence or absence of lung cancer. Next, accuracy, sensitivity, and specificity in the validation cohort were calculated using the discriminant thus prepared, with the lung cancer patient group as a positive sample group and, on the other hand, the healthy subject group, the pancreatic cancer patient group, the biliary tract cancer patient group, the colorectal cancer patient group, the stomach cancer patient group, the liver cancer patient group, and the benign pancreaticobiliary disease patient group as a negative sample group. The discriminant performance of the selected polynucleotides was validated using the independent samples.

[0602] Most of polynucleotides consisting of the nucleotide sequences represented by these SEQ ID NOs (SEQ ID NOs: 1 to 174, and 561 to 579 corresponding to the miRNA markers of Table 1) or complementary sequences thereof mentioned above were able to provide relatively high accuracy, sensitivity, and specificity in the determination of the presence or absence of lung cancer, and furthermore, were able to specifically discriminate lung cancer from the other cancers. For example, among the combinations of multiple polynucleotides selected from the group consisting of polynucleotides consisting of the nucleotide sequences represented by SEQ ID NOs: 1, 2, 3, 4, 5,7,9,10,11,19,21,26,29,31,52,53,63,65,69,72,87,90,113,124,125,126,128,130,143, 148, 160, 162, 561, 562, 563, 564, 565, 566, 567, 568, 569, 570, 571, 572, 573, 574, 575, 576, 577, 578 and 579 or complementary sequences thereof (the cancer type-specific polynucleotide group 1) as polynucleotides capable of specifically binding to target markers, combinations comprising at least one or more polynucleotide(s) selected from the group consisting of polynucleotides consisting of the nucleotide sequences represented by SEQ ID NOs: 1, 2, 3, 10, 63, 113, 124, 125, 126, 128, 130, 143, 160, 561, 568, 573 and 578 or complementary sequences thereof (the cancer type-specific polynucleotide group 2) included in the cancer type-specific polynucleotide group 1 were able to specifically discriminate lung cancer from the other cancers with high accuracy.

[0603] The number of the polynucleotides with cancer type specificity in the combination can be 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or more for the combination. The combinations of 4 or more of these polynucleotides were able to exhibit discriminant accuracy of 90% or higher.

[0604] Specifically, the discriminant accuracy of the measurement using the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 1 or a complementary sequence thereof is shown in Table 8-1. For example, the measurement using the combination of one polynucleotide comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 1 or a complementary sequence thereof exhibited accuracy of 94.2% in the training cohort and accuracy of 91.4% in the validation cohort. Also, for example, the measurement using the combinations of two polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 1 or a complementary sequence thereof exhibited accuracy of 98.7% in the training cohort and accuracy of 97.5% in the validation cohort. Furthermore, for example, the measurement using the combinations of three polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 1 or a complementary sequence thereof exhibited accuracy of 99.2% in the training cohort and accuracy of 98.5% in the validation cohort. Furthermore, for example, the measurement using the combinations of four polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 1 or a complementary sequence thereof exhibited accuracy of 99.7% in the training cohort and accuracy of 99.0% in the validation cohort.

[0605] Specifically, the discriminant accuracy of the measurement using the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 2 or a complementary sequence thereof is shown in Table 8-2. For example, the measurement using the combination of one polynucleotide comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 2 or a complementary sequence thereof exhibited accuracy of 94.0% in the training cohort and accuracy of 92.4% in the validation cohort. Also, for example, the measurement using the combinations of two polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 2 or a complementary sequence thereof exhibited accuracy of 97.2% in the training cohort and accuracy of 96.0% in the validation cohort. Furthermore, for example, the measurement using the combinations of three polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 2 or a complementary sequence thereof exhibited accuracy of 99.5% in the training cohort and accuracy of 98.0% in the validation cohort. Furthermore, for example, the measurement using the combinations of four polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 2 or a complementary sequence thereof exhibited accuracy of 100% in the training cohort and accuracy of 98.0% in the validation cohort.

[0606] Specifically, the discriminant accuracy of the measurement using the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 3 or a complementary sequence thereof is shown in Table 8-3. For example, the measurement using the combination of one polynucleotide comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 3 or a complementary sequence thereof exhibited accuracy of 85.7% in the training cohort and accuracy of 84.3% in the validation cohort. Also, for example, the measurement using the

combinations of two polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 3 or a complementary sequence thereof exhibited accuracy of 97.0% in the training cohort and accuracy of 97.0% in the validation cohort. Furthermore, for example, the measurement using the combinations of three polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 3 or a complementary sequence thereof exhibited accuracy of 99.0% in the training cohort and accuracy of 98.5% in the validation cohort. Furthermore, for example, the measurement using the combinations of four polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 3 or a complementary sequence thereof exhibited accuracy of 99.5% in the training cohort and accuracy of 100% in the validation cohort.

[0607] Specifically, the discriminant accuracy of the measurement using the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 10 or a complementary sequence thereof is shown in Table 8-4. For example, the measurement using the combination of one polynucleotide comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 10 or a complementary sequence thereof exhibited accuracy of 64.0% in the training cohort and accuracy of 61.6% in the validation cohort. Also, for example, the measurement using the combinations of two polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 10 or a complementary sequence thereof exhibited accuracy of 94.0% in the training cohort and accuracy of 92.4% in the validation cohort. Furthermore, for example, the measurement using the combinations of three polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 10 or a complementary sequence thereof exhibited accuracy of 99.2% in the training cohort and accuracy of 99.0% in the validation cohort. Furthermore, for example, the measurement using the combinations of four polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 10 or a complementary sequence thereof exhibited accuracy of 99.2% in the training cohort and accuracy of 99.5% in the validation cohort.

[0608] Specifically, the discriminant accuracy of the measurement using the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 63 or a complementary sequence thereof is shown in Table 8-5. For example, the measurement using the combination of one polynucleotide comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 63 or a complementary sequence thereof exhibited accuracy of 79.4% in the training cohort and accuracy of 80.8% in the validation cohort. Also, for example, the measurement using the combinations of two polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 63 or a complementary sequence thereof exhibited accuracy of 95.7% in the training cohort and accuracy of 97.5% in the validation cohort. Furthermore, for example, the measurement using the combinations of three polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 63 or a complementary sequence thereof exhibited accuracy of 98.2% in the training cohort and accuracy of 98.0% in the validation cohort. Furthermore, for example, the measurement using the combinations of four polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 63 or a complementary sequence thereof exhibited accuracy of 99.5% in the training cohort and accuracy of 97.5% in the validation cohort.

[0609] Specifically, the discriminant accuracy of the measurement using the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 113 or a complementary sequence thereof is shown in Table 8-6. For example, the measurement using the combination of one polynucleotide comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 113 or a complementary sequence thereof exhibited accuracy of 67.8% in the training cohort and accuracy of 69.2% in the validation cohort. Also, for example, the measurement using the combinations of two polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 113 or a complementary sequence thereof exhibited accuracy of 97.7% in the training cohort and accuracy of 95.5% in the validation cohort. Furthermore, for example, the measurement using the combinations of three polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 113 or a complementary sequence thereof exhibited accuracy of 99.5% in the training cohort and accuracy of 99.0% in the validation cohort. Furthermore, for example, the measurement using the combinations of four polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 113 or a complementary sequence thereof exhibited accuracy of 99.5% in the training cohort and accuracy of 99.0% in the validation cohort.

[0610] Specifically, the discriminant accuracy of the measurement using the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 124 or a complementary sequence thereof is shown in Table 8-7. For example, the measurement using the combination of one polynucleotide comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 124 or a complementary sequence thereof exhibited accuracy of 79.6% in the training cohort and accuracy of 76.8% in the validation cohort. Also, for example, the measurement using the combinations of two polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 124 or a complementary sequence thereof exhibited accuracy of 95.0% in the training

cohort and accuracy of 91.4% in the validation cohort. Furthermore, for example, the measurement using the combinations of three polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 124 or a complementary sequence thereof exhibited accuracy of 98.5% in the training cohort and accuracy of 97.5% in the validation cohort. Furthermore, for example, the measurement using the combinations of four polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 124 or a complementary sequence thereof exhibited accuracy of 99.0% in the training cohort and accuracy of 99.0% in the validation cohort.

[0611] Specifically, the discriminant accuracy of the measurement using the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 125 or a complementary sequence thereof is shown in Table 8-8. For example, the measurement using the combination of one polynucleotide comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 125 or a complementary sequence thereof exhibited accuracy of 77.6% in the training cohort and accuracy of 73.7% in the validation cohort. Also, for example, the measurement using the combinations of two polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 125 or a complementary sequence thereof exhibited accuracy of 94.7% in the training cohort and accuracy of 93.4% in the validation cohort. Furthermore, for example, the measurement using the combinations of three polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 125 or a complementary sequence thereof exhibited accuracy of 99.0% in the training cohort and accuracy of 96.5% in the validation cohort. Furthermore, for example, the measurement using the combinations of four polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO:125 or a complementary sequence thereof exhibited accuracy of 99.5% in the training cohort and accuracy of 99.0% in the validation cohort.

[0612] Specifically, the discriminant accuracy of the measurement using the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 126 or a complementary sequence thereof is shown in Table 8-9. For example, the measurement using the combination of one polynucleotide comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 126 or a complementary sequence thereof exhibited accuracy of 90.4% in the training cohort and accuracy of 92.4% in the validation cohort. Also, for example, the measurement using the combinations of two polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 126 or a complementary sequence thereof exhibited accuracy of 96.7% in the training cohort and accuracy of 95.5% in the validation cohort. Furthermore, for example, the measurement using the combinations of three polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 126 or a complementary sequence thereof exhibited accuracy of 99.7% in the training cohort and accuracy of 98.0% in the validation cohort. Furthermore, for example, the measurement using the combinations of four polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 126 or a complementary sequence thereof exhibited accuracy of 99.7% in the training cohort and accuracy of 99.0% in the validation cohort.

[0613] Specifically, the discriminant accuracy of the measurement using the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 128 or a complementary sequence thereof is shown in Table 8-10. For example, the measurement using the combination of one polynucleotide comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 128 or a complementary sequence thereof exhibited accuracy of 81.4% in the training cohort and accuracy of 81.3% in the validation cohort. Also, for example, the measurement using the combinations of two polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 128 or a complementary sequence thereof exhibited accuracy of 96.2% in the training cohort and accuracy of 94.9% in the validation cohort. Furthermore, for example, the measurement using the combinations of three polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 128 or a complementary sequence thereof exhibited accuracy of 98.7% in the training cohort and accuracy of 97.5% in the validation cohort. Furthermore, for example, the measurement using the combinations of four polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 128 or a complementary sequence thereof exhibited accuracy of 99.2% in the training cohort and accuracy of 99.5% in the validation cohort.

[0614] Specifically, the discriminant accuracy of the measurement using the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 130 or a complementary sequence thereof is shown in Table 8-11. For example, the measurement using the combination of one polynucleotide comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 130 or a complementary sequence thereof exhibited accuracy of 83.4% in the training cohort and accuracy of 87.4% in the validation cohort. Also, for example, the measurement using the combinations of two polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 130 or a complementary sequence thereof exhibited accuracy of 96.2% in the training cohort and accuracy of 94.4% in the validation cohort. Furthermore, for example, the measurement using the combinations of three polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by

SEQ ID NO: 130 or a complementary sequence thereof exhibited accuracy of 99.2% in the training cohort and accuracy of 98.5% in the validation cohort. Furthermore, for example, the measurement using the combinations of four polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 130 or a complementary sequence thereof exhibited accuracy of 99.5% in the training cohort and accuracy of 99.5% in the validation cohort.

[0615] Specifically, the discriminant accuracy of the measurement using the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 143 or a complementary sequence thereof is shown in Table 8-12. For example, the measurement using the combination of one polynucleotide comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 143 or a complementary sequence thereof exhibited accuracy of 64.6% in the training cohort and accuracy of 66.2% in the validation cohort. Also, for example, the measurement using the combinations of two polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 143 or a complementary sequence thereof exhibited accuracy of 96.0% in the training cohort and accuracy of 93.9% in the validation cohort. Furthermore, for example, the measurement using the combinations of three polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 143 or a complementary sequence thereof exhibited accuracy of 98.7% in the training cohort and accuracy of 98.0% in the validation cohort. Furthermore, for example, the measurement using the combinations of four polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 143 or a complementary sequence thereof exhibited accuracy of 99.0% in the training cohort and accuracy of 98.0% in the validation cohort.

[0616] Specifically, the discriminant accuracy of the measurement using the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 160 or a complementary sequence thereof is shown in Table 8-13. For example, the measurement using the combination of one polynucleotide comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 160 or a complementary sequence thereof exhibited accuracy of 70.9% in the training cohort and accuracy of 67.2% in the validation cohort. Also, for example, the measurement using the combinations of two polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 160 or a complementary sequence thereof exhibited accuracy of 96.0% in the training cohort and accuracy of 92.4% in the validation cohort. Furthermore, for example, the measurement using the combinations of three polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 160 or a complementary sequence thereof exhibited accuracy of 99.2% in the training cohort and accuracy of 98.5% in the validation cohort. Furthermore, for example, the measurement using the combinations of four polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 160 or a complementary sequence thereof exhibited accuracy of 99.5% in the training cohort and accuracy of 99.0% in the validation cohort.

[0617] Specifically, the discriminant accuracy of the measurement using the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 561 or a complementary sequence thereof is shown in Table 8-14. For example, the measurement using the combination of one polynucleotide comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 561 or a complementary sequence thereof exhibited accuracy of 84.9% in the training cohort and accuracy of 81.8% in the validation cohort. Also, for example, the measurement using the combinations of two polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 561 or a complementary sequence thereof exhibited accuracy of 96.5% in the training cohort and accuracy of 97.5% in the validation cohort. Furthermore, for example, the measurement using the combinations of three polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 561 or a complementary sequence thereof exhibited accuracy of 98.7% in the training cohort and accuracy of 98.0% in the validation cohort. Furthermore, for example, the measurement using the combinations of four polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 561 or a complementary sequence thereof exhibited accuracy of 100% in the training cohort and accuracy of 99.0% in the validation cohort.

[0618] Specifically, the discriminant accuracy of the measurement using the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 568 or a complementary sequence thereof is shown in Table 8-15. For example, the measurement using the combination of one polynucleotide comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 568 or a complementary sequence thereof exhibited accuracy of 60.2% in the training cohort and accuracy of 67.2% in the validation cohort. Also, for example, the measurement using the combinations of two polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 568 or a complementary sequence thereof exhibited accuracy of 97.0% in the training cohort and accuracy of 96.0% in the validation cohort. Furthermore, for example, the measurement using the combinations of three polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 568 or a complementary sequence thereof exhibited accuracy of 99.0% in the training cohort and accuracy of 96.0% in the validation cohort. Furthermore, for example, the measurement using the combinations of four polynu-

cleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 568 or a complementary sequence thereof exhibited accuracy of 99.5% in the training cohort and accuracy of 98.5% in the validation cohort.

[0619] Specifically, the discriminant accuracy of the measurement using the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 573 or a complementary sequence thereof is shown in Table 8-16. For example, the measurement using the combination of one polynucleotide comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 573 or a complementary sequence thereof exhibited accuracy of 53.0% in the training cohort and accuracy of 53.5% in the validation cohort. Also, for example, the measurement using the combinations of two polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 573 or a complementary sequence thereof exhibited accuracy of 96.5% in the training cohort and accuracy of 95.5% in the validation cohort. Furthermore, for example, the measurement using the combinations of three polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 573 or a complementary sequence thereof exhibited accuracy of 98.7% in the training cohort and accuracy of 98.0% in the validation cohort. Furthermore, for example, the measurement using the combinations of four polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 573 or a complementary sequence thereof exhibited accuracy of 99.2% in the training cohort and accuracy of 98.5% in the validation cohort.

[0620] Specifically, the discriminant accuracy of the measurement using the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 578 or a complementary sequence thereof is shown in Table 8-17. For example, the measurement using the combination of one polynucleotide comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 578 or a complementary sequence thereof exhibited accuracy of 52.8% in the training cohort and accuracy of 53.5% in the validation cohort. Also, for example, the measurement using the combinations of two polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 578 or a complementary sequence thereof exhibited accuracy of 96.2% in the training cohort and accuracy of 94.9% in the validation cohort. Furthermore, for example, the measurement using the combinations of three polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 578 or a complementary sequence thereof exhibited accuracy of 98.5% in the training cohort and accuracy of 96.5% in the validation cohort. Furthermore, for example, the measurement using the combinations of four polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 578 or a complementary sequence thereof exhibited accuracy of 99.2% in the training cohort and accuracy of 99.0% in the validation cohort.

[0621] The measurement values of the nucleotide sequences represented by SEQ ID NOs: 1, 113, 126, and 561 were compared among 17 lung cancer patients, 99 healthy subjects, 75 pancreatic cancer patients, 62 biliary tract cancer patients, 32 colorectal cancer patients, 35 stomach cancer patients, 32 esophageal cancer patients, 33 liver cancer patients, and 13 benign pancreaticobiliary disease patients in the training cohort. As a result, a scatter diagram that significantly separated the discriminant score of the lung cancer patient group from the discriminant scores of the other groups was obtained in the training cohort (see Figure 4A). These results were also reproducible for the validation cohort (see Figure 4B).

