



(11) **EP 3 150 707 A1**

(12) **EUROPEAN PATENT APPLICATION**
published in accordance with Art. 153(4) EPC

(43) Date of publication:
05.04.2017 Bulletin 2017/14

(21) Application number: **15800550.4**

(22) Date of filing: **29.05.2015**

(51) Int Cl.:
C12N 15/09 (2006.01) **C12M 1/00** (2006.01)
C12M 1/34 (2006.01) **C12Q 1/68** (2006.01)
G01N 33/53 (2006.01) **G01N 33/574** (2006.01)
G01N 37/00 (2006.01)

(86) International application number:
PCT/JP2015/065696

(87) International publication number:
WO 2015/182781 (03.12.2015 Gazette 2015/48)

(84) Designated Contracting States:
AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HR HU IE IS IT LI LT LU LV MC MK MT NL NO PL PT RO RS SE SI SK SM TR
Designated Extension States:
BA ME
Designated Validation States:
MA

(30) Priority: **30.05.2014 JP 2014113523**
11.09.2014 JP 2014185730

(71) Applicants:
• **Toray Industries, Inc.**
Tokyo 103-8666 (JP)
• **National Cancer Center**
Tokyo 104-0045 (JP)

(72) Inventors:
• **KAWAUCHI Junpei**
Kamakura-shi
Kanagawa 248-8555 (JP)

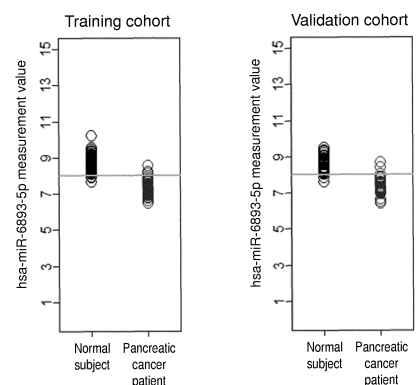
- **NOBUMASA Hitoshi**
Kamakura-shi
Kanagawa 248-8555 (JP)
- **KOZONO Satoko**
Kamakura-shi
Kanagawa 248-8555 (JP)
- **KONDOU Satoshi**
Kamakura-shi
Kanagawa 248-8555 (JP)
- **SUDO Hiroko**
Kamakura-shi
Kanagawa 248-8555 (JP)
- **OCHIAI Atsushi**
Kashiwa-shi
Chiba 277-8577 (JP)
- **KOJIMA Motohiro**
Kashiwa-shi
Chiba 277-8577 (JP)

(74) Representative: **Denison, Christopher Marcus et al**
Mewburn Ellis LLP
City Tower
40 Basinghall Street
London EC2V 5DE (GB)

(54) **PANCREATIC CANCER DETECTION KIT, DEVICE, AND DETECTION METHOD**

(57) This invention provides a kit or a device for the detection of pancreatic cancer, comprising a nucleic acid(s) capable of specifically binding to a miRNA(s) in a sample from a subject, and a method for detecting pancreatic cancer, comprising measuring the miRNA(s) *in vitro*.

Fig. 2



EP 3 150 707 A1

Description

TECHNICAL FIELD

5 **[0001]** The present invention relates to a kit or a device for the detection of pancreatic cancer, comprising a nucleic acid capable of specifically binding to a particular miRNA, which is used for examining the presence or absence of pancreatic cancer in a subject, and a method for detecting pancreatic cancer, comprising measuring an expression level of the miRNA using the nucleic acid.

10 BACKGROUND ART

[0002] The pancreas serves as an exocrine gland that secretes pancreatic juice as a digestive juice and sends the juice into the digestive tract through the pancreatic duct, while also functioning as an endocrine gland that secretes hormones such as insulin and glucagon into blood.

15 **[0003]** Since the pancreas is surrounded by many organs such as the stomach, the duodenum, the small intestine, the liver, and the gallbladder, pancreatic cancer is not only difficult to detect early but has properties such as a lack of subjective symptoms, very rapid progression, and metastasis to other organs and thus has very poor prognosis as compared with other cancers. According to the 2011 statistics of cancer type-specific mortality in Japan disclosed by the Center for Cancer Control and Information Services, National Cancer Center (Tokyo, Japan), the number of pancreatic cancer deaths climbed to 28,829 people, and 5-year relative survival rates by cancer type in 2003 to 2005 were lowest in pancreatic cancer with 7.1% for males and 6.9% for females.

20 **[0004]** As described in Non-Patent Literature 1, the basic therapy of pancreatic cancer is practiced by surgery, systemic chemotherapy, radiotherapy, or a combination thereof depending on a stage of progression. Although 15 to 20% pancreatic cancer patients undergo surgery for potential cure, the great majority of patients who do not undergo surgery are considered to have local progression or metastasis. The median survival time is reportedly 8 to 12 months for locally advanced cancer and 3 to 6 months for metastatic cancer, which are very poor as compared with other cancers.

25 **[0005]** The UICC (Unio Internationalis Contra Cancrum) stages of progression of pancreatic cancer are defined in General Rules for the Study of Pancreatic Cancer, the 5th edition (edited by Japan Pancreas Society, KANEHARA & Co., LTD., 2013, p. 55) and classified into stages 0, IA, IB, IIA, IIB, III, IVa, and IVb according to the size of primary tumor, lymph node metastasis, distant metastasis, etc. Stages I to III occupy half or more of the number of 5-year survivals, and stages IVa and IVb occupy 70% or more of the progressed stages at the time of diagnosis. Also, pancreatic cancer differs in symptoms among sites of origin. Carcinoma of the head of the pancreas often manifests jaundice, whereas carcinoma of the tail of the pancreas has few symptoms. Therefore, the carcinoma of the tail of the pancreas tends to result in delayed diagnosis as compared with the carcinoma of the head of the pancreas.

30 **[0006]** As described in Non-Patent Literature 2, abdominal ultrasonography is very useful as convenient and limitedly invasive examination in outpatient settings or medical examination for the diagnosis of pancreatic cancer. However, it is often difficult to visualize pancreatic cancer having a small tumor size or a lesion on the pancreatic tail side. In ordinary medical checkup, the prevalence of pancreatic cancer found in pancreatic images by abdominal ultrasonography is approximately 1%, and the detection rate of pancreatic cancer is approximately 0.06% or lower. For example, CA19-9, Span-1, CA50, CA242, Dupan-2, TAG-72, and urinary fucose as carbohydrate antigens, and CEA, POA, and TPS as non-carbohydrate antigens are known as tumor markers for the detection of pancreatic cancer. As for how to use these tumor markers, a subject is suspected of having a cancer when their concentrations in blood are higher or lower than predetermined reference values. For example, as described in Non-Patent Literature 3, the reference value of CEA is set to 5 ng/mL, and the reference value of CA19-9 is set to 37 U/mL. A subject is suspected of having a cancer including pancreatic cancer when their concentrations exhibit these values or higher. However, the evaluation of tumor markers often examines advanced pancreatic cancer and does not show abnormal values for early pancreatic cancer in many cases. Even combinatorial use of tumor markers and abdominal ultrasonography in medical examination results in low rates of detection of pancreatic cancer. The implementation of such medical examinations for the detection of pancreatic cancer is controversial from the viewpoint of cost effectiveness.

35 **[0007]** As shown in Patent Literatures 1 to 4, there are reports, albeit at a research stage, on the determination of pancreatic 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.

[0008] Patent Literature 1 discloses a method for detecting pancreatic cancer by combining hsa-miR-125a-3p with dozens of other miRNAs in blood.

40 **[0009]** Patent Literature 2 discloses a method for detecting pancreatic cancer by combining a hsa-miR-204-3p precursor, a hsa-miR-423-5p precursor, or a hsa-miR-328-5p precursor with several hundreds of other miRNAs in blood or tissues.

45 **[0010]** Patent Literature 3 discloses a method for detecting pancreatic cancer by combining hsa-miR-575, hsa-miR-

16-5p, or hsa-miR-24-3p with several hundreds of other miRNAs in blood.

[0011] Patent Literature 4 discloses a method for detecting pancreatic cancer by combining hsa-miR-451a with dozens of other miRNAs in blood or tissues.

5 **[0012]** Patent Literature 5 discloses a method for detecting pancreatic cancer by combining a hsa-miR-150-3p precursor or a hsa-miR-187-5p precursor with several hundreds of other miRNAs in blood or tissues.

[0013] Non-Patent Literature 4 discloses hsa-miR-423-5p, hsa-miR-1246, hsa-miR-150-3p, hsa-miR-550a-5p, hsa-miR-371a-5p, hsa-miR-1469, hsa-miR-575, hsa-miR-564, hsa-miR-125a-3p, hsa-miR-451a, hsa-miR-1908-5p and the like in plasma as miRNAs that have significant difference in their expression levels between pancreatic cancer patients and healthy subjects.

10 **[0014]** Non-Patent Literature 5 discloses miR-3188, miR-16-5p, and the like in plasma as miRNAs that have significant difference in their expression levels between pancreatic cancer patients and healthy subjects.

[0015] Non-Patent Literature 6 discloses miR-550a-5p, miR-1290, miR-24-3p, miR-486-3p, miR-423-5p, miR-125a-3p, and the like in serum as miRNAs that have significant difference in their expression levels between pancreatic cancer patients and healthy subjects.

15 **[0016]** Non-Patent Literature 7 discloses miR-602 in tissues as a miRNA that have significant difference in its expression level between pancreatic cancer patients and healthy subjects.

PRIOR ART LITERATURE

20 Patent Literature

[0017]

Patent Literature 1: JP Patent Publication (Kohyo) No. 2012-507300 A (2012)

25 Patent Literature 2: Published U.S. Patent Application No. 2010/0286232

Patent Literature 3: International Publication No. WO 2013/107459

Patent Literature 4: Published U.S. Patent Application No. 2013/0310276

Patent Literature 5: Published U.S. Patent Application No. 2008/0306018

30 Non-Patent Literature

[0018]

35 Non-Patent Literature 1: Tetsuya Mine, "Suizo (Pancreas), Journal of the Japan Pancreas Society", Japan Pancreas Society, 2007, Vol. 22, p.105-113

Non-Patent Literature 2: Japan Pancreas Society, "2009 Scientific evidence based clinical practice guidelines for pancreatic cancer" CQ1 diagnosis methods <http://www.suizou.org/PCMG2009/cq1/cq1-3.html>

Non-Patent Literature 3: Kiyoshi Kurokawa et al. ed., LAB DATA, 2013, p. 633, 636 (Igaku-Shoin Ltd., Tokyo, Japan)

Non-Patent Literature 4: Ali S. et al, 2010, American Journal of Translational Research, Vol. 3, (1), p. 28-47

40 Non-Patent Literature 5: Ganepola GA. et al., 2014, World Journal of Gastrointestinal Oncology., Vol. 6, (1), p. 22-33

Non-Patent Literature 6: Li A. et al., 2013, Clinical Cancer Research, Vol. 19, (13), p. 3600-3610

Non-Patent Literature 7: Zhang J. et al., 2014, Oncology Reports, Vol. 31, (3), p. 1157-1164

SUMMARY OF INVENTION

45

Problem to be Solved by Invention

[0019] An object of the present invention is to find novel tumor markers for pancreatic cancer and to provide a method that can effectively detect pancreatic cancer using nucleic acids capable of specifically binding to the markers. As described in Non-Patent Literature 2, for example, CA19-9, Span-1, CA50, CA242, Dupan-2, TAG-72, and urinary fucose as carbohydrate antigens and CEA, POA, and TPS as non-carbohydrate antigens are known as tumor markers for the detection of pancreatic cancer. The pancreatic cancer detection sensitivity of these tumor markers is 70 to 80% for CA19-9, 70 to 80% for Span-1, 50 to 60% for Dupan-2, 30 to 60% for CEA, and 60% for CA50. In addition, their specificity is not much high, and their false positive rates are as high as 20 to 30%. Therefore, there may be the possibility of false detection of other cancers and/or benign tumors and/or benign diseases of the pancreas and/or peripancreatic organs, etc. Particularly, the detection sensitivity of early pancreatic cancer is generally low, and the positive rate of CA19-9 is merely 1/2 (52%) for pancreatic cancer having a tumor size of 2 cm or smaller. Therefore, these tumor markers are not useful for the detection of early pancreatic cancer. Furthermore, the tumor markers based on carbohydrate antigens

exhibit false negatives in Lewis blood type negative cases, in which the subjects do not produce the antigens. Therefore, this examination is unsuitable for some subjects.

5 [0020] As described below, there are reports, albeit at a research stage, on the determination of pancreatic cancer using the expression levels of microRNAs (miRNAs) in biological samples including blood, none of which, however, have yet been brought into practical use.

[0021] Patent Literature 1 describes a method for diagnosing various cancers including pancreatic cancer by combining hsa-miR-125a-3p with a large number (dozens) of other miRNAs in blood. This literature, however, neither describes specific detection performance thereof such as accuracy, sensitivity, or specificity nor describes a specific method for diagnosing pancreatic cancer using blood.

10 [0022] Patent Literature 2 describes a method for detecting pancreatic cancer by combining a hsa-miR-204-3p precursor, a hsa-miR-423-5p precursor, or a hsa-miR-328-5p precursor with several hundreds of other miRNAs in blood or tissues. This literature, however, neither describes specific detection performance thereof such as accuracy, sensitivity, or specificity nor describes a specific method for diagnosing pancreatic cancer using blood.

15 [0023] The method described in Patent Literature 3 diagnoses pancreatic cancer by combining hsa-miR-575, hsa-miR-16-5p, or hsa-miR-24-3p with several hundreds of other miRNAs and does not state that diagnosis can be conducted by combining several miRNAs.

[0024] Patent Literature 4 employs hsa-miR-451a in combination with dozens or more of other miRNAs in pancreatic cancer tissues for the diagnosis of pancreatic cancer. This literature, however, does not describe a specific method for diagnosing pancreatic cancer using blood.

20 [0025] Patent Literature 5 employs a hsa-miR-150-3p precursor or a hsa-miR-187-5p precursor in combination with several hundreds or more of other miRNAs in pancreatic cancer tissues for the diagnosis of pancreatic cancer. This literature, however, neither describes specific detection performance thereof such as accuracy, sensitivity, or specificity nor describes a specific method for diagnosing pancreatic cancer using blood.

25 [0026] In Non-Patent Literature 4, examples of the miRNAs that have significant difference in their expression levels in plasma between pancreatic cancer patients and healthy subjects include miR-423-5p, miR-1246, miR-150-3p, miR-550a-5p, miR-371a-5p, miR-1469, miR-575, miR-564, miR-125a-3p, miR-451a, and miR-1908-5p. This literature, however, does not describe specific detection performance thereof such as accuracy, sensitivity, or specificity.

[0027] In Non-Patent Literature 5, examples of the miRNAs that have significant difference in their expression levels in plasma between pancreatic cancer patients and healthy subjects include miR-3188 and miR-16-5p. However, as a result of validation, these miRNAs were excluded from the analytes due to their low reliability.

30 [0028] In Non-Patent Literature 6, examples of the miRNAs that have significant difference in their expression levels in serum between pancreatic cancer patients and healthy subjects include miR-550a-5p, miR-1290, miR-24-3p, miR-486-3p, miR-423-5p, and miR-125a-3p. This literature, however, neither describes the specific detection performance, such as accuracy, sensitivity, or specificity, of miR-550a-5p, miR-24-3p, miR-486-3p, miR-423-5p, and miR-125a-3p nor validated the detection performance of miR-1290 in an independent sample group.

[0029] In Non-Patent Literature 7, examples of the miRNA that have significant difference in its expression level in pancreatic tissues between pancreatic cancer patients and healthy subjects include miR-602. This literature, however, neither describes specific detection performance thereof such as accuracy, sensitivity, or specificity nor describes a specific method for diagnosing pancreatic cancer using blood.

40 [0030] As mentioned above, the existing tumor markers exhibit low performance in the detection of pancreatic cancer, or neither performance nor detection methods are specifically shown as to the markers at a research stage. Therefore, use of these markers might require carrying out needless extra examination due to the false detection of healthy subjects as being pancreatic cancer patients, or might waste therapeutic opportunity because of overlooking pancreatic cancer patients. In addition, the measurement of dozens to several hundreds of miRNAs increases examination costs and is therefore difficult to use in large-scale screening such as medical checkup. Furthermore, the collection of pancreatic tissues for measuring the tumor markers is highly invasive to patients and is not favorable. Hence, there is a demand for a highly accurate pancreatic cancer marker that is detectable from blood, which can be collected in less invasive manner, and is capable of correctly determining a pancreatic cancer patient as a pancreatic cancer patient and a healthy subject as a healthy subject. Particularly, a highly sensitive pancreatic cancer marker is desired because tumor resection based on early detection is only radical cure for pancreatic cancer.

Means for Solution of Problem

55 [0031] The present inventors have conducted diligent studies to attain the object and consequently completed the present invention by finding several genes usable as markers for the detection of pancreatic cancer from blood, which can be collected with limited invasiveness, and finding that pancreatic cancer can be significantly detected by using nucleic acids capable of specifically binding to any of these markers.

<Summary of Invention>

[0032] The present invention has the following features:

5 (1) A kit for the detection of pancreatic cancer, comprising a nucleic acid(s) capable of specifically binding to at least one or more polynucleotides selected from the group consisting of the following pancreatic cancer markers: miR-6893-5p, miR-6075, miR-6820-5p, miR-4294, miR-6729-5p, miR-4476, miR-6836-3p, miR-6765-3p, miR-6799-5p, miR-4530, miR-7641, miR-4454, miR-615-5p, miR-8073, miR-663a, miR-4634, miR-4450, miR-4792, miR-665, miR-7975, miR-7109-5p, miR-6789-5p, miR-4497, miR-6877-5p, miR-6880-5p, miR-7977, miR-4734, miR-6821-5p, miR-8089, miR-5585-3p, miR-6085, miR-6845-5p, miR-4651, miR-4433-3p, miR-1231, miR-4665-5p, miR-7114-5p, miR-1238-5p, miR-8069, miR-4732-5p, miR-619-5p, miR-3622a-5p, miR-1260a, miR-6741-5p, miR-6781-5p, miR-6125, miR-6805-5p, miR-6132, miR-6872-3p, miR-6875-5p, miR-1908-3p, miR-4433b-3p, miR-4736, miR-5100, miR-6724-5p, miR-7107-5p, miR-6726-5p, miR-3185, miR-4638-5p, miR-1273g-3p, miR-6778-5p, miR-328-5p, miR-3679-3p, miR-1228-3p, miR-6779-5p, miR-4723-5p, miR-6850-5p, miR-760, miR-7704, miR-8072, miR-4486, miR-1913, miR-4656, miR-1260b, miR-7106-5p, miR-6889-5p, miR-6780b-5p, miR-6090, miR-4534, miR-4449, miR-5195-3p, miR-1202, miR-4467, miR-6515-3p, miR-4281, miR-4505, miR-4484, miR-6805-3p, miR-3135b, miR-3162-5p, miR-6768-5p, miR-6721-5p, miR-1227-5p, miR-6722-3p, miR-4286, miR-4746-3p, miR-6727-5p, miR-6816-5p, miR-4741, miR-4508, miR-940, miR-4327, miR-4665-3p, miR-718, miR-1203, miR-663b, miR-4258, miR-4649-5p, miR-4516, miR-3619-3p, miR-6826-5p, miR-6757-5p, miR-3131, miR-1343-3p, miR-6775-5p, miR-6813-5p, and miR-3940-5p.

(2) The kit according to (1), wherein miR-6893-5p is hsa-miR-6893-5p, miR-6075 is hsa-miR-6075, miR-6820-5p is hsa-miR-6820-5p, miR-4294 is hsa-miR-4294, miR-6729-5p is hsa-miR-6729-5p, miR-4476 is hsa-miR-4476, miR-6836-3p is hsa-miR-6836-3p, miR-6765-3p is hsa-miR-6765-3p, miR-6799-5p is hsa-miR-6799-5p, miR-4530 is hsa-miR-4530, miR-7641 is hsa-miR-7641, miR-4454 is hsa-miR-4454, miR-615-5p is hsa-miR-615-5p, miR-8073 is hsa-miR-8073, miR-663a is hsa-miR-663a, miR-4634 is hsa-miR-4634, miR-4450 is hsa-miR-4450, miR-4792 is hsa-miR-4792, miR-665 is hsa-miR-665, miR-7975 is hsa-miR-7975, miR-7109-5p is hsa-miR-7109-5p, miR-6789-5p is hsa-miR-6789-5p, miR-4497 is hsa-miR-4497, miR-6877-5p is hsa-miR-6877-5p, miR-6880-5p is hsa-miR-6880-5p, miR-7977 is hsa-miR-7977, miR-4734 is hsa-miR-4734, miR-6821-5p is hsa-miR-6821-5p, miR-8089 is hsa-miR-8089, miR-5585-3p is hsa-miR-5585-3p, miR-6085 is hsa-miR-6085, miR-6845-5p is hsa-miR-6845-5p, miR-4651 is hsa-miR-4651, miR-4433-3p is hsa-miR-4433-3p, miR-1231 is hsa-miR-1231, miR-4665-5p is hsa-miR-4665-5p, miR-7114-5p is hsa-miR-7114-5p, miR-1238-5p is hsa-miR-1238-5p, miR-8069 is hsa-miR-8069, miR-4732-5p is hsa-miR-4732-5p, miR-619-5p is hsa-miR-619-5p, miR-3622a-5p is hsa-miR-3622a-5p, miR-1260a is hsa-miR-1260a, miR-6741-5p is hsa-miR-6741-5p, miR-6781-5p is hsa-miR-6781-5p, miR-6125 is hsa-miR-6125, miR-6805-5p is hsa-miR-6805-5p, miR-6132 is hsa-miR-6132, miR-6872-3p is hsa-miR-6872-3p, miR-6875-5p is hsa-miR-6875-5p, miR-1908-3p is hsa-miR-1908-3p, miR-4433b-3p is hsa-miR-4433b-3p, miR-4736 is hsa-miR-4736, miR-5100 is hsa-miR-5100, miR-6724-5p is hsa-miR-6724-5p, miR-7107-5p is hsa-miR-7107-5p, miR-6726-5p is hsa-miR-6726-5p, miR-3185 is hsa-miR-3185, miR-4638-5p is hsa-miR-4638-5p, miR-1273g-3p is hsa-miR-1273g-3p, miR-6778-5p is hsa-miR-6778-5p, miR-328-5p is hsa-miR-328-5p, miR-3679-3p is hsa-miR-3679-3p, miR-1228-3p is hsa-miR-1228-3p, miR-6779-5p is hsa-miR-6779-5p, miR-4723-5p is hsa-miR-4723-5p, miR-6850-5p is hsa-miR-6850-5p, miR-760 is hsa-miR-760, miR-7704 is hsa-miR-7704, miR-8072 is hsa-miR-8072, miR-4486 is hsa-miR-4486, miR-1913 is hsa-miR-1913, miR-4656 is hsa-miR-4656, miR-1260b is hsa-miR-1260b, miR-7106-5p is hsa-miR-7106-5p, miR-6889-5p is hsa-miR-6889-5p, miR-6780b-5p is hsa-miR-6780b-5p, miR-6090 is hsa-miR-6090, miR-4534 is hsa-miR-4534, miR-4449 is hsa-miR-4449, miR-5195-3p is hsa-miR-5195-3p, miR-1202 is hsa-miR-1202, miR-4467 is hsa-miR-4467, miR-6515-3p is hsa-miR-6515-3p, miR-4281 is hsa-miR-4281, miR-4505 is hsa-miR-4505, miR-4484 is hsa-miR-4484, miR-6805-3p is hsa-miR-6805-3p, miR-3135b is hsa-miR-3135b, miR-3162-5p is hsa-miR-3162-5p, miR-6768-5p is hsa-miR-6768-5p, miR-6721-5p is hsa-miR-6721-5p, miR-1227-5p is hsa-miR-1227-5p, miR-6722-3p is hsa-miR-6722-3p, miR-4286 is hsa-miR-4286, miR-4746-3p is hsa-miR-4746-3p, miR-6727-5p is hsa-miR-6727-5p, miR-6816-5p is hsa-miR-6816-5p, miR-4741 is hsa-miR-4741, miR-4508 is hsa-miR-4508, miR-940 is hsa-miR-940, miR-4327 is hsa-miR-4327, miR-4665-3p is hsa-miR-4665-3p, miR-718 is hsa-miR-718, miR-1203 is hsa-miR-1203, miR-663b is hsa-miR-663b, miR-4258 is hsa-miR-4258, miR-4649-5p is hsa-miR-4649-5p, miR-4516 is hsa-miR-4516, miR-3619-3p is hsa-miR-3619-3p, miR-6826-5p is hsa-miR-6826-5p, miR-6757-5p is hsa-miR-6757-5p, miR-3131 is hsa-miR-3131, miR-1343-3p is hsa-miR-1343-3p, miR-6775-5p is hsa-miR-6775-5p, miR-6813-5p is hsa-miR-6813-5p, and miR-3940-5p is hsa-miR-3940-5p.

(3) The kit according to (1) or (2), wherein the nucleic acid(s) is a polynucleotide(s) 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: 1 to 104, 464 to 473, and 492 to 494 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: 1 to 104, 464 to 473, and 492 to 494;
- (c) a polynucleotide consisting of a nucleotide sequence complementary to a nucleotide sequence represented by any of SEQ ID NOs: 1 to 104, 464 to 473, and 492 to 494 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: 1 to 104, 464 to 473, and 492 to 494 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).

(4) The kit according to any of (1) to (3), further comprising, in addition to the nucleic acid(s), a nucleic acid(s) capable of specifically binding to at least one or more polynucleotides selected from the group consisting of miR-125a-3p, miR-204-3p, miR-1469, miR-575, miR-150-3p, miR-423-5p, miR-564, miR-3188, miR-1246, miR-602, miR-1290, miR-16-5p, miR-451a, miR-24-3p, miR-187-5p, miR-1908-5p, miR-371a-5p, and miR-550a-5p.

(5) The kit according to (4), wherein miR-125a-3p is hsa-miR-125a-3p, miR-204-3p is hsa-miR-204-3p, miR-1469 is hsa-miR-1469, miR-575 is hsa-miR-575, miR-150-3p is hsa-miR-150-3p, miR-423-5p is hsa-miR-423-5p, miR-564 is hsa-miR-564, miR-3188 is hsa-miR-3188, miR-1246 is hsa-miR-1246, miR-602 is hsa-miR-602, miR-1290 is hsa-miR-1290, miR-16-5p is hsa-miR-16-5p, miR-451a is hsa-miR-451a, miR-24-3p is hsa-miR-24-3p, miR-187-5p is hsa-miR-187-5p, miR-1908-5p is hsa-miR-1908-5p, miR-371a-5p is hsa-miR-371a-5p, and miR-550a-5p is hsa-miR-550a-5p.

(6) The kit according to (4) or (5), wherein the nucleic acid(s) further comprise a polynucleotide(s) 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: 105 to 122 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: 105 to 122;

(h) a polynucleotide consisting of a nucleotide sequence complementary to a nucleotide sequence represented by any of SEQ ID NOs: 105 to 122 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: 105 to 122 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).

(7) The kit according to any of (1) to (6), further comprising, in addition to the nucleic acid(s), a nucleic acid(s) capable of specifically binding to at least one or more polynucleotides selected from the group consisting of miR-4417, miR-4707-5p, miR-7847-3p, miR-2861, miR-4513, miR-7111-5p, miR-6777-5p, miR-7113-3p, miR-4648, miR-3184-5p, miR-4271, miR-6791-5p, miR-642a-3p, miR-7108-5p, miR-128-1-5p, miR-5196-5p, miR-3178, miR-3656, miR-92a-2-5p, miR-6769b-5p, miR-4689, miR-6076, miR-92b-5p, miR-6774-5p, miR-486-3p, miR-6806-5p, miR-6842-5p, miR-6716-5p, miR-557, miR-4673, miR-4674, miR-4442, miR-1915-3p, miR-4687-3p, and miR-92b-3p.

(8) The kit according to claim (7), wherein miR-4417 is hsa-miR-4417, miR-4707-5p is hsa-miR-4707-5p, miR-7847-3p is hsa-miR-7847-3p, miR-2861 is hsa-miR-2861, miR-4513 is hsa-miR-4513, miR-7111-5p is hsa-miR-7111-5p, miR-6777-5p is hsa-miR-6777-5p, miR-7113-3p is hsa-miR-7113-3p, miR-4648 is hsa-miR-4648, miR-3184-5p is hsa-miR-3184-5p, miR-4271 is hsa-miR-4271, miR-6791-5p is hsa-miR-6791-5p, miR-642a-3p is hsa-miR-642a-3p, miR-7108-5p is hsa-miR-7108-5p, miR-128-1-5p is hsa-miR-128-1-5p, miR-5196-5p is hsa-miR-5196-5p, miR-3178 is hsa-miR-3178, miR-3656 is hsa-miR-3656, miR-92a-2-5p is hsa-miR-92a-2-5p, miR-6769b-5p is hsa-miR-6769b-5p, miR-4689 is hsa-miR-4689, miR-6076 is hsa-miR-6076, miR-92b-5p is hsa-miR-92b-5p, miR-6774-5p is hsa-miR-6774-5p, miR-486-3p is hsa-miR-486-3p, miR-6806-5p is hsa-miR-6806-5p, miR-6842-5p is hsa-miR-6842-5p, miR-6716-5p is hsa-miR-6716-5p, miR-557 is hsa-miR-557, miR-4673 is hsa-miR-4673, miR-4674 is hsa-miR-4674, miR-4442 is hsa-miR-4442, miR-1915-3p is hsa-miR-1915-3p, miR-4687-3p is hsa-miR-4687-3p, and miR-92b-3p is hsa-miR-92b-3p.

(9) The kit according to (7) or (8), wherein the nucleic acid(s) is a polynucleotide(s) 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: 349 to 383 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;

(1) a polynucleotide comprising a nucleotide sequence represented by any of SEQ ID NOs: 349 to 383;

(m) a polynucleotide consisting of a nucleotide sequence complementary to a nucleotide sequence represented by any of SEQ ID NOs: 349 to 383 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: 349 to 383 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 kit according to any one of (1) to (9), 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 pancreatic cancer markers according to (1) or (2).

(11) A device for the detection of pancreatic cancer, comprising a nucleic acid(s) capable of specifically binding to at least one or more polynucleotides selected from the group consisting of pancreatic cancer markers miR-6893-5p, miR-6075, miR-6820-5p, miR-4294, miR-6729-5p, miR-4476, miR-6836-3p, miR-6765-3p, miR-6799-5p, miR-4530, miR-7641, miR-4454, miR-615-5p, miR-8073, miR-663a, miR-4634, miR-4450, miR-4792, miR-665, miR-7975, miR-7109-5p, miR-6789-5p, miR-4497, miR-6877-5p, miR-6880-5p, miR-7977, miR-4734, miR-6821-5p, miR-8089, miR-5585-3p, miR-6085, miR-6845-5p, miR-4651, miR-4433-3p, miR-1231, miR-4665-5p, miR-7114-5p, miR-1238-5p, miR-8069, miR-4732-5p, miR-619-5p, miR-3622a-5p, miR-1260a, miR-6741-5p, miR-6781-5p, miR-6125, miR-6805-5p, miR-6132, miR-6872-3p, miR-6875-5p, miR-1908-3p, miR-4433b-3p, miR-4736, miR-5100, miR-6724-5p, miR-7107-5p, miR-6726-5p, miR-3185, miR-4638-5p, miR-1273g-3p, miR-6778-5p, miR-328-5p, miR-3679-3p, miR-1228-3p, miR-6779-5p, miR-4723-5p, miR-6850-5p, miR-760, miR-7704, miR-8072, miR-4486, miR-1913, miR-4656, miR-1260b, miR-7106-5p, miR-6889-5p, miR-6780b-5p, miR-6090, miR-4534, miR-4449, miR-5195-3p, miR-1202, miR-4467, miR-6515-3p, miR-4281, miR-4505, miR-4484, miR-6805-3p, miR-3135b, miR-3162-5p, miR-6768-5p, miR-6721-5p, miR-1227-5p, miR-6722-3p, miR-4286, miR-4746-3p, miR-6727-5p, miR-6816-5p, miR-4741, miR-4508, miR-940, miR-4327, miR-4665-3p, miR-718, miR-1203, miR-663b, miR-4258, miR-4649-5p, miR-4516, miR-3619-3p, miR-6826-5p, miR-6757-5p, miR-3131, miR-1343-3p, miR-6775-5p, miR-6813-5p, and miR-3940-5p.

(12) The device according to (11), wherein miR-6893-5p is hsa-miR-6893-5p, miR-6075 is hsa-miR-6075, miR-6820-5p is hsa-miR-6820-5p, miR-4294 is hsa-miR-4294, miR-6729-5p is hsa-miR-6729-5p, miR-4476 is hsa-miR-4476, miR-6836-3p is hsa-miR-6836-3p, miR-6765-3p is hsa-miR-6765-3p, miR-6799-5p is hsa-miR-6799-5p, miR-4530 is hsa-miR-4530, miR-7641 is hsa-miR-7641, miR-4454 is hsa-miR-4454, miR-615-5p is hsa-miR-615-5p, miR-8073 is hsa-miR-8073, miR-663a is hsa-miR-663a, miR-4634 is hsa-miR-4634, miR-4450 is hsa-miR-4450, miR-4792 is hsa-miR-4792, miR-665 is hsa-miR-665, miR-7975 is hsa-miR-7975, miR-7109-5p is hsa-miR-7109-5p, miR-6789-5p is hsa-miR-6789-5p, miR-4497 is hsa-miR-4497, miR-6877-5p is hsa-miR-6877-5p, miR-6880-5p is hsa-miR-6880-5p, miR-7977 is hsa-miR-7977, miR-4734 is hsa-miR-4734, miR-6821-5p is hsa-miR-6821-5p, miR-8089 is hsa-miR-8089, miR-5585-3p is hsa-miR-5585-3p, miR-6085 is hsa-miR-6085, miR-6845-5p is hsa-miR-6845-5p, miR-4651 is hsa-miR-4651, miR-4433-3p is hsa-miR-4433-3p, miR-1231 is hsa-miR-1231, miR-4665-5p is hsa-miR-4665-5p, miR-7114-5p is hsa-miR-7114-5p, miR-1238-5p is hsa-miR-1238-5p, miR-8069 is hsa-miR-8069, miR-4732-5p is hsa-miR-4732-5p, miR-619-5p is hsa-miR-619-5p, miR-3622a-5p is hsa-miR-3622a-5p, miR-1260a is hsa-miR-1260a, miR-6741-5p is hsa-miR-6741-5p, miR-6781-5p is hsa-miR-6781-5p, miR-6125 is hsa-miR-6125, miR-6805-5p is hsa-miR-6805-5p, miR-6132 is hsa-miR-6132, miR-6872-3p is hsa-miR-6872-3p, miR-6875-5p is hsa-miR-6875-5p, miR-1908-3p is hsa-miR-1908-3p, miR-4433b-3p is hsa-miR-4433b-3p, miR-4736 is hsa-miR-4736, miR-5100 is hsa-miR-5100, miR-6724-5p is hsa-miR-6724-5p, miR-7107-5p is hsa-miR-7107-5p, miR-6726-5p is hsa-miR-6726-5p, miR-3185 is hsa-miR-3185, miR-4638-5p is hsa-miR-4638-5p, miR-1273g-3p is hsa-miR-1273g-3p, miR-6778-5p is hsa-miR-6778-5p, miR-328-5p is hsa-miR-328-5p, miR-3679-3p is hsa-miR-3679-3p, miR-1228-3p is hsa-miR-1228-3p, miR-6779-5p is hsa-miR-6779-5p, miR-4723-5p is hsa-miR-4723-5p, miR-6850-5p is hsa-miR-6850-5p, miR-760 is hsa-miR-760, miR-7704 is hsa-miR-7704, miR-8072 is hsa-miR-8072, miR-4486 is hsa-miR-4486, miR-1913 is hsa-miR-1913, miR-4656 is hsa-miR-4656, miR-1260b is hsa-miR-1260b, miR-7106-5p is hsa-miR-7106-5p, miR-6889-5p is hsa-miR-6889-5p, miR-6780b-5p is hsa-miR-6780b-5p, miR-6090 is hsa-miR-6090, miR-4534 is hsa-miR-4534, miR-4449 is hsa-miR-4449, miR-5195-3p is hsa-miR-5195-3p, miR-1202 is hsa-miR-1202, miR-4467 is hsa-miR-4467, miR-6515-3p is hsa-miR-6515-3p, miR-4281 is hsa-miR-4281, miR-4505 is hsa-miR-4505, miR-4484 is hsa-miR-4484, miR-6805-3p is hsa-miR-6805-3p, miR-3135b is hsa-miR-3135b, miR-3162-5p is hsa-miR-3162-5p, miR-6768-5p is hsa-miR-6768-5p, miR-6721-5p is hsa-miR-6721-5p,

miR-1227-5p is hsa-miR-1227-5p, miR-6722-3p is hsa-miR-6722-3p, miR-4286 is hsa-miR-4286, miR-4746-3p is hsa-miR-4746-3p, miR-6727-5p is hsa-miR-6727-5p, miR-6816-5p is hsa-miR-6816-5p, miR-4741 is hsa-miR-4741, miR-4508 is hsa-miR-4508, miR-940 is hsa-miR-940, miR-4327 is hsa-miR-4327, miR-4665-3p is hsa-miR-4665-3p, miR-718 is hsa-miR-718, miR-1203 is hsa-miR-1203, miR-663b is hsa-miR-663b, miR-4258 is hsa-miR-4258, miR-4649-5p is hsa-miR-4649-5p, miR-4516 is hsa-miR-4516, miR-3619-3p is hsa-miR-3619-3p, miR-6826-5p is hsa-miR-6826-5p, miR-6757-5p is hsa-miR-6757-5p, miR-3131 is hsa-miR-3131, miR-1343-3p is hsa-miR-1343-3p, miR-6775-5p is hsa-miR-6775-5p, miR-6813-5p is hsa-miR-6813-5p, and miR-3940-5p is hsa-miR-3940-5p.

(13) The device according to (11) or (12), wherein the nucleic acid(s) is a polynucleotide(s) 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: 1 to 104, 464 to 473, and 492 to 494 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: 1 to 104, 464 to 473, and 492 to 494;

(c) a polynucleotide consisting of a nucleotide sequence complementary to a nucleotide sequence represented by any of SEQ ID NOs: 1 to 104, 464 to 473, and 492 to 494 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: 1 to 104, 464 to 473, and 492 to 494 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).

(14) The device according to any one of (11) to (13), wherein the device further comprises a nucleic acid(s) capable of specifically binding to at least one or more polynucleotides selected from the group consisting of other pancreatic cancer markers miR-125a-3p, miR-204-3p, miR-1469, miR-575, miR-150-3p, miR-423-5p, miR-564, miR-3188, miR-1246, miR-602, miR-1290, miR-16-5p, miR-451a, miR-24-3p, miR-187-5p, miR-1908-5p, miR-371a-5p, and miR-550a-5p.

(15) The device according to (14), wherein miR-125a-3p is hsa-miR-125a-3p, miR-204-3p is hsa-miR-204-3p, miR-1469 is hsa-miR-1469, miR-575 is hsa-miR-575, miR-150-3p is hsa-miR-150-3p, miR-423-5p is hsa-miR-423-5p, miR-564 is hsa-miR-564, miR-3188 is hsa-miR-3188, miR-1246 is hsa-miR-1246, miR-602 is hsa-miR-602, miR-1290 is hsa-miR-1290, miR-16-5p is hsa-miR-16-5p, miR-451a is hsa-miR-451a, miR-24-3p is hsa-miR-24-3p, miR-187-5p is hsa-miR-187-5p, miR-1908-5p is hsa-miR-1908-5p, miR-371a-5p is hsa-miR-371a-5p, and miR-550a-5p is hsa-miR-550a-5p.

(16) The device according to (14) or (15), wherein the nucleic acid(s) is a polynucleotide(s) 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: 105 to 122 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: 105 to 122;

(h) a polynucleotide consisting of a nucleotide sequence complementary to a nucleotide sequence represented by any of SEQ ID NOs: 105 to 122 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: 105 to 122 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).

(17) The device according to any one of (11) to (16), wherein the device further comprises a nucleic acid(s) capable of specifically binding to at least one or more polynucleotides selected from the group consisting of other pancreatic cancer markers miR-4417, miR-4707-5p, miR-7847-3p, miR-2861, miR-4513, miR-7111-5p, miR-6777-5p, miR-7113-3p, miR-4648, miR-3184-5p, miR-4271, miR-6791-5p, miR-642a-3p, miR-7108-5p, miR-128-1-5p, miR-5196-5p, miR-3178, miR-3656, miR-92a-2-5p, miR-6769b-5p, miR-4689, miR-6076, miR-92b-5p, miR-6774-5p, miR-486-3p, miR-6806-5p, miR-6842-5p, miR-6716-5p, miR-557, miR-4673, miR-4674, miR-4442, miR-1915-3p, miR-4687-3p and miR-92b-3p.

(18) The device according to (17), wherein miR-4417 is hsa-miR-4417, miR-4707-5p is hsa-miR-4707-5p, miR-7847-3p is hsa-miR-7847-3p, miR-2861 is hsa-miR-2861, miR-4513 is hsa-miR-4513, miR-7111-5p is hsa-miR-7111-5p, miR-6777-5p is hsa-miR-6777-5p, miR-7113-3p is hsa-miR-7113-3p, miR-4648 is hsa-miR-4648, miR-3184-5p is hsa-miR-3184-5p, miR-4271 is hsa-miR-4271, miR-6791-5p is hsa-miR-6791-5p, miR-642a-3p is hsa-miR-642a-3p, miR-7108-5p is hsa-miR-7108-5p, miR-128-1-5p is hsa-miR-128-1-5p, miR-5196-5p is hsa-miR-5196-5p, miR-3178 is hsa-miR-3178, miR-3656 is hsa-miR-3656, miR-92a-2-5p is hsa-miR-92a-2-5p, miR-6769b-5p is hsa-miR-6769b-5p, miR-4689 is hsa-miR-4689, miR-6076 is hsa-miR-6076, miR-92b-5p is hsa-miR-92b-5p, miR-6774-5p is hsa-miR-6774-5p, miR-486-3p is hsa-miR-486-3p, miR-6806-5p is hsa-miR-6806-5p, miR-6842-5p is hsa-miR-6842-5p, miR-6716-5p is hsa-miR-6716-5p, miR-557 is hsa-miR-557, miR-4673 is hsa-miR-4673, miR-4674 is hsa-miR-4674, miR-4442 is hsa-miR-4442, miR-1915-3p is hsa-miR-1915-3p, miR-4687-3p is hsa-miR-4687-3p, and miR-92b-3p is hsa-miR-92b-3p.

(19) The device according to (17) or (18), wherein the nucleic acid(s) is a polynucleotide(s) 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: 349 to 383 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: 349 to 383;

(m) a polynucleotide consisting of a nucleotide sequence complementary to a nucleotide sequence represented by any of SEQ ID NOs: 349 to 383 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: 349 to 383 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).

(20) The device according to any one of (11) to (19), wherein the device is for measurement based on a hybridization technique.

(21) The device according to (20), wherein the hybridization technique is a nucleic acid array technique.

(22) The device according to any one of (11) to (21), 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 pancreatic cancer markers according to (11) or (12).

(23) A method for detecting pancreatic cancer, comprising: measuring an expression level(s) of a target nucleic acid(s) in a sample from a subject using a kit according to any one of (1) to (10) or a device according to any one of (11) to (22); and evaluating *in vitro* whether or not the subject has pancreatic cancer using both of the measured expression level(s) and a control expression level(s) in a sample from a healthy subject measured in the same way.

(24) The method according to (23), wherein the subject is a human.

(25) The method according to (23) or (24), wherein the sample is blood, serum, or plasma.

<Definition of Terms>

[0033] The terms used herein are defined as described below.

[0034] The term "pancreatic cancer" used herein refers to any malignant tumor formed in the pancreas. Specifically, the "pancreatic cancer" includes serous cystadenoma, mucinous cystadenocarcinoma, intraductal papillary-mucinous carcinoma, invasive ductal carcinoma, acinar cell carcinoma, neuroendocrine cancer, and the like ("General Rules for the Study of Pancreatic Cancer", the 6th edition, revised version, 2013, Japan Pancreas Society, KANEHARA & Co., LTD., p. 21-22).

[0035] The term "benign tumors and/or benign diseases of the pancreas and/or peripancreatic organs" used herein refers to diseases with nonmalignant tumors in the pancreas, the liver, and the bile duct.

[0036] Abbreviations or terms such as "nucleotide", "polynucleotide", "DNA", and "RNA" used herein 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.

[0037] The term "polynucleotide" used herein refers to 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 a DNA and an 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 nucleotides (i.e., a variant sequence) and a sequence comprising one or more modified nucleotides (i.e., a modified sequence), which are different from the natural sequence. Herein, the term "polynucleotide" is used interchangeably with the term "nucleic acid."

5 **[0038]** 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.

[0039] The term "gene" used herein is intended to include not only RNA and double-stranded DNA but also 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.

10 **[0040]** 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 their 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 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 499 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t. Regardless whether or not there is a difference in functional region, the "gene" can comprise, for example, expression control regions, coding region, exons, or introns. The "gene" may be contained in a cell or may exist alone after being released from a cell. Alternatively, the "gene" may be in a state enclosed in a vesicle called exosome.

15 **[0041]** The term "exosome" used herein is a vesicle that is encapsulated by lipid bilayer and secreted from a cell. The exosome is derived from a multivesicular endosome and may incorporate biomaterials such as "genes" (e.g., RNA or DNA) or proteins when released into an extracellular environment. The exosome is known to be contained in a body fluid such as blood, serum, plasma, serum or lymph.