[Table 8-1]

	Training cohort			Validation cohort		
SEQ ID NO:	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
1	94.2	100	94.0	91.4	87.5	91.6
1_113	98.7	100	98.7	97.5	100	97.4
1_52_126	99.2	100	99.2	98.5	100	98.4
1_53_113_125	99.2	100	99.2	98.5	100	98.4
1_10_63_113	99.2	100	99.2	98.5	100	98.4
1_19_113_143	99.2	100	99.2	99.0	100	98.9
1_10_113_126	99.7	100	99.7	99.0	100	98.9
1_2_10_113	99.7	100	99.7	98.5	100	98.4

[Table 8-2]

	Training cohort			Validation cohort		
SEQ ID NO:	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
2	94.0	94.1	94.0	92.4	100	92.1
2_126	97.2	100	97.1	96.0	100	95.8
1_2_113	99.5	100	99.5	98.0	100	97.9
2_19_53_113	99.2	100	99.2	97.5	100	97.4
2_72_113_125	99.0	100	99.0	96.5	100	96.3
2_19_72_113	99.0	100	99.0	97.0	100	96.8
2_19_113_579	98.5	100	98.4	96.5	100	96.3
1_2_19_113	100	100	100	98.0	100	97.9

[Table 8-3]

	Training cohort			Validation cohort		
SEQ ID NO:	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
3	85.7	94.1	85.3	84.3	100	83.7
3_126	97.0	94.1	97.1	97.0	100	96.8
1_3_113	99.0	100	99.0	98.5	100	98.4
3_125_128_568	98.5	100	98.4	97.0	100	96.8
1_3_10_113	99.2	100	99.2	99.0	100	98.9
3_113_125_126	99.5	94.1	99.7	100	100	100
1_3_126_573	98.5	100	98.4	98.0	100	97.9
3_126_130_561	98.2	94.1	98.4	98.0	100	97.9

[Table 8-4]

	Training cohort			Validation cohort		
SEQ ID NO:	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
10	64.0	82.4	63.2	61.6	75.0	61.1
2_10	94.0	100	93.7	92.4	100	92.1
1_10_113	99.2	100	99.2	99.0	100	98.9
1_10_113_143	99.0	100	98.9	99.5	100	99.5
1_10_113_569	99.2	100	99.2	99.0	100	98.9
1_10_113_562	98.7	100	98.7	99.0	100	98.9
1_10_113_578	99.2	100	99.2	98.5	100	98.4
1_7_10_113	99.2	100	99.2	99.0	100	98.9

[Table 8-5]

	Training cohort			Validation cohort		
SEQ ID NO:	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
63	79.4	94.1	78.7	80.8	75.0	81.1
63_126	95.7	94.1	95.8	97.5	100	97.4
1_63_113	98.2	100	98.2	98.0	100	97.9
1_63_567_578	99.5	100	99.5	97.5	100	97.4
1_53_63_578	98.2	100	98.2	98.0	100	97.9
1_63_162_573	98.0	100	97.9	97.5	87.5	97.9
1_63_162_578	98.5	100	98.4	98.0	100	97.9
1_63_576_578	98.7	100	98.7	98.0	100	97.9

[Table 8-6]

	Training cohort			Validation cohort		
SEQ ID NO:	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
113	67.8	76.5	67.5	69.2	100	67.9
2_113	97.7	100	97.6	95.5	100	95.3
1_19_113	99.5	100	99.5	99.0	100	98.9
1_10_113_567	99.5	100	99.5	99.0	100	98.9
1_53_63_113	99.0	100	99.0	98.0	100	97.9
1_53_113_143	99.0	100	99.0	98.0	100	97.9
2_19_113_125	99.0	100	99.0	98.0	100	97.9
2_10_113_130	99.2	100	99.2	99.5	100	99.5

[Table 8-7]

	Training cohort			Validation cohort		
SEQ ID NO:	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
124	79.6	94.1	79.0	76.8	100	75.8
2_124	95.0	100	94.8	91.4	100	91.1
1_113_124	98.5	100	98.4	97.5	100	97.4
113_124_125_126	99.0	94.1	99.2	99.0	100	98.9
124_125_128_568	98.0	100	97.9	94.9	100	94.7
113_124_125_162	99.0	100	99.0	98.0	100	97.9
52_124_126_561	98.0	94.1	98.2	98.0	100	97.9
19_113_124_126	98.0	94.1	98.2	99.0	100	98.9

[Table 8-8]

	Training cohort			Validation cohort		
SEQ ID NO:	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
125	77.6	82.4	77.4	73.7	87.5	73.2
113_125	94.7	100	94.5	93.4	100	93.2
2_113_125	99.0	100	99.0	96.5	100	96.3
1_113_125_160	99.5	100	99.5	98.5	100	98.4
31_113_125_568	99.0	100	98.9	98.0	100	97.9
2_53_113_125	99.2	100	99.2	98.0	100	97.9
1_10_113_125	99.5	100	99.5	99.0	100	98.9
1_113_125_143	99.2	100	99.2	99.0	100	98.9

[Table 8-9]

	Training cohort			Validation cohort		
SEQ ID NO:	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
126	90.4	94.1	90.3	92.4	100	92.1
1_126	96.7	100	96.6	95.5	100	95.3
1_113_126	99.7	100	99.7	98.0	100	97.9
1_126_561_573	98.5	100	98.4	97.5	100	97.4
113_125_126_568	98.5	100	98.4	98.5	100	98.4
113_125_126_561	99.0	94.1	99.2	98.5	100	98.4
1_113_125_126	99.7	100	99.7	99.0	100	98.9
1_52_126_561	99.5	100	99.5	98.0	100	97.9

[Table 8-10]

	Training cohort			Validation cohort		
SEQ ID NO:	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
128	81.4	82.4	81.4	81.3	87.5	81.1
1_128	96.2	100	96.1	94.9	100	94.7
1_113_128	98.7	100	98.7	97.5	100	97.4
26_113_125_128	97.7	94.1	97.9	98.5	100	98.4
1_113_125_128	99.0	100	99.0	99.0	100	98.9
1_10_113_128	99.2	100	99.2	99.5	100	99.5
31_113_125_128	97.5	94.1	97.6	99.0	100	98.9
2_19_113_128	99.0	100	99.0	97.0	100	96.8

[Table 8-11]

	Training cohort			Validation cohort		
SEQ ID NO:	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
130	83.4	88.2	83.2	87.4	100	86.8
1_130	96.2	100	96.1	94.4	100	94.2
1_113_130	99.2	100	99.2	98.5	100	98.4
1_3_130_143	97.7	100	97.6	99.0	100	98.9
1_10_113_130	99.5	100	99.5	99.5	100	99.5
1_63_130_578	98.7	100	98.7	98.5	100	98.4
124_125_130_568	98.5	100	98.4	96.5	100	96.3
2_19_113_130	99.0	100	99.0	98.0	100	97.9

[Table 8-12]

	Training cohort			Validation cohort		
SEQ ID NO:	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
143	64.6	58.8	64.8	66.2	62.5	66.3
1_143	96.0	100	95.8	93.9	87.5	94.2
1_113_143	98.7	100	98.7	98.0	100	97.9
1_3_126_143	99.0	100	98.9	98.0	100	97.9
1_63_130_143	97.7	100	97.6	98.0	100	97.9
1_10_52_143	98.0	100	97.9	100	100	100
2_19_113_143	98.5	100	98.4	96.5	100	96.3
63_124_130_143	96.2	94.1	96.3	96.0	100	95.8

[Table 8-13]

	Training cohort			Validation cohort		
SEQ ID NO:	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
160	70.9	70.6	70.9	67.2	37.5	68.4
2_160	96.0	100	95.8	92.4	100	92.1
1_113_160	99.2	100	99.2	98.5	100	98.4
1_10_113_160	99.2	100	99.2	99.0	100	98.9
7_113_125_160	99.0	100	99.0	97.5	100	97.4
1_113_160_567	99.5	100	99.5	98.0	100	97.9
1_113_160_578	98.7	100	98.7	98.0	100	97.9
2_19_113_160	99.5	100	99.5	98.0	100	97.9

[Table 8-14]

	Training cohort			Validation cohort		
SEQ ID NO:	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
561	84.9	88.2	84.8	81.8	87.5	81.6
126_561	96.5	94.1	96.6	97.5	100	97.4
1_113_561	98.7	100	98.7	98.0	100	97.9
113_125_130_561	97.7	94.1	97.9	99.5	100	99.5
7_126_143_561	98.5	100	98.4	98.5	100	98.4
1_113_126_561	100	100	100	99.0	100	98.9
1_126_561_568	98.7	100	98.7	98.0	100	97.9
7_113_126_561	99.2	94.1	99.5	98.5	100	98.4

[Table 8-15]

	Training cohort			Validation cohort		
SEQ ID NO:	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
568	60.2	58.8	60.3	67.2	100	65.8
1_568	97.0	100	96.8	96.0	100	95.8
1_2_568	99.0	100	98.9	96.0	100	95.8
7_125_126_568	99.2	100	99.2	98.0	100	97.9
124_125_126_568	98.5	100	98.4	98.0	100	97.9
7_113_125_568	98.5	100	98.4	98.0	100	97.9
1_113_125_568	99.5	100	99.5	98.0	100	97.9
113_125_128_568	97.5	100	97.4	98.5	100	98.4

[Table 8-16]

	Training cohort			Validation cohort		
SEQ ID NO:	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
573	53.0	35.3	53.8	53.5	12.5	55.3
1_573	96.5	100	96.3	95.5	100	95.3
1_113_573	98.7	100	98.7	98.0	100	97.9
113_125_126_573	98.2	94.1	98.4	99.5	100	99.5
1_113_125_573	99.2	100	99.2	98.5	100	98.4
1_53_113_573	98.7	100	98.7	97.5	100	97.4
1_124_126_573	97.7	100	97.6	96.5	100	96.3
1_63_130_573	98.7	100	98.7	98.0	100	97.9

[Table 8-17]

	Training cohort			Validation cohort		
SEQ ID NO:	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
578	52.8	52.9	52.8	53.5	50.0	53.7
1_578	96.2	100	96.1	94.9	100	94.7
1_113_578	98.5	100	98.4	96.5	100	96.3
1_126_567_578	98.5	100	98.4	97.5	100	97.4
1_19_113_578	99.2	100	99.2	99.0	100	98.9
31_126_561_578	97.5	94.1	97.6	97.5	100	97.4
1_126_160_578	98.7	100	98.7	97.0	100	96.8
1_113_125_578	98.7	100	98.7	98.5	100	98.4

Industrial Applicability

[0622] According to the present invention, lung cancer can be effectively detected by a simple and inexpensive method. This permits early detection, diagnosis and treatment of lung cancer. The method of the present invention can detect lung cancer with limited invasiveness using the blood of a patient and therefore allows lung cancer to be detected conveniently and rapidly.

SEQUENCE LISTING

[0623]

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<120> Kit and method for detecting lung cancer

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<150> JP 2014-125561
<151> 2014-06-18

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ccuugucucc uuucccuag 79

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ugcccaggcu ggagcgagug caguggugca gucaguccua gcucacugca gccucgaacu 60

ccugggcu 68

<210> 214
<211> 84
<212> RNA
<213> Homo sapiens

<400> 214

ugugcagugg gaaggggggc cgauacacug uacgagagug aguagcaggu cucacaguga 60

accggucucu uucccuacug uguc 84

<210> 215
<211> 77
<212> RNA
<213> Homo sapiens

<400> 215

caugagaaau ccugcugguc aaccauagcc cuggucagac ucuccggggc ugugauugac 60

cagcaggacu ucucaug 77

<210> 216
<211> 80
<212> RNA
<213> Homo sapiens

<400> 216

uggcagaccc uugcucucuc acucucccua augggggcuga agacagcuca ggggcagggu 60

gggggguguu guuuuuguuu 80

<210> 217
<211> 67
<212> RNA
<213> Homo sapiens

<400> 217

ugguggggggu ggggggguguu guuuuuguuu uugagacaga gucuugcucc gucgcccagg 60

ccggagu 67

<210> 218
<211> 81
<212> RNA
<213> Homo sapiens

<400> 218

cucccuggga gggcguggau gaugguggga gaggagcccc acuguggaag ucugaccccc 60

acaucgcccc accuucccca g 81

<210> 219
<211> 63
<212> RNA
<213> Homo sapiens

<400> 219

aauggguggg ugcuggуggg agccgugccc uggccacuca uucggcucuc ucccucaccc 60

uag 63

<210> 220
<211> 49
<212> RNA
<213> Homo sapiens

<400> 220
uucccagcca acgcaccaaa aaugauaugg gucuguuguc uggagaaac 49

<210> 221
<211> 105
<212> RNA
<213> Homo sapiens

<400> 221

gcgggcggcg gcggcggcag cagcagcagg ugcggggcgg cggccgcgcu ggccgcucga 60

cuccgcagcu gcucguucug cuucuccagc uugcgcacca gcucc 105

<210> 222
<211> 82

<212> RNA
<213> Homo sapiens

<400> 222

ugagcuguug gauucggggc cguagcacug ucugagaggu uuacauuucu cacagugaac 60

cggucucuuu uucagcugcu uc 82

<210> 223
<211> 93
<212> RNA
<213> Homo sapiens

<400> 223

uacuuauggc accccacucc ugguaccaua gucauaaguu aggagauguu agagcuguga 60

guaccaugac uuaagugugg uggcuuaaac aug 93

<210> 224
<211> 87
<212> RNA
<213> Homo sapiens

<400> 224

gugaggcggg gccaggaggg uguguggcgu gggugcugcg gggccgucag ggugccugcg 60

ggacgcucac cuggcuggcc cgcccag 87

<210> 225
<211> 61
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<213> Homo sapiens

<400> 225

gagggcagcg uggguguggc ggaggcaggc gugaccguuu gccgcccucu cgcugcucua 60

g 61

<210> 226
<211> 87
<212> RNA
<213> Homo sapiens

<400> 226

accgcaggga aaaugaggga cuuuuggggg cagauguguu uccauuccac uaucauaaug 60

ccccuaaaaa uccuuauugc ucuugca 87

<210> 227
<211> 51
<212> RNA
<213> Homo sapiens

<400> 227
agagaugaag cgggggggcg gggucuugcu cuauugccua cgcugaucuc a 51

<210> 228
<211> 66
<212> RNA
<213> Homo sapiens

<400> 228

ccgagugggg cggggcaggu cccugcaggg acugugacac ugaaggaccu gcaccuucgc 60

ccacag 66

<210> 229
<211> 66
<212> RNA
<213> Homo sapiens

<400> 229

ccuggagggg ggcacugcgc aagcaaagcc agggacccug agaggcuuug cuuccugcuc 60

cccuag 66

<210> 230
<211> 76
<212> RNA
<213> Homo sapiens

<400> 230

acugacuuug agucucuccu cagggugcug caggcaaagc uggggaccca gggagagacg 60

uaagugaggg gagaug 76

<210> 231
<211> 153
<212> RNA
<213> Homo sapiens

<400> 231

gcuccgcccc acgucgcaug cgccccggga acgcgugggg cggagcuucc ggaggccccg 60

cucugcugcc gacccugugg agcggagggu gaagccuccg gaugccaguc ccucaucgcu 120

ggccuggucg cgcuguggcg aaggggggcgg agc 153

<210> 232
<211> 153

<212> RNA
<213> Homo sapiens

<400> 232

gcuccgcccc acgucgcaug cgccccggga acgcgugggg cggagcuucc ggaggccccg 60

cccugcugcc gacccugugg agcggagggu gaagccuccg gaugccaguc ccucaucgcu 120

ggcccggucg cgcuguggcg aaggggggcgg agc 153

<210> 233
<211> 67
<212> RNA
<213> Homo sapiens

<400> 233

gcgcccuccc ucucucccgg gugugcaaau gugugugugc gguguuaugc cggacaagag 60

ggaggug 67

<210> 234
<211> 74
<212> RNA
<213> Homo sapiens

<400> 234

gcagcccggu gagcgcucgc uggccuggca gugcgucgga agaacagggc ggguggggcc 60

gcgcacaucu cugc 74

<210> 235
<211> 87
<212> RNA
<213> Homo sapiens

<400> 235

cccucaucuc ugggcagggg cuuauuguag gagucucuga agagagcugu ggacugaccu 60

gcuuuaaccc uucccccaggu ucccauu 87

<210> 236
<211> 67
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<213> Homo sapiens

<400> 236

ggcagccagg gggaugggcg agcuugggcc cauuccuuuc cuuacccuac cccccauccc 60

ccuguag 67

<210> 237
<211> 82
<212> RNA
<213> Homo sapiens

<400> 237

cugacuuuuu uagggaguag aaggguggggg agcaugaaca auguuucuca cucccuaccc 60

cuccacuccc caaaaaaguc ag 82

<210> 238
<211> 89
<212> RNA
<213> Homo sapiens

<400> 238

agccuguggg aaagagaaga gcagggcagg gugaaggccc ggcggagaca cucugcccac 60

cccacacccu gccuaugggc cacacagcu 89

<210> 239
<211> 71
<212> RNA
<213> Homo sapiens

<400> 239

ggugaguggg agccgguggg gcuggaguaa gggcacgccc ggggcugccc caccugcuga 60

ccacccuccc c 71

<210> 240
<211> 84
<212> RNA
<213> Homo sapiens

<400> 240

auggucccuc ccaauccagc cauuccucag accagguggc ucccgagcca ccccaggcug 60

uaggaugggg gugagaggug cuag 84

<210> 241
<211> 68
<212> RNA
<213> Homo sapiens

<400> 241

gcauccugua cugagcugcc ccgaggcccu ucaugcugcc cagcucgggg cagcucagua 60

caggauac 68

<210> 242
<211> 64
<212> RNA
<213> Homo sapiens

<400> 242

uccuguacug agcugccccg agcugggcag caugaagggc cucggggcag cucaguacag 60

gaug 64

<210> 243
<211> 65
<212> RNA
<213> Homo sapiens

<400> 243

gggugcucgg ggcaggcggc ugggagcggc ccucacauug auggcuccug ccaccuccuc 60

cgcag 65

<210> 244
<211> 67
<212> RNA
<213> Homo sapiens

<400> 244

gugggagggg agaggcagca agcacacagg gccugggacu agcaugcuga ccucccuccu 60

gccccag 67

<210> 245
<211> 63
<212> RNA
<213> Homo sapiens

<400> 245

cuugcccggg agaaggaggu ggccuggaga gcugcugucu ccagccgccg ccugucucca 60

cag 63

<210> 246
<211> 70
<212> RNA
<213> Homo sapiens

<400> 246

acaaauagcu ucagggaguc aggggagggc agaaauagau ggccuucccc ugcugggaag 60

aaagugggguc 70

<210> 247
<211> 102
<212> RNA
<213> Homo sapiens

<400> 247

gcuuaucgag gaaaagaucg aggugggguug gggcgggcuc uggggauuug gucucacagc 60

ccggauccca gcccacuuac cuugguuacu cuccuuccuu cu 102

<210> 248
<211> 90
<212> RNA
<213> Homo sapiens

<400> 248

gugucucucu ggagacccug cagccuuccc acccaccagg gagcuuucca ugggcugugg 60

ggaaggcguc agugucgggu gagggaacac 90

<210> 249
<211> 87
<212> RNA
<213> Homo sapiens

<400> 249

guguggccgg caggcgggug ggcgggggcg gccgguggga accccgcccc gccccgcgcc 60

cgcacucacc cgcccgucuc cccacag 87

<210> 250
<211> 69
<212> RNA
<213> Homo sapiens

<400> 250

cuuucggcca gcgggacggc auccgaggug ggcuaggcuc gggcccgugg cgggugcggg 60

ggugggagg 69

<210> 251
<211> 66
<212> RNA
<213> Homo sapiens

<400> 251

cagagcaggg cagggaaggu gggagagggg cccagcugac ccuccuguca cccgcuccuu 60

gcccag 66

<210> 252

<211> 64
<212> RNA
<213> Homo sapiens

<400> 252

gaaggcgagg gguagaagag cacagggguu cugauaaacc cuucugccug cauucuacuc 60

ccag 64

<210> 253
<211> 73
<212> RNA
<213> Homo sapiens

<400> 253

accuuuccag cucaucccac cucugccacc aaaacacuca ucgcgggguc agagggagug 60

ccaaaaaagg uaa 73

<210> 254
<211> 67
<212> RNA
<213> Homo sapiens

<400> 254

cugguccauu ucccugccau ucccuuggcu ucaauuuacu cccagggcug gcagugacau 60

gggucaa 67

<210> 255
<211> 63
<212> RNA
<213> Homo sapiens

<400> 255

gagucgagga cugguggaag ggccuuuccc cucagaccaa ggcccuggcc ccagcuucuu 60

cuc 63

<210> 256
<211> 67
<212> RNA
<213> Homo sapiens

<400> 256

aauagauuau uggucaccac cuccaguuuc ugaauuugug agacuggggu ggggccugag 60

aauuugc 67

<210> 257
<211> 68

<212> RNA
<213> Homo sapiens

<400> 257

gaauggaaga agaaggcggu cggucugcgg gagccaggcc gcagagccau ccgccuucug 60

uccauguc 68

<210> 258
<211> 60
<212> RNA
<213> Homo sapiens

<400> 258
caaggugggg gagaugggggg uugaacuuca uuucucaugc ucaucccccau cuccuuucag 60

<210> 259
<211> 64
<212> RNA
<213> Homo sapiens

<400> 259

gagcucuggg aggggcuggg uuuggcagga caguuuccaa gcccugucuc cucccaucuu 60

ccag 64

<210> 260
<211> 100
<212> RNA
<213> Homo sapiens

<400> 260

gaggugggag gauugcuuga gucagggugg uugaggcugc aguaaguugu gaucauacca 60

cugcacucca gccugaguga cagagcaaga ccuugucuca 100

<210> 261
<211> 81
<212> RNA
<213> Homo sapiens

<400> 261

uacaggugca ggggaacugu agaugaaaag gcuuggcacu ugagggaaag ccucaguuca 60

uucucauuuu gcucaccugu u 81

<210> 262
<211> 78
<212> RNA
<213> Homo sapiens

<400> 262

gggcccagaa gggggcgcag ucacugacgu gaagggacca caucccgcuu caugucagug 60

acuccugccc cuuggucu 78

<210> 263
<211> 87
<212> RNA
<213> Homo sapiens

<400> 263

cccaggcgcc cgcucccgac ccacgccgcg ccgccggguc ccuccucccc ggagaggcug 60

ggcucgggac gcgcggcuca gcucggg 87

<210> 264
<211> 81
<212> RNA
<213> Homo sapiens

<400> 264

cauccuccuu acgucccacc ccccacuccu guuucuggug aaauauucaa acaggagugg 60

gggugggaca uaaggaggau a 81

<210> 265
<211> 86
<212> RNA
<213> Homo sapiens

<400> 265

ggcuuagaaa cagucccuag guaggauuug gggaggagcu aagaagcccc uacagggccc 60

agaggugggg acugagccuu aguugg 86

<210> 266
<211> 80
<212> RNA
<213> Homo sapiens

<400> 266

ugagaggccg caccuugccu ugcugcccgg gccgugcacc cgugggcccc agggcgacgc 60

ggcgggggcg gcccuagcga 80

<210> 267
<211> 73
<212> RNA

<213> Homo sapiens

<400> 267

gaaaacaacc aggugggcuu cccggagggc ggaacaccca gccccagcau ccagggcuca 60

ccuaccacgu uug 73

<210> 268
<211> 64
<212> RNA
<213> Homo sapiens

<400> 268

aaccccgggc cggaggucaa gggcgucgcu ucucccuaau guugccucuu uuccacggcc 60

ucag 64

<210> 269
<211> 74
<212> RNA
<213> Homo sapiens

<400> 269

ccugcaggag gcagugggcg agcaggcggg gcagcccaau gccaugggcc ugaucucacc 60

gcugccuccu uccc 74

<210> 270
<211> 102
<212> RNA
<213> Homo sapiens

<400> 270

gugggagggc ccaggcgcgg gcaggggugg ggguggcaga gcgcuguccc gggggcgggg 60

ccgaagcgcg gcgaccguaa cuccuucugc uccgucccgc ag 102

<210> 271
<211> 69
<212> RNA
<213> Homo sapiens

<400> 271

gaaccucggg gcaugggggа gggaggcugg acaggagagg gcucacccag gcccuguccu 60

cugccccag 69

<210> 272
<211> 99

<212> RNA
<213> Homo sapiens

<400> 272

gcaagggaca gggagggucg uggcgacacu cgcgccagcu cccgggacgg cugggcucgg 60

gcuggucgcc gaccuccgac ccuccacuag augccuggc 99

<210> 273
<211> 71
<212> RNA
<213> Homo sapiens

<400> 273

gugucugugc cggucccagg agaaccugca gaggcaucgg gucagcggug cuccugcggg 60

ccgacacuca c 71

<210> 274
<211> 61
<212> RNA
<213> Homo sapiens

<400> 274

ucucguuuga ucucggaagc uaagcagggu ugggccuggu uaguacuugg augggaaacu 60

u 61

<210> 275
<211> 53
<212> RNA
<213> Homo sapiens

<400> 275
guuugaucuc ggaagcuaag cagggucggg ccugguuagu acuuggaugg gag 53

<210> 276
<211> 103
<212> RNA
<213> Homo sapiens

<400> 276

gugucggcug uggcgugacu gucccucugu gucccccacu aggcccacug cucaguggag 60

cguggaggac gaggaggagg ccguccacga gcaaugccag cau 103

<210> 277
<211> 64
<212> RNA
<213> Homo sapiens

<400> 277

ugcucuguag gcaugaggca gggcccaggu uccaugugau gcugaagcuc ugacauuccu 60

gcag 64

<210> 278
<211> 63
<212> RNA
<213> Homo sapiens

<400> 278

ugguggcggc gguaguuaug ggcuucucuu ucucaccagc agccccuggg ccgccgccuc 60

ccu 63

<210> 279
<211> 58
<212> RNA
<213> Homo sapiens

<400> 279
agggccagag gagccuggag uggucggguc gacugaaccc agguucccuc uggccgca 58

<210> 280
<211> 72
<212> RNA
<213> Homo sapiens

<400> 280

ugugggacug caaaugggag cucagcaccu gccugccacc cacgcagacc agccccugcu 60

cuguucccac ag 72

<210> 281
<211> 64
<212> RNA
<213> Homo sapiens

<400> 281

ccccgggccc ggcguucccu ccccuuccgu gcgccagugg aggccggggu ggggcggggc 60

gggg 64

<210> 282
<211> 64
<212> RNA
<213> Homo sapiens

<400> 282

ccccgggccc ggcguucccu ccccuuccgu gcgccagugg aggccggggu ggggcggggc 60

gggg 64

<210> 283
<211> 89
<212> RNA
<213> Homo sapiens

<400> 283

ucuccguuua ucccaccacu gccaccauua uugcuacugu ucagcaggug cugcuggugg 60

ugauggugau agucuggugg gggcggugg 89

<210> 284
<211> 51
<212> RNA
<213> Homo sapiens

<400> 284
acagaccccg gggagcccgg cggugaagcu ccugguaucc ugggugucug a 51

<210> 285
<211> 115
<212> RNA
<213> Homo sapiens

<400> 285

gagcaaaaac cagagaacaa caugggagcg uuccuaaccc cuaaggcaac uggaugggag 60

accugaccca uccaguucuc ugagggggcu cuuguguguu cuacaagguu guuca 115

<210> 286
<211> 85
<212> RNA
<213> Homo sapiens

<400> 286

ggcgccuccu gcucugcugu gccgccaggg ccucccccuag cgcgccuucu ggagaggcuu 60

ugugcggaua cggggcugga ggccu 85

<210> 287
<211> 70
<212> RNA
<213> Homo sapiens

<400> 287

gucccuggggg gcugggaugg gccauggugu gcucugaucc cccuguggguc ucuuggcccc 60

caggaacucc 70

<210> 288
<211> 82
<212> RNA
<213> Homo sapiens

<400> 288

gugaguggga ggccagggca cggcaggggg agcugcaggg cuaugggagg ggccccagcg 60

ucugagcccu guccuccccgc ag 82

<210> 289
<211> 82
<212> RNA
<213> Homo sapiens

<400> 289

gugaguggga ggccagggca cggcaggggg agcugcaggg cuaugggagg ggccccagcg 60

ucugagcccu guccuccccgc ag 82

<210> 290
<211> 73
<212> RNA
<213> Homo sapiens

<400> 290

cuggguguuug aggcgaugug gggauguaga gacaacuucc cagucucauu uccucauccu 60

gccaggccac cau 73

<210> 291
<211> 84
<212> RNA
<213> Homo sapiens

<400> 291

ccgcagccgc cgcgccgggc ccggguuggc cgcugacccc cgcggggccc ccggcggccg 60

gggcgggggc gggggcugcc ccgg 84

<210> 292
<211> 69
<212> RNA
<213> Homo sapiens

<400> 292

gggcuuaggg augggaggcc aggaugaaga uuaaucccua aucccccaaca cuggccuugc 60

uauccccag 69

<210> 293
<211> 80
<212> RNA
<213> Homo sapiens

<400> 293

gcgucaagau ggcggcgggg agguaggcag agcaggacgc cgcugcugcc gccgccaccg 60

ccgccuccgc uccagucgcc 80

<210> 294
<211> 62
<212> RNA
<213> Homo sapiens

<400> 294

gugaguggggg cucccgggac ggcgcccgcc cuggcccugg cccggcgacg ucucacgguc 60

cc 62

<210> 295
<211> 67
<212> RNA
<213> Homo sapiens

<400> 295

ccugcaggca gaagugggggc ugacagggca gaggguugcg cccccucacc aucccuucug 60

ccugcag 67

<210> 296
<211> 67
<212> RNA
<213> Homo sapiens

<400> 296

ccugcaggca gaagugggggc ugacagggca gaggguugcg cccccucacc aucccuucug 60

ccugcag 67

<210> 297
<211> 67
<212> RNA
<213> Homo sapiens

<400> 297

ccugcaggca gaaguggggc ugacagggca gaggguugcg cccccucacc aucccuucug 60

ccugcag 67

<210> 298
<211> 67
<212> RNA
<213> Homo sapiens

<400> 298

ccugcaggca gaaguggggc ugacagggca gaggguugcg cccccucacc aucccuucug 60

ccugcag 67

<210> 299
<211> 59
<212> RNA
<213> Homo sapiens

<400> 299
cgggcucugg gugcaguggg gguucccacg ccgcggcaac caccacuguc ucuccccag 59

<210> 300
<211> 67
<212> RNA
<213> Homo sapiens

<400> 300

guggcacuca aacuguggggc gcacuuucug cucucuggug aaagugccgc caucuuuuga 60

guguuac 67

<210> 301
<211> 88
<212> RNA
<213> Homo sapiens

<400> 301

guggggccag gcgguggugg gcacugcugg ggugggcaca gcagccaugc agagcgggca 60

uuugaccccg ugccacccuu uuccccag 88

<210> 302
<211> 94
<212> RNA
<213> Homo sapiens

<400> 302

cacggugucc ccugguggaa ccuggcaggg ggagagguaa ggucuuucag ccucuccaaa 60

gcccaugguc agguacucag gugggggagc ccug 94

<210> 303
<211> 109
<212> RNA
<213> Homo sapiens

<400> 303

ggucgggcuc accaugacac agugugagac cucgggcuac aacacaggac ccgggcgcug 60

cucugacccc ucgugucuug uguugcagcc ggagggacgc agguccgca 109

<210> 304
<211> 90
<212> RNA
<213> Homo sapiens

<400> 304

ucuaagaaac gcaguggucu cugaagccug caggggcagg ccagcccugc acugaacgcc 60

uguucuugcc agguggcaga agguugcugc 90

<210> 305
<211> 87
<212> RNA
<213> Homo sapiens

<400> 305

cacuguucua ugguuaguuu ugcagguuug cauccagcug ugugauauuc ugcugugcaa 60

auccaugcaa aacugacugu gguagug 87

<210> 306
<211> 96
<212> RNA
<213> Homo sapiens

<400> 306

acauugcuac uuacaauuag uuuugcaggu uugcauuuca gcguauauau guauaugugg 60

cugugcaaau ccaugcaaaa cugauuguga uaaugu 96

<210> 307
<211> 90
<212> RNA
<213> Homo sapiens

<400> 307

guggguacgg cccagugggg gggagaggga cacgcccugg gcucugccca gggugcagcc 60

ggacugacug agccccugug ccgcccccag 90

<210> 308
<211> 72
<212> RNA
<213> Homo sapiens

<400> 308

cuugggaaug gcaaggaaac cguuaccauu acugaguuua guaaugguaa ugguucucuu 60

gcuauaccca ga 72

<210> 309
<211> 82
<212> RNA
<213> Homo sapiens

<400> 309

uguggGcagg gcccugggga gcugaggcuc uggggguggc cggggcugac ccugggccuc 60

ugcucccCag ugucugaccg cg 82

<210> 310
<211> 110
<212> RNA
<213> Homo sapiens

<400> 310

ccuggccucc ugcagugcca cgcuccgugu auuugacaag cugaguugga cacuccaugu 60

gguagagugu caguuuguca aauaccccaa gugcggcaca ugcuuaccag 110

<210> 311
<211> 73
<212> RNA
<213> Homo sapiens

<400> 311

gugggcgggg gcaggugugu ggugggguggu ggccugcggu gagcagggcc cucacaccug 60

ccucgccccc cag 73

<210> 312
<211> 86
<212> RNA
<213> Homo sapiens

<400> 312

ugccagucuc uaggucccug agacccuuua accugugagg acauccaggg ucacagguga 60

gguucuuggg agccuggcgu cuggcc 86

<210> 313
<211> 96
<212> RNA
<213> Homo sapiens

<400> 313

cgggccccgg gcgggcggga gggacgggac gcggugcagu guuguuuuuu cccccgccaa 60

uauugcacuc gucccggccu ccggcccccc cggccc 96

<210> 314
<211> 85
<212> RNA
<213> Homo sapiens

<400> 314

ggcugagccg caguaguucu ucaguggcaa gcuuuauguc cugacccagc uaaagcugcc 60

aguugaagaa cuguugcccu cugcc 85

<210> 315
<211> 67
<212> RNA
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agggacccuc ccaacuc 77

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ugcagcacca cggcccaggc ggcauuggug ucacc 95

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cggaaggcgg agcggcggau cuggacaccc agcggu 96

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aucccgaggc uuugcacag 79

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ccuccag 67

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gggacggggg cugugcuggg gcagcugga 89

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uggagaggcc 70

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gcaggggcug gugcugggcg gggggcggcg gg 92

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cucag 65

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ccaggugcac ag 72

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gggcggcgcc guguccgcga ccgcguaccc ugac 94

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cccgcccggc gcccguccgc ccgcgggguc 89

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uccgagccug ggucucccuc uucccccccaa cccccc 96

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gucagggccc cucaucuucc ccuccuuucc cag 93

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gcacugggag gggcccucac 80

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gaccuggaca uguuugugcc caguacuguc aguuugcag 99

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gggccaggcu gugggggcg 78

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ccgcgccuuu gucugugucc cacag 85

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cucagccccu ggg 73

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cggggagccc cugg 74

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acucggcgug gcguc 15

Claims

1. Use of a kit in the *in vitro* diagnosis of lung cancer, the kit comprising a nucleic acid capable of specifically binding to lung cancer marker miR-6768-5p.