20 **[0042]** The term "transcript" used herein refers to an RNA synthesized from the DNA sequence of a gene as a template. RNA polymerase binds to a site called promoter located upstream of the gene and adds ribonucleotides complementary to the nucleotide sequence of the DNA to the 3' end to synthesize an RNA. This RNA contains not only the gene itself but the whole sequence from a transcription initiation site to the end of a polyA sequence, including expression control regions, coding region, exons, or introns.

25 **[0043]** Unless otherwise specified, the term "microRNA (miRNA)" used herein is intended to mean a 15- to 25-nucleotide non-coding RNA that is transcribed as an RNA precursor having a hairpin-like structure, cleaved by a dsRNA-cleaving enzyme having RNase III cleavage activity, and integrated into a protein complex called RISC, and that is involved in the suppression of translation of mRNA. 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 499. 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).

30 **[0044]** The term "probe" used herein includes a polynucleotide that is used for specifically detecting an RNA resulting from the expression of a gene or a polynucleotide derived from the RNA, and/or a polynucleotide complementary thereto.

[0045] The term "primer" used herein includes a polynucleotide that specifically recognizes and amplifies an RNA resulting from the expression of a gene or a polynucleotide derived from the RNA, and/or a polynucleotide complementary thereto.

35 **[0046]** In this context, the complementary polynucleotide (complementary strand or reverse strand) means a polynucleotide in a complementary relationship based on 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 499 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.

40 **[0047]** The term "stringent conditions" used herein refers to conditions under which a nucleic acid probe hybridizes to its target sequence to a detectably 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) x 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 complementary 100% 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.

5 **[0048]** The term "T_m 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.

[0049] 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 or 2 or more nucleotides in a nucleotide sequence represented by any of SEQ ID NOs: 1 to 499 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 percent (%) 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 sequences 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 sequences thereof.

15 **[0050]** The term "several" used herein means an integer of approximately 10, 9, 8, 7, 6, 5, 4, 3, or 2.

[0051] The variant as used herein can be prepared by use of a well-known technique such as site-directed mutagenesis or mutagenesis using PCR.

[0052] The term "percent (%) identity" used herein can be determined with or without an introduced gap, using a protein or gene search system based on BLAST or FASTA (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).

[0053] The term "derivative" used herein is meant to include unlimitedly 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).

[0054] As used herein, the "nucleic acid" capable of specifically binding to a polynucleotide selected from the pancreatic 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 pancreatic cancer in a subject, for diagnosing the presence or absence or the severity of pancreatic cancer, the presence or absence or the degree of amelioration of pancreatic cancer, or the therapeutic sensitivity of pancreatic cancer, or for screening for a candidate substance useful in the prevention, amelioration, or treatment of pancreatic 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 499 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 pancreatic 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*.

[0055] 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.

[0056] 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.

[0057] 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" is regarded as being a more significant difference between subjects to be compared.

[0058] 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 pancreatic cancer to be detected early, leading to the complete resection of cancer sites and reduction in the rate of recurrence.

[0059] 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 pancreatic cancer patients, leading to reduction in burden on patients and reduction in medical expense.

[0060] 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 are identified correctly to all samples, and serves as a primary index for evaluating detection performance.

[0061] 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 pancreatic cancer develops, as pancreatic cancer progresses, or as therapeutic effects on pancreatic cancer are exerted. Specifically, the "sample" refers to a pancreatic tissue, a peripancreatic 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.

[0062] The term "hsa-miR-6893-5p gene" or "hsa-miR-6893-5p" used herein includes the hsa-miR-6893-5p gene (miRBase Accession No. MIMAT0027686) described in SEQ ID NO: 1, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6893-5p gene can be obtained by a method described in Ladewig E et al., 2012, *Genome Res.*, Vol. 22, p. 1634-1645. Also, "hsa-mir-6893" (miRBase Accession No. MI0022740, SEQ ID NO: 123) having a hairpin-like structure is known as a precursor of "hsa-miR-6893-5p".

[0063] 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: 2, 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: 124) having a hairpin-like structure is known as a precursor of "hsa-miR-6075".

[0064] The term "hsa-miR-6820-5p gene" or "hsa-miR-6820-5p" used herein includes the hsa-miR-6820-5p gene (miRBase Accession No. MIMAT0027540) described in SEQ ID NO: 3, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6820-5p gene can be obtained by a method described in Ladewig E et al., 2012, *Genome Res.*, Vol. 22, p. 1634-1645. Also, "hsa-mir-6820" (miRBase Accession No. MI0022665, SEQ ID NO: 125) having a hairpin-like structure is known as a precursor of "hsa-miR-6820-5p".

[0065] The term "hsa-miR-4294 gene" or "hsa-miR-4294" used herein includes the hsa-miR-4294 gene (miRBase Accession No. MIMAT0016849) described in SEQ ID NO: 4, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4294 gene can be obtained by a method described in Goff LA et al., 2009, *PLoS One.*, Vol. 4, e7192. Also, "hsa-mir-4294" (miRBase Accession No. MI0015827, SEQ ID NO: 126) having a hairpin-like structure is known as a precursor of "hsa-miR-4294".

[0066] 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: 5, 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: 127) having a hairpin-like structure is known as a precursor of "hsa-miR-6729-5p".

[0067] The term "hsa-miR-4476 gene" or "hsa-miR-4476" used herein includes the hsa-miR-4476 gene (miRBase Accession No. MIMAT0019003) described in SEQ ID NO: 6, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4476 gene can be obtained by a method described in Jima DD et al., 2010, *Blood.*, Vol. 116, e118-e127. Also, "hsa-mir-4476" (miRBase Accession No. MI0016828, SEQ ID NO: 128) having a hairpin-like structure is known as a precursor of "hsa-miR-4476".

[0068] 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: 7, 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: 129) having a hairpin-like structure is known as a precursor of "hsa-miR-6836-3p".

[0069] 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: 8, 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: 130) having a hairpin-like structure is known as a precursor of "hsa-miR-6765-3p".

[0070] The term "hsa-miR-6799-5p gene" or "hsa-miR-6799-5p" used herein includes the hsa-miR-6799-5p gene (miRBase Accession No. MIMAT0027498) described in SEQ ID NO: 9, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6799-5p gene can be obtained by a method described in Ladewig E et al., 2012, *Genome Res.*, Vol. 22, p. 1634-1645. Also, "hsa-mir-6799" (miRBase Accession No. MI0022644, SEQ ID NO: 131) having a hairpin-like structure is known as a precursor of "hsa-miR-6799-5p".

[0071] The term "hsa-miR-4530 gene" or "hsa-miR-4530" used herein includes the hsa-miR-4530 gene (miRBase Accession No. MIMAT0019069) described in SEQ ID NO: 10, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4530 gene can be obtained by a method described in n Jima DD et al., 2010, *Blood.*, Vol. 116, e118-e127. Also, "hsa-mir-4530" (miRBase Accession No. MI0016897, SEQ ID NO: 132) having a hairpin-like structure is known as a precursor of "hsa-miR-4530".

[0072] 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: 11, 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: 133 and 134) having a hairpin-like structure are known as precursors of "hsa-miR-7641".

5 **[0073]** 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: 12, 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: 135) having a hairpin-like structure is known as a precursor of "hsa-miR-4454".

10 **[0074]** The term "hsa-miR-615-5p gene" or "hsa-miR-615-5p" used in the present specification includes the hsa-miR-615-5p gene (miRBase Accession No. MIMAT0004804) described in SEQ ID NO: 13, 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, 2006, Proc Natl Acad Sci, Vol. 103, p. 3687-3692. Also, "hsa-mir-615" (miRBase Accession No. MI0003628, SEQ ID NO: 136) having a hairpin-like structure is known as a precursor of "hsa-miR-615-5p".

15 **[0075]** The term "hsa-miR-8073 gene" or "hsa-miR-8073" used herein includes the hsa-miR-8073 gene (miRBase Accession No. MIMAT0031000) described in SEQ ID NO: 14, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-8073 gene can be obtained by a method described in Wang HJ et al., 2013, Shock., Vol. 39, p. 480-487. Also, "hsa-mir-8073" (miRBase Accession No. MI0025909, SEQ ID NO: 137) having a hairpin-like structure is known as a precursor of "hsa-miR-8073".

20 **[0076]** 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: 15, 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, 2006, Proc Natl Acad Sci, Vol. 103, p. 3687-3692. Also, "hsa-mir-663a" (miRBase Accession No. MI0003672, SEQ ID NO: 138) having a hairpin-like structure is known as a precursor of "hsa-miR-663a".

25 **[0077]** The term "hsa-miR-4634 gene" or "hsa-miR-4634" used herein includes the hsa-miR-4634 gene (miRBase Accession No. MIMAT0019691) described in SEQ ID NO: 16, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4634 gene can be obtained by a method described in Persson H et al., 2011, Cancer Res., Vol. 71, p. 78-86. Also, "hsa-mir-4634" (miRBase Accession No. MI0017261, SEQ ID NO: 139) having a hairpin-like structure is known as a precursor of "hsa-miR-4634".

30 **[0078]** The term "hsa-miR-4450 gene" or "hsa-miR-4450" used herein includes the hsa-miR-4450 gene (miRBase Accession No. MIMAT0018971) described in SEQ ID NO: 17, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4450 gene can be obtained by a method described in Jima DD et al., 2010, Blood., Vol. 116, e118-e127. Also, "hsa-mir-4450" (miRBase Accession No. MI0016795, SEQ ID NO: 140) having a hairpin-like structure is known as a precursor of "hsa-miR-4450".

35 **[0079]** 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: 18, 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: 141) having a hairpin-like structure is known as a precursor of "hsa-miR-4792".

40 **[0080]** The term "hsa-miR-665 gene" or "hsa-miR-665" used herein includes the hsa-miR-665 gene (miRBase Accession No. MIMAT0004952) described in SEQ ID NO: 19, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-665 gene can be obtained by a method described in Berezikov E et al., 2006, Genome Res., Vol. 16, p. 1289-1298. Also, "hsa-mir-665" (miRBase Accession No. MI0005563, SEQ ID NO: 142) having a hairpin-like structure is known as a precursor of "hsa-miR-665".

45 **[0081]** 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: 20, 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. [Epub prior to print]. Also, "hsa-mir-7975" (miRBase Accession No. MI0025751, SEQ ID NO: 143) having a hairpin-like structure is known as a precursor of "hsa-miR-7975".

50 **[0082]** The term "hsa-miR-7109-5p gene" or "hsa-miR-7109-5p" used herein includes the hsa-miR-7109-5p gene (miRBase Accession No. MIMAT0028115) described in SEQ ID NO: 21, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-7109-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res., Vol. 22, p. 1634-1645. Also, "hsa-mir-7109" (miRBase Accession No. MI0022960, SEQ ID NO: 144) having a hairpin-like structure is known as a precursor of "hsa-miR-7109-5p".

55 **[0083]** The term "hsa-miR-6789-5p gene" or "hsa-miR-6789-5p" used herein includes the hsa-miR-6789-5p gene (miRBase Accession No. MIMAT0027478) described in SEQ ID NO: 22, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6789-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res., Vol. 22, p. 1634-1645. Also, "hsa-mir-6789" (miRBase Accession No. MI0022634, SEQ ID NO: 145) having a hairpin-like structure is known as a precursor of "hsa-miR-6789-5p".

[0084] 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: 23, 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: 146) having a hairpin-like structure is known as a precursor of "hsa-miR-4497".

[0085] 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: 24, 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: 147) having a hairpin-like structure is known as a precursor of "hsa-miR-6877-5p".

[0086] 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: 25, 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: 148) having a hairpin-like structure is known as a precursor of "hsa-miR-6880-5p".

[0087] 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: 26, 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.* [Epub prior to print]. Also, "hsa-mir-7977" (miRBase Accession No. MI0025753, SEQ ID NO: 149) having a hairpin-like structure is known as a precursor of "hsa-miR-7977".

[0088] The term "hsa-miR-4734 gene" or "hsa-miR-4734" used herein includes the hsa-miR-4734 gene (miRBase Accession No. MIMAT0019859) described in SEQ ID NO: 27, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4734 gene can be obtained by a method described in Persson H et al., 2011, *Cancer Res.*, Vol. 71, p. 78-86. Also, "hsa-mir-4734" (miRBase Accession No. MI0017371, SEQ ID NO: 150) having a hairpin-like structure is known as a precursor of "hsa-miR-4734".

[0089] The term "hsa-miR-6821-5p gene" or "hsa-miR-6821-5p" used herein includes the hsa-miR-6821-5p gene (miRBase Accession No. MIMAT0027542) described in SEQ ID NO: 28, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6821-5p gene can be obtained by a method described in Ladewig E et al., 2012, *Genome Res.*, Vol. 22, p. 1634-1645. Also, "hsa-mir-6821" (miRBase Accession No. MI0022666, SEQ ID NO: 151) having a hairpin-like structure is known as a precursor of "hsa-miR-6821-5p".

[0090] The term "hsa-miR-8089 gene" or "hsa-miR-8089" used herein includes the hsa-miR-8089 gene (miRBase Accession No. MIMAT0031016) described in SEQ ID NO: 29, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-8089 gene can be obtained by a method described in Wang HJ et al., 2013, *Shock.*, Vol. 39, p. 480-487. Also, "hsa-mir-8089" (miRBase Accession No. MI0025925, SEQ ID NO: 152) having a hairpin-like structure is known as a precursor of "hsa-miR-8089".

[0091] The term "hsa-miR-5585-3p gene" or "hsa-miR-5585-3p" used herein includes the hsa-miR-5585-3p gene (miRBase Accession No. MIMAT0022286) described in SEQ ID NO: 30, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-5585-3p gene can be obtained by a method described in Friedlander MR et al., 2012, *Nucleic Acids Res.*, Vol. 40, p. 37-52. Also, "hsa-mir-5585" (miRBase Accession No. MI0019142, SEQ ID NO: 153) having a hairpin-like structure is known as a precursor of "hsa-miR-5585-3p".

[0092] The term "hsa-miR-6085 gene" or "hsa-miR-6085" used herein includes the hsa-miR-6085 gene (miRBase Accession No. MIMAT0023710) described in SEQ ID NO: 31, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6085 gene can be obtained by a method described in Voellencle C et al., 2012, *RNA.*, Vol. 18, p. 472-484. Also, "hsa-mir-6085" (miRBase Accession No. MI0020362, SEQ ID NO: 154) having a hairpin-like structure is known as a precursor of "hsa-miR-6085".

[0093] 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: 32, 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: 155) having a hairpin-like structure is known as a precursor of "hsa-miR-6845-5p".

[0094] 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: 33, 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: 156) having a hairpin-like structure is known as a precursor of "hsa-miR-4651".

[0095] 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: 34, 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: 157) having a hairpin-like structure is known as a precursor of "hsa-miR-4433-3p".

[0096] The term "hsa-miR-1231 gene" or "hsa-miR-1231" used herein includes the hsa-miR-1231 gene (miRBase Accession No. MIMAT0005586) described in SEQ ID NO: 35, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-1231 gene can be obtained by a method described in Berezikov E et al., 2007, Mol Cell., Vol. 28, p. 328-336. Also, "hsa-mir-1231" (miRBase Accession No. MI0006321, SEQ ID NO: 158) having a hairpin-like structure is known as a precursor of "hsa-miR-1231".

[0097] The term "hsa-miR-4665-5p gene" or "hsa-miR-4665-5p" used herein includes the hsa-miR-4665-5p gene (miRBase Accession No. MIMAT0019739) described in SEQ ID NO: 36, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4665-5p gene can be obtained by a method described in Persson H et al., 2011, Cancer Res., Vol. 71, p. 78-86. Also, "hsa-mir-4665" (miRBase Accession No. MI0017295, SEQ ID NO: 159) having a hairpin-like structure is known as a precursor of "hsa-miR-4665-5p".

[0098] The term "hsa-miR-7114-5p gene" or "hsa-miR-7114-5p" used herein includes the hsa-miR-7114-5p gene (miRBase Accession No. MIMAT0028125) described in SEQ ID NO: 37, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-7114-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res., Vol. 22, p. 1634-1645. Also, "hsa-mir-7114" (miRBase Accession No. MI0022965, SEQ ID NO: 160) having a hairpin-like structure is known as a precursor of "hsa-miR-7114-5p".

[0099] The term "hsa-miR-1238-5p gene" or "hsa-miR-1238-5p" used herein includes the hsa-miR-1238-5p gene (miRBase Accession No. MIMAT0022947) described in SEQ ID NO: 38, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-1238-5p gene can be obtained by a method described in Berezikov E et al., 2007, Mol Cell., Vol. 28, p. 328-336. Also, "hsa-mir-1238" (miRBase Accession No. MI0006328, SEQ ID NO: 161) having a hairpin-like structure is known as a precursor of "hsa-miR-1238-5p".

[0100] 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: 39, 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: 162) having a hairpin-like structure is known as a precursor of "hsa-miR-8069".

[0101] The term "hsa-miR-4732-5p gene" or "hsa-miR-4732-5p" used herein includes the hsa-miR-4732-5p gene (miRBase Accession No. MIMAT0019855) described in SEQ ID NO: 40, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4732-5p gene can be obtained by a method described in Persson H et al., 2011, Cancer Res., Vol. 71, p. 78-86. Also, "hsa-mir-4732" (miRBase Accession No. MI0017369, SEQ ID NO: 163) having a hairpin-like structure is known as a precursor of "hsa-miR-4732-5p".

[0102] 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: 41, 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, 2006, Proc Natl Acad Sci, Vol. 103, p. 3687-3692. Also, "hsa-mir-619" (miRBase Accession No. MI0003633, SEQ ID NO: 164) having a hairpin-like structure is known as a precursor of "hsa-miR-619-5p".

[0103] The term "hsa-miR-3622a-5p gene" or "hsa-miR-3622a-5p" used herein includes the hsa-miR-3622a-5p gene (miRBase Accession No. MIMAT0018003) described in SEQ ID NO: 42, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-3622a-5p gene can be obtained by a method described in Witten D et al., 2010, BMC Biol., Vol. 8, p. 58. Also, "hsa-mir-3622a" (miRBase Accession No. MI0016013, SEQ ID NO: 165) having a hairpin-like structure is known as a precursor of "hsa-miR-3622a-5p".

[0104] 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: 43, 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: 166) having a hairpin-like structure is known as a precursor of "hsa-miR-1260a".

[0105] 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: 44, 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: 167) having a hairpin-like structure is known as a precursor of "hsa-miR-6741-5p".

[0106] 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: 45, 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: 168) having a hairpin-like structure is known as a precursor of "hsa-miR-6781-5p".

[0107] 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: 46, 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: 169) having a hairpin-like structure is known as a precursor of "hsa-miR-6125".

5 **[0108]** The term "hsa-miR-6805-5p gene" or "hsa-miR-6805-5p" used herein includes the hsa-miR-6805-5p gene (miRBase Accession No. MIMAT0027510) described in SEQ ID NO: 47, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6805-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res., Vol. 22, p. 1634-1645. Also, "hsa-mir-6805" (miRBase Accession No. MI0022650, SEQ ID NO: 170) having a hairpin-like structure is known as a precursor of "hsa-miR-6805-5p".

10 **[0109]** The term "hsa-miR-6132 gene" or "hsa-miR-6132" used herein includes the hsa-miR-6132 gene (miRBase Accession No. MIMAT0024616) described in SEQ ID NO: 48, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6132 gene can be obtained by a method described in Dannemann M, 2012, Genome Biol Evol., Vol. 4, p. 552-564. Also, "hsa-mir-6132" (miRBase Accession No. MI0021277, SEQ ID NO: 171) having a hairpin-like structure is known as a precursor of "hsa-miR-6132".

15 **[0110]** 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: 49, 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: 172) having a hairpin-like structure is known as a precursor of "hsa-miR-6872-3p".

20 **[0111]** 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: 50, 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: 173) having a hairpin-like structure is known as a precursor of "hsa-miR-6875-5p".

25 **[0112]** 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: 51, 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: 174) having a hairpin-like structure is known as a precursor of "hsa-miR-1908-3p".

30 **[0113]** 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: 52, 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: 175) having a hairpin-like structure is known as a precursor of "hsa-miR-4433b-3p".

35 **[0114]** The term "hsa-miR-4736 gene" or "hsa-miR-4736" used herein includes the hsa-miR-4736 gene (miRBase Accession No. MIMAT0019862) described in SEQ ID NO: 53, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4736 gene can be obtained by a method described in Persson H et al., 2011, Cancer Res., Vol. 71, p. 78-86. Also, "hsa-mir-4736" (miRBase Accession No. MI0017373, SEQ ID NO: 176) having a hairpin-like structure is known as a precursor of "hsa-miR-4736".

40 **[0115]** The term "hsa-miR-5100 gene" or "hsa-miR-5100" used herein includes the hsa-miR-5100 gene (miRBase Accession No. MIMAT0022259) described in SEQ ID NO: 54, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-5100 gene can be obtained by a method described in Tandon M et al., 2012, Oral Dis., Vol. 18, p. 127-131. Also, "hsa-mir-5100" (miRBase Accession No. MI0019116, SEQ ID NO: 177) having a hairpin-like structure is known as a precursor of "hsa-miR-5100".

45 **[0116]** The term "hsa-miR-6724-5p gene" or "hsa-miR-6724-5p" used herein includes the hsa-miR-6724-5p gene (miRBase Accession No. MIMAT0025856) described in SEQ ID NO: 55 a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6724-5p gene can be obtained by a method described in Li Y et al., 2012, Gene., Vol. 497, p. 330-335. Also, "hsa-mir-6724" (miRBase Accession No. MI0022559, SEQ ID NO: 178) having a hairpin-like structure is known as a precursor of "hsa-miR-6724-5p".

50 **[0117]** The term "hsa-miR-7107-5p gene" or "hsa-miR-7107-5p" used herein includes the hsa-miR-7107-5p gene (miRBase Accession No. MIMAT0028111) described in SEQ ID NO: 56, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-7107-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res., Vol. 22, p. 1634-1645. Also, "hsa-mir-7107" (miRBase Accession No. MI0022958, SEQ ID NO: 179) having a hairpin-like structure is known as a precursor of "hsa-miR-7107-5p".

55 **[0118]** 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: 57, 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".

[0119] 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: 58, 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: 181) having a hairpin-like structure is known as a precursor of "hsa-miR-3185".

[0120] The term "hsa-miR-4638-5p gene" or "hsa-miR-4638-5p" used herein includes the hsa-miR-4638-5p gene (miRBase Accession No. MIMAT0019695) described in SEQ ID NO: 59, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4638-5p gene can be obtained by a method described in Persson H et al., 2011, Cancer Res., Vol. 71, p. 78-86. Also, "hsa-mir-4638" (miRBase Accession No. MI0017265, SEQ ID NO: 182) having a hairpin-like structure is known as a precursor of "hsa-miR-4638-5p".

[0121] 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: 60, 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: 183) having a hairpin-like structure is known as a precursor of "hsa-miR-1273g-3p".

[0122] The term "hsa-miR-6778-5p gene" or "hsa-miR-6778-5p" used herein includes the hsa-miR-6778-5p gene (miRBase Accession No. MIMAT0027456) described in SEQ ID NO: 61, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6778-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res., Vol. 22, p. 1634-1645. Also, "hsa-mir-6778" (miRBase Accession No. MI0022623, SEQ ID NO: 184) having a hairpin-like structure is known as a precursor of "hsa-miR-6778-5p".

[0123] The term "hsa-miR-328-5p gene" or "hsa-miR-328-5p" used herein includes the hsa-miR-328-5p gene (miRBase Accession No. MIMAT0026486) described in SEQ ID NO: 62, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-328-5p gene can be obtained by a method described in Kim J et al., 2004, Proc Natl Acad Sci, Vol. 101, p. 360-365. Also, "hsa-mir-328" (miRBase Accession No. MI0000804, SEQ ID NO: 185) having a hairpin-like structure is known as a precursor of "hsa-miR-328-5p".

[0124] The term "hsa-miR-3679-3p gene" or "hsa-miR-3679-3p" used herein includes the hsa-miR-3679-3p gene (miRBase Accession No. MIMAT0018105) described in SEQ ID NO: 63, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-3679-3p 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: 186) having a hairpin-like structure is known as a precursor of "hsa-miR-3679-3p".

[0125] 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: 64, 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: 187) having a hairpin-like structure is known as a precursor of "hsa-miR-1228-3p".

[0126] 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: 65, 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: 188) having a hairpin-like structure is known as a precursor of "hsa-miR-6779-5p".

[0127] The term "hsa-miR-4723-5p gene" or "hsa-miR-4723-5p" used herein includes the hsa-miR-4723-5p gene (miRBase Accession No. MIMAT0019838) described in SEQ ID NO: 66, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4723-5p gene can be obtained by a method described in Persson H et al., 2011, Cancer Res., Vol. 71, p. 78-86. Also, "hsa-mir-4723" (miRBase Accession No. MI0017359, SEQ ID NO: 189) having a hairpin-like structure is known as a precursor of "hsa-miR-4723-5p".

[0128] The term "hsa-miR-6850-5p gene" or "hsa-miR-6850-5p" used herein includes the hsa-miR-6850-5p gene (miRBase Accession No. MIMAT0027600) described in SEQ ID NO: 67, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6850-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res., Vol. 22, p. 1634-1645. Also, "hsa-mir-6850" (miRBase Accession No. MI0022696, SEQ ID NO: 190) having a hairpin-like structure is known as a precursor of "hsa-miR-6850-5p".

[0129] 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: 68, 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: 191) having a hairpin-like structure is known as a precursor of "hsa-miR-760".

[0130] The term "hsa-miR-7704 gene" or "hsa-miR-7704" used herein includes the hsa-miR-7704 gene (miRBase Accession No. MIMAT0030019) described in SEQ ID NO: 69, a homolog or an ortholog of a different organism species,

and the like. The hsa-miR-7704 gene can be obtained by a method described in Swaminathan S et al., 2013, *Biochem Biophys Res Commun.*, Vol. 434, p. 228-234. Also, "hsa-mir-7704" (miRBase Accession No. MI0025240, SEQ ID NO: 192) having a hairpin-like structure is known as a precursor of "hsa-miR-7704".

5 **[0131]** 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: 70, 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: 193) having a hairpin-like structure is known as a precursor of "hsa-miR-8072".

10 **[0132]** The term "hsa-miR-4486 gene" or "hsa-miR-4486" used herein includes the hsa-miR-4486 gene (miRBase Accession No. MIMAT0019020) described in SEQ ID NO: 71, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4486 gene can be obtained by a method described in Jima DD et al., 2010, *Blood.*, Vol. 116, e118-e127. Also, "hsa-mir-4486" (miRBase Accession No. MI0016847, SEQ ID NO: 194) having a hairpin-like structure is known as a precursor of "hsa-miR-4486".

15 **[0133]** 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: 72, 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: 195) having a hairpin-like structure is known as a precursor of "hsa-miR-1913".

20 **[0134]** The term "hsa-miR-4656 gene" or "hsa-miR-4656" used herein includes the hsa-miR-4656 gene (miRBase Accession No. MIMAT0019723) described in SEQ ID NO: 73, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4656 gene can be obtained by a method described in Persson H et al., 2011, *Cancer Res.*, Vol. 71, p. 78-86. Also, "hsa-mir-4656" (miRBase Accession No. MI0017284, SEQ ID NO: 196) having a hairpin-like structure is known as a precursor of "hsa-miR-4656".

25 **[0135]** 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: 74, 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: 197) having a hairpin-like structure is known as a precursor of "hsa-miR-1260b".

30 **[0136]** The term "hsa-miR-7106-5p gene" or "hsa-miR-7106-5p" used herein includes the hsa-miR-7106-5p gene (miRBase Accession No. MIMAT0028109) described in SEQ ID NO: 75, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-7106-5p gene can be obtained by a method described in Ladewig E et al., 2012, *Genome Res.*, Vol. 22, p. 1634-1645. Also, "hsa-mir-7106" (miRBase Accession No. MI0022957, SEQ ID NO: 198) having a hairpin-like structure is known as a precursor of "hsa-miR-7106-5p".

35 **[0137]** 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: 76, 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: 199) having a hairpin-like structure is known as a precursor of "hsa-miR-6889-5p".

40 **[0138]** 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: 77, 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: 200) having a hairpin-like structure is known as a precursor of "hsa-miR-6780b-5p".

45 **[0139]** The term "hsa-miR-6090 gene" or "hsa-miR-6090" used herein includes the hsa-miR-6090 gene (miRBase Accession No. MIMAT0023715) described in SEQ ID NO: 78, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6090 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-6090" (miRBase Accession No. MI0020367, SEQ ID NO: 201) having a hairpin-like structure is known as a precursor of "hsa-miR-6090".

50 **[0140]** 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: 79, 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: 202) having a hairpin-like structure is known as a precursor of "hsa-miR-4534".

55 **[0141]** The term "hsa-miR-4449 gene" or "hsa-miR-4449" used herein includes the hsa-miR-4449 gene (miRBase Accession No. MIMAT0018968) described in SEQ ID NO: 80, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4449 gene can be obtained by a method described in Jima DD et al., 2010, *Blood.*, Vol. 116, e118-e127. Also, "hsa-mir-4449" (miRBase Accession No. MI0016792, SEQ ID NO: 203) having a hairpin-like structure is known as a precursor of "hsa-miR-4449".

[0142] 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: 81, 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: 204) having a hairpin-like structure is known as a precursor of "hsa-miR-5195-3p".

[0143] 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: 82, 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: 205) having a hairpin-like structure is known as a precursor of "hsa-miR-1202".

[0144] 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: 83, 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: 206) having a hairpin-like structure is known as a precursor of "hsa-miR-4467".

[0145] The term "hsa-miR-6515-3p gene" or "hsa-miR-6515-3p" used herein includes the hsa-miR-6515-3p gene (miRBase Accession No. MIMAT0025487) described in SEQ ID NO: 84, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6515-3p 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-6515" (miRBase Accession No. MI0022227, SEQ ID NO: 207) having a hairpin-like structure is known as a precursor of "hsa-miR-6515-3p".

[0146] The term "hsa-miR-4281 gene" or "hsa-miR-4281" used herein includes the hsa-miR-4281 gene (miRBase Accession No. MIMAT0016907) described in SEQ ID NO: 85, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4281 gene can be obtained by a method described in Goff LA et al., 2009, *PLoS One.*, Vol. 4, e7192. Also, "hsa-mir-4281" (miRBase Accession No. MI0015885, SEQ ID NO: 208) having a hairpin-like structure is known as a precursor of "hsa-miR-4281".

[0147] The term "hsa-miR-4505 gene" or "hsa-miR-4505" used herein includes the hsa-miR-4505 gene (miRBase Accession No. MIMAT0019041) described in SEQ ID NO: 86, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4505 gene can be obtained by a method described in Jima DD et al., 2010, *Blood.*, Vol. 116, e118-e127. Also, "hsa-mir-4505" (miRBase Accession No. MI0016868, SEQ ID NO: 209) having a hairpin-like structure is known as a precursor of "hsa-miR-4505".

[0148] The term "hsa-miR-4484 gene" or "hsa-miR-4484" used herein includes the hsa-miR-4484 gene (miRBase Accession No. MIMAT0019018) described in SEQ ID NO: 87, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4484 gene can be obtained by a method described in Jima DD et al., 2010, *Blood.*, Vol. 116, e118-e127. Also, "hsa-mir-4484" (miRBase Accession No. MI0016845, SEQ ID NO: 210) having a hairpin-like structure is known as a precursor of "hsa-miR-4484".

[0149] The term "hsa-miR-6805-3p gene" or "hsa-miR-6805-3p" used herein includes the hsa-miR-6805-3p gene (miRBase Accession No. MIMAT0027511) described in SEQ ID NO: 88, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6805-3p gene can be obtained by a method described in Ladewig E et al., 2012, *Genome Res.*, Vol. 22, p. 1634-1645. Also, "hsa-mir-6805" (miRBase Accession No. MI0022650, SEQ ID NO: 211) having a hairpin-like structure is known as a precursor of "hsa-miR-6805-3p".

[0150] 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: 89, 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, e118-e127. Also, "hsa-mir-3135b" (miRBase Accession No. MI0016809, SEQ ID NO: 212) having a hairpin-like structure is known as a precursor of "hsa-miR-3135b".

[0151] 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: 90, 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: 213) having a hairpin-like structure is known as a precursor of "hsa-miR-3162-5p".

[0152] 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: 91, 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: 214) having a hairpin-like structure is known as a precursor of "hsa-miR-6768-5p".

[0153] 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: 92, 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: 215) having a hairpin-like structure is known as a precursor of "hsa-miR-6721-5p".

[0154] The term "hsa-miR-1227-5p gene" or "hsa-miR-1227-5p" used herein includes the hsa-miR-1227-5p gene (miRBase Accession No. MIMAT0022941) described in SEQ ID NO: 93, 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: 216) having a hairpin-like structure is known as a precursor of "hsa-miR-1227-5p".

[0155] 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: 94, 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: 217) having a hairpin-like structure is known as a precursor of "hsa-miR-6722-3p".

[0156] 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: 95, 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: 218) having a hairpin-like structure is known as a precursor of "hsa-miR-4286".

[0157] 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: 96, 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: 219) having a hairpin-like structure is known as a precursor of "hsa-miR-4746-3p".

[0158] 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: 97, 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: 220) having a hairpin-like structure is known as a precursor of "hsa-miR-6727-5p".

[0159] 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: 98, 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: 221) having a hairpin-like structure is known as a precursor of "hsa-miR-6816-5p".

[0160] The term "hsa-miR-4741 gene" or "hsa-miR-4741" used herein includes the hsa-miR-4741 gene (miRBase Accession No. MIMAT0019871) described in SEQ ID NO: 99, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4741 gene can be obtained by a method described in Persson H et al., 2011, Cancer Res., Vol. 71, p. 78-86. Also, "hsa-mir-4741" (miRBase Accession No. MI0017379, SEQ ID NO: 222) having a hairpin-like structure is known as a precursor of "hsa-miR-4741".

[0161] The term "hsa-miR-4508 gene" or "hsa-miR-4508" used herein includes the hsa-miR-4508 gene (miRBase Accession No. MIMAT0019045) described in SEQ ID NO: 100, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4508 gene can be obtained by a method described in Jima DD et al., 2010, Blood., Vol. 116, e118-e127. Also, "hsa-mir-4508" (miRBase Accession No. MI0016872, SEQ ID NO: 223) having a hairpin-like structure is known as a precursor of "hsa-miR-4508".

[0162] 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: 101, 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, A Cancer Res., Vol. 67, p. 6031-6043. Also, "hsa-mir-940" (miRBase Accession No. MI0005762, SEQ ID NO: 224) having a hairpin-like structure is known as a precursor of "hsa-miR-940".

[0163] The term "hsa-miR-4327 gene" or "hsa-miR-4327" used herein includes the hsa-miR-4327 gene (miRBase Accession No. MIMAT0016889) described in SEQ ID NO: 102, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4327 gene can be obtained by a method described in Goff LA et al., 2009, PLoS One., Vol. 4, e7192. Also, "hsa-mir-4327" (miRBase Accession No. MI0015867, SEQ ID NO: 225) having a hairpin-like structure is known as a precursor of "hsa-miR-4327".

[0164] 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: 103, 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: 159) having a hairpin-like structure is known as a precursor of "hsa-miR-4665-3p".

[0165] The term "hsa-miR-718 gene" or "hsa-miR-718" used herein includes the hsa-miR-718 gene (miRBase Acces-

sion No. MIMAT0012735) described in SEQ ID NO: 104, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-718 gene can be obtained by a method described in Artzi S et al., 2008, BMC Bioinformatics., Vol. 9, p. 39. Also, "hsa-mir-718" (miRBase Accession No. MI0012489, SEQ ID NO: 226) having a hairpin-like structure is known as a precursor of "hsa-miR-718".

5 **[0166]** 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: 105, 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: 227) having a hairpin-like structure is known as a precursor of "hsa-miR-125a-3p".

10 **[0167]** The term "hsa-miR-204-3p gene" or "hsa-miR-204-3p" used herein includes the hsa-miR-204-3p gene (miR-Base Accession No. MIMAT0022693) described in SEQ ID NO: 106, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-204-3p gene can be obtained by a method described in Lim LP et al., 2003, Science., Vol. 299, p. 1540. Also, "hsa-mir-204" (miRBase Accession No. MI0000284, SEQ ID NO: 228) having a hairpin-like structure is known as a precursor of "hsa-miR-204-3p".

15 **[0168]** The term "hsa-miR-1469 gene" or "hsa-miR-1469" used herein includes the hsa-miR-1469 gene (miRBase Accession No. MIMAT0007347) described in SEQ ID NO: 107, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-1469 gene can be obtained by a method described in Kawaji H et al., 2008, BMC Genomics, Vol. 9, p. 157. Also, "hsa-mir-1469" (miRBase Accession No. MI0007074, SEQ ID NO: 229) having a hairpin-like structure is known as a precursor of "hsa-miR-1469".

20 **[0169]** The term "hsa-miR-575 gene" or "hsa-miR-575" used herein includes the hsa-miR-575 gene (miRBase Accession No. MIMAT0003240) described in SEQ ID NO: 108, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-575 gene can be obtained by a method described in Cummins JM, 2006, Proc Natl Acad Sci, Vol. 103, p. 3687-3692. Also, "hsa-mir-575" (miRBase Accession No. MI0003582, SEQ ID NO: 230) having a hairpin-like structure is known as a precursor of "hsa-miR-575".

25 **[0170]** The term "hsa-miR-150-3p gene" or "hsa-miR-150-3p" used herein includes the hsa-miR-150-3p gene (miR-Base Accession No. MIMAT0004610) described in SEQ ID NO: 109, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-150-3p 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-150" (miRBase Accession No. MI0000479, SEQ ID NO: 231) having a hairpin-like structure is known as a precursor of "hsa-miR-150-3p".

30 **[0171]** The term "hsa-miR-423-5p gene" or "hsa-miR-423-5p" used herein includes the hsa-miR-423-5p gene (miR-Base Accession No. MIMAT0004748) described in SEQ ID NO: 110, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-423-5p gene can be obtained by a method described in Kasashima K et al., 2004, Biochem Biophys Res Commun., Vol. 322, p. 403-410. Also, "hsa-mir-423" (miRBase Accession No. MI0001445, SEQ ID NO: 232) having a hairpin-like structure is known as a precursor of "hsa-miR-423-5p".

35 **[0172]** 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: 111, 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, 2006, Proc Natl Acad Sci, Vol. 103, p. 3687-3692. Also, "hsa-mir-564" (miRBase Accession No. MI0003570, SEQ ID NO: 233) having a hairpin-like structure is known as a precursor of "hsa-miR-564".

40 **[0173]** 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: 112, 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: 234) having a hairpin-like structure is known as a precursor of "hsa-miR-3188".

45 **[0174]** The term "hsa-miR-1246 gene" or "hsa-miR-1246" used herein includes the hsa-miR-1246 gene (miRBase Accession No. MIMAT0005898) described in SEQ ID NO: 113, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-1246 gene can be obtained by a method described in Morin RD et al., 2008, Genome Res., Vol. 18, p. 610-621. Also, "hsa-mir-1246" (miRBase Accession No. MI0006381, SEQ ID NO: 235) having a hairpin-like structure is known as a precursor of "hsa-miR-1246".

50 **[0175]** The term "hsa-miR-602 gene" or "hsa-miR-602" used herein includes the hsa-miR-602 gene (miRBase Accession No. MIMAT0003270) described in SEQ ID NO: 114, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-602 gene can be obtained by a method described in Cummins JM, 2006, Proc Natl Acad Sci, Vol. 103, p. 3687-3692. Also, "hsa-mir-602" (miRBase Accession No. MI0003615, SEQ ID NO: 236) having a hairpin-like structure is known as a precursor of "hsa-miR-602".

55 **[0176]** The term "hsa-miR-1290 gene" or "hsa-miR-1290" used herein includes the hsa-miR-1290 gene (miRBase Accession No. MIMAT0005880) described in SEQ ID NO: 115, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-1290 gene can be obtained by a method described in Morin RD et al., 2008, Genome Res., Vol. 18, p. 610-621. Also, "hsa-mir-1290" (miRBase Accession No. MI0006352, SEQ ID NO: 237) having a hairpin-like

structure is known as a precursor of "hsa-miR-1290".

[0177] The term "hsa-miR-16-5p gene" or "hsa-miR-16-5p" used herein includes the hsa-miR-16-5p gene (miRBase Accession No. MIMAT0000069) described in SEQ ID NO: 116, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-16-5p 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-16-1 and hsa-mir-16-2" (miRBase Accession Nos. MI0000070 and MI0000115, SEQ ID NOs: 238 and 239) having a hairpin-like structure are known as precursors of "hsa-miR-16-5p".

[0178] 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: 117, 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 Y et al., 2005, *Nucleic Acids Res.*, Vol. 33, p. 2697-2706. Also, "hsa-mir-451a" (miRBase Accession No. MI0001729, SEQ ID NO: 240) having a hairpin-like structure are known as precursors of "hsa-miR-451a".

[0179] The term "hsa-miR-24-3p gene" or "hsa-miR-24-3p" used herein includes the hsa-miR-24-3p gene (miRBase Accession No. MIMAT0000080) described in SEQ ID NO: 118, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-24-3p gene can be obtained by a method described in Lagos-Quintana M et al., 2001, *Science.*, Vol. 294, p. 853-858. Also, "hsa-mir-24-1 and hsa-mir-24-2" (miRBase Accession Nos. MI0000080 and MI0000081, SEQ ID NOs: 241 and 242) having a hairpin-like structure are known as precursors of "hsa-miR-24-3p".

[0180] 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: 119, 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: 243) having a hairpin-like structure are known as precursors of "hsa-miR-187-5p".

[0181] 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: 120, 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: 244) having a hairpin-like structure are known as precursors of "hsa-miR-1908-5p".

[0182] 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: 121, 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: 245) having a hairpin-like structure are known as precursors of "hsa-miR-371a-5p".

[0183] The term "hsa-miR-550a-5p gene" or "hsa-miR-550a-5p" used herein includes the hsa-miR-550a-5p gene (miRBase Accession No. MIMAT0004800) described in SEQ ID NO: 122, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-550a-5p gene can be obtained by a method described in Cummins JM, 2006, *Proc Natl Acad Sci*, Vol. 103, p. 3687-3692. Also, "hsa-mir-550a-1 and hsa-mir-550a-2" (miRBase Accession Nos. MI0003600 and MI0003601, SEQ ID NOs: 246 and 247) having a hairpin-like structure are known as precursors of "hsa-miR-550a-5p".

[0184] 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: 349, 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: 384) having a hairpin-like structure are known as precursors of "hsa-miR-4417".

[0185] The term "hsa-miR-4707-5p gene" or "hsa-miR-4707-5p" used herein includes the hsa-miR-4707-5p gene (miRBase Accession No. MIMAT0019807) described in SEQ ID NO: 350, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4707-5p gene can be obtained by a method described in Persson H et al., 2011, *Cancer Res*, Vol. 71, p. 78-86. Also, "hsa-mir-4707" (miRBase Accession No. MI0017340, SEQ ID NO: 385) having a hairpin-like structure are known as precursors of "hsa-miR-4707-5p".

[0186] 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: 351, 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: 386) having a hairpin-like structure are known as precursors of "hsa-miR-7847-3p".

[0187] The term "hsa-miR-2861 gene" or "hsa-miR-2861" used herein includes the hsa-miR-2861 gene (miRBase Accession No. MIMAT0013802) described in SEQ ID NO: 352, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-2861 gene can be obtained by a method described in Li H et al., 2009, *J Clin Invest*, Vol. 119, p. 3666-3677. Also, "hsa-mir-2861" (miRBase Accession No. MI0013006, SEQ ID NO: 387) having a hairpin-like structure are known as precursors of "hsa-miR-2861".

[0188] The term "hsa-miR-4513 gene" or "hsa-miR-4513" used herein includes the hsa-miR-4513 gene (miRBase Accession No. MIMAT0019050) described in SEQ ID NO: 353, a homolog or an ortholog of a different organism species,

and the like. The hsa-miR-4513 gene can be obtained by a method described in Jima DD et al., 2010, Blood, Vol. 116, e118-e127. Also, "hsa-mir-4513" (miRBase Accession No. MI0016879, SEQ ID NO: 388) having a hairpin-like structure are known as precursors of "hsa-miR-4513".

[0189] The term "hsa-miR-7111-5p gene" or "hsa-miR-7111-5p" used herein includes the hsa-miR-7111-5p gene (miRBase Accession No. MIMAT0028119) described in SEQ ID NO: 354, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-7111-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-7111" (miRBase Accession No. MI0022962, SEQ ID NO: 389) having a hairpin-like structure are known as precursors of "hsa-miR-7111-5p".

[0190] The term "hsa-miR-6777-5p gene" or "hsa-miR-6777-5p" used herein includes the hsa-miR-6777-5p gene (miRBase Accession No. MIMAT0027454) described in SEQ ID NO: 355, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6777-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6777" (miRBase Accession No. MI0022622, SEQ ID NO: 390) having a hairpin-like structure are known as precursors of "hsa-miR-6777-5p".

[0191] 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: 356, 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: 391) having a hairpin-like structure are known as precursors of "hsa-miR-7113-3p".

[0192] 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: 357, 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: 392) having a hairpin-like structure are known as precursors of "hsa-miR-4648".

[0193] 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: 358, 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: 393) having a hairpin-like structure are known as precursors of "hsa-miR-3184-5p".

[0194] 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: 359, 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: 394) having a hairpin-like structure are known as precursors of "hsa-miR-4271".

[0195] 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: 360, 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: 395) having a hairpin-like structure are known as precursors of "hsa-miR-6791-5p".