2. The use according to claim 1, wherein the nucleic acid is a polynucleotide selected from the group consisting of the following polynucleotides (a) to (e):

(a) a polynucleotide consisting of a nucleotide sequence represented by SEQ ID NO: 1 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, a variant thereof, a derivative thereof, or a fragment thereof comprising 15 or more consecutive nucleotides,
(b) a polynucleotide comprising a nucleotide sequence represented by SEQ ID NO: 1,
(c) a polynucleotide consisting of a nucleotide sequence complementary to a nucleotide sequence represented by SEQ ID NO: 1 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, a variant thereof, a derivative thereof, or a fragment thereof comprising 15 or more consecutive nucleotides,
(d) a polynucleotide comprising a nucleotide sequence complementary to a nucleotide sequence represented by SEQ ID NO: 1 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, and
(e) a polynucleotide hybridizing under stringent conditions to any of the polynucleotides (a) to (d).

3. The use according to claim 1 or 2, wherein the kit further comprises a nucleic acid capable of specifically binding to at least one or more polynucleotide(s) selected from the group consisting of other lung cancer markers: miR-6836-3p, miR-6782-5p, miR-3663-3p, miR-1908-3p, miR-6726-5p, miR-4258, miR-1343-3p, miR-4516, miR-6875-5p, miR-4651, miR-6825-5p, miR-6840-3p, miR-6780b-5p, miR-6749-5p, miR-8063, miR-6784-5p, miR-3679-5p, miR-3184-5p, miR-663b, miR-6880-5p, miR-1908-5p, miR-92a-2-5p, miR-7975, miR-7110-5p, miR-6842-5p, miR-6857-5p, miR-5572, miR-3197, miR-6131, miR-6889-5p, miR-4454, miR-1199-5p, miR-1247-3p, miR-6800-5p, miR-6872-3p, miR-4649-5p, miR-6791-5p, miR-4433b-3p, miR-3135b, miR-128-2-5p, miR-4675, miR-4472, miR-6785-5p, miR-6741-5p, miR-7977, miR-3665, miR-128-1-5p, miR-4286, miR-6765-3p, miR-4632-5p, miR-365a-5p, miR-6088, miR-6816-5p, miR-6885-5p, miR-711, miR-6765-5p, miR-3180, miR-4442, miR-4792, miR-6721-5p, miR-6798-5p, miR-3162-5p, miR-6126, miR-4758-5p, miR-2392, miR-486-3p, miR-6727-5p, miR-4728-5p,

miR-6746-5p, miR-4270, miR-3940-5p, miR-4725-3p, miR-7108-5p, miR-3656, miR-6879-5p, miR-6738-5p, miR-1260a, miR-4446-3p, miR-3131, miR-4463, miR-3185, miR-6870-5p, miR-6779-5p, miR-1273g-3p, miR-8059, miR-4697-5p, miR-4674, miR-4433-3p, miR-4257, miR-1915-5p, miR-4417, miR-1343-5p, miR-6781-5p, miR-4695-5p, miR-1237-5p, miR-6775-5p, miR-7845-5p, miR-4746-3p, miR-7641, miR-7847-3p, miR-6806-5p, miR-4467, miR-4726-5p, miR-4648, miR-6089, miR-1260b, miR-4532, miR-5195-3p, miR-3188, miR-6848-5p, miR-1233-5p, miR-6717-5p, miR-3195, miR-6757-5p, miR-8072, miR-4745-5p, miR-6511a-5p, miR-6776-5p, miR-371a-5p, miR-1227-5p, miR-7150, miR-1915-3p, miR-187-5p, miR-614, miR-1225-5p, miR-451a, miR-939-5p, miR-223-3p, miR-125a-3p, miR-92b-5p, miR-22-3p, miR-6073, miR-6845-5p, miR-6769b-5p, miR-4665-3p, miR-1913, miR-1228-3p, miR-940, miR-296-3p, miR-4690-5p, miR-548q, miR-663a, miR-1249, miR-1202, miR-7113-3p, miR-1225-3p, miR-4783-3p, miR-4448 and miR-4534, and/or; miR-19b-3p, miR-1228-5p, miR-1307-3p, miR-4271, miR-642b-3p, miR-6075, miR-6125, miR-887-3p, miR-6851-5p, miR-6763-5p, miR-3928-3p, miR-4443, miR-3648, miR-149-3p, miR-4689, miR-4763-3p, miR-6729-5p, miR-3196, miR-8069, miR-1268a, miR-4739, miR-1268b, miR-5698, miR-6752-5p, miR-4507, miR-564, miR-4497, miR-6877-5p, miR-6087, miR-4731-5p, miR-615-5p, miR-760, miR-6891-5p, miR-6887-5p, miR-4525, miR-1914-3p, miR-619-5p, miR-5001-5p, miR-6722-3p, miR-3621, miR-4298, miR-675-5p and miR-4655-5p.

4. The use according to claim 3, wherein the nucleic acid is a polynucleotide selected from the group consisting of the following polynucleotides (a') to (e'):

(a') a polynucleotide consisting of a nucleotide sequence represented by any of SEQ ID NOs: 2 to 125, 127 to 130, 132 to 134, and 561 to 578 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, a variant thereof, a derivative thereof, or a fragment thereof comprising 15 or more consecutive nucleotides,
(b') a polynucleotide comprising a nucleotide sequence represented by any of SEQ ID NOs: 2 to 125, 127 to 130, 132 to 134, and 561 to 578,
(c') a polynucleotide consisting of a nucleotide sequence complementary to a nucleotide sequence represented by any of SEQ ID NOs: 2 to 125, 127 to 130, 132 to 134, and 561 to 578 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, a variant thereof, a derivative thereof, or a fragment thereof comprising 15 or more consecutive nucleotides,
(d') a polynucleotide comprising a nucleotide sequence complementary to a nucleotide sequence represented by any of SEQ ID NOs: 2 to 125, 127 to 130, 132 to 134, and 561 to 578 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, and
(e') a polynucleotide hybridizing under stringent conditions to any of the polynucleotides (a') to (d'), and/or;

a polynucleotide selected from the group consisting of the following polynucleotides (f) to (o):

(f) a polynucleotide consisting of a nucleotide sequence represented by any of SEQ ID NOs: 126, 131 and 579 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, a variant thereof, a derivative thereof, or a fragment thereof comprising 15 or more consecutive nucleotides,
(g) a polynucleotide comprising a nucleotide sequence represented by any of SEQ ID NOs: 126, 131 and 579
(h) a polynucleotide consisting of a nucleotide sequence complementary to a nucleotide sequence represented by any of SEQ ID NOs: 126, 131 and 579 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, a variant thereof, a derivative thereof, or a fragment thereof comprising 15 or more consecutive nucleotides,
(i) a polynucleotide comprising a nucleotide sequence complementary to a nucleotide sequence represented by any of SEQ ID NOs: 126, 131 and 579 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t,
(j) a polynucleotide hybridizing under stringent conditions to any of the polynucleotides (f) to (i);
(k) a polynucleotide consisting of a nucleotide sequence represented by any of SEQ ID NOs: 135 to 174 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, a variant thereof, a derivative thereof, or a fragment thereof comprising 15 or more consecutive nucleotides,
(l) a polynucleotide comprising a nucleotide sequence represented by any of SEQ ID NOs: 135 to 174,
(m) a polynucleotide consisting of a nucleotide sequence complementary to a nucleotide sequence represented by any of SEQ ID NOs: 135 to 174 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, a variant thereof, a derivative thereof, or a fragment thereof comprising 15 or more consecutive nucleotides,
(n) a polynucleotide comprising a nucleotide sequence complementary to a nucleotide sequence represented by any of SEQ ID NOs: 135 to 174 or a nucleotide sequence derived from the nucleotide sequence by the

replacement of u with t, and
(o) a polynucleotide hybridizing under stringent conditions to any of the polynucleotides (k) to (n).

5. The use according to any one of claims 1 to 4, wherein the kit comprises at least two or more nucleic acids capable of specifically binding to at least two or more polynucleotides, respectively, selected from all of the lung cancer markers according to claim 1 or 3.

6. Use of a device in the *in vitro* diagnosis of lung cancer, comprising a nucleic acid capable of specifically binding to a polynucleotide of lung cancer marker miR-6768-5p.

7. The use according to claim 6, wherein the nucleic acid is a polynucleotide selected from the group consisting of the following polynucleotides (a) to (e):

(a) a polynucleotide consisting of a nucleotide sequence represented by SEQ ID NO: 1 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, a variant thereof, a derivative thereof, or a fragment thereof comprising 15 or more consecutive nucleotides,
(b) a polynucleotide comprising a nucleotide sequence represented by SEQ ID NO: 1,
(c) a polynucleotide consisting of a nucleotide sequence complementary to a nucleotide sequence represented by SEQ ID NO: 1 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, a variant thereof, a derivative thereof, or a fragment thereof comprising 15 or more consecutive nucleotides,
(d) a polynucleotide comprising a nucleotide sequence complementary to a nucleotide sequence represented by SEQ ID NO: 1 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, and
(e) a polynucleotide hybridizing under stringent conditions to any of the polynucleotides (a) to (d).

8. The use according to claim 6 or 7, wherein the device further comprises a nucleic acid capable of specifically binding to at least one or more polynucleotide(s) selected from the group consisting of other lung cancer markers: miR-6836-3p, miR-6782-5p, miR-3663-3p, miR-1908-3p, miR-6726-5p, miR-4258, miR-1343-3p, miR-4516, miR-6875-5p, miR-4651, miR-6825-5p, miR-6840-3p, miR-6780b-5p, miR-6749-5p, miR-8063, miR-6784-5p, miR-3679-5p, miR-3184-5p, miR-663b, miR-6880-5p, miR-1908-5p, miR-92a-2-5p, miR-7975, miR-7110-5p, miR-6842-5p, miR-6857-5p, miR-5572, miR-3197, miR-6131, miR-6889-5p, miR-4454, miR-1199-5p, miR-1247-3p, miR-6800-5p, miR-6872-3p, miR-4649-5p, miR-6791-5p, miR-4433b-3p, miR-3135b, miR-128-2-5p, miR-4675, miR-4472, miR-6785-5p, miR-6741-5p, miR-7977, miR-3665, miR-128-1-5p, miR-4286, miR-6765-3p, miR-4632-5p, miR-365a-5p, miR-6088, miR-6816-5p, miR-6885-5p, miR-711, miR-6765-5p, miR-3180, miR-4442, miR-4792, miR-6721-5p, miR-6798-5p, miR-3162-5p, miR-6126, miR-4758-5p, miR-2392, miR-486-3p, miR-6727-5p, miR-4728-5p, miR-6746-5p, miR-4270, miR-3940-5p, miR-4725-3p, miR-7108-5p, miR-3656, miR-6879-5p, miR-6738-5p, miR-1260a, miR-4446-3p, miR-3131, miR-4463, miR-3185, miR-6870-5p, miR-6779-5p, miR-1273g-3p, miR-8059, miR-4697-5p, miR-4674, miR-4433-3p, miR-4257, miR-1915-5p, miR-4417, miR-1343-5p, miR-6781-5p, miR-4695-5p, miR-1237-5p, miR-6775-5p, miR-7845-5p, miR-4746-3p, miR-7641, miR-7847-3p, miR-6806-5p, miR-4467, miR-4726-5p, miR-4648, miR-6089, miR-1260b, miR-4532, miR-5195-3p, miR-3188, miR-6848-5p, miR-1233-5p, miR-6717-5p, miR-3195, miR-6757-5p, miR-8072, miR-4745-5p, miR-6511a-5p, miR-6776-5p, miR-371a-5p, miR-1227-5p, miR-7150, miR-1915-3p, miR-187-5p, miR-614, miR-1225-5p, miR-451a, miR-939-5p, miR-223-3p, miR-125a-3p, miR-92b-5p, miR-22-3p, miR-6073, miR-6845-5p, miR-6769b-5p, miR-4665-3p, miR-1913, miR-1228-3p, miR-940, miR-296-3p, miR-4690-5p, miR-548q, miR-663a, miR-1249, miR-1202, miR-7113-3p, miR-1225-3p, miR-4783-3p, miR-4448 and miR-4534, and /or; miR-19b-3p, miR-1228-5p, miR-1307-3p, miR-4271, miR-642b-3p, miR-6075, miR-6125, miR-887-3p, miR-6851-5p, miR-6763-5p, miR-3928-3p, miR-4443, miR-3648, miR-149-3p, miR-4689, miR-4763-3p, miR-6729-5p, miR-3196, miR-8069, miR-1268a, miR-4739, miR-1268b, miR-5698, miR-6752-5p, miR-4507, miR-564, miR-4497, miR-6877-5p, miR-6087, miR-4731-5p, miR-615-5p, miR-760, miR-6891-5p, miR-6887-5p, miR-4525, miR-1914-3p, miR-619-5p, miR-5001-5p, miR-6722-3p, miR-3621, miR-4298, miR-675-5p and miR-4655-5p.

9. The use according to claim 8, wherein the nucleic acid is a polynucleotide selected from the group consisting of the following polynucleotides (a') to (e'):

(a') a polynucleotide consisting of a nucleotide sequence represented by any of SEQ ID NOs: 2 to 125, 127 to 130, 132 to 134, and 561 to 578 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, a variant thereof, a derivative thereof, or a fragment thereof comprising 15 or more consecutive nucleotides,

(b') a polynucleotide comprising a nucleotide sequence represented by any of SEQ ID NOs: 2 to 125, 127 to 130, 132 to 134, and 561 to 578,
(c') a polynucleotide consisting of a nucleotide sequence complementary to a nucleotide sequence represented by any of SEQ ID NOs: 2 to 125, 127 to 130, 132 to 134, and 561 to 578 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, a variant thereof, a derivative thereof, or a fragment thereof comprising 15 or more consecutive nucleotides,
(d') a polynucleotide comprising a nucleotide sequence complementary to a nucleotide sequence represented by any of SEQ ID NOs: 2 to 125, 127 to 130, 132 to 134, and 561 to 578 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, and
(e') a polynucleotide hybridizing under stringent conditions to any of the polynucleotides (a') to (d'), and/or;

a polynucleotide selected from the group consisting of the following polynucleotides (f) to (o):

(f) a polynucleotide consisting of a nucleotide sequence represented by any of SEQ ID NOs: 126, 131 and 579or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, a variant thereof, a derivative thereof, or a fragment thereof comprising 15 or more consecutive nucleotides,
(g) a polynucleotide comprising a nucleotide sequence represented by any of SEQ ID NOs: 126, 131 and 579,
(h) a polynucleotide consisting of a nucleotide sequence complementary to a nucleotide sequence represented by any of SEQ ID NOs: 126, 131 and 579or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, a variant thereof, a derivative thereof, or a fragment thereof comprising 15 or more consecutive nucleotides,
(i) a polynucleotide comprising a nucleotide sequence complementary to a nucleotide sequence represented by any of SEQ ID NOs: 126, 131 and 579 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t,
(j) a polynucleotide hybridizing under stringent conditions to any of the polynucleotides (f) to (i);
(k) a polynucleotide consisting of a nucleotide sequence represented by any of SEQ ID NOs: 135 to 174 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, a variant thereof, a derivative thereof, or a fragment thereof comprising 15 or more consecutive nucleotides,
(l) a polynucleotide comprising a nucleotide sequence represented by any of SEQ ID NOs: 135 to 174,
(m) a polynucleotide consisting of a nucleotide sequence complementary to a nucleotide sequence represented by any of SEQ ID NOs: 135 to 174 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, a variant thereof, a derivative thereof, or a fragment thereof comprising 15 or more consecutive nucleotides,
(n) a polynucleotide comprising a nucleotide sequence complementary to a nucleotide sequence represented by any of SEQ ID NOs: 135 to 174 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, and
(o) a polynucleotide hybridizing under stringent conditions to any of the polynucleotides (k) to (n).

10. The use according to any one of claims 6 to 9, wherein the device is a device for measurement by a hybridization technique.

11. The use according to claim 10, wherein the hybridization technique is a nucleic acid array technique.

12. The use according to any one of claims 6 to 11, wherein the device comprises at least two or more nucleic acids capable of specifically binding to at least two or more polynucleotides, respectively, selected from all of the lung cancer markers according to claim 6

13. A method for detecting lung cancer, comprising measuring an expression level of a target nucleic acid in a sample from a subject using the kit as defined in any one of claims 1 to 5 or use of the device as defined in any one of claims 6 to 12, and evaluating *in vitro* whether or not the subject has lung cancer using both of the measured expression level and a control expression level of in a sample from a healthy subject measured in the same way.