[0196] The term "hsa-miR-642a-3p gene" or "hsa-miR-642a-3p" used herein includes the hsa-miR-642a-3p gene (miRBase Accession No. MIMAT0020924) described in SEQ ID NO: 361, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-642a-3p gene can be obtained by a method described in Cummins JM et al., 2006, Proc Natl Acad Sci USA, Vol. 103, p. 3687-3692, Landgraf P et al., 2007, Cell, Vol. 129, p. 1401-1414, Zaragosi LE et al., 2011, Genome Biol, Vol. 12, R64, etc. Also, "hsa-mir-642a" (miRBase Accession No. MI0003657, SEQ ID NO: 396) having a hairpin-like structure is known as a precursor of "hsa-miR-642a-3p".

[0197] 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: 362, 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: 397) having a hairpin-like structure is known as a precursor of "hsa-miR-7108-5p".

[0198] 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: 363, 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, Kasashima K et al., 2004, Biochem Biophys Res Commun, Vol. 322, p. 403-410, Landgraf P et al., 2007, Cell, Vol. 129, p. 1401-1414, Meunier J et al., 2013, Genome Res, Vol. 23, p. 34-45, etc. Also, "hsa-mir-128-1" (miRBase Accession No. MI0000447, SEQ ID NO: 398) having a hairpin-like structure is known as a precursor of "hsa-miR-128-1-5p".

[0199] The term "hsa-miR-5196-5p gene" or "hsa-miR-5196-5p" used herein includes the hsa-miR-5196-5p gene (miRBase Accession No. MIMAT0021128) described in SEQ ID NO: 364, a homolog or an ortholog of a different organism

species, and the like. The hsa-miR-5196-5p gene can be obtained by a method described in Schotte D et al., 2011, *Leukemia*, Vol. 25, p. 1389-1399. Also, "hsa-mir-5196" (miRBase Accession No. MI0018175, SEQ ID NO: 399) having a hairpin-like structure is known as a precursor of "hsa-miR-5196-5p".

[0200] The term "hsa-miR-3178 gene" or "hsa-miR-3178" used herein includes the hsa-miR-3178 gene (miRBase Accession No. MIMAT0015055) described in SEQ ID NO: 365, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-3178 gene can be obtained by a method described in Stark MS et al., 2010, *PLoS One*, Vol. 5, e9685. Also, "hsa-mir-3178" (miRBase Accession No. MI0014212, SEQ ID NO: 400) having a hairpin-like structure is known as a precursor of "hsa-miR-3178".

[0201] 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: 366, 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: 401) having a hairpin-like structure is known as a precursor of "hsa-miR-3656".

[0202] 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: 367, 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, Dostie J et al., 2003, *RNA*, Vol. 9, p. 180-186, Houbaviy HB et al., 2003, *Dev Cell*, Vol. 5, p. 351-358, Suh MR et al., 2004, *Dev Biol*, Vol. 270, p. 488-498, Kasashima K et al., 2004, *Biochem Biophys Res Commun*, Vol. 322, p. 403-410, Fu H et al., 2005, *FEBS Lett*, Vol. 579, p. 3849-3854, Landgraf P et al., 2007, *Cell*, Vol. 129, p. 1401-1414, Lui WO et al., 2007, *Cancer Res*, Vol. 67, p. 6031-6043, etc. Also, "hsa-mir-92a-2" (miRBase Accession No. MI0000094, SEQ ID NO: 402) having a hairpin-like structure is known as a precursor of "hsa-miR-92a-2-5p".

[0203] 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: 368, 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: 403) having a hairpin-like structure is known as a precursor of "hsa-miR-6769b-5p".

[0204] 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: 369, 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: 404) having a hairpin-like structure is known as a precursor of "hsa-miR-4689".

[0205] The term "hsa-miR-6076 gene" or "hsa-miR-6076" used herein includes the hsa-miR-6076 gene (miRBase Accession No. MIMAT0023701) described in SEQ ID NO: 370, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6076 gene can be obtained by a method described in Voellenkle C et al., 2012, *RNA*, Vol. 18, p. 472-484. Also, "hsa-mir-6076" (miRBase Accession No. MI0020353, SEQ ID NO: 405) having a hairpin-like structure is known as a precursor of "hsa-miR-6076".

[0206] 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: 371, 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 USA*, Vol. 103, p. 3687-3692, Landgraf P et al., 2007, *Cell*, Vol. 129, p. 1401-1414, Lui WO et al., 2007, *Cancer Res*, Vol. 67, p. 6031-6043, etc. Also, "hsa-mir-92b" (miRBase Accession No. MI0003560, SEQ ID NO: 406) having a hairpin-like structure is known as a precursor of "hsa-miR-92b-5p".

[0207] The term "hsa-miR-6774-5p gene" or "hsa-miR-6774-5p" used herein includes the hsa-miR-6774-5p gene (miRBase Accession No. MIMAT0027448) described in SEQ ID NO: 372, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6774-5p gene can be obtained by a method described in Ladewig E et al., 2012, *Genome Res*, Vol. 22, p. 1634-1645. Also, "hsa-mir-6774" (miRBase Accession No. MI0022619, SEQ ID NO: 407) having a hairpin-like structure is known as a precursor of "hsa-miR-6774-5p".

[0208] 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: 373, 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, Landgraf P et al., 2007, *Cell*, Vol. 129, p. 1401-1414, Meunier J et al., 2013, *Genome Res*, Vol. 23, p. 34-45, etc. Also, "hsa-mir-486 and hsa-mir-486-2" (miRBase Accession Nos. MI0002470 and MI0023622, SEQ ID NOs: 408 and 409) having a hairpin-like structure are known as precursors of "hsa-miR-486-3p".

[0209] 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: 374, 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: 410)

having a hairpin-like structure is known as a precursor of "hsa-miR-6806-5p".

[0210] 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: 375, 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: 411) having a hairpin-like structure is known as a precursor of "hsa-miR-6842-5p".

[0211] The term "hsa-miR-6716-5p gene" or "hsa-miR-6716-5p" used herein includes the hsa-miR-6716-5p gene (miRBase Accession No. MIMAT0025844) described in SEQ ID NO: 376, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6716-5p gene can be obtained by a method described in Li Y et al., 2012, Gene, Vol. 497, p. 330-335. Also, "hsa-mir-6716" (miRBase Accession No. MI0022550, SEQ ID NO: 412) having a hairpin-like structure is known as a precursor of "hsa-miR-6716-5p".

[0212] The term "hsa-miR-557 gene" or "hsa-miR-557" used herein includes the hsa-miR-557 gene (miRBase Accession No. MIMAT0003221) described in SEQ ID NO: 377, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-557 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-557" (miRBase Accession No. MI0003563, SEQ ID NO: 413) having a hairpin-like structure is known as a precursor of "hsa-miR-557".

[0213] The term "hsa-miR-4673 gene" or "hsa-miR-4673" used herein includes the hsa-miR-4673 gene (miRBase Accession No. MIMAT0019755) described in SEQ ID NO: 378, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4673 gene can be obtained by a method described in Persson H et al., 2011, Cancer Res, Vol. 71, p. 78-86. Also, "hsa-mir-4673" (miRBase Accession No. MI0017304, SEQ ID NO: 414) having a hairpin-like structure is known as a precursor of "hsa-miR-4673".

[0214] 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: 379, 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: 415) having a hairpin-like structure is known as a precursor of "hsa-miR-4674".

[0215] 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: 380, 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: 416) having a hairpin-like structure is known as a precursor of "hsa-miR-4442".

[0216] 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: 381, 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: 417) having a hairpin-like structure is known as a precursor of "hsa-miR-1915-3p".

[0217] The term "hsa-miR-4687-3p gene" or "hsa-miR-4687-3p" used herein includes the hsa-miR-4687-3p gene (miRBase Accession No. MIMAT0019775) described in SEQ ID NO: 382, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4687-3p gene can be obtained by a method described in Persson H et al., 2011, Cancer Res, Vol. 71, p. 78-86. Also, "hsa-mir-4687" (miRBase Accession No. MI0017319, SEQ ID NO: 418) having a hairpin-like structure is known as a precursor of "hsa-miR-4687-3p".

[0218] The term "hsa-miR-92b-3p gene" or "hsa-miR-92b-3p" used herein includes the hsa-miR-92b-3p gene (miRBase Accession No. MIMAT0003218) described in SEQ ID NO: 383, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-92b-3p gene can be obtained by a method described in Cummins JM et al., 2006, Proc Natl Acad Sci USA, Vol. 103, p. 3687-3692, Landgraf P et al., 2007, Cell, Vol. 129, p. 1401-1414, Lui WO et al., 2007, Cancer Res, Vol. 67, p. 6031-6043. Also, "hsa-mir-92b" (miRBase Accession No. MI0003560, SEQ ID NO: 419) having a hairpin-like structure is known as a precursor of "hsa-miR-92b-3p".

[0219] The term "hsa-miR-1203 gene" or "hsa-miR-1203" used herein includes the hsa-miR-1203 gene (miRBase Accession No. MIMAT0005866) described in SEQ ID NO: 464, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-1203 gene can be obtained by a method described in Marton S et al., 2008, Leukemia., Vol. 22, p. 330-338. Also, "hsa-mir-1203" (miRBase Accession No. MI0006335, SEQ ID NO: 467) having a hairpin-like structure is known as a precursor of "hsa-miR-1203".

[0220] 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: 465, 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: 475) having a hairpin-like structure is known as a precursor of "hsa-miR-663b".

[0221] 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: 466, 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: 476) having a hairpin-like structure is known as a precursor of "hsa-miR-4258".

5 **[0222]** 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: 467, 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: 477) having a hairpin-like structure is known as a precursor of "hsa-miR-4649-5p".

10 **[0223]** 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: 468, 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: 478) having a hairpin-like structure is known as a precursor of "hsa-miR-4516".

15 **[0224]** The term "hsa-miR-3619-3p gene" or "hsa-miR-3619-3p" used herein includes the hsa-miR-3619-3p gene (miRBase Accession No. MIMAT0019219) described in SEQ ID NO: 469, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-3619-3p gene can be obtained by a method described in Witten D et al., 2010, BMC Biol., Vol. 8, p. 58. Also, "hsa-mir-3619" (miRBase Accession No. MI0016009, SEQ ID NO: 479) having a hairpin-like structure is known as a precursor of "hsa-miR-3619-3p".

20 **[0225]** The term "hsa-miR-6826-5p gene" or "hsa-miR-6826-5p" used herein includes the hsa-miR-6826-5p gene (miRBase Accession No. MIMAT0027552) described in SEQ ID NO: 470, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6826-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res., Vol. 22, p. 1634-1645. Also, "hsa-mir-6826" (miRBase Accession No. MI0022671, SEQ ID NO: 480) having a hairpin-like structure is known as a precursor of "hsa-miR-6826-5p".

25 **[0226]** 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: 471, 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: 481) having a hairpin-like structure is known as a precursor of "hsa-miR-6757-5p".

30 **[0227]** 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: 472, 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: 482) having a hairpin-like structure is known as a precursor of "hsa-miR-3131".

35 **[0228]** 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: 473, 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: 483) having a hairpin-like structure is known as a precursor of "hsa-miR-1343-3p".

40 **[0229]** 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: 492, 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: 495) having a hairpin-like structure is known as a precursor of "hsa-miR-6775-5p".

45 **[0230]** The term "hsa-miR-6813-5p gene" or "hsa-miR-6813-5p" used herein includes the hsa-miR-6813-5p gene (miRBase Accession No. MIMAT0027526) described in SEQ ID NO: 493, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6813-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6813" (miRBase Accession No. MI0022658, SEQ ID NO: 496) having a hairpin-like structure is known as a precursor of "hsa-miR-6813-5p".

50 **[0231]** The term "hsa-miR-3940-5p gene" or "hsa-miR-3940-5p" used herein includes the hsa-miR-3940-5p gene (miRBase Accession No. MIMAT0019229) described in SEQ ID NO: 494, 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: 497) having a hairpin-like structure is known as a precursor of "hsa-miR-3940-5p".

55 **[0232]** A mature miRNA may become a variant due to the sequence cleaved shorter or longer by one to several flanking nucleotides, or due to substitution of nucleotides, 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 122, 349 to 383, 464 to

473, and 492 to 494 as well as a large number of the nucleotide sequence variants and fragments represented by SEQ ID NOs: 248 to 348, 420 to 463, 484 to 491, and 498 to 499, called isomiRs. These variants can also be obtained as miRNAs having a nucleotide sequence represented by any of SEQ ID NOs: 1 to 122, 349 to 383, 464 to 473, and 492 to 494. Specifically, among the variants of polynucleotides consisting of the nucleotide sequence represented by any of SEQ ID NOs: 6, 10, 12, 13, 15, 18, 19, 23, 30, 33, 34, 41, 43, 46, 48, 51, 55, 59, 60, 62, 63, 64, 66, 68, 71, 74, 80, 83, 86, 87, 89, 90, 92, 95, 99, 100, 101, 105, 106, 109, 110, 112, 113, 115, 116, 117, 118, 119, 121, 349, 350, 352, 353, 357, 359, 361, 363, 364, 365, 366, 367, 369, 371, 373, 376, 378, 379, 380, 381, 382, 383, 465, 468, 472, 473, and 492 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t according to the present invention, examples of the longest variants registered in miRBase Release 20 include polynucleotides represented by SEQ ID NOs: 248, 250, 251, 253, 255, 257, 259, 262, 265, 267, 268, 272, 275, 277, 278, 279, 282, 285, 287, 289, 291, 292, 294, 296, 298, 300, 302, 305, 306, 307, 309, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 337, 339, 341, 342, 344, 346, 420, 422, 424, 426, 428, 430, 432, 434, 436, 438, 440, 442, 444, 446, 448, 450, 452, 454, 456, 458, 460, 462, 484, 486, 488, 490, and 498, respectively. Also, among the variants of polynucleotides consisting of a nucleotide sequence represented by any of SEQ ID NOs: 6, 10, 12, 13, 15, 18, 19, 23, 30, 33, 34, 41, 43, 46, 48, 51, 55, 59, 60, 62, 63, 64, 66, 68, 71, 74, 80, 83, 86, 87, 89, 90, 92, 95, 99, 100, 101, 105, 106, 109, 110, 112, 113, 115, 116, 117, 118, 119, 121, 349, 350, 352, 353, 357, 359, 361, 363, 364, 365, 366, 367, 369, 371, 373, 376, 378, 379, 380, 381, 382, 383, 465, 468, 472, 473 and 492 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t according to the present invention, examples of shortest variants registered in the miRBase Release 20 include polynucleotides having sequences represented by SEQ ID NOs: 249, 252, 254, 256, 258, 260, 261, 263, 264, 266, 269, 270, 271, 273, 274, 276, 280, 281, 283, 284, 286, 288, 290, 293, 295, 297, 299, 301, 303, 304, 308, 311, 313, 315, 317, 319, 321, 323, 325, 327, 329, 331, 333, 335, 338, 340, 343, 345, 347, 348, 421, 423, 425, 427, 429, 431, 433, 435, 437, 439, 441, 443, 445, 447, 449, 451, 453, 455, 457, 459, 461, 463, 485, 487, 489, 491, and 499, respectively. In addition to these variants and fragments, examples thereof include a large number of isomiR polynucleotides of SEQ ID NOs: 6, 10, 12, 13, 15, 18, 19, 23, 30, 33, 34, 41, 43, 46, 48, 51, 55, 59, 60, 62, 63, 64, 66, 68, 71, 74, 80, 83, 86, 87, 89, 90, 92, 95, 99, 100, 101, 105, 106, 109, 110, 112, 113, 115, 116, 117, 118, 119, 121, 349, 350, 352, 353, 357, 359, 361, 363, 364, 365, 366, 367, 369, 371, 373, 376, 378, 379, 380, 381, 382, 383, 465, 468, 472, 473 and 492 registered in the miRBase. Examples of the polynucleotide comprising a nucleotide sequence represented by any of SEQ ID NOs: 1 to 122, 349 to 383, 464 to 473 and 492 to 494 include a polynucleotide represented by any of SEQ ID NOs: 123 to 247, 384 to 419, 474 to 483, and 495 to 497, which are their respective precursors.

[0233] The names and miRBase Accession Nos. (registration numbers) of the genes represented by SEQ ID NOs: 1 to 499 are shown in Table 1.

[0234] 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.

[0235]

[Table 1]

SEQ ID NO:	Gene name	miRBase registration No.
1	hsa-miR-6893-5p	MIMAT0027686
2	hsa-miR-6075	MIMAT0023700
3	hsa-miR-6820-5p	MIMAT0027540
4	hsa-miR-4294	MIMAT0016849
5	hsa-miR-6729-5p	MIMAT0027359
6	hsa-miR-4476	MIMAT0019003
7	hsa-miR-6836-3p	MIMAT0027575
8	hsa-miR-6765-3p	MIMAT0027431
9	hsa-miR-6799-5p	MIMAT0027498
10	hsa-miR-4530	MIMAT0019069
11	hsa-miR-7641	MIMAT0029782
12	hsa-miR-4454	MIMAT0018976
13	hsa-miR-615-5p	MIMAT0004804
14	hsa-miR-8073	MIMAT0031000

EP 3 150 707 A1

(continued)

5
10
15
20
25
30
35
40
45
50
55

SEQ ID NO:	Gene name	miRBase registration No.
15	hsa-miR-663a	MIMAT0003326
16	hsa-miR-4634	MIMAT0019691
17	hsa-miR-4450	MIMAT0018971
18	hsa-miR-4792	MIMAT0019964
19	hsa-miR-665	MIMAT0004952
20	hsa-miR-7975	MIMAT0031178
21	hsa-miR-7109-5p	MIMAT0028115
22	hsa-miR-6789-5p	MIMAT0027478
23	hsa-miR-4497	MIMAT0019032
24	hsa-miR-6877-Sp	MIMAT0027654
25	hsa-miR-6880-Sp	MIMAT0027660
26	hsa-miR-7977	MIMAT0031180
27	hsa-miR-4734	MIMAT0019859
28	hsa-miR-6821-Sp	MIMAT0027542
29	hsa-miR-8089	MIMAT0031016
30	hsa-miR-5585-3p	MIMAT0022286
31	hsa-miR-6085	MIMAT0023710
32	hsa-miR-6845-5p	MIMAT0027590
33	hsa-miR-4651	MIMAT0019715
34	hsa-miR-4433-3p	MIMAT0018949
35	hsa-miR-1231	MIMAT0005586
36	hsa-miR-4665-5p	MIMAT0019739
37	hsa-miR-7114-5p	MIMAT0028125
38	hsa-miR-1238-5p	MIMAT0022947
39	hsa-miR-8069	MIMAT0030996
40	hsa-miR-4732-5p	MIMAT0019855
41	hsa-miR-619-5p	MIMAT0026622
42	hsa-miR-3622a-5p	MIMAT0018003
43	hsa-miR-1260a	MIMAT0005911
44	hsa-miR-6741-5p	MIMAT0027383
45	hsa-miR-6781-5p	MIMAT0027462
46	hsa-miR-6125	MIMAT0024598
47	hsa-miR-6805-5p	MIMAT0027510
48	hsa-miR-6132	MIMAT0024616
49	hsa-miR-6872-3p	MIMAT0027645
50	hsa-miR-6875-5p	MIMAT0027650
51	hsa-miR-1908-3p	MIMAT0026916
52	hsa-miR-4433b-3p	MIMAT0030414

EP 3 150 707 A1

(continued)

5
10
15
20
25
30
35
40
45
50
55

SEQ ID NO:	Gene name	miRBase registration No.
53	hsa-miR-4736	MIMAT0019862
54	hsa-miR-5100	MIMAT0022259
55	hsa-miR-6724-5p	MIMAT0025856
56	hsa-miR-7107-5p	MIMAT0028111
57	hsa-miR-6726-5p	MIMAT0027353
58	hsa-miR-3185	MIMAT0015065
59	hsa-miR-4638-5p	MIMAT0019695
60	hsa-miR-1273g-3p	MIMAT0022742
61	hsa-miR-6778-5p	MIMAT0027456
62	hsa-miR-328-5p	MIMAT0026486
63	hsa-miR-3679-3p	MIMAT0018105
64	hsa-miR-1228-3p	MIMAT0005583
65	hsa-miR-6779-5p	MIMAT0027458
66	hsa-miR-4723-5p	MIMAT0019838
67	hsa-miR-6850-5p	MIMAT0027600
68	hsa-miR-760	MIMAT0004957
69	hsa-miR-7704	MIMAT0030019
70	hsa-miR-8072	MIMAT0030999
71	hsa-miR-4486	MIMAT0019020
72	hsa-miR-1913	MIMAT0007888
73	hsa-miR-4656	MIMAT0019723
74	hsa-miR-1260b	MIMAT0015041
75	hsa-miR-7106-5p	MIMAT0028109
76	hsa-miR-6889-5p	MIMAT0027678
77	hsa-miR-6780b-5p	MIMAT0027572
78	hsa-miR-6090	MIMAT0023715
79	hsa-miR-4534	MIMAT0019073
80	hsa-miR-4449	MIMAT0018968
81	hsa-miR-5195-3p	MIMAT0021127
82	hsa-miR-1202	MIMAT0005865
83	hsa-miR-4467	MIMAT0018994
84	hsa-miR-6515-3p	MIMAT0025487
85	hsa-miR-4281	MIMAT0016907
86	hsa-miR-4505	MIMAT0019041
87	hsa-miR-4484	MIMAT0019018
88	hsa-miR-6805-3p	MIMAT0027511
89	hsa-miR-3135b	MIMAT0018985
90	hsa-miR-3162-5p	MIMAT0015036

EP 3 150 707 A1

(continued)

5

10

15

20

25

30

35

40

45

50

55

SEQ ID NO:	Gene name	miRBase registration No.
91	hsa-miR-6768-5p	MIMAT0027436
92	hsa-miR-6721-5p	MIMAT0025852
93	hsa-miR-1227-5p	MIMAT0022941
94	hsa-miR-6722-3p	MIMAT0025854
95	hsa-miR-4286	MIMAT0016916
96	hsa-miR-4746-3p	MIMAT0019881
97	hsa-miR-6727-5p	MIMAT0027355
98	hsa-miR-6816-5p	MIMAT0027532
99	hsa-miR-4741	MIMAT0019871
100	hsa-miR-4508	MIMAT0019045
101	hsa-miR-940	MIMAT0004983
102	hsa-miR-4327	MIMAT0016889
103	hsa-miR-4665-3p	MIMAT0019740
104	hsa-miR-718	MIMAT0012735
105	hsa-miR-125a-3p	MIMAT0004602
106	hsa-miR-204-3p	MIMAT0022693
107	hsa-miR-1469	MIMAT0007347
108	hsa-miR-575	MIMAT0003240
109	hsa-miR-150-3p	MIMAT0004610
110	hsa-miR-423-5p	MIMAT0004748
111	hsa-miR-564	MIMAT0003228
112	hsa-miR-3188	MIMAT0015070
113	hsa-miR-1246	MIMAT0005898
114	hsa-miR-602	MIMAT0003270
115	hsa-miR-1290	MIMAT0005880
116	hsa-miR-16-5p	MIMAT0000069
117	hsa-miR-451a	MIMAT0001631
118	hsa-miR-24-3p	MIMAT0000080
119	hsa-miR-187-5p	MIMAT0004561
120	hsa-miR-1908-5p	MIMAT0007881
121	hsa-miR-371a-5p	MIMAT0004687
122	hsa-miR-550a-5p	MIMAT0004800
123	hsa-mir-6893	MI0022740
124	hsa-mir-6075	MI0020352
125	hsa-mir-6820	MI0022665
126	hsa-mir-4294	MI0015827
127	hsa-mir-6729	MI0022574
128	hsa-mir-4476	MI0016828