14. The method according to claim 13, wherein the subject is a human.

15. The method according to claim 13 or 14, wherein the sample is blood, serum, or plasma.

16. Use of a marker in the *in vitro* diagnosis of lung cancer, the marker comprising polynucleotide miR-6768-5p.

17. The use according to claim 16, wherein the marker further comprises at least one polynucleotide(s) selected from the group consisting of the following other lung cancer markers: miR-.6836-3p, miR-6782-5p, miR-3663-3p, miR-1908-3p, miR-6726-5p, miR-4258, miR-1343-3p, miR-4516, miR-6875-5p, miR-4651, miR-6825-5p, miR-6840-3p, miR-6780b-5p, miR-6749-5p, miR-8063, miR-6784-5p, miR-3679-5p, miR-3184-5p, miR-663b, miR-6880-5p, miR-1908-5p, miR-92a-2-5p, miR-7975, miR-7110-5p, miR-6842-5p, miR-6857-5p, miR-5572, miR-3197, miR-6131, miR-6889-5p, miR-4454, miR-1199-5p, miR-1247-3p, miR-6800-5p, miR-6872-3p, miR-4649-5p, miR-6791-5p, miR-4433b-3p, miR-3135b, miR-128-2-5p, miR-4675, miR-4472, miR-6785-5p, miR-6741-5p, miR-7977, miR-3665, miR-128-1-5p, miR-4286, miR-6765-3p, miR-4632-5p, miR-365a-5p, miR-6088, miR-6816-5p, miR-6885-5p, miR-711, miR-6765-5p, miR-3180, miR-4442, miR-4792, miR-6721-5p, miR-6798-5p, miR-3162-5p, miR-6126, miR-4758-5p, miR-2392, miR-486-3p, miR-6727-5p, miR-4728-5p, miR-6746-5p, miR-4270, miR-3940-5p, miR-4725-3p, miR-7108-5p, miR-3656, miR-6879-5p, miR-6738-5p, miR-1260a, miR-4446-3p, miR-3131, miR-4463, miR-3185, miR-6870-5p, miR-6779-5p, miR-1273g-3p, miR-8059, miR-4697-5p, miR-4674, miR-4433-3p, miR-4257, miR-1915-5p, miR-4417, miR-1343-5p, miR-6781-5p, miR-4695-5p, miR-1237-5p, miR-6775-5p, miR-7845-5p, miR-4746-3p, miR-7641, miR-7847-3p, miR-6806-5p, miR-4467, miR-4726-5p, miR-4648, miR-6089, miR-1260b, miR-4532, miR-5195-3p, miR-3188, miR-6848-5p, miR-1233-5p, miR-6717-5p, miR-3195, miR-6757-5p, miR-8072, miR-4745-5p, miR-6511a-5p, miR-6776-5p, miR-371a-5p, miR-1227-5p, miR-7150, miR-1915-3p, miR-187-5p, miR-614, miR-1225-5p, miR-451a, miR-939-5p, miR-223-3p, miR-125a-3p, miR-92b-5p, miR-22-3p, miR-6073, miR-6845-5p, miR-6769b-5p, miR-4665-3p, miR-1913, miR-1228-3p, miR-940, miR-296-3p, miR-4690-5p, miR-548q, miR-663a, miR-1249, miR-1202, miR-7113-3p, miR-1225-3p, miR-4783-3p, miR-4448 and miR-4534, and/or;
miR-19b-3p, miR-1228-5p, miR-1307-3p, miR-4271, miR-642b-3p, miR-6075, miR-6125, miR-887-3p, miR-6851-5p, miR-6763-5p, miR-3928-3p, miR-4443, miR-3648, miR-149-3p, miR-4689, miR-4763-3p, miR-6729-5p, miR-3196, miR-8069, miR-1268a, miR-4739, miR-1268b, miR-5698, miR-6752-5p, miR-4507, miR-564, miR-4497, miR-6877-5p, miR-6087, miR-4731-5p, miR-615-5p, miR-760, miR-6891-5p, miR-6887-5p, miR-4525, miR-1914-3p, miR-619-5p, miR-5001-5p, miR-6722-3p, miR-3621, miR-4298, miR-675-5p and miR-4655-5p.

Patentansprüche

1. Verwendung eines Sets bei der In-vitro-Diagnose von Lungenkrebs, wobei das Set eine Nucleinsäure umfasst, die in der Lage ist, spezifisch an den Lungenkrebsmarker miR-6768-5p zu binden.

2. Verwendung nach Anspruch 1, wobei die Nucleinsäure ein Polynucleotid ist, das aus der aus den folgenden Polynucleotiden (a) bis (e) bestehenden Gruppe ausgewählt ist:

   (a) einem Polynucleotid, das aus einer Nucleotidsequenz, die durch SEQ ID NO: 1 dargestellt ist, oder einer Nucleotidsequenz, die von der Nucleotidsequenz durch Ersatz von u mit t stammt, besteht, einer Variante davon, einem Derivat davon oder einem Fragment davon, das 15 oder mehr aufeinanderfolgende Nucleotide umfasst,
   (b) einem Polynucleotid, das eine Nucleotidsequenz, die durch SEQ ID NO: 1 dargestellt ist, umfasst,
   (c) einem Polynucleotid, das aus einer Nucleotidsequenz besteht, die zu einer Nucleotidsequenz, die durch SEQ ID NO: 1 dargestellt ist, oder einer Nucleotidsequenz, die von der Nucleotidsequenz durch Ersatz von u mit t stammt, komplementär ist, einer Variante davon, einem Derivat davon oder einem Fragment davon, das 15 oder mehr aufeinanderfolgende Nucleotide umfasst,
   (d) einem Polynucleotid, das eine Nucleotidsequenz umfasst, die zu einer Nucleotidsequenz, die durch SEQ ID NO: 1 dargestellt ist, oder einer Nucleotidsequenz, die von der Nucleotidsequenz durch Ersatz von u mit t stammt, komplementär ist, und
   (e) einem Polynucleotid, das unter stringenten Konditionen an ein beliebiges der Polynucleotide (a) bis (d) hybridisiert.

3. Verwendung nach Anspruch 1 oder 2, wobei das Set ferner eine Nucleinsäure umfasst, die in der Lage ist, an zumindest ein Polynucleotid oder mehrere Polynucleotide spezifisch zu binden, das bzw. die aus der aus folgenden anderen Lungenkrebsmarkern bestehenden Gruppe ausgewählt ist bzw. sind: miR-6836-3p, miR-6782-5p, miR-3663-3p, miR-1908-3p, miR-6726-5p, miR-4258, miR-1343-3p, miR-4516, miR-6875-5p, miR-4651, miR-6825-5p, miR-6840-3p, miR-6780b-5p, miR-6749-5p, miR-8063, miR-6784-5p, miR-3679-5p, miR-3184-5p, miR-663b, miR-6880-5p, miR-1908-5p, miR-92a-2-5p, miR-7975, miR-7110-5p, miR-6842-5p, miR-6857-5p, miR-5572, miR-3197, miR-6131, miR-6889-5p, miR-4454, miR-1199-5p, miR-1247-3p, miR-6800-5p, miR-6872-3p, miR-4649-5p, miR-6791-5p, miR-4433b-3p, miR-3135b, miR-128-2-5p, miR-4675, miR-4472, miR-6785-5p, miR-6741-5p, miR-7977, miR-3665, miR-128-1-5p, miR-4286, miR-6765-3p, miR-4632-5p, miR-365a-5p, miR-6088, miR-6816-5p, miR-

6885-5p, miR-711, miR-6765-5p, miR-3180, miR-4442, miR-4792, miR-6721-5p, miR-6798-5p, miR-3162-5p, miR-6126, miR-4758-5p, miR-2392, miR-486-3p, miR-6727-5p, miR-4728-5p, miR-6746-5p, miR-4270, miR-3940-5p, miR-4725-3p, miR-7108-5p, miR-3656, miR-6879-5p, miR-6738-5p, miR-1260a, miR-4446-3p, miR-3131, miR-4463, miR-3185, miR-6870-5p, miR-6779-5p, miR-1273g-3p, miR-8059, miR-4697-5p, miR-4674, miR-4433-3p, miR-4257, miR-1915-5p, miR-4417, miR-1343-5p, miR-6781-5p, miR-4695-5p, miR-1237-5p, miR-6775-5p, miR-7845-5p, miR-4746-3p, miR-7641, miR-7847-3p, miR-6806-5p, miR-4467, miR-4726-5p, miR-4648, miR-6089, miR-1260b, miR-4532, miR-5195-3p, miR-3188, miR-6848-5p, miR-1233-5p, miR-6717-5p, miR-3195, miR-6757-5p, miR-8072, miR-4745-5p, miR-6511 a-Sp, miR-6776-5p, miR-371a-5p, miR-1227-5p, miR-7150, miR-1915-3p, miR-187-5p, miR-614, miR-1225-5p, miR-451a, miR-939-5p, miR-223-3p, miR-125a-3p, miR-92b-5p, miR-22-3p, miR-6073, miR-6845-5p, miR-6769b-5p, miR-4665-3p, miR-1913, miR-1228-3p, miR-940, miR-296-3p, miR-4690-5p, miR-548q, miR-663a, miR-1249, miR-1202, miR-7113-3p, miR-1225-3p, miR-4783-3p, miR-4448 und miR-4534 und/oder

miR-19b-3p, miR-1228-5p, miR-1307-3p, miR-4271, miR-642b-3p, miR-6075, miR-6125, miR-887-3p, miR-6851-5p, miR-6763-5p, miR-3928-3p, miR-4443, miR-3648, miR-149-3p, miR-4689, miR-4763-3p, miR-6729-5p, miR-4507, miR-564, miR-4497, miR-6877-5p, miR-6087, miR-4731-5p, miR-615-5p, miR-760, miR-6891-5p, miR-6887-5p, miR-4525, miR-1914-3p, miR-619-5p, miR-5001-5p, miR-6722-3p, miR-3621, miR-4298, miR-675-5p und miR-4655-5p.

4. Verwendung nach Anspruch 3, wobei die Nucleinsäure ein Polynucleotid ist, das aus der aus den folgenden Polynucleotiden (a') bis (e') bestehenden Gruppe ausgewählt ist:

(a') einem Polynucleotid, das aus einer Nucleotidsequenz, die durch eine beliebige der SEQ ID NOs: 2 bis 125, 127 bis 130, 132 bis 134 und 561 bis 578 dargestellt ist, oder einer Nucleotidsequenz, die von der Nucleotidsequenz durch Ersatz von u mit t stammt, besteht, einer Variante davon, einem Derivat davon oder einem Fragment davon, das 15 oder mehr aufeinanderfolgende Nucleotide umfasst,
(b') einem Polynucleotid, das eine Nucleotidsequenz, die durch eine beliebige der SEQ ID NOs: 2 bis 125, 127 bis 130, 132 bis 134 und 561 bis 578 dargestellt ist, umfasst, (c') einem Polynucleotid, das aus einer Nucleotidsequenz besteht, die zu einer Nucleotidsequenz, die durch eine beliebige der SEQ ID NOs: 2 bis 125, 127 bis 130, 132 bis 134 und 561 bis 578 dargestellt ist, oder einer Nucleotidsequenz, die von der Nucleotidsequenz durch Ersatz von u mit t stammt, komplementär ist, einer Variante davon, einem Derivat davon oder einem Fragment davon, das 15 oder mehr aufeinanderfolgende Nucleotide umfasst,
(d') einem Polynucleotid, das eine Nucleotidsequenz umfasst, die zu einer Nucleotidsequenz, die durch eine beliebige der SEQ ID NOs: 2 bis 125, 127 bis 130, 132 bis 134 und 561 bis 578 dargestellt ist, oder einer Nucleotidsequenz, die von der Nucleotidsequenz durch Ersatz von u mit t stammt, komplementär ist, und
(e') einem Polynucleotid, das unter stringenten Bedingungen an ein beliebiges der Polynucleotide (a') bis (d') hybridisiert, und/oder;

ein Polynucleotid, das aus der aus den folgenden Polynucleotiden (f) bis (o) bestehenden Gruppe ausgewählt ist:

(f) einem Polynucleotid, das aus einer Nucleotidsequenz, die durch eine beliebige der SEQ ID NOs: 126, 131 und 579 dargestellt ist, oder einer Nucleotidsequenz, die von der Nucleotidsequenz durch Ersatz von u mit t stammt, besteht, einer Variante davon, einem Derivat davon oder einem Fragment davon, das 15 oder mehr aufeinanderfolgende Nucleotide umfasst,
(g) einem Polynucleotid, das eine Nucleotidsequenz, die durch eine beliebige der SEQ ID NOs: 126, 131 und 579 dargestellt ist, umfasst,
(h) einem Polynucleotid, das aus einer Nucleotidsequenz besteht, die zu einer Nucleotidsequenz, die durch eine beliebige der SEQ ID NOs: 126, 131 und 579 dargestellt ist, oder einer Nucleotidsequenz, die von der Nucleotidsequenz durch Ersatz von u mit t stammt, komplementär ist, einer Variante davon, einem Derivat davon oder einem Fragment davon, das 15 oder mehr aufeinanderfolgende Nucleotide umfasst,
(i) einem Polynucleotid, das eine Nucleotidsequenz umfasst, die zu einer Nucleotidsequenz, die durch eine beliebige der SEQ ID NOs: 126, 131 und 579 dargestellt ist, oder einer Nucleotidsequenz, die von der Nucleotidsequenz durch Ersatz von u mit t stammt, komplementär ist,
(j) einem Polynucleotid, das unter stringenten Bedingungen an ein beliebiges der Polynucleotide (f) bis (i) hybridisiert;
(k) einem Polynucleotid, das aus einer Nucleotidsequenz, die durch eine beliebige der SEQ ID NOs: 135 bis 174 dargestellt ist, oder einer Nucleotidsequenz, die von der Nucleotidsequenz durch Ersatz von u mit t stammt, besteht, einer Variante davon, einem Derivat davon oder einem Fragment davon, das 15 oder mehr aufeinanderfolgende Nucleotide umfasst,

(l) einem Polynucleotid, das eine Nucleotidsequenz, die durch eine beliebige der SEQ ID NOs: 135 bis 174 dargestellt ist, umfasst,
(m) einem Polynucleotid, das aus einer Nucleotidsequenz besteht, die zu einer Nucleotidsequenz, die durch eine beliebige der SEQ ID NOs: 135 bis 174 dargestellt ist, oder einer Nucleotidsequenz, die von der Nucleotidsequenz durch Ersatz von u mit t stammt, komplementär ist, einer Variante davon, einem Derivat davon oder einem Fragment davon, das 15 oder mehr aufeinanderfolgende Nucleotide umfasst,
(n) einem Polynucleotid, das eine Nucleotidsequenz umfasst, die zu einer Nucleotidsequenz, die durch eine beliebige der SEQ ID NOs: 135 bis 174 dargestellt ist, oder einer Nucleotidsequenz, die von der Nucleotidsequenz durch Ersatz von u mit t stammt, komplementär ist, und
(o) einem Polynucleotid, das unter stringenten Bedingungen an ein beliebiges der Polynucleotide (k) bis (n) hybridisiert.

5. Verwendung nach einem der Ansprüche 1 bis 4, wobei das Set zumindest zwei oder mehr Nucleinsäuren umfasst, die in der Lage sind, jeweils spezifisch an zumindest zwei oder mehr Polynucleotide zu binden, die aus allen Lungenkrebsmarkern nach Anspruch 1 oder 3 ausgewählt sind.

6. Verwendung einer Vorrichtung bei der In-vitro-Diagnose von Lungenkrebs, die eine Nucleinsäure umfasst, die in der Lage ist, spezifisch an ein Polynucleotid des Lungenkrebsmarkers miR-6768-5p zu binden.

7. Verwendung nach Anspruch 6, wobei die Nucleinsäure ein Polynucleotid ist, das aus der aus den folgenden Polynucleotiden (a) bis (e) bestehenden Gruppe ausgewählt ist:

(a) einem Polynucleotid, das aus einer Nucleotidsequenz, die durch SEQ ID NO: 1 dargestellt ist, oder einer Nucleotidsequenz, die von der Nucleotidsequenz durch Ersatz von u mit t stammt, besteht, einer Variante davon, einem Derivat davon oder einem Fragment davon, das 15 oder mehr aufeinanderfolgende Nucleotide umfasst,
(b) einem Polynucleotid, das eine Nucleotidsequenz, die durch SEQ ID NO: 1 dargestellt ist, umfasst,
(c) einem Polynucleotid, das aus einer Nucleotidsequenz besteht, die zu einer Nucleotidsequenz, die durch SEQ ID NO: 1 dargestellt ist, oder einer Nucleotidsequenz, die durch Ersatz von u mit t stammt, komplementär ist, einer Variante davon, einem Derivat davon oder einem Fragment davon, das 15 oder mehr aufeinanderfolgende Nucleotide umfasst,
(d) einem Polynucleotid, das eine Nucleotidsequenz umfasst, die zu einer Nucleotidsequenz, die durch SEQ ID NO: 1 dargestellt ist, oder einer Nucleotidsequenz, die durch Ersatz von u mit t stammt, komplementär ist, und
(e) einem Polynucleotid, das unter stringenten Konditionen an ein beliebiges der Polynucleotide (a) bis (d) hybridisiert.

8. Verwendung nach Anspruch 6 oder 7, wobei die Vorrichtung ferner eine Nucleinsäure umfasst, die in der Lage ist, an zumindest ein Polynucleotid oder mehrere Polynucleotide spezifisch zu binden, das bzw. die aus der aus folgenden anderen Lungenkrebsmarkern bestehenden Gruppe ausgewählt ist bzw. sind: miR-6836-3p, miR-6782-5p, miR-3663-3p, miR-1908-3p, miR-6726-5p, miR-4258, miR-1343-3p, miR-4516, miR-6875-5p, miR-4651, miR-6825-5p, miR-6840-3p, miR-6780b-5p, miR-6749-5p, miR-8063, miR-6784-5p, miR-3679-5p, miR-3184-5p, miR-663b, miR-6880-5p, miR-1908-5p, miR-92a-2-5p, miR-7975, miR-7110-5p, miR-6842-5p, miR-6857-5p, miR-5572, miR-3197, miR-6131, miR-6889-5p, miR-4454, miR-1199-5p, miR-1247-3p, miR-6800-5p, miR-6872-3p, miR-4649-5p, miR-6791-5p, miR-4433b-3p, miR-3135b, miR-128-2-5p, miR-4675, miR-4472, miR-6785-5p, miR-6741-5p, miR-7977, miR-3665, miR-128-1-5p, miR-4286, miR-6765-3p, miR-4632-5p, miR-365a-5p, miR-6088, miR-6816-5p, miR-6885-5p, miR-711, miR-6765-5p, miR-3180, miR-4442, miR-4792, miR-6721-5p, miR-6798-5p, miR-3162-5p, miR-6126, miR-4758-5p, miR-2392, miR-486-3p, miR-6727-5p, miR-4728-5p, miR-6746-5p, miR-4270, miR-3940-5p, miR-4725-3p, miR-7108-5p, miR-3656, miR-6879-5p, miR-6738-5p, miR-1260a, miR-4446-3p, miR-3131, miR-4463, miR-3185, miR-6870-5p, miR-6779-5p, miR-1273g-3p, miR-8059, miR-4697-5p, miR-4674, miR-4433-3p, miR-4257, miR-1915-5p, miR-4417, miR-1343-5p, miR-6781-5p, miR-4695-5p, miR-1237-5p, miR-6775-5p, miR-7845-5p, miR-4746-3p, miR-7641, miR-7847-3p, miR-6806-5p, miR-4467, miR-4726-5p, miR-4648, miR-6089, miR-1260b, miR-4532, miR-5195-3p, miR-3188, miR-6848-5p, miR-1233-5p, miR-6717-5p, miR-3195, miR-6757-5p, miR-8072, miR-4745-5p, miR-6511 a-Sp, miR-6776-5p, miR-371a-5p, miR-1227-5p, miR-7150, miR-1915-3p, miR-187-5p, miR-614, miR-1225-5p, miR-451a, miR-939-5p, miR-223-3p, miR-125a-3p, miR-92b-5p, miR-22-3p, miR-6073, miR-6845-5p, miR-6769b-5p, miR-4665-3p, miR-1913, miR-1228-3p, miR-940, miR-296-3p, miR-4690-5p, miR-548q, miR-663a, miR-1249, miR-1202, miR-7113-3p, miR-1225-3p, miR-4783-3p, miR-4448 und miR-4534 und/oder
miR-19b-3p, miR-1228-5p, miR-1307-3p, miR-4271, miR-642b-3p, miR-6075, miR-6125, miR-887-3p, miR-

6851-5p, miR-6763-5p, miR-3928-3p, miR-4443, miR-3648, miR-149-3p, miR-4689, miR-4763-3p, miR-6729-5p, miR-4507, miR-564, miR-4497, miR-6877-5p, miR-6087, miR-4731-5p, miR-615-5p, miR-760, miR-6891-5p, miR-6887-5p, miR-4525, miR-1914-3p, miR-619-5p, miR-5001-5p, miR-6722-3p, miR-3621, miR-4298, miR-675-5p und miR-4655-5p.

9. Verwendung nach Anspruch 8, wobei die Nucleinsäure ein Polynucleotid ist, das aus der aus den folgenden Polynucleotiden (a') bis (e') bestehenden Gruppe ausgewählt ist:

(a') einem Polynucleotid, das aus einer Nucleotidsequenz, die durch eine beliebige der SEQ ID NOs: 2 bis 125, 127 bis 130, 132 bis 134 und 561 bis 578 dargestellt ist, oder einer Nucleotidsequenz, die von der Nucleotidsequenz durch Ersatz von u mit t stammt, besteht, einer Variante davon, einem Derivat davon oder einem Fragment davon, das 15 oder mehr aufeinanderfolgende Nucleotide umfasst,
(b') einem Polynucleotid, das eine Nucleotidsequenz, die durch eine beliebige der SEQ ID NOs: 2 bis 125, 127 bis 130, 132 bis 134 und 561 bis 578 dargestellt ist, umfasst, (c') einem Polynucleotid, das aus einer Nucleotidsequenz besteht, die zu einer Nucleotidsequenz, die durch eine beliebige der SEQ ID NOs: 2 bis 125, 127 bis 130, 132 bis 134 und 561 bis 578 dargestellt ist, oder einer Nucleotidsequenz, die von der Nucleotidsequenz durch Ersatz von u mit t stammt, komplementär ist, einer Variante davon, einem Derivat davon oder einem Fragment davon, das 15 oder mehr aufeinanderfolgende Nucleotide umfasst,
(d') einem Polynucleotid, das eine Nucleotidsequenz umfasst, die zu einer Nucleotidsequenz, die durch eine beliebige der SEQ ID NOs: 2 bis 125, 127 bis 130, 132 bis 134 und 561 bis 578 dargestellt ist, oder einer Nucleotidsequenz, die von der Nucleotidsequenz durch Ersatz von u mit t stammt, komplementär ist, und
(e') einem Polynucleotid, das unter stringenten Bedingungen an ein beliebiges der Polynucleotide (a') bis (d') hybridisiert, und/oder;

ein Polynucleotid, das aus der aus den folgenden Polynucleotiden (f) bis (o) bestehenden Gruppe ausgewählt ist:

(f) einem Polynucleotid, das aus einer Nucleotidsequenz, die durch eine beliebige der SEQ ID NOs: 126, 131 und 579 dargestellt ist, oder einer Nucleotidsequenz, die von der Nucleotidsequenz durch Ersatz von u mit t stammt, besteht, einer Variante davon, einem Derivat davon oder einem Fragment davon, das 15 oder mehr aufeinanderfolgende Nucleotide umfasst,
(g) einem Polynucleotid, das eine Nucleotidsequenz, die durch eine beliebige der SEQ ID NOs: 126, 131 und 579 dargestellt ist, umfasst,
(h) einem Polynucleotid, das aus einer Nucleotidsequenz besteht, die zu einer Nucleotidsequenz, die durch eine beliebige der SEQ ID NOs: 126, 131 und 579 dargestellt ist, oder einer Nucleotidsequenz, die von der Nucleotidsequenz durch Ersatz von u mit t stammt, komplementär ist, einer Variante davon, einem Derivat davon oder einem Fragment davon, das 15 oder mehr aufeinanderfolgende Nucleotide umfasst,
(i) einem Polynucleotid, das eine Nucleotidsequenz umfasst, die zu einer Nucleotidsequenz, die durch eine beliebige der SEQ ID NOs: 126, 131 und 579 dargestellt ist, oder einer Nucleotidsequenz, die von der Nucleotidsequenz durch Ersatz von u mit t stammt, komplementär ist,
(j) einem Polynucleotid, das unter stringenten Bedingungen an ein beliebiges der Polynucleotide (f) bis (i) hybridisiert;
(k) einem Polynucleotid, das aus einer Nucleotidsequenz, die durch eine beliebige der SEQ ID NOs: 135 bis 174 dargestellt ist, oder einer Nucleotidsequenz, die von der Nucleotidsequenz durch Ersatz von u mit t stammt, besteht, einer Variante davon, einem Derivat davon oder einem Fragment davon, das 15 oder mehr aufeinanderfolgende Nucleotide umfasst,
(l) einem Polynucleotid, das eine Nucleotidsequenz, die durch eine beliebige der SEQ ID NOs: 135 bis 174 dargestellt ist, umfasst,
(m) einem Polynucleotid, das aus einer Nucleotidsequenz besteht, die zu einer Nucleotidsequenz, die durch eine beliebige der SEQ ID NOs: 135 bis 174 dargestellt ist, oder einer Nucleotidsequenz, die von der Nucleotidsequenz durch Ersatz von u mit t stammt, komplementär ist, einer Variante davon, einem Derivat davon oder einem Fragment davon, das 15 oder mehr aufeinanderfolgende Nucleotide umfasst,
(n) einem Polynucleotid, das eine Nucleotidsequenz umfasst, die zu einer Nucleotidsequenz, die durch eine beliebige der SEQ ID NOs: 135 bis 174 dargestellt ist, oder einer Nucleotidsequenz, die von der Nucleotidsequenz durch Ersatz von u mit t stammt, komplementär ist, und
(o) einem Polynucleotid, das unter stringenten Bedingungen an ein beliebiges der Polynucleotide (k) bis (n) hybridisiert.

10. Verwendung nach einem der Ansprüche 6 bis 9, wobei die Vorrichtung eine Vorrichtung zum Messen durch ein

Hybridisierungsverfahren ist.

11. Verwendung nach Anspruch 10, wobei das Hybridisierungsverfahren ein Nucleinsäurearrayverfahren ist.

12. Verwendung nach einem der Ansprüche 6 bis 11, wobei die Vorrichtung zumindest zwei oder mehr Nucleinsäuren umfasst, die in der Lage sind, jeweils spezifisch an zumindest zwei oder mehr Polynucleotide zu binden, die aus allen Lungenkrebsmarkern nach Anspruch 6 ausgewählt sind.

13. Verfahren zum Detektieren von Lungenkrebs, das das Messen eines Expressionsausmaßes einer Zielnucleinsäure in einer Probe aus einem Individuum unter Verwendung eines Sets wie in einem der Ansprüche 1 bis 5 definiert oder Verwendung einer Vorrichtung wie in einem der Ansprüche 6 bis 12 definiert und das In-vitro-Bewerten, ob das Individuum an Lungenkrebs leidet, unter Verwendung sowohl des gemessenen Expressionsausmaßes als auch eines Kontrollexpressionsausmaßes in einer Probe aus einem gesundem Individuum, das auf dieselbe Weise gemessen wurde, umfasst.

14. Verfahren nach Anspruch 13, wobei das Individuum ein Mensch ist.

15. Verfahren nach Anspruch 13 oder 14, wobei die Probe Blut, Serum oder Plasma ist.

16. Verwendung eines Markers bei der In-vitro-Diagnostik von Lungenkrebs, wobei der Marker das Polynucleotid miR-6768-5p umfasst.

17. Verwendung nach Anspruch 16, wobei der Marker ferner zumindest ein Polynucleotid bzw. Polynucleotide umfasst, das bzw. die aus der aus folgenden anderen Lungenkrebsmarkern bestehenden Gruppe ausgewählt ist bzw. sind: miR-6836-3p, miR-6782-5p, miR-3663-3p, miR-1908-3p, miR-6726-5p, miR-4258, miR-1343-3p, miR-4516, miR-6875-5p, miR-4651, miR-6825-5p, miR-6840-3p, miR-6780b-5p, miR-6749-5p, miR-8063, miR-6784-5p, miR-3679-5p, miR-3184-5p, miR-663b, miR-6880-5p, miR-1908-5p, miR-92a-2-5p, miR-7975, miR-7110-5p, miR-6842-5p, miR-6857-5p, miR-5572, miR-3197, miR-6131, miR-6889-5p, miR-4454, miR-1199-5p, miR-1247-3p, miR-6800-5p, miR-6872-3p, miR-4649-5p, miR-6791-5p, miR-4433b-3p, miR-3135b, miR-128-2-5p, miR-4675, miR-4472, miR-6785-5p, miR-6741-5p, miR-7977, miR-3665, miR-128-1-5p, miR-4286, miR-6765-3p, miR-4632-5p, miR-365a-5p, miR-6088, miR-6816-5p, miR-6885-5p, miR-711, miR-6765-5p, miR-3180, miR-4442, miR-4792, miR-6721-5p, miR-6798-5p, miR-3162-5p, miR-6126, miR-4758-5p, miR-2392, miR-486-3p, miR-6727-5p, miR-4728-5p, miR-6746-5p, miR-4270, miR-3940-5p, miR-4725-3p, miR-7108-5p, miR-3656, miR-6879-5p, miR-6738-5p, miR-1260a, miR-4446-3p, miR-3131, miR-4463, miR-3185, miR-6870-5p, miR-6779-5p, miR-1273g-3p, miR-8059, miR-4697-5p, miR-4674, miR-4433-3p, miR-4257, miR-1915-5p, miR-4417, miR-1343-5p, miR-6781-5p, miR-4695-5p, miR-1237-5p, miR-6775-5p, miR-7845-5p, miR-4746-3p, miR-7641, miR-7847-3p, miR-6806-5p, miR-4467, miR-4726-5p, miR-4648, miR-6089, miR-1260b, miR-4532, miR-5195-3p, miR-3188, miR-6848-5p, miR-1233-5p, miR-6717-5p, miR-3195, miR-6757-5p, miR-8072, miR-4745-5p, miR-6511a-Sp, miR-6776-5p, miR-371a-5p, miR-1227-5p, miR-7150, miR-1915-3p, miR-187-5p, miR-614, miR-1225-5p, miR-451a, miR-939-5p, miR-223-3p, miR-125a-3p, miR-92b-5p, miR-22-3p, miR-6073, miR-6845-5p, miR-6769b-5p, miR-4665-3p, miR-1913, miR-1228-3p, miR-940, miR-296-3p, miR-4690-5p, miR-548q, miR-663a, miR-1249, miR-1202, miR-7113-3p, miR-1225-3p, miR-4783-3p, miR-4448 und miR-4534 und/oder
miR-19b-3p, miR-1228-5p, miR-1307-3p, miR-4271, miR-642b-3p, miR-6075, miR-6125, miR-887-3p, miR-6851-5p, miR-6763-5p, miR-3928-3p, miR-4443, miR-3648, miR-149-3p, miR-4689, miR-4763-3p, miR-6729-5p, miR-4507, miR-564, miR-4497, miR-6877-5p, miR-6087, miR-4731-5p, miR-615-5p, miR-760, miR-6891-5p, miR-6887-5p, miR-4525, miR-1914-3p, miR-619-5p, miR-5001-5p, miR-6722-3p, miR-3621, miR-4298, miR-675-5p und miR-4655-5p.

Revendications

1. Utilisation d'un kit dans le diagnostic *in vitro* du cancer du poumon, le kit comprenant un acide nucléique capable de spécifiquement se lier au marqueur du cancer du poumon miR-6768-5p.

2. Utilisation selon la revendication 1, dans laquelle l'acide nucléique est un polynucléotide sélectionné dans le groupe consistant en les polynucléotides (a) à (e) suivants :

(a) un polynucléotide consistant en une séquence de nucléotides représentée par SEQ ID NO: 1 ou une séquence

de nucléotides dérivée de la séquence de nucléotides par le remplacement de u par t, un variant de celle-ci, un dérivé de celle-ci, ou un fragment de celle-ci comprenant 15 nucléotides consécutifs ou plus,
(b) un polynucléotide comprenant une séquence de nucléotides représentée par SEQ ID NO: 1,
(c) un polynucléotide consistant en une séquence de nucléotides complémentaire à une séquence de nucléotides représentée par SEQ ID NO: 1 ou une séquence de nucléotides dérivée de la séquence de nucléotides par le remplacement de u par t, un variant de celle-ci, un dérivé de celle-ci, ou un fragment de celle-ci comprenant 15 nucléotides consécutifs ou plus,
(d) un polynucléotide comprenant une séquence de nucléotides complémentaire à une séquence de nucléotides représentée par SEQ ID NO: 1 ou une séquence de nucléotides dérivée de la séquence de nucléotides par le remplacement de u par t, et
(e) un polynucléotide qui s'hybride dans des conditions stringentes à l'un quelconque des polynucléotides (a) à (d) .

3. Utilisation selon la revendication 1 ou 2, dans laquelle le kit comprend en outre un acide nucléique capable de spécifiquement se lier à au moins un ou plusieurs polynucléotide (s) sélectionné(s) dans le groupe consistant en d'autres marqueurs du cancer du poumon : miR-6836-3p, miR-6782-5p, miR-3663-3p, miR-1908-3p, miR-6726-5p, miR-4258, miR-1343-3p, miR-4516, miR-6875-5p, miR-4651, miR-6825-5p, miR-6840-3p, miR-6780b-5p, miR-6749-5p, miR-8063, miR-6784-5p, miR-3679-5p, miR-3184-5p, miR-663b, miR-6880-5p, miR-1908-5p, miR-92a-2-5p, miR-7975, miR-7110-5p, miR-6842-5p, miR-6857-5p, miR-5572, miR-3197, miR-6131, miR-6889-5p, miR-4454, miR-1199-5p, miR-1247-3p, miR-6800-5p, miR-6872-3p, miR-4649-5p, miR-6791-5p, miR-4433b-3p, miR-3135b, miR-128-2-5p, miR-4675, miR-4472, miR-6785-5p, miR-6741-5p, miR-7977, miR-3665, miR-128-1-5p, miR-4286, miR-6765-3p, miR-4632-5p, miR-365a-5p, miR-6088, miR-6816-5p, miR-6885-5p, miR-711, miR-6765-5p, miR-3180, miR-4442, miR-4792, miR-6721-5p, miR-6798-5p, miR-3162-5p, miR-6126, miR-4758-5p, miR-2392, miR-486-3p, miR-6727-5p, miR-4728-5p, miR-6746-5p, miR-4270, miR-3940-5p, miR-4725-3p, miR-7108-5p, miR-3656, miR-6879-5p, miR-6738-5p, miR-1260a, miR-4446-3p, miR-3131, miR-4463, miR-3185, miR-6870-5p, miR-6779-5p, miR-1273g-3p, miR-8059, miR-4697-5p, miR-4674, miR-4433-3p, miR-4257, miR-1915-5p, miR-4417, miR-1343-5p, miR-6781-5p, miR-4695-5p, miR-1237-5p, miR-6775-5p, miR-7845-5p, miR-4746-3p, miR-7641, miR-7847-3p, miR-6806-5p, miR-4467, miR-4726-5p, miR-4648, miR-6089, miR-1260b, miR-4532, miR-5195-3p, miR-3188, miR-6848-5p, miR-1233-5p, miR-6717-5p, miR-3195, miR-6757-5p, miR-8072, miR-4745-5p, miR-6511a-5p, miR-6776-5p, miR-371a-5p, miR-1227-5p, miR-7150, miR-1915-3p, miR-187-5p, miR-614, miR-1225-5p, miR-451a, miR-939-5p, miR-223-3p, miR-125a-3p, miR-92b-5p, miR-22-3p, miR-6073, miR-6845-5p, miR-6769b-5p, miR-4665-3p, miR-1913, miR-1228-3p, miR-940, miR-296-3p, miR-4690-5p, miR-548q, miR-663a, miR-1249, miR-1202, miR-7113-3p, miR-1225-3p, miR-4783-3p, miR-4448 et miR-4534, et/ou ;
miR-19b-3p, miR-1228-5p, miR-1307-3p, miR-4271, miR-642b-3p, miR-6075, miR-6125, miR-887-3p, miR-6851-5p, miR-6763-5p, miR-3928-3p, miR-4443, miR-3648, miR-149-3p, miR-4689, miR-4763-3p, miR-6729-5p, miR-3196, miR-8069, miR-1268a, miR-4739, miR-1268b, miR-5698, miR-6752-5p, miR-4507, miR-564, miR-4497, miR-6877-5p, miR-6087, miR-4731-5p, miR-615-5p, miR-760, miR-6891-5p, miR-6887-5p, miR-4525, miR-1914-3p, miR-619-5p, miR-5001-5p, miR-6722-3p, miR-3621, miR-4298, miR-675-5p et miR-4655-5p.