EP 3 150 707 A1

(continued)

SEQ ID NO:	Gene name	miRBase registration No.	
5	129	hsa-mir-6836	MI0022682
	130	hsa-mir-6765	MI0022610
	131	hsa-mir-6799	MI0022644
	132	hsa-mir-4530	MI0016897
10	133	hsa-mir-7641-1	MI0024975
	134	hsa-mir-7641-2	MI0024976
	135	hsa-mir-4454	MI0016800
15	136	hsa-mir-615	MI0003628
	137	hsa-mir-8073	MI0025909
	138	hsa-mir-663a	MI0003672
	139	hsa-mir-4634	MI0017261
20	140	hsa-mir-4450	MI0016795
	141	hsa-mir-4792	MI0017439
	142	hsa-mir-665	MI0005563
25	143	hsa-mir-7975	MI0025751
	144	hsa-mir-7109	MI0022960
	145	hsa-mir-6789	MI0022634
	146	hsa-mir-4497	MI0016859
30	147	hsa-mir-6877	MI0022724
	148	hsa-mir-6880	MI0022727
	149	hsa-mir-7977	MI0025753
35	150	hsa-mir-4734	MI0017371
	151	hsa-mir-6821	MI0022666
	152	hsa-mir-8089	MI0025925
	153	hsa-mir-5585	MI0019142
40	154	hsa-mir-6085	MI0020362
	155	hsa-mir-6845	MI0022691
	156	hsa-mir-4651	MI0017279
45	157	hsa-mir-4433	MI0016773
	158	hsa-mir-1231	MI0006321
	159	hsa-mir-4665	MI0017295
	160	hsa-mir-7114	MI0022965
50	161	hsa-mir-1238	MI0006328
	162	hsa-mir-8069	MI0025905
	163	hsa-mir-4732	MI0017369
55	164	hsa-mir-619	MI0003633
	165	hsa-mir-3622a	MI0016013
	166	hsa-mir-1260a	MI0006394

EP 3 150 707 A1

(continued)

SEQ ID NO:	Gene name	miRBase registration No.
5 167	hsa-mir-6741	MI0022586
168	hsa-mir-6781	MI0022626
169	hsa-mir-6125	MI0021259
170	hsa-mir-6805	MI0022650
10 171	hsa-mir-6132	MI0021277
172	hsa-mir-6872	MI0022719
173	hsa-mir-6875	MI0022722
15 174	hsa-mir-1908	MI0008329
175	hsa-mir-4433b	MI0025511
176	hsa-mir-4736	MI0017373
177	hsa-mir-5100	MI0019116
20 178	hsa-mir-6724	MI0022559
179	hsa-mir-7107	MI0022958
180	hsa-mir-6726	MI0022571
25 181	hsa-mir-3185	MI0014227
182	hsa-mir-4638	MI0017265
183	hsa-mir-1273g	MI0018003
184	hsa-mir-6778	MI0022623
30 185	hsa-mir-328	MI0000804
186	hsa-mir-3679	MI0016080
187	hsa-mir-1228	MI0006318
35 188	hsa-mir-6779	MI0022624
189	hsa-mir-4723	MI0017359
190	hsa-mir-6850	MI0022696
191	hsa-mir-760	MI0005567
40 192	hsa-mir-7704	MI0025240
193	hsa-mir-8072	MI0025908
194	hsa-mir-4486	MI0016847
45 195	hsa-mir-1913	MI0008334
196	hsa-mir-4656	MI0017284
197	hsa-mir-1260b	MI0014197
198	hsa-mir-7106	MI0022957
50 199	hsa-mir-6889	MI0022736
200	hsa-mir-6780b	MI0022681
201	hsa-mir-6090	MI0020367
55 202	hsa-mir-4534	MI0016901
203	hsa-mir-4449	MI0016792
204	hsa-mir-5195	MI0018174

EP 3 150 707 A1

(continued)

SEQ ID NO:	Gene name	miRBase registration No.
5 205	hsa-mir-1202	MI0006334
206	hsa-mir-4467	MI0016818
207	hsa-mir-6515	MI0022227
208	hsa-mir-4281	MI0015885
10 209	hsa-mir-4505	MI0016868
210	hsa-mir-4484	MI0016845
211	hsa-mir-6805	MI0022650
15 212	hsa-mir-3135b	MI0016809
213	hsa-mir-3162	MI0014192
214	hsa-mir-6768	MI0022613
215	hsa-mir-6721	MI0022556
20 216	hsa-mir-1227	MI0006316
217	hsa-mir-6722	MI0022557
218	hsa-mir-4286	MI0015894
25 219	hsa-mir-4746	MI0017385
220	hsa-mir-6727	MI0022572
221	hsa-mir-6816	MI0022661
222	hsa-mir-4741	MI0017379
30 223	hsa-mir-4508	MI0016872
224	hsa-mir-940	MI0005762
225	hsa-mir-4327	MI0015867
35 226	hsa-mir-718	MI0012489
227	hsa-mir-125a	MI0000469
228	hsa-mir-204	MI0000284
229	hsa-mir-1469	MI0007074
40 230	hsa-mir-575	MI0003582
231	hsa-mir-150	MI0000479
232	hsa-mir-423	MI0001445
45 233	hsa-mir-564	MI0003570
234	hsa-mir-3188	MI0014232
235	hsa-mir-1246	MI0006381
236	hsa-mir-602	MI0003615
50 237	hsa-mir-1290	MI0006352
238	hsa-mir-16-1	MI0000070
239	hsa-mir-16-2	MI0000115
55 240	hsa-mir-451a	MI0001729
241	hsa-mir-24-1	MI0000080
242	hsa-mir-24-2	MI0000081

EP 3 150 707 A1

(continued)

5

10

15

20

25

30

35

40

45

50

55

SEQ ID NO:	Gene name	miRBase registration No.
243	hsa-mir-187	MI0000274
244	hsa-mir-1908	MI0008329
245	hsa-mir-371a	MI0000779
246	hsa-mir-550a-1	MI0003600
247	hsa-mir-550a-2	MI0003601
248	isomiR example 1 of SEQ ID NO: 6	-
249	isomiR example 2 of SEQ ID NO: 6	-
250	isomiR example 1 of SEQ ID NO: 10	-
251	isomiR example 1 of SEQ ID NO: 12	-
252	isomiR example 2 of SEQ ID NO: 12	-
253	isomiR example 1 of SEQ ID NO: 13	-
254	isomiR example 2 of SEQ ID NO: 13	-
255	isomiR example 1 of SEQ ID NO: 15	-
256	isomiR example 2 of SEQ ID NO: 15	-
257	isomiR example 1 of SEQ ID NO: 18	-
258	isomiR example 2 of SEQ ID NO: 18	-
259	isomiR example 1 of SEQ ID NO: 19	-
260	isomiR example 2 of SEQ ID NO: 19	-
261	isomiR example 1 of SEQ ID NO: 20	-
262	isomiR example 1 of SEQ ID NO: 23	-
263	isomiR example 2 of SEQ ID NO: 23	-
264	isomiR example 1 of SEQ ID NO: 27	-
265	isomiR example 1 of SEQ ID NO: 30	-
266	isomiR example 2 of SEQ ID NO: 30	-
267	isomiR example 1 of SEQ ID NO: 33	-
268	isomiR example 1 of SEQ ID NO: 34	-
269	isomiR example 2 of SEQ ID NO: 34	-
270	isomiR example 1 of SEQ ID NO: 36	-
271	isomiR example 1 of SEQ ID NO: 40	-
272	isomiR example 1 of SEQ ID NO: 41	-
273	isomiR example 2 of SEQ ID NO: 41	-
274	isomiR example 1 of SEQ ID NO: 42	-
275	isomiR example 1 of SEQ ID NO: 43	-
276	isomiR example 2 of SEQ ID NO: 43	-
277	isomiR example 1 of SEQ ID NO: 46	-
278	isomiR example 1 of SEQ ID NO: 48	-
279	isomiR example 1 of SEQ ID NO: 51	-
280	isomiR example 2 of SEQ ID NO: 51	-

EP 3 150 707 A1

(continued)

5

10

15

20

25

30

35

40

45

50

55

SEQ ID NO:	Gene name	miRBase registration No.
281	isomiR example 1 of SEQ ID NO: 54	-
282	isomiR example 1 of SEQ ID NO: 55	-
283	isomiR example 2 of SEQ ID NO: 55	-
284	isomiR example 1 of SEQ ID NO: 58	-
285	isomiR example 1 of SEQ ID NO: 59	-
286	isomiR example 2 of SEQ ID NO: 59	-
287	isomiR example 1 of SEQ ID NO: 60	-
288	isomiR example 2 of SEQ ID NO: 60	-
289	isomiR example 1 of SEQ ID NO: 62	-
290	isomiR example 2 of SEQ ID NO: 62	-
291	isomiR example 1 of SEQ ID NO: 63	-
292	isomiR example 1 of SEQ ID NO: 64	-
293	isomiR example 2 of SEQ ID NO: 64	-
294	isomiR example 1 of SEQ ID NO: 66	-
295	isomiR example 2 of SEQ ID NO: 66	-
296	isomiR example 1 of SEQ ID NO: 68	-
297	isomiR example 2 of SEQ ID NO: 68	-
298	isomiR example 1 of SEQ ID NO: 71	-
299	isomiR example 1 of SEQ ID NO: 72	-
300	isomiR example 1 of SEQ ID NO: 74	-
301	isomiR example 2 of SEQ ID NO: 74	-
302	isomiR example 1 of SEQ ID NO: 80	-
303	isomiR example 2 of SEQ ID NO: 80	-
304	isomiR example 1 of SEQ ID NO: 82	-
305	isomiR example 1 of SEQ ID NO: 83	-
306	isomiR example 1 of SEQ ID NO: 86	-
307	isomiR example 1 of SEQ ID NO: 87	-
308	isomiR example 2 of SEQ ID NO: 87	-
309	isomiR example 1 of SEQ ID NO: 89	-
310	isomiR example 1 of SEQ ID NO: 90	-
311	isomiR example 2 of SEQ ID NO: 90	-
312	isomiR example 1 of SEQ ID NO: 92	-
313	isomiR example 2 of SEQ ID NO: 92	-
314	isomiR example 1 of SEQ ID NO: 95	-
315	isomiR example 2 of SEQ ID NO: 95	-
316	isomiR example 1 of SEQ ID NO: 99	-
317	isomiR example 2 of SEQ ID NO: 99	-
318	isomiR example 1 of SEQ ID NO: 100	-

EP 3 150 707 A1

(continued)

5
10
15
20
25
30
35
40
45
50
55

SEQ ID NO:	Gene name	miRBase registration No.
319	isomiR example 2 of SEQ ID NO: 100	-
320	isomiR example 1 of SEQ ID NO: 101	-
321	isomiR example 2 of SEQ ID NO: 101	-
322	isomiR example 1 of SEQ ID NO: 105	-
323	isomiR example 2 of SEQ ID NO: 105	-
324	isomiR example 1 of SEQ ID NO: 106	-
325	isomiR example 2 of SEQ ID NO: 106	-
326	isomiR example 1 of SEQ ID NO: 109	-
327	isomiR example 2 of SEQ ID NO: 109	-
328	isomiR example 1 of SEQ ID NO: 110	-
329	isomiR example 2 of SEQ ID NO: 110	-
330	isomiR example 1 of SEQ ID NO: 112	-
331	isomiR example 2 of SEQ ID NO: 112	-
332	isomiR example 1 of SEQ ID NO: 113	-
333	isomiR example 2 of SEQ ID NO: 113	-
334	isomiR example 1 of SEQ ID NO: 115	-
335	isomiR example 2 of SEQ ID NO: 115	-
336	isomiR example 1 of SEQ ID NO: 116	-
337	isomiR example 2 of SEQ ID NO: 116	-
338	isomiR example 3 of SEQ ID NO: 116	-
339	isomiR example 1 of SEQ ID NO: 117	-
340	isomiR example 2 of SEQ ID NO: 117	-
341	isomiR example 1 of SEQ ID NO: 118	-
342	isomiR example 2 of SEQ ID NO: 118	-
343	isomiR example 3 of SEQ ID NO: 118	-
344	isomiR example 1 of SEQ ID NO: 119	-
345	isomiR example 2 of SEQ ID NO: 119	-
346	isomiR example 1 of SEQ ID NO: 121	-
347	isomiR example 2 of SEQ ID NO: 121	-
348	isomiR example 1 of SEQ ID NO: 122	-
349	hsa-miR-4417	MIMAT0018929
350	hsa-miR-4707-5p	MIMAT0019807
351	hsa-miR-7847-3p	MIMAT0030422
352	hsa-miR-2861	MIMAT0013802
353	hsa-miR-4513	MIMAT0019050
354	hsa-miR-7111-5p	MIMAT0028119
355	hsa-miR-6777-Sp	MIMAT0027454
356	hsa-miR-7113-3p	MIMAT0028124

EP 3 150 707 A1

(continued)

5
10
15
20
25
30
35
40
45
50
55

SEQ ID NO:	Gene name	miRBase registration No.
357	hsa-miR-4648	MIMAT0019710
358	hsa-miR-3184-5p	MIMAT0015064
359	hsa-miR-4271	MIMAT0016901
360	hsa-miR-6791-5p	MIMAT0027482
361	hsa-miR-642a-3p	MIMAT0020924
362	hsa-miR-7108-5p	MIMAT0028113
363	hsa-miR-128-1-Sp	MIMAT0026477
364	hsa-miR-5196-5p	MIMAT0021128
365	hsa-miR-3178	MIMAT0015055
366	hsa-miR-3656	MIMAT0018076
367	hsa-miR-92a-2-5p	MIMAT0004508
368	hsa-miR-6769b-5p	MIMAT0027620
369	hsa-miR-4689	MIMAT0019778
370	hsa-miR-6076	MIMAT0023701
371	hsa-miR-92b-5p	MIMAT0004792
372	hsa-miR-6774-5p	MIMAT0027448
373	hsa-miR-486-3p	MIMAT0004762
374	hsa-miR-6806-5p	MIMAT0027512
375	hsa-miR-6842-5p	MIMAT0027586
376	hsa-miR-6716-5p	MIMAT0025844
377	hsa-miR-557	MIMAT0003221
378	hsa-miR-4673	MIMAT0019755
379	hsa-miR-4674	MIMAT0019756
380	hsa-miR-4442	MIMAT0018960
381	hsa-miR-1915-3p	MIMAT0007892
382	hsa-miR-4687-3p	MIMAT0019775
383	hsa-miR-92b-3p	MIMAT0003218
384	hsa-mir-4417	MI0016753
385	hsa-mir-4707	MI0017340
386	hsa-mir-7847	MI0025517
387	hsa-mir-2861	MI0013006
388	hsa-mir-4513	MI0016879
389	hsa-mir-7111	MI0022962
390	hsa-mir-6777	MI0022622
391	hsa-mir-7113	MI0022964
392	hsa-mir-4648	MI0017275
393	hsa-mir-3184	MI0014226
394	hsa-mir-4271	MI0015879

EP 3 150 707 A1

(continued)

5
10
15
20
25
30
35
40
45
50
55

SEQ ID NO:	Gene name	miRBase registration No.
395	hsa-mir-6791	MI0022636
396	hsa-mir-642a	MI0003657
397	hsa-mir-7108	MI0022959
398	hsa-mir-128-1	MI0000447
399	hsa-mir-5196	MI0018175
400	hsa-mir-3178	MI0014212
401	hsa-mir-3656	MI0016056
402	hsa-mir-92a-2	MI0000094
403	hsa-mir-6769b	MI0022706
404	hsa-mir-4689	MI0017322
405	hsa-mir-6076	MI0020353
406	hsa-mir-92b	MI0003560
407	hsa-mir-6774	MI0022619
408	hsa-mir-486	MI0002470
409	hsa-mir-486-2	MI0023622
410	hsa-mir-6806	MI0022651
411	hsa-mir-6842	MI0022688
412	hsa-mir-6716	MI0022550
413	hsa-mir-557	MI0003563
414	hsa-mir-4673	MI0017304
415	hsa-mir-4674	MI0017305
416	hsa-mir-4442	MI0016785
417	hsa-mir-1915	MI0008336
418	hsa-mir-4687	MI0017319
419	hsa-mir-92b	MI0003560
420	isomiR example 1 of SEQ ID NO: 349	-
421	isomiR example 2 of SEQ ID NO: 349	-
422	isomiR example 1 of SEQ ID NO: 350	-
423	isomiR example 2 of SEQ ID NO: 350	-
424	isomiR example 1 of SEQ ID NO: 352	-
425	isomiR example 2 of SEQ ID NO: 352	-
426	isomiR example 1 of SEQ ID NO: 353	-
427	isomiR example 2 of SEQ ID NO: 353	-
428	isomiR example 1 of SEQ ID NO: 357	-
429	isomiR example 2 of SEQ ID NO: 357	-
430	isomiR example 1 of SEQ ID NO: 359	-
431	isomiR example 2 of SEQ ID NO: 359	-
432	isomiR example 1 of SEQ ID NO: 361	-

EP 3 150 707 A1

(continued)

5

10

15

20

25

30

35

40

45

50

55

SEQ ID NO:	Gene name	miRBase registration No.
433	isomiR example 2 of SEQ ID NO: 361	-
434	isomiR example 1 of SEQ ID NO: 363	-
435	isomiR example 2 of SEQ ID NO: 363	-
436	isomiR example 1 of SEQ ID NO: 364	-
437	isomiR example 2 of SEQ ID NO: 364	-
438	isomiR example 1 of SEQ ID NO: 365	-
439	isomiR example 2 of SEQ ID NO: 365	-
440	isomiR example 1 of SEQ ID NO: 366	-
441	isomiR example 2 of SEQ ID NO: 366	-
442	isomiR example 1 of SEQ ID NO: 367	-
443	isomiR example 2 of SEQ ID NO: 367	-
444	isomiR example 1 of SEQ ID NO: 369	-
445	isomiR example 2 of SEQ ID NO: 369	-
446	isomiR example 1 of SEQ ID NO: 371	-
447	isomiR example 2 of SEQ ID NO: 371	-
448	isomiR example 1 of SEQ ID NO: 373	-
449	isomiR example 2 of SEQ ID NO: 373	-
450	isomiR example 1 of SEQ ID NO: 376	-
451	isomiR example 2 of SEQ ID NO: 376	-
452	isomiR example 1 of SEQ ID NO: 378	-
453	isomiR example 2 of SEQ ID NO: 378	-
454	isomiR example 1 of SEQ ID NO: 379	-
455	isomiR example 2 of SEQ ID NO: 379	-
456	isomiR example 1 of SEQ ID NO: 380	-
457	isomiR example 2 of SEQ ID NO: 380	-
458	isomiR example 1 of SEQ ID NO: 381	-
459	isomiR example 2 of SEQ ID NO: 381	-
460	isomiR example 1 of SEQ ID NO: 382	-
461	isomiR example 2 of SEQ ID NO: 382	-
462	isomiR example 1 of SEQ ID NO: 383	-
463	isomiR example 2 of SEQ ID NO: 383	-
464	hsa-miR-1203	MIMAT0005866
465	hsa-miR-663b	MIMAT0005867
466	hsa-miR-4258	MIMAT0016879
467	hsa-miR-4649-5p	MIMAT0019711
468	hsa-miR-4516	MIMAT0019053
469	hsa-miR-3619-3p	MIMAT0019219
470	hsa-miR-6826-5p	MIMAT0027552

EP 3 150 707 A1

(continued)

SEQ ID NO:	Gene name	miRBase registration No.
5 471	hsa-miR-6757-5p	MIMAT0027414
472	hsa-miR-3131	MIMAT0014996
473	hsa-miR-1343-3p	MIMAT0019776
10 474	hsa-mir-1203	MI0006335
475	hsa-mir-663b	MI0006336
476	hsa-mir-4258	MI0015857
477	hsa-mir-4649	MI0017276
15 478	hsa-mir-4516	MI0016882
479	hsa-mir-3619	MI0016009
480	hsa-mir-6826	MI0022671
481	hsa-mir-6757	MI0022602
20 482	hsa-mir-3131	MI0014151
483	hsa-mir-1343	MI0017320
484	isomiR example 1 of SEQ ID NO: 465	-
25 485	isomiR example 2 of SEQ ID NO: 465	-
486	isomiR example 1 of SEQ ID NO: 468	-
487	isomiR example 2 of SEQ ID NO: 468	-
30 488	isomiR example 1 of SEQ ID NO: 472	-
489	isomiR example 2 of SEQ ID NO: 472	-
490	isomiR example 1 of SEQ ID NO: 473	-
491	isomiR example 2 of SEQ ID NO: 473	-
35 492	hsa-miR-6775-5p	MIMAT0027450
493	hsa-miR-6813-5p	MIMAT0027526
494	hsa-miR-3940-5p	MIMAT0019229
40 495	hsa-miR-6775-5p	MI0022620
496	hsa-mir-6813	MI0022658
497	hsa-miR-3940-5p	MI0016597
498	isomiR example 1 of SEQ ID NO: 494	-
45 499	isomiR example 2 of SEQ ID NO: 494	-

[0236] The present specification encompasses the contents described in the specifications and/or drawings of Japanese Patent Application No. 2014-113523 and No. 2014-185730 from which the present application claims priorities.

50 Advantageous Effect of Invention

[0237] According to the present invention, pancreatic cancer can be detected easily and in high accuracy.

[0238] For example, the presence or absence of pancreatic cancer in patients can be easily detected by using, as indicators, the determined expression levels of several miRNAs in blood, serum, and/or plasma of the patients, which
55 can be collected with limited invasiveness.

BRIEF DESCRIPTION OF THE DRAWINGS

[0239]

5 [Figure 1] This figure shows the relationship between the nucleotide sequences of hsa-miR-4665-5p represented by SEQ ID NO: 36 and hsa-miR-4665-3p represented by SEQ ID NO: 103, which are produced from a precursor hsa-mir-4665 represented by SEQ ID NO: 159.

10 [Figure 2] Left diagram: the expression level measurement values of hsa-miR-6893-5p (SEQ ID NO: 1) in healthy subjects (100 persons) and pancreatic cancer patients (67 persons) selected as a training cohort were each plotted on the ordinate. The horizontal line in the diagram depicts a threshold (8.02) that was optimized by Fisher's discriminant analysis and discriminated between the two groups. Right diagram: the expression level measurement values of hsa-miR-6893-5p (SEQ ID NO: 1) in healthy subjects (50 persons) and pancreatic cancer patients (33 persons) selected as a validation cohort were each plotted on the ordinate. The horizontal line in the diagram depicts the threshold (8.02) that was set in the training cohort and discriminated between the two groups.