4. Utilisation selon la revendication 3, dans laquelle l'acide nucléique est un polynucléotide sélectionné dans le groupe consistant en les polynucléotides (a') à (e') suivants :

(a') un polynucléotide consistant en une séquence de nucléotides représentée par l'une quelconque de SEQ ID NO: 2 à 125, 127 à 130, 132 à 134, et 561 à 578 ou une séquence de nucléotides dérivée de la séquence de nucléotides par le remplacement de u par t, un variant de celle-ci, un dérivé de celle-ci, ou un fragment de celle-ci comprenant 15 nucléotides consécutifs ou plus,
(b') un polynucléotide comprenant une séquence de nucléotides représentée par l'une quelconque de SEQ ID NO: 2 à 125, 127 à 130, 132 à 134, et 561 à 578,
(c') un polynucléotide consistant en une séquence de nucléotides complémentaire à une séquence de nucléotides représentée par l'une quelconque de SEQ ID NO: 2 à 125, 127 à 130, 132 à 134, et 561 à 578 ou une séquence de nucléotides dérivée de la séquence de nucléotides par le remplacement de u par t, un variant de celle-ci, un dérivé de celle-ci, ou un fragment de celle-ci comprenant 15 nucléotides consécutifs ou plus,
(d') un polynucléotide comprenant une séquence de nucléotides complémentaire à une séquence de nucléotides représentée par l'une quelconque de SEQ ID NO: 2 à 125, 127 à 130, 132 à 134, et 561 à 578 ou une séquence de nucléotides dérivée de la séquence de nucléotides par le remplacement de u par t, et
(e') un polynucléotide qui s'hybride dans des conditions stringentes à l'un quelconque des polynucléotides (a') à (d'), et/ou ;

un polynucléotide sélectionné dans le groupe consistant en les polynucléotides (f) à (o) suivants :

(f) un polynucléotide consistant en une séquence de nucléotides représentée par l'une quelconque de SEQ ID NO: 126, 131 et 579 ou une séquence de nucléotides dérivée de la séquence de nucléotides par le remplacement de u par t, un variant de celle-ci, un dérivé de celle-ci, ou un fragment de celle-ci comprenant 15 nucléotides consécutifs ou plus,
(g) un polynucléotide comprenant une séquence de nucléotides représentée par l'une quelconque de SEQ ID NO: 126, 131 et 579
(h) un polynucléotide consistant en une séquence de nucléotides complémentaire à une séquence de nucléotides représentée par l'une quelconque de SEQ ID NO: 126, 131 et 579 ou une séquence de nucléotides dérivée de la séquence de nucléotides par le remplacement de u par t, un variant de celle-ci, un dérivé de celle-ci, ou un fragment de celle-ci comprenant 15 nucléotides consécutifs ou plus,
(i) un polynucléotide comprenant une séquence de nucléotides complémentaire à une séquence de nucléotides représentée par l'une quelconque de SEQ ID NO: 126, 131 et 579 ou une séquence de nucléotides dérivée de la séquence de nucléotides par le remplacement de u par t,
(j) un polynucléotide qui s'hybride dans des conditions stringentes à l'un quelconque des polynucléotides (f) à (i) ;
(k) un polynucléotide consistant en une séquence de nucléotides représentée par l'une quelconque de SEQ ID NO: 135 à 174 ou une séquence de nucléotides dérivée de la séquence de nucléotides par le remplacement de u par t, un variant de celle-ci, un dérivé de celle-ci, ou un fragment de celle-ci comprenant 15 nucléotides consécutifs ou plus,
(1) un polynucléotide comprenant une séquence de nucléotides représentée par l'une quelconque de SEQ ID NO: 135 à 174,
(m) un polynucléotide consistant en une séquence de nucléotides complémentaire à une séquence de nucléotides représentée par l'une quelconque de SEQ ID NO: 135 à 174 ou une séquence de nucléotides dérivée de la séquence de nucléotides par le remplacement de u par t, un variant de celle-ci, un dérivé de celle-ci, ou un fragment de celle-ci comprenant 15 nucléotides consécutifs ou plus,
(n) un polynucléotide comprenant une séquence de nucléotides complémentaire à une séquence de nucléotides représentée par l'une quelconque de SEQ ID NO: 135 à 174 ou une séquence de nucléotides dérivée de la séquence de nucléotides par le remplacement de u par t, et
(o) un polynucléotide qui s'hybride dans des conditions stringentes à l'un quelconque des polynucléotides (k) à (n) .

5. Utilisation selon l'une quelconque des revendications 1 à 4, dans laquelle le kit comprend au moins deux acides nucléiques ou plus capables de spécifiquement se lier à au moins deux polynucléotides ou plus, respectivement, sélectionnés parmi tous les marqueurs du cancer du poumon selon la revendication 1 ou 3.

6. Utilisation d'un dispositif dans le diagnostic *in vitro* du cancer du poumon, comprenant un acide nucléique capable de spécifiquement se lier à un polynucléotide de marqueur du cancer du poumon miR-6768-5p.

7. Utilisation selon la revendication 6, dans laquelle l'acide nucléique est un polynucléotide sélectionné dans le groupe consistant en les polynucléotides (a) à (e) suivants :

(a) un polynucléotide consistant en une séquence de nucléotides représentée par SEQ ID NO: 1 ou une séquence de nucléotides dérivée de la séquence de nucléotides par le remplacement de u par t, un variant de celle-ci, un dérivé de celle-ci, ou un fragment de celle-ci comprenant 15 nucléotides consécutifs ou plus,
(b) un polynucléotide comprenant une séquence de nucléotides représentée par SEQ ID NO: 1,
(c) un polynucléotide consistant en une séquence de nucléotides complémentaire à une séquence de nucléotides représentée par SEQ ID NO: 1 ou une séquence de nucléotides dérivée de la séquence de nucléotides par le remplacement de u par t, un variant de celle-ci, un dérivé de celle-ci, ou un fragment de celle-ci comprenant 15 nucléotides consécutifs ou plus,
(d) un polynucléotide comprenant une séquence de nucléotides complémentaire à une séquence de nucléotides représentée par SEQ ID NO: 1 ou une séquence de nucléotides dérivée de la séquence de nucléotides par le remplacement de u par t, et
(e) un polynucléotide qui s'hybride dans des conditions stringentes à l'un quelconque des polynucléotides (a) à (d) .

8. Utilisation selon la revendication 6 ou 7, dans laquelle le dispositif comprend en outre un acide nucléique capable de spécifiquement se lier à au moins un ou plusieurs polynucléotide(s) sélectionné(s) dans le groupe consistant en

d'autres marqueurs du cancer du poumon : miR-6836-3p, miR-6782-5p, miR-3663-3p, miR-1908-3p, miR-6726-5p, miR-4258, miR-1343-3p, miR-4516, miR-6875-5p, miR-4651, miR-6825-5p, miR-6840-3p, miR-6780b-5p, miR-6749-5p, miR-8063, miR-6784-5p, miR-3679-5p, miR-3184-5p, miR-663b, miR-6880-5p, miR-1908-5p, miR-92a-2-5p, miR-7975, miR-7110-5p, miR-6842-5p, miR-6857-5p, miR-5572, miR-3197, miR-6131, miR-6889-5p, miR-4454, miR-1199-5p, miR-1247-3p, miR-6800-5p, miR-6872-3p, miR-4649-5p, miR-6791-5p, miR-4433b-3p, miR-3135b, miR-128-2-5p, miR-4675, miR-4472, miR-6785-5p, miR-6741-5p, miR-7977, miR-3665, miR-128-1-5p, miR-4286, miR-6765-3p, miR-4632-5p, miR-365a-5p, miR-6088, miR-6816-5p, miR-6885-5p, miR-711, miR-6765-5p, miR-3180, miR-4442, miR-4792, miR-6721-5p, miR-6798-5p, miR-3162-5p, miR-6126, miR-4758-5p, miR-2392, miR-486-3p, miR-6727-5p, miR-4728-5p, miR-6746-5p, miR-4270, miR-3940-5p, miR-4725-3p, miR-7108-5p, miR-3656, miR-6879-5p, miR-6738-5p, miR-1260a, miR-4446-3p, miR-3131, miR-4463, miR-3185, miR-6870-5p, miR-6779-5p, miR-1273g-3p, miR-8059, miR-4697-5p, miR-4674, miR-4433-3p, miR-4257, miR-1915-5p, miR-4417, miR-1343-5p, miR-6781-5p, miR-4695-5p, miR-1237-5p, miR-6775-5p, miR-7845-5p, miR-4746-3p, miR-7641, miR-7847-3p, miR-6806-5p, miR-4467, miR-4726-5p, miR-4648, miR-6089, miR-1260b, miR-4532, miR-5195-3p, miR-3188, miR-6848-5p, miR-1233-5p, miR-6717-5p, miR-3195, miR-6757-5p, miR-8072, miR-4745-5p, miR-6511a-5p, miR-6776-5p, miR-371a-5p, miR-1227-5p, miR-7150, miR-1915-3p, miR-187-5p, miR-614, miR-1225-5p, miR-451a, miR-939-5p, miR-223-3p, miR-125a-3p, miR-92b-5p, miR-22-3p, miR-6073, miR-6845-5p, miR-6769b-5p, miR-4665-3p, miR-1913, miR-1228-3p, miR-940, miR-296-3p, miR-4690-5p, miR-548q, miR-663a, miR-1249, miR-1202, miR-7113-3p, miR-1225-3p, miR-4783-3p, miR-4448 et miR-4534, et/ou ;
miR-19b-3p, miR-1228-5p, miR-1307-3p, miR-4271, miR-642b-3p, miR-6075, miR-6125, miR-887-3p, miR-6851-5p, miR-6763-5p, miR-3928-3p, miR-4443, miR-3648, miR-149-3p, miR-4689, miR-4763-3p, miR-6729-5p, miR-3196, miR-8069, miR-1268a, miR-4739, miR-1268b, miR-5698, miR-6752-5p, miR-4507, miR-564, miR-4497, miR-6877-5p, miR-6087, miR-4731-5p, miR-615-5p, miR-760, miR-6891-5p, miR-6887-5p, miR-4525, miR-1914-3p, miR-619-5p, miR-5001-5p, miR-6722-3p, miR-3621, miR-4298, miR-675-5p et miR-4655-5p.

9. Utilisation selon la revendication 8, dans laquelle l'acide nucléique est un polynucléotide sélectionné dans le groupe consistant en les polynucléotides (a') à (e') suivants :

(a') un polynucléotide consistant en une séquence de nucléotides représentée par l'une quelconque de SEQ ID NO: 2 à 125, 127 à 130, 132 à 134, et 561 à 578 ou une séquence de nucléotides dérivée de la séquence de nucléotides par le remplacement de u par t, un variant de celle-ci, un dérivé de celle-ci, ou un fragment de celle-ci comprenant 15 nucléotides consécutifs ou plus,
(b') un polynucléotide comprenant une séquence de nucléotides représentée par l'une quelconque de SEQ ID NO: 2 à 125, 127 à 130, 132 à 134, et 561 à 578,
(c') un polynucléotide consistant en une séquence de nucléotides complémentaire à une séquence de nucléotides représentée par l'une quelconque de SEQ ID NO: 2 à 125, 127 à 130, 132 à 134, et 561 à 578 ou une séquence de nucléotides dérivée de la séquence de nucléotides par le remplacement de u par t, un variant de celle-ci, un dérivé de celle-ci, ou un fragment de celle-ci comprenant 15 nucléotides consécutifs ou plus,
(d') un polynucléotide comprenant une séquence de nucléotides complémentaire à une séquence de nucléotides représentée par l'une quelconque de SEQ ID NO: 2 à 125, 127 à 130, 132 à 134, et 561 à 578 ou une séquence de nucléotides dérivée de la séquence de nucléotides par le remplacement de u par t, et
(e') un polynucléotide qui s'hybride dans des conditions stringentes à l'un quelconque des polynucléotides (a') à (d'), et/ou ;

un polynucléotide sélectionné dans le groupe consistant en les polynucléotides (f) à (o) suivants :

(f) un polynucléotide consistant en une séquence de nucléotides représentée par l'une quelconque de SEQ ID NO: 126, 131 et 579 ou une séquence de nucléotides dérivée de la séquence de nucléotides par le remplacement de u par t, un variant de celle-ci, un dérivé de celle-ci, ou un fragment de celle-ci comprenant 15 nucléotides consécutifs ou plus,
(g) un polynucléotide comprenant une séquence de nucléotides représentée par l'une quelconque de SEQ ID NO: 126, 131 et 579,
(h) un polynucléotide consistant en une séquence de nucléotides complémentaire à une séquence de nucléotides représentée par l'une quelconque de SEQ ID NO: 126, 131 et 579 ou une séquence de nucléotides dérivée de la séquence de nucléotides par le remplacement de u par t, un variant de celle-ci, un dérivé de celle-ci, ou un fragment de celle-ci comprenant 15 nucléotides consécutifs ou plus,
(i) un polynucléotide comprenant une séquence de nucléotides complémentaire à une séquence de nucléotides représentée par l'une quelconque de SEQ ID NO: 126, 131 et 579 ou une séquence de nucléotides dérivée de la séquence de nucléotides par le remplacement de u par t,

(j) un polynucléotide qui s'hybride dans des conditions stringentes à l'un quelconque des polynucléotides (f) à (i) ;
(k) un polynucléotide consistant en une séquence de nucléotides représentée par l'une quelconque de SEQ ID NO: 135 à 174 ou une séquence de nucléotides dérivée de la séquence de nucléotides par le remplacement de u par t, un variant de celle-ci, un dérivé de celle-ci, ou un fragment de celle-ci comprenant 15 nucléotides consécutifs ou plus, (1) un polynucléotide comprenant une séquence de nucléotides représentée par l'une quelconque de SEQ ID NO: 135 à 174,
(m) un polynucléotide consistant en une séquence de nucléotides complémentaire à une séquence de nucléotides représentée par l'une quelconque de SEQ ID NO: 135 à 174 ou une séquence de nucléotides dérivée de la séquence de nucléotides par le remplacement de u par t, un variant de celle-ci, un dérivé de celle-ci, ou un fragment de celle-ci comprenant 15 nucléotides consécutifs ou plus,
(n) un polynucléotide comprenant une séquence de nucléotides complémentaire à une séquence de nucléotides représentée par l'une quelconque de SEQ ID NO: 135 à 174 ou une séquence de nucléotides dérivée de la séquence de nucléotides par le remplacement de u par t, et
(o) un polynucléotide qui s'hybride dans des conditions stringentes à l'un quelconque des polynucléotides (k) à (n) .

10. Utilisation selon l'une quelconque des revendications 6 à 9, dans laquelle le dispositif est un dispositif pour une mesure par une technique d'hybridation.

11. Utilisation selon la revendication 10, dans laquelle la technique d'hybridation est une technique par réseau d'acide nucléique.

12. Utilisation selon l'une quelconque des revendications 6 à 11, dans laquelle le dispositif comprend au moins deux acides nucléiques ou plus capables de spécifiquement se lier à au moins deux polynucléotides ou plus, respectivement, sélectionnés parmi tous les marqueurs du cancer de poumon selon la revendication 6.

13. Procédé de détection du cancer du poumon, comprenant la mesure d'un taux d'expression d'un acide nucléique cible dans un échantillon d'un sujet en utilisant le kit tel que défini dans l'une quelconque des revendications 1 à 5 ou en utilisant le dispositif tel que défini dans l'une quelconque des revendications 6 à 12, et l'évaluation *in vitro* du fait que le sujet présente ou non un cancer du poumon en utilisant à la fois le taux d'expression mesuré et un taux d'expression de contrôle dans un échantillon d'un sujet en bonne santé mesuré de la même manière.

14. Procédé selon la revendication 13, dans lequel le sujet est un humain.

15. Procédé selon la revendication 13 ou 14, dans lequel l'échantillon est du sang, du sérum, ou du plasma.

16. Utilisation d'un marqueur dans le diagnostic *in vitro* du cancer du poumon, le marqueur comprenant le polynucléotide miR-6768-5p.

17. Utilisation selon la revendication 16, dans laquelle le marqueur comprend en outre au moins un polynucléotide sélectionné dans le groupe consistant en les autres marqueurs du cancer du poumon suivants : miR-6836-3p, miR-6782-5p, miR-3663-3p, miR-1908-3p, miR-6726-5p, miR-4258, miR-1343-3p, miR-4516, miR-6875-5p, miR-4651, miR-6825-5p, miR-6840-3p, miR-6780b-5p, miR-6749-5p, miR-8063, miR-6784-5p, miR-3679-5p, miR-3184-5p, miR-663b, miR-6880-5p, miR-1908-5p, miR-92a-2-5p, miR-7975, miR-7110-5p, miR-6842-5p, miR-6857-5p, miR-5572, miR-3197, miR-6131, miR-6889-5p, miR-4454, miR-1199-5p, miR-1247-3p, miR-6800-5p, miR-6872-3p, miR-4649-5p, miR-6791-5p, miR-4433b-3p, miR-3135b, miR-128-2-5p, miR-4675, miR-4472, miR-6785-5p, miR-6741-5p, miR-7977, miR-3665, miR-128-1-5p, miR-4286, miR-6765-3p, miR-4632-5p, miR-365a-5p, miR-6088, miR-6816-5p, miR-6885-5p, miR-711, miR-6765-5p, miR-3180, miR-4442, miR-4792, miR-6721-5p, miR-6798-5p, miR-3162-5p, miR-6126, miR-4758-5p, miR-2392, miR-486-3p, miR-6727-5p, miR-4728-5p, miR-6746-5p, miR-4270, miR-3940-5p, miR-4725-3p, miR-7108-5p, miR-3656, miR-6879-5p, miR-6738-5p, miR-1260a, miR-4446-3p, miR-3131, miR-4463, miR-3185, miR-6870-5p, miR-6779-5p, miR-1273g-3p, miR-8059, miR-4697-5p, miR-4674, miR-4433-3p, miR-4257, miR-1915-5p, miR-4417, miR-1343-5p, miR-6781-5p, miR-4695-5p, miR-1237-5p, miR-6775-5p, miR-7845-5p, miR-4746-3p, miR-7641, miR-7847-3p, miR-6806-5p, miR-4467, miR-4726-5p, miR-4648, miR-6089, miR-1260b, miR-4532, miR-5195-3p, miR-3188, miR-6848-5p, miR-1233-5p, miR-6717-5p, miR-3195, miR-6757-5p, miR-8072, miR-4745-5p, miR-6511a-5p, miR-6776-5p, miR-371a-5p, miR-1227-5p, miR-7150, miR-1915-3p, miR-187-5p, miR-614, miR-1225-5p, miR-451a, miR-939-5p, miR-223-3p, miR-125a-3p, miR-92b-5p, miR-22-3p, miR-6073, miR-6845-5p, miR-6769b-5p, miR-4665-3p, miR-1913, miR-1228-3p, miR-940, miR-296-3p, miR-4690-5p, miR-548q, miR-663a, miR-1249, miR-1202, miR-7113-3p, miR-1225-3p, miR-4783-3p, miR-4448 et miR-

4534, et/ou ;
miR-19b-3p, miR-1228-5p, miR-1307-3p, miR-4271, miR-642b-3p, miR-6075, miR-6125, miR-887-3p, miR-6851-5p, miR-6763-5p, miR-3928-3p, miR-4443, miR-3648, miR-149-3p, miR-4689, miR-4763-3p, miR-6729-5p, miR-3196, miR-8069, miR-1268a, miR-4739, miR-1268b, miR-5698, miR-6752-5p, miR-4507, miR-564, miR-4497, miR-6877-5p, miR-6087, miR-4731-5p, miR-615-5p, miR-760, miR-6891-5p, miR-6887-5p, miR-4525, miR-1914-3p, miR-619-5p, miR-5001-5p, miR-6722-3p, miR-3621, miR-4298, miR-675-5p et miR-4655-5p.

Fig. 1

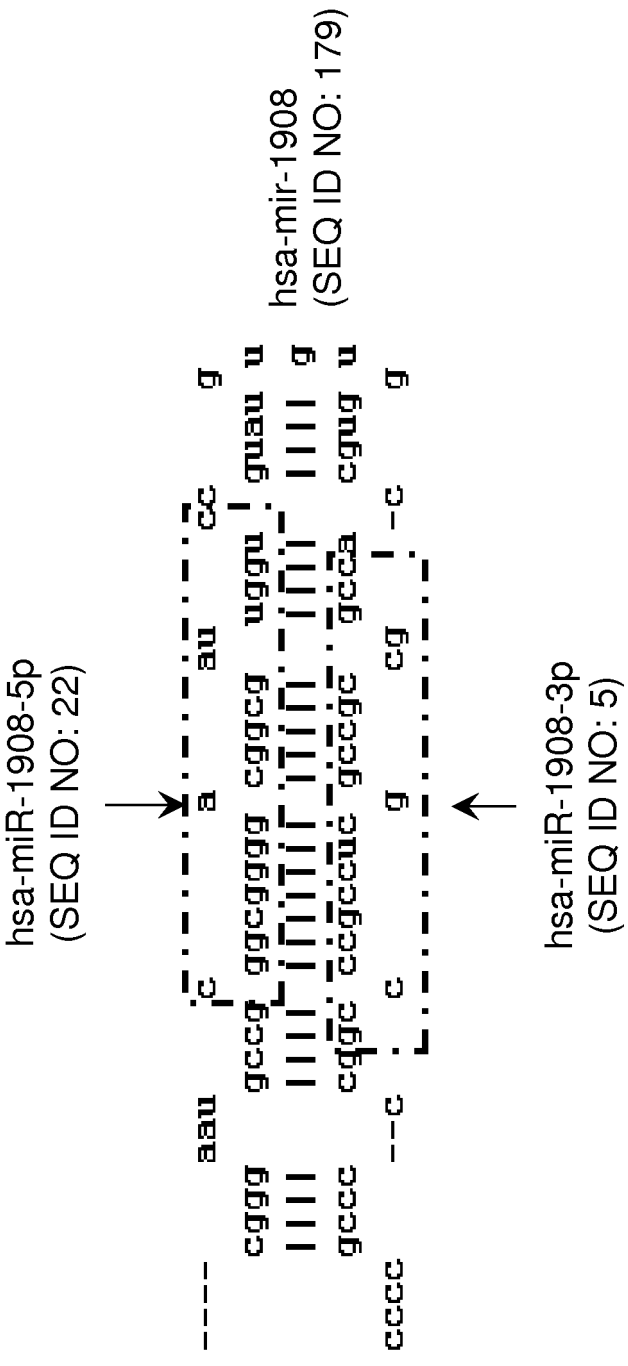

hsa-miR-1908-5p
(SEQ ID NO: 22)
hsa-miR-1908-3p
(SEQ ID NO: 5)
hsa-mir-1908
(SEQ ID NO: 179)

Fig. 2

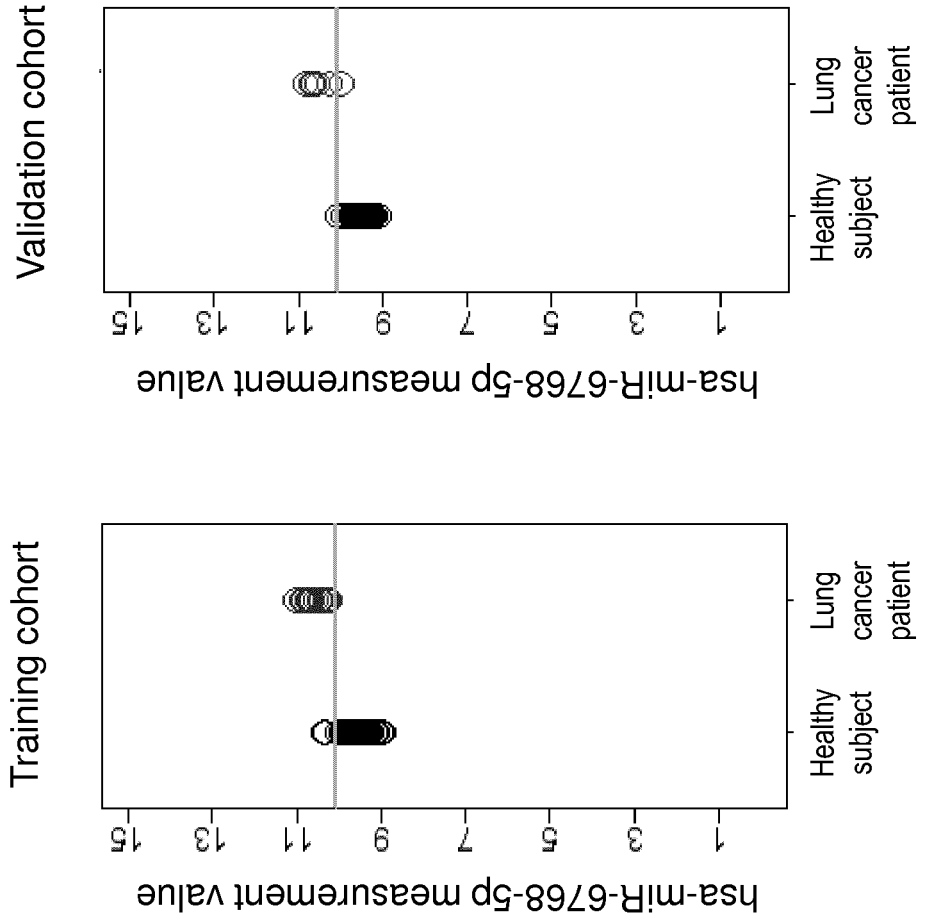

Validation cohort
hsa-miR-6768-5p measurement value
1
3
5
7
9
11
13
15
Healthy subject
Lung cancer patient
Training cohort
hsa-miR-6768-5p measurement value
1
3
5
7
9
11
13
15
Healthy subject
Lung cancer patient

Fig. 3

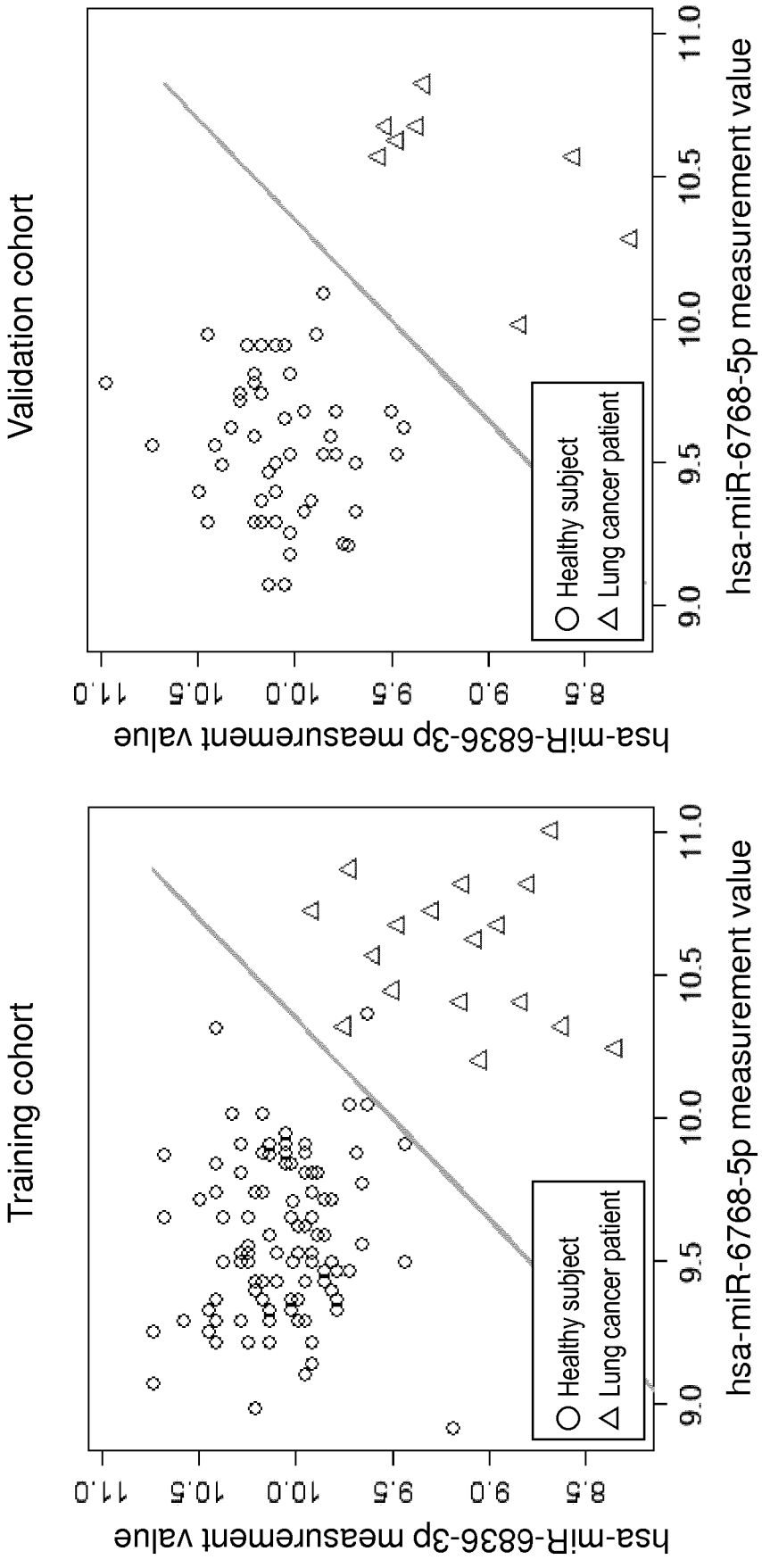
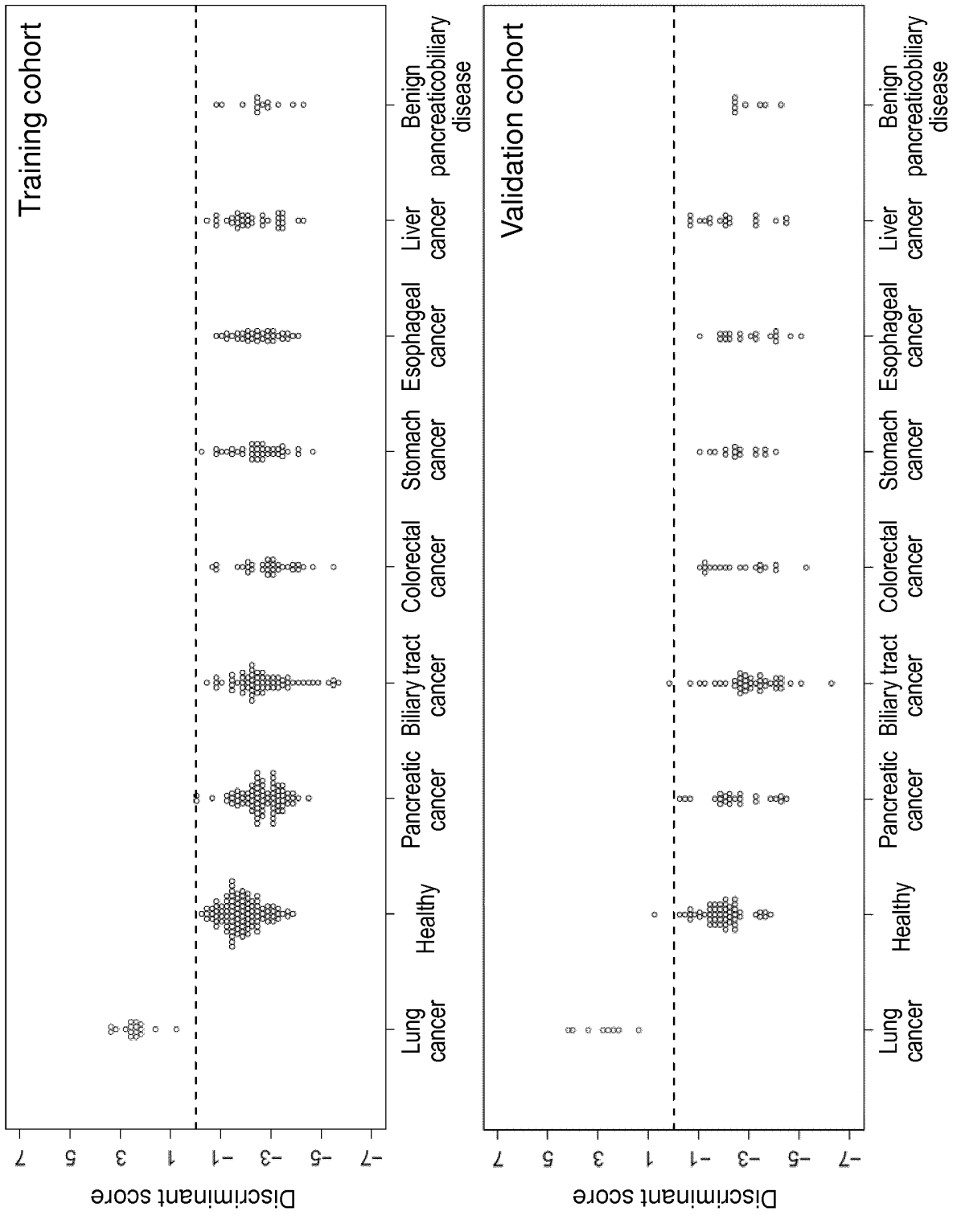

Training cohort
Validation cohort
hsa-miR-6836-3p measurement value
hsa-miR-6768-5p measurement value
8.5
9.0
9.5
10.0
10.5
11.0
○ Healthy subject
△ Lung cancer patient

Fig. 4


A
Training cohort
Discriminant score
7
5
3
1
-1
-3
-5
-7
Lung cancer
Healthy
Pancreatic cancer
Biliary tract cancer
Colorectal cancer
Stomach cancer
Esophageal cancer
Liver cancer
Benign pancreaticobiliary disease
B
Validation cohort
Discriminant score
7
5
3
1
-1
-3
-5
-7
Lung cancer
Healthy
Pancreatic cancer
Biliary tract cancer
Colorectal cancer
Stomach cancer
Esophageal cancer
Liver cancer
Benign pancreaticobiliary disease

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