15 [Figure 3] Left diagram: the expression level measurement values of hsa-miR-6893-5p (SEQ ID NO: 1) in healthy subjects (100 persons, circles) and pancreatic cancer patients (67 persons, triangles) selected as a training cohort were each plotted on the abscissa against their expression level measurement values of hsa-miR-6075 (SEQ ID NO: 2) on the ordinate. The line in the diagram depicts a discriminant function ($0 = 1.74x + y + 5.14$) that was optimized by Fisher's discriminant analysis and discriminated between the two groups. Right diagram: the expression level measurement values of hsa-miR-6893-5p (SEQ ID NO: 1) in healthy subjects (50 persons, circles) and pancreatic cancer patients (33 persons, triangles) selected as a validation cohort were each plotted on the abscissa against their expression level measurement values of hsa-miR-6075 (SEQ ID NO: 2) on the ordinate. The line in the diagram depicts the threshold ($0 = 1.74x + y + 5.14$) that was set in the training cohort and discriminated between the two groups.

20 [Figure 4] Upper diagram: a discriminant ($1.64 \times \text{hsa-miR-6075} + 1.02 \times \text{hsa-miR-6836-3p} - 0.35 \times \text{hsa-miR-6799-5p} - 0.06 \times \text{hsa-miR-125a-3p} - 20.67$) was prepared by use of Fisher's discriminant analysis from the expression level measurement values of hsa-miR-6075 (SEQ ID NO: 2), hsa-miR-6836-3p (SEQ ID NO: 7), hsa-miR-6799-5p (SEQ ID NO: 9), and hsa-miR-125a-3p (SEQ ID NO: 105) in 67 pancreatic cancer patients, 93 healthy subjects, 35 colorectal cancer patients, 37 stomach cancer patients, 32 esophageal cancer patients, 38 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 groups. Lower diagram: discriminant scores obtained from the discriminant prepared from the training cohort as to the expression level measurement values of hsa-miR-6075 (SEQ ID NO: 2), hsa-miR-6799-5p (SEQ ID NO: 9), hsa-miR-125a-3p (SEQ ID NO: 105), and hsa-miR-6836-3p (SEQ ID NO: 7) in 33 pancreatic cancer patients, 57 healthy subjects, 15 colorectal cancer patients, 13 stomach cancer patients, 18 esophageal cancer patients, 12 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 both of the groups.

MODES FOR CARRYING OUT THE INVENTION

[0240] Hereinafter, the present invention will be further described in detail.

45 1. Target nucleic acid for pancreatic cancer

[0241] Primary target nucleic acids, as pancreatic cancer markers, for detecting the presence and/or absence of pancreatic cancer or pancreatic cancer cells using the nucleic acid probes or the primers for the detection of pancreatic cancer defined above according to the present invention comprise at least one or more miRNAs selected from the group consisting of the following miRNAs: hsa-miR-6893-5p, hsa-miR-6075, hsa-miR-6820-5p, hsa-miR-4294, hsa-miR-6729-5p, hsa-miR-4476, hsa-miR-6836-3p, hsa-miR-6765-3p, hsa-miR-6799-5p, hsa-miR-4530, hsa-miR-7641, hsa-miR-4454, hsa-miR-615-5p, hsa-miR-8073, hsa-miR-663a, hsa-miR-4634, hsa-miR-4450, hsa-miR-4792, hsa-miR-665, hsa-miR-7975, hsa-miR-7109-5p, hsa-miR-6789-5p, hsa-miR-4497, hsa-miR-6877-5p, hsa-miR-6880-5p, hsa-miR-7977, hsa-miR-4734, hsa-miR-6821-5p, hsa-miR-8089, hsa-miR-5585-3p, hsa-miR-6085, hsa-miR-6845-5p, hsa-miR-4651, hsa-miR-4433-3p, hsa-miR-1231, hsa-miR-4665-5p, hsa-miR-7114-5p, hsa-miR-1238-5p, hsa-miR-8069, hsa-miR-4732-5p, hsa-miR-619-5p, hsa-miR-3622a-5p, hsa-miR-1260a, hsa-miR-6741-5p, hsa-miR-6781-5p, hsa-miR-6125, hsa-miR-6805-5p, hsa-miR-6132, hsa-miR-6872-3p, hsa-miR-6875-5p, hsa-miR-1908-3p, hsa-miR-4433b-3p, hsa-miR-4736, hsa-miR-5100, hsa-miR-6724-5p, hsa-miR-7107-5p, hsa-miR-6726-5p, hsa-miR-3185, hsa-miR-

4638-5p, hsa-miR-1273g-3p, hsa-miR-6778-5p, hsa-miR-328-5p, hsa-miR-3679-3p, hsa-miR-1228-3p, hsa-miR-6779-5p, hsa-miR-4723-5p, hsa-miR-6850-5p, hsa-miR-760, hsa-miR-7704, hsa-miR-8072, hsa-miR-4486, hsa-miR-1913, hsa-miR-4656, hsa-miR-1260b, hsa-miR-7106-5p, hsa-miR-6889-5p, hsa-miR-6780b-5p, hsa-miR-6090, hsa-miR-4534, hsa-miR-4449, hsa-miR-5195-3p, hsa-miR-1202, hsa-miR-4467, hsa-miR-6515-3p, hsa-miR-4281, hsa-miR-4505, hsa-miR-4484, hsa-miR-6805-3p, hsa-miR-3135b, hsa-miR-3162-5p, hsa-miR-6768-5p, hsa-miR-6721-5p, hsa-miR-1227-5p, hsa-miR-6722-3p, hsa-miR-4286, hsa-miR-4746-3p, hsa-miR-6727-5p, hsa-miR-6816-5p, hsa-miR-4741, hsa-miR-4508, hsa-miR-940, hsa-miR-4327, hsa-miR-4665-3p, hsa-miR-718, hsa-miR-1203, hsa-miR-663b, hsa-miR-4258, hsa-miR-4649-5p, hsa-miR-4516, hsa-miR-3619-3p, hsa-miR-6826-5p, hsa-miR-6757-5p, hsa-miR-3131, hsa-miR-1343-3p, hsa-miR-6775-5p, hsa-miR-6813-5p and hsa-miR-3940-5p. Furthermore, at least one or more miRNAs selected from the group consisting of the following other pancreatic cancer markers that can be combined with these miRNAs, i.e., hsa-miR-125a-3p, hsa-miR-204-3p, hsa-miR-1469, hsa-miR-575, hsa-miR-150-3p, hsa-miR-423-5p, hsa-miR-564, hsa-miR-3188, hsa-miR-1246, hsa-miR-602, hsa-miR-1290, hsa-miR-16-5p, hsa-miR-451a, hsa-miR-24-3p, hsa-miR-187-5p, hsa-miR-1908-5p, hsa-miR-371a-5p and hsa-miR-550a-5p can also be preferably used as target nucleic acids. Moreover, at least one or more miRNAs selected from the group consisting of the following other pancreatic cancer markers that can be combined with these miRNAs, i.e., hsa-miR-4417, hsa-miR-4707-5p, hsa-miR-7847-3p, hsa-miR-2861, hsa-miR-4513, hsa-miR-7111-5p, hsa-miR-6777-5p, hsa-miR-7113-3p, hsa-miR-4648, hsa-miR-3184-5p, hsa-miR-4271, hsa-miR-6791-5p, hsa-miR-642a-3p, hsa-miR-7108-5p, hsa-miR-128-1-5p, hsa-miR-5196-5p, hsa-miR-3178, hsa-miR-3656, hsa-miR-92a-2-5p, hsa-miR-6769b-5p, hsa-miR-4689, hsa-miR-6076, hsa-miR-92b-5p, hsa-miR-6774-5p, hsa-miR-486-3p, hsa-miR-6806-5p, hsa-miR-6842-5p, hsa-miR-6716-5p, hsa-miR-557, hsa-miR-4673, hsa-miR-4674, hsa-miR-4442, hsa-miR-1915-3p, hsa-miR-4687-3p and hsa-miR-92b-3p can also be preferably used as target nucleic acids.

[0242] These miRNAs include, for example, a human gene comprising a nucleotide sequence represented by any of SEQ NOs: 1 to 122 and 349 to 383, 464 to 473, and 492 to 494 (i.e., hsa-miR-6893-5p, hsa-miR-6075, hsa-miR-6820-5p, hsa-miR-4294, hsa-miR-6729-5p, hsa-miR-4476, hsa-miR-6836-3p, hsa-miR-6765-3p, hsa-miR-6799-5p, hsa-miR-4530, hsa-miR-7641, hsa-miR-4454, hsa-miR-615-5p, hsa-miR-8073, hsa-miR-663a, hsa-miR-4634, hsa-miR-4450, hsa-miR-4792, hsa-miR-665, hsa-miR-7975, hsa-miR-7109-5p, hsa-miR-6789-5p, hsa-miR-4497, hsa-miR-6877-5p, hsa-miR-6880-5p, hsa-miR-7977, hsa-miR-4734, hsa-miR-6821-5p, hsa-miR-8089, hsa-miR-5585-3p, hsa-miR-6085, hsa-miR-6845-5p, hsa-miR-4651, hsa-miR-4433-3p, hsa-miR-1231, hsa-miR-4665-5p, hsa-miR-7114-5p, hsa-miR-1238-5p, hsa-miR-8069, hsa-miR-4732-5p, hsa-miR-619-5p, hsa-miR-3622a-5p, hsa-miR-1260a, hsa-miR-6741-5p, hsa-miR-6781-5p, hsa-miR-6125, hsa-miR-6805-5p, hsa-miR-6132, hsa-miR-6872-3p, hsa-miR-6875-5p, hsa-miR-1908-3p, hsa-miR-4433b-3p, hsa-miR-4736, hsa-miR-5100, hsa-miR-6724-5p, hsa-miR-7107-5p, hsa-miR-6726-5p, hsa-miR-3185, hsa-miR-4638-5p, hsa-miR-1273g-3p, hsa-miR-6778-5p, hsa-miR-328-5p, hsa-miR-3679-3p, hsa-miR-1228-3p, hsa-miR-6779-5p, hsa-miR-4723-5p, hsa-miR-6850-5p, hsa-miR-760, hsa-miR-7704, hsa-miR-8072, hsa-miR-4486, hsa-miR-1913, hsa-miR-4656, hsa-miR-1260b, hsa-miR-7106-5p, hsa-miR-6889-5p, hsa-miR-6780b-5p, hsa-miR-6090, hsa-miR-4534, hsa-miR-4449, hsa-miR-5195-3p, hsa-miR-1202, hsa-miR-4467, hsa-miR-6515-3p, hsa-miR-4281, hsa-miR-4505, hsa-miR-4484, hsa-miR-6805-3p, hsa-miR-3135b, hsa-miR-3162-5p, hsa-miR-6768-5p, hsa-miR-6721-5p, hsa-miR-1227-5p, hsa-miR-6722-3p, hsa-miR-4286, hsa-miR-4746-3p, hsa-miR-6727-5p, hsa-miR-6816-5p, hsa-miR-4741, hsa-miR-4508, hsa-miR-940, hsa-miR-4327, hsa-miR-4665-3p, hsa-miR-718, hsa-miR-125a-3p, hsa-miR-204-3p, hsa-miR-1469, hsa-miR-575, hsa-miR-150-3p, hsa-miR-423-5p, hsa-miR-564, hsa-miR-3188, hsa-miR-1246, hsa-miR-602, hsa-miR-1290, hsa-miR-16-5p, hsa-miR-451a, hsa-miR-24-3p, hsa-miR-187-5p, hsa-miR-1908-5p, hsa-miR-371a-5p, hsa-miR-550a-5p, hsa-miR-4417, hsa-miR-4707-5p, hsa-miR-7847-3p, hsa-miR-2861, hsa-miR-4513, hsa-miR-7111-5p, hsa-miR-6777-5p, hsa-miR-7113-3p, hsa-miR-4648, hsa-miR-3184-5p, hsa-miR-4271, hsa-miR-6791-5p, hsa-miR-642a-3p, hsa-miR-7108-5p, hsa-miR-128-1-5p, hsa-miR-5196-5p, hsa-miR-3178, hsa-miR-3656, hsa-miR-92a-2-5p, hsa-miR-6769b-5p, hsa-miR-4689, hsa-miR-6076, hsa-miR-92b-5p, hsa-miR-6774-5p, hsa-miR-486-3p, hsa-miR-6806-5p, hsa-miR-6842-5p, hsa-miR-6716-5p, hsa-miR-557, hsa-miR-4673, hsa-miR-4674, hsa-miR-4442, hsa-miR-1915-3p, hsa-miR-4687-3p, hsa-miR-92b-3p, hsa-miR-1203, hsa-miR-663b, hsa-miR-4258, hsa-miR-4649-5p, hsa-miR-4516, hsa-miR-3619-3p, hsa-miR-6826-5p, hsa-miR-6757-5p, hsa-miR-3131, hsa-miR-1343-3p, hsa-miR-6775-5p, hsa-miR-6813-5p and hsa-miR-3940-5p, respectively), a congener, a transcript thereof, or/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.

[0243] The target nucleic acid is preferably a human gene comprising a nucleotide sequence represented by any of SEQ ID NOs: 1 to 499 or a transcript thereof, more preferably the transcript, i.e., a miRNA or its precursor RNA (pri-miRNA or pre-miRNA).

[0244] The first target gene is the hsa-miR-6893-5p 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 pancreatic cancer.

[0245] The second 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

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 pancreatic cancer.

[0401] The 158th target gene is the hsa-miR-1203 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 pancreatic cancer.

[0402] The 159th 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 pancreatic cancer.

[0403] The 160th 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 pancreatic cancer.

[0404] The 161st target gene is the hsa-mir-4649 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 pancreatic cancer.

[0405] The 162nd 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 pancreatic cancer.

[0406] The 163rd target gene is the hsa-mir-3619 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 pancreatic cancer.

[0407] The 164th target gene is the hsa-mir-6826 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 pancreatic cancer.

[0408] The 165th target gene is the hsa-mir-6757 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 pancreatic cancer.

[0409] The 166th 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 pancreatic cancer.

[0410] The 167th target gene is the hsa-mir-1343 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 pancreatic cancer.

[0411] The 168th 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 pancreatic cancer.

[0412] The 169th target gene is the hsa-miR-6813-5p 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 pancreatic cancer.

[0413] The 170th 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 pancreatic cancer.

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

[0414] In the present invention, a nucleic acid capable of specifically binding to any of the target nucleic acids as the pancreatic 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 pancreatic cancer.

[0415] In the present invention, the nucleic acid probes or the primers that can be used for detecting pancreatic cancer or for diagnosing pancreatic cancer enable qualitative and/or quantitative measurement of the presence, expression level, or existing amount (abundance) of: any of human-derived hsa-miR-6893-5p, hsa-miR-6075, hsa-miR-6820-5p, hsa-miR-4294, hsa-miR-6729-5p, hsa-miR-4476, hsa-miR-6836-3p, hsa-miR-6765-3p, hsa-miR-6799-5p, hsa-miR-4530, hsa-miR-7641, hsa-miR-4454, hsa-miR-615-5p, hsa-miR-8073, hsa-miR-663a, hsa-miR-4634, hsa-miR-4450, hsa-miR-4792, hsa-miR-665, hsa-miR-7975, hsa-miR-7109-5p, hsa-miR-6789-5p, hsa-miR-4497, hsa-miR-6877-5p, hsa-miR-6880-5p, hsa-miR-7977, hsa-miR-4734, hsa-miR-6821-5p, hsa-miR-8089, hsa-miR-5585-3p, hsa-miR-6085, hsa-miR-6845-5p, hsa-miR-4651, hsa-miR-4433-3p, hsa-miR-1231, hsa-miR-4665-5p, hsa-miR-7114-5p, hsa-miR-1238-5p, hsa-miR-8069, hsa-miR-4732-5p, hsa-miR-619-5p, hsa-miR-3622a-5p, hsa-miR-1260a, hsa-miR-6741-5p, hsa-miR-6781-5p, hsa-miR-6125, hsa-miR-6805-5p, hsa-miR-6132, hsa-miR-6872-3p, hsa-miR-6875-5p, hsa-miR-1908-3p, hsa-miR-4433b-3p, hsa-miR-4736, hsa-miR-5100, hsa-miR-6724-5p, hsa-miR-7107-5p, hsa-miR-6726-5p,

hsa-miR-3185, hsa-miR-4638-5p, hsa-miR-1273g-3p, hsa-miR-6778-5p, hsa-miR-328-5p, hsa-miR-3679-3p, hsa-miR-1228-3p, hsa-miR-6779-5p, hsa-miR-4723-5p, hsa-miR-6850-5p, hsa-miR-760, hsa-miR-7704, hsa-miR-8072, hsa-miR-4486, hsa-miR-1913, hsa-miR-4656, hsa-miR-1260b, hsa-miR-7106-5p, hsa-miR-6889-5p, hsa-miR-6780b-5p, hsa-miR-6090, hsa-miR-4534, hsa-miR-4449, hsa-miR-5195-3p, hsa-miR-1202, hsa-miR-4467, hsa-miR-6515-3p, hsa-miR-4281, hsa-miR-4505, hsa-miR-4484, hsa-miR-6805-3p, hsa-miR-3135b, hsa-miR-3162-5p, hsa-miR-6768-5p, hsa-miR-6721-5p, hsa-miR-1227-5p, hsa-miR-6722-3p, hsa-miR-4286, hsa-miR-4746-3p, hsa-miR-6727-5p, hsa-miR-6816-5p, hsa-miR-4741, hsa-miR-4508, hsa-miR-940, hsa-miR-4327, hsa-miR-4665-3p, hsa-miR-718, hsa-miR-1203, hsa-miR-663b, hsa-miR-4258, hsa-miR-4649-5p, hsa-miR-4516, hsa-miR-3619-3p, hsa-miR-6826-5p, hsa-miR-6757-5p, hsa-miR-3131, hsa-miR-1343-3p, hsa-miR-6775-5p, hsa-miR-6813-5p, and hsa-miR-3940-5p, as target nucleic acids for pancreatic cancer, or a combination thereof; and hsa-miR-125a-3p, hsa-miR-204-3p, hsa-miR-1469, hsa-miR-575, hsa-miR-150-3p, hsa-miR-423-5p, hsa-miR-564, hsa-miR-3188, hsa-miR-1246, hsa-miR-602, hsa-miR-1290, hsa-miR-16-5p, hsa-miR-451a, hsa-miR-24-3p, hsa-miR-187-5p, hsa-miR-1908-5p, hsa-miR-371a-5p, and hsa-miR-550a-5p, that can be further optionally combined therewith or a combination thereof; and hsa-miR-4417, hsa-miR-4707-5p, hsa-miR-7847-3p, hsa-miR-2861, hsa-miR-4513, hsa-miR-7111-5p, hsa-miR-6777-5p, hsa-miR-7113-3p, hsa-miR-4648, hsa-miR-3184-5p, hsa-miR-4271, hsa-miR-6791-5p, hsa-miR-642a-3p, hsa-miR-7108-5p, hsa-miR-128-1-5p, hsa-miR-5196-5p, hsa-miR-3178, hsa-miR-3656, hsa-miR-92a-2-5p, hsa-miR-6769b-5p, hsa-miR-4689, hsa-miR-6076, hsa-miR-92b-5p, hsa-miR-6774-5p, hsa-miR-486-3p, hsa-miR-6806-5p, hsa-miR-6842-5p, hsa-miR-6716-5p, hsa-miR-557, hsa-miR-4673, hsa-miR-4674, hsa-miR-4442, hsa-miR-1915-3p, hsa-miR-4687-3p and hsa-miR-92b-3p, that can be further optionally combined therewith or a combination thereof; congeners thereof: transcripts thereof: or variants or derivatives thereof.

[0416] The expression levels of the target nucleic acids described above are increased or decreased (hereinafter, referred to as "increased/decreased") depending on the types of the target nucleic acids in subjects having pancreatic cancer as compared with healthy subjects. Hence, the composition of the present invention can be effectively used for measuring expression levels of the target nucleic acids in body fluids from subjects (e.g., humans) suspected of having pancreatic cancer and body fluids from healthy subjects and thereby detecting pancreatic cancer through the comparison thereof. The composition of the invention can also be effectively used for measuring expression levels of the target nucleic acids in body fluids from subjects (e.g., humans) suspected of having pancreatic cancer and body fluids from colorectal cancer patients, stomach cancer patients, esophageal cancer patients, liver cancer patients, and benign pancreaticobiliary disease patients and thereby specifically detecting pancreatic cancer while distinguished from other cancers, benign diseases or the like, through the comparison thereof.

[0417] 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 at least one of SEQ ID NOs: 1 to 104, 464 to 473, and 492 to 494, or a primer for amplifying a polynucleotide consisting of a nucleotide sequence represented by at least one of SEQ ID NOs: 1 to 104, 464 to 473, and 492 to 494.

[0418] The nucleic acid probe or the primer that can be used in the present invention may further 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: 105 to 122, or a primer for amplifying a polynucleotide consisting of a nucleotide sequence represented by at least one of SEQ ID NOs: 105 to 122.

[0419] The nucleic acid probe or the primer that can be used in the present invention may further 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: 349 to 383, or a primer for amplifying a polynucleotide consisting of a nucleotide sequence represented by at least one of SEQ ID NOs: 349 to 383.

[0420] Specifically, these nucleic acid probes or primers comprise a combination of one or more polynucleotides selected from: a group of polynucleotides comprising nucleotide sequences represented by any of SEQ ID NOs: 1 to 122, 349 to 383, 464 to 473, and 492 to 494 or nucleotide sequences derived from the nucleotide sequences by the replacement of u with t, and a group of complementary polynucleotides thereof; a group of polynucleotides respectively hybridizing under stringent conditions (mentioned later) to DNAs consisting of nucleotide sequences complementary to these nucleotide sequences, and a group of complementary polynucleotides thereof; and a group of polynucleotides comprising 15 or more, preferably 17 or more consecutive nucleotides and being from the nucleotide sequences of these polynucleotide groups. These polynucleotides can be used as nucleic acid probes and primers for detecting the pancreatic cancer markers as target nucleic acids.

[0421] More specifically, examples of the nucleic acid probes or the primers that can be used in the present invention include one or more polynucleotides 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: 1 to 104, 464 to 473, and 492 to 494 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: 1 to 104, 464 to 473,

and 492 to 494;

(c) a polynucleotide consisting of a nucleotide sequence complementary to a nucleotide sequence represented by any of SEQ ID NOs: 1 to 104, 464 to 473, and 492 to 494 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: 1 to 104, 464 to 473, and 492 to 494 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).

[0422] In addition to at least one or more polynucleotides selected from any of the polynucleotides (a) to (e), the nucleic acid probes or the primers that can be used in the present invention may further comprise any of the following polynucleotides (f) to (j):

(f) a polynucleotide consisting of a nucleotide sequence represented by any of SEQ ID NOs: 105 to 122 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: 105 to 122;

(h) a polynucleotide consisting of a nucleotide sequence complementary to a nucleotide sequence represented by any of SEQ ID NOs: 105 to 122 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: 105 to 122 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).

[0423] In addition to at least one or more polynucleotides selected from any of the polynucleotides (a) to (j), the nucleic acid probes or the primers that can be used in the present invention may further comprise any of the following polynucleotides (k) to (o):

(k) a polynucleotide consisting of a nucleotide sequence represented by any of SEQ ID NOs: 349 to 383 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: 349 to 383;

(m) a polynucleotide consisting of a nucleotide sequence complementary to a nucleotide sequence represented by any of SEQ ID NOs: 349 to 383 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: 349 to 383 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).

[0424] For the above-mentioned polynucleotides, the "fragment thereof comprising 15 or more consecutive nucleotides" can comprise, but is not limited to, the number of nucleotides in the range of, for example, from 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, from 19 consecutive nucleotides to less than the total number of nucleotides of the sequence, or the like, and is from the nucleotide sequence of each polynucleotide.

[0425] These polynucleotides or fragments thereof used in the present invention may each be DNA or may each be RNA.

[0426] The polynucleotides that can be used in the present invention can be prepared by use of a general technique such as a DNA recombination technique, a PCR method, or a method using an automatic DNA/RNA synthesizer.

[0427] The DNA recombination technique and the PCR method may employ techniques described in, for example, Ausubel et al., *Current Protocols in Molecular Biology*, John Wiley & Sons, US (1993); and Sambrook et al., *Molecular Cloning - A Laboratory Manual*, Cold Spring Harbor Laboratory Press, US (1989).

[0428] The human-derived hsa-miR-6893-5p, hsa-miR-6075, hsa-miR-6820-5p, hsa-miR-4294, hsa-miR-6729-5p, hsa-miR-4476, hsa-miR-6836-3p, hsa-miR-6765-3p, hsa-miR-6799-5p, hsa-miR-4530, hsa-miR-7641, hsa-miR-4454, hsa-miR-615-5p, hsa-miR-8073, hsa-miR-663a, hsa-miR-4634, hsa-miR-4450, hsa-miR-4792, hsa-miR-665, hsa-miR-7975, hsa-miR-7109-5p, hsa-miR-6789-5p, hsa-miR-4497, hsa-miR-6877-5p, hsa-miR-6880-5p, hsa-miR-7977, hsa-miR-4734, hsa-miR-6821-5p, hsa-miR-8089, hsa-miR-5585-3p, hsa-miR-6085, hsa-miR-6845-5p, hsa-miR-4651, hsa-

miR-4433-3p, hsa-miR-1231, hsa-miR-4665-5p, hsa-miR-7114-5p, hsa-miR-1238-5p, hsa-miR-8069, hsa-miR-4732-5p, hsa-miR-619-5p, hsa-miR-3622a-5p, hsa-miR-1260a, hsa-miR-6741-5p, hsa-miR-6781-5p, hsa-miR-6125, hsa-miR-6805-5p, hsa-miR-6132, hsa-miR-6872-3p, hsa-miR-6875-5p, hsa-miR-1908-3p, hsa-miR-4433b-3p, hsa-miR-4736, hsa-miR-5100, hsa-miR-6724-5p, hsa-miR-7107-5p, hsa-miR-6726-5p, hsa-miR-3185, hsa-miR-4638-5p, hsa-miR-1273g-3p, hsa-miR-6778-5p, hsa-miR-328-5p, hsa-miR-3679-3p, hsa-miR-1228-3p, hsa-miR-6779-5p, hsa-miR-4723-5p, hsa-miR-6850-5p, hsa-miR-760, hsa-miR-7704, hsa-miR-8072, hsa-miR-4486, hsa-miR-1913, hsa-miR-4656, hsa-miR-1260b, hsa-miR-7106-5p, hsa-miR-6889-5p, hsa-miR-6780b-5p, hsa-miR-6090, hsa-miR-4534, hsa-miR-4449, hsa-miR-5195-3p, hsa-miR-1202, hsa-miR-4467, hsa-miR-6515-3p, hsa-miR-4281, hsa-miR-4505, hsa-miR-4484, hsa-miR-6805-3p, hsa-miR-3135b, hsa-miR-3162-5p, hsa-miR-6768-5p, hsa-miR-6721-5p, hsa-miR-1227-5p, hsa-miR-6722-3p, hsa-miR-4286, hsa-miR-4746-3p, hsa-miR-6727-5p, hsa-miR-6816-5p, hsa-miR-4741, hsa-miR-4508, hsa-miR-940, hsa-miR-4327, hsa-miR-4665-3p, hsa-miR-718, hsa-miR-125a-3p, hsa-miR-204-3p, hsa-miR-1469, hsa-miR-575, hsa-miR-150-3p, hsa-miR-423-5p, hsa-miR-564, hsa-miR-3188, hsa-miR-1246, hsa-miR-602, hsa-miR-1290, hsa-miR-16-5p, hsa-miR-451a, hsa-miR-24-3p, hsa-miR-187-5p, hsa-miR-1908-5p, hsa-miR-371a-5p, hsa-miR-550a-5p, hsa-miR-4417, hsa-miR-4707-5p, hsa-miR-7847-3p, hsa-miR-2861, hsa-miR-4513, hsa-miR-7111-5p, hsa-miR-6777-5p, hsa-miR-7113-3p, hsa-miR-4648, hsa-miR-3184-5p, hsa-miR-4271, hsa-miR-6791-5p, hsa-miR-642a-3p, hsa-miR-7108-5p, hsa-miR-128-1-5p, hsa-miR-5196-5p, hsa-miR-3178, hsa-miR-3656, hsa-miR-92a-2-5p, hsa-miR-6769b-5p, hsa-miR-4689, hsa-miR-6076, hsa-miR-92b-5p, hsa-miR-6774-5p, hsa-miR-486-3p, hsa-miR-6806-5p, hsa-miR-6842-5p, hsa-miR-6716-5p, hsa-miR-557, hsa-miR-4673, hsa-miR-4674, hsa-miR-4442, hsa-miR-1915-3p, hsa-miR-4687-3p, hsa-miR-92b-3p, hsa-miR-1203, hsa-miR-663b, hsa-miR-4258, hsa-miR-4649-5p, hsa-miR-4516, hsa-miR-3619-3p, hsa-miR-6826-5p, hsa-miR-6757-5p, hsa-miR-3131, hsa-miR-1343-3p, hsa-miR-6775-5p, hsa-miR-6813-5p and hsa-miR-3940-5p represented by SEQ ID NOs: 1 to 122, 349 to 383, 464 to 473, and 492 to 494 are known in the art, and their obtainment 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.

[0429] Such nucleic acid probes or primers can be chemically synthesized using an automatic DNA synthesizer. In general, the 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 synthesizer is commercially available from, for example, Polygen GmbH, ABI, or Applied Biosystems, Inc.

[0430] Alternatively, the polynucleotides of the present invention can also be prepared by cDNA cloning methods. The cDNA cloning technique may employ, for example, microRNA Cloning Kit Wako.

[0431] In this context, the sequences of the nucleic acid probes and the primers for detecting the polynucleotide consisting of a nucleotide sequence represented by any of SEQ ID NOs: 1 to 122, 349 to 383, 464 to 473, and 492 to 494 do not exist as miRNAs or precursors thereof in the living body or *in vivo*. For example, the nucleotide sequences represented by SEQ ID NO: 36 and SEQ ID NO: 103 are produced from the precursor represented by SEQ ID NO: 159. This precursor has a hairpin-like structure as shown in Figure 1, and the nucleotide sequences represented by SEQ ID NO: 36 and SEQ ID NO: 103 have mismatch sequences with each other. As such, a nucleotide sequence completely complementary to the nucleotide sequence represented by SEQ ID NO: 36 or SEQ ID NO: 103 does not naturally occur *in vivo*. Therefore, the nucleic acid probes and the primers for detecting the nucleotide sequence represented by any of SEQ ID NOs: 1 to 122, 349 to 383, 464 to 473, and 492 to 494 have artificial nucleotide sequences that do not exist in the living body or *in vivo*.

3. Kit or device for detection of pancreatic cancer

[0432] The present invention also provides a kit or a device for the detection of pancreatic cancer, comprising one or more polynucleotides (which may include a variant, a fragment, or a derivative thereof) that can be used as nucleic acid probes or primers in the present invention for measuring target nucleic acids as pancreatic cancer markers.

[0433] The target nucleic acids as pancreatic cancer markers according to the present invention are at least one nucleic acid selected from the following group A:

Group A:

miR-6893-5p, miR-6075, miR-6820-5p, miR-4294, miR-6729-5p, miR-4476, miR-6836-3p, miR-6765-3p, miR-6799-5p, miR-4530, miR-7641, miR-4454, miR-615-5p, miR-8073, miR-663a, miR-4634, miR-4450, miR-4792, miR-665, miR-7975, miR-7109-5p, miR-6789-5p, miR-4497, miR-6877-5p, miR-6880-5p, miR-7977, miR-4734, miR-6821-5p, miR-8089, miR-5585-3p, miR-6085, miR-6845-5p, miR-4651, miR-4433-3p, miR-1231, miR-4665-5p, miR-7114-5p, miR-1238-5p, miR-8069, miR-4732-5p, miR-619-5p, miR-3622a-5p, miR-1260a, miR-6741-5p, miR-6781-5p, miR-6125, miR-6805-5p, miR-6132, miR-6872-3p, miR-6875-5p, miR-1908-3p, miR-4433b-3p, miR-4736, miR-5100, miR-6724-5p, miR-7107-5p, miR-6726-5p, miR-3185, miR-4638-5p, miR-1273g-3p, miR-6778-5p, miR-328-5p, miR-3679-3p, miR-1228-3p, miR-6779-5p, miR-4723-5p, miR-6850-5p,

EP 3 150 707 A1

miR-760, miR-7704, miR-8072, miR-4486, miR-1913, miR-4656, miR-1260b, miR-7106-5p, miR-6889-5p, miR-6780b-5p, miR-6090, miR-4534, miR-4449, miR-5195-3p, miR-1202, miR-4467, miR-6515-3p, miR-4281, miR-4505, miR-4484, miR-6805-3p, miR-3135b, miR-3162-5p, miR-6768-5p, miR-6721-5p, miR-1227-5p, miR-6722-3p, miR-4286, miR-4746-3p, miR-6727-5p, miR-6816-5p, miR-4741, miR-4508, miR-940, miR-4327, miR-4665-3p, miR-718, miR-1203, miR-663b, miR-4258, miR-4649-5p, miR-4516, miR-3619-3p, miR-6826-5p, miR-6757-5p, miR-3131, miR-1343-3p, miR-6775-5p, miR-6813-5p, and miR-3940-5p.

[0434] Additional target nucleic acids that may be optionally used in the measurement are at least one nucleic acid selected from the following group B:

Group B:

miR-125a-3p, miR-204-3p, miR-1469, miR-575, miR-150-3p, miR-423-5p, miR-564, miR-3188, miR-1246, miR-602, miR-1290, miR-16-5p, miR-451a, miR-24-3p, miR-187-5p, miR-1908-5p, miR-371a-5p, and miR-550a-5p.

[0435] Additional target nucleic acids that may be further optionally used in the measurement are at least one nucleic acid selected from the following group C:

Group C:

miR-4417, miR-4707-5p, miR-7847-3p, miR-2861, miR-4513, miR-7111-5p, miR-6777-5p, miR-7113-3p, miR-4648, miR-3184-5p, miR-4271, miR-6791-5p, miR-642a-3p, miR-7108-5p, miR-128-1-5p, miR-5196-5p, miR-3178, miR-3656, miR-92a-2-5p, miR-6769b-5p, miR-4689, miR-6076, miR-92b-5p, miR-6774-5p, miR-486-3p, miR-6806-5p, miR-6842-5p, miR-6716-5p, miR-557, miR-4673, miR-4674, miR-4442, miR-1915-3p, miR-4687-3p, and miR-92b-3p.

[0436] The kit or the device of the present invention comprises one or more nucleic acids capable of specifically binding to any of the target nucleic acids as the pancreatic cancer markers described above, preferably one or more polynucleotides selected from the polynucleotides described in the preceding Section 2, or variants thereof.

[0437] Specifically, the kit or the device of the present invention can comprise at least one or more polynucleotides comprising (or consisting of) a nucleotide sequence represented by any of SEQ ID NOs: 1 to 104, 464 to 473, and 492 to 494 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, a polynucleotide(s) hybridizing under stringent conditions to any of these polynucleotides, or a variant(s) or a fragment(s) comprising 15 or more consecutive nucleotides of any of these polynucleotide sequences.

[0438] The kit or the device of the present invention can further comprise one or more polynucleotides comprising (or consisting of) a nucleotide sequence represented by any of SEQ ID NOs: 105 to 122 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, a polynucleotide(s) comprising (or consisting of) a complementary sequence thereof, a polynucleotide(s) hybridizing under stringent conditions to any of these polynucleotides, a variant(s) or a fragment(s) comprising 15 or more consecutive nucleotides of any of these polynucleotide sequences.

[0439] The kit or the device of the present invention can further comprise one or more polynucleotides comprising (or consisting of) a nucleotide sequence represented by any of SEQ ID NOs: 349 to 383 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, a polynucleotide(s) hybridizing under stringent conditions to any of these polynucleotides, a variant(s) or a fragment(s) comprising 15 or more consecutive nucleotides of any of these polynucleotide sequences.

[0440] The fragment or fragments that can be comprised in the kit or the device of the present invention is/are, for example, one or more polynucleotides, preferably two or more polynucleotides, selected from the group consisting of the following polynucleotides (1) to (3):

(1) a polynucleotide comprising 15 or more consecutive nucleotides that are from a nucleotide sequence derived from a nucleotide sequence represented by any of SEQ ID NOs: 1 to 104, 464 to 473, and 492 to 494 by the replacement of u with t, or a complementary sequence thereof;

(2) a polynucleotide comprising 15 or more consecutive nucleotides that are from a nucleotide sequence derived from a nucleotide sequence represented by any of SEQ ID NOs: 105 to 122 by the replacement of u with t, or a complementary sequence thereof; and

(3) a polynucleotide comprising 15 or more consecutive nucleotides that are from a nucleotide sequence derived from a nucleotide sequence represented by any of SEQ ID NOs: 349 to 383 by the replacement of u with t, or a complementary sequence thereof.

5 [0441] In a preferred embodiment, the polynucleotide is a polynucleotide consisting of a nucleotide sequence represented by any of SEQ ID NOs: 1 to 104, 464 to 473, and 492 to 494 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.

10 [0442] In a preferred embodiment, the polynucleotide is a polynucleotide consisting of a nucleotide sequence represented by any of SEQ ID NOs: 105 to 122 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.

15 [0443] In a preferred embodiment, the polynucleotide is a polynucleotide consisting of a nucleotide sequence represented by any of SEQ ID NOs: 349 to 383 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.

[0444] 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.

20 [0445] In the present invention, the size of the polynucleotide fragment is 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.

25 [0446] Specific examples of the aforementioned combination constituting the kit or the device of the present invention can include the above-mentioned polynucleotides relevant to the combinations of SEQ ID NOs shown in Table 1 (i.e., SEQ ID NOs: 1 to 122, 349 to 383, 464 to 473, and 492 to 494 corresponding to the miRNA markers in Table 1). However, these are given merely for illustrative purposes, and all of various other possible combinations are included in the present invention.

30 [0447] The combination constituting the kit or the device for discriminating a pancreatic cancer patient from a healthy subject according to the present invention is desirably, for example, a combination of two or more polynucleotides consisting of the nucleotide sequences represented by SEQ ID NOs shown in Table 1. Usually, a combination of two of these polynucleotides can produce adequate performance.

35 [0448] The specific combination of two polynucleotides that consist of the above-mentioned nucleotide sequences or the complementary sequences thereof for discriminating a pancreatic cancer patient from a healthy subject is preferably a combination comprising at least one or more polynucleotides of the newly found polynucleotides consisting of the nucleotide sequences represented by SEQ ID NOs: 1 to 104, 349 to 383, 464 to 473, and 492 to 494, among the combinations constituted by two polynucleotides of the polynucleotides consisting of the nucleotide sequences represented by SEQ ID NOs: 1 to 122, 349 to 383, 464 to 473, and 492 to 494.

40 [0449] The combination of two polynucleotides that consist of the above-mentioned nucleotide sequences or the complementary sequences thereof for discriminating a pancreatic cancer patient from a healthy subject is preferably a combination of a plurality of polynucleotides comprising at least one polynucleotide selected from the group consisting of polynucleotides consisting of the nucleotide sequences represented by SEQ ID NOs: 1, 2, 4, 7, 15, 24, 105, 107, and 108 or complementary sequences thereof, with any of the polynucleotides of the other SEQ ID NOs.

45 [0450] Non-limiting examples of the combination comprising a polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 1 or a complementary sequence thereof among the combinations constituted by two polynucleotides of the polynucleotides consisting of the nucleotide sequences represented by SEQ ID NOs: 1 to 122, 349 to 383, 464 to 473, and 492 to 494 for discriminating a pancreatic cancer patient from a healthy subject are listed below:

- (1) a combination of SEQ ID NOs: 1 and 77 (markers: hsa-miR-6893-5p and hsa-miR-6780b-5p);
- (2) a combination of SEQ ID NOs: 1 and 119 (markers: hsa-miR-6893-5p and hsa-miR-187-5p); and
- (3) a combination of SEQ ID NOs: 1 and 20 (markers: hsa-miR-6893-5p and hsa-miR-7975).

50 [0451] Non-limiting examples of the combination comprising a polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 2 or a complementary sequence thereof among the combinations constituted by two polynucleotides of the polynucleotides consisting of the nucleotide sequences represented by SEQ ID NOs: 1 to 122, 349 to 383, 464 to 473, and 492 to 494 for discriminating a pancreatic cancer patient from a healthy subject are further listed below:

- (1) a combination of SEQ ID NOs: 2 and 105 (markers: hsa-miR-6075 and hsa-miR-125a-3p);
- (2) a combination of SEQ ID NOs: 2 and 16 (markers: hsa-miR-6075 and hsa-miR-4634); and

(3) a combination of SEQ ID NOs: 2 and 10 (markers: hsa-miR-6075 and hsa-miR-4530).

[0452] Non-limiting examples of the combination comprising a polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 4 or a complementary sequence thereof among the combinations constituted by two polynucleotides of the polynucleotides consisting of the nucleotide sequences represented by SEQ ID NOs: 1 to 122, 349 to 383, 464 to 473, and 492 to 494 for discriminating a pancreatic cancer patient from a healthy subject are further listed below:

- (1) a combination of SEQ ID NOs: 4 and 105 (markers: hsa-miR-4294 and hsa-miR-125a-3p);
- (2) a combination of SEQ ID NOs: 4 and 119 (markers: hsa-miR-4294 and hsa-miR-187-5p); and
- (3) a combination of SEQ ID NOs: 4 and 45 (markers: hsa-miR-4294 and hsa-miR-6781-5p).

[0453] Non-limiting examples of the combination comprising a polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 7 or a complementary sequence thereof among the combinations constituted by two polynucleotides of the polynucleotides consisting of the nucleotide sequences represented by SEQ ID NOs: 1 to 122, 349 to 383, 464 to 473, and 492 to 494 for discriminating a pancreatic cancer patient from a healthy subject are further listed below:

- (1) a combination of SEQ ID NOs: 7 and 105 (markers: hsa-miR-6836-3p and hsa-miR-125a-3p);
- (2) a combination of SEQ ID NOs: 7 and 34 (markers: hsa-miR-6836-3p and hsa-miR-4433-3p); and
- (3) a combination of SEQ ID NOs: 7 and 12 (markers: hsa-miR-6836-3p and hsa-miR-4454).

[0454] Non-limiting examples of the combination comprising a polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 105 or a complementary sequence thereof among the combinations constituted by two polynucleotides of the polynucleotides consisting of the nucleotide sequences represented by SEQ ID NOs: 1 to 122, 349 to 383, 464 to 473, and 492 to 494 for discriminating a pancreatic cancer patient from a healthy subject are further listed below:

- (1) a combination of SEQ ID NOs: 18 and 105 (markers: hsa-miR-4792 and hsa-miR-125a-3p);
- (2) a combination of SEQ ID NOs: 46 and 105 (markers: hsa-miR-6125 and hsa-miR-125a-3p); and
- (3) a combination of SEQ ID NOs: 105 and 494 (markers: hsa-miR-125a-3p and hsa-miR-3940-5p).

[0455] The combination of polynucleotides with cancer type specificity capable of discriminating a pancreatic 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 one polynucleotide selected from the group consisting of polynucleotides consisting of the nucleotide sequences represented by SEQ ID NOs: 2, 4, 6, 7, 9, 10, 25, 28, 30, 31, 38, 48, 82, 103, 105, 108, and 464 or complementary sequences thereof (hereinafter, this group is referred to as "cancer type-specific polynucleotide group 1"); and any of the polynucleotides of the other SEQ ID NOs.

[0456] The combination of polynucleotides with cancer type specificity capable of discriminating a pancreatic 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.

[0457] The combination of polynucleotides with cancer type specificity capable of discriminating a pancreatic cancer patient not only from a healthy subject but also from other cancer patients is more preferably a combination comprising at least one or more polynucleotides selected from the group consisting of polynucleotides consisting of the nucleotide sequences represented by SEQ ID NOs: 2, 4, 7, 10, and 25 or complementary sequences thereof (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. The number of the polynucleotides with cancer type specificity may be 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or more in the combination and is more preferably 4 or more in the combination. Usually, the combination of 4 polynucleotides of these polynucleotides can produce adequate performance.

[0458] 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 three polynucleotides selected from the cancer type-specific polynucleotide group 1 or complementary sequences thereof are listed below:

- (1) a combination of SEQ ID NOs: 2, 9, 105, and 7 (markers: hsa-miR-6075, hsa-miR-6799-5p, hsa-miR-125a-3p, and hsa-miR-6836-3p);
- (2) a combination of SEQ ID NOs: 2, 7, 108, and 464 (markers: hsa-miR-6075, hsa-miR-6836-3p, hsa-miR-575,

and hsa-miR-1203);

(3) a combination of SEQ ID NOs: 2, 31, 48, and 38 (markers: hsa-miR-6075, hsa-miR-6085, hsa-miR-6132, and hsa-miR-1238-5p);

(4) a combination of SEQ ID NOs: 2, 31, 28, and 48 (markers: hsa-miR-6075, hsa-miR-6085, hsa-miR-6821-5p, and hsa-miR-6132); and

(5) a combination of SEQ ID NOs: 2, 25, 105, and 10 (markers: hsa-miR-6075, hsa-miR-6880-5p, hsa-miR-125a-3p, and hsa-miR-4530).

[0459] Non-limiting examples of the combination of the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 4 or a complementary sequence thereof, with polynucleotides consisting of nucleotide sequences represented by SEQ ID NOs of three polynucleotides selected from the cancer type-specific polynucleotide group 1 or complementary sequences thereof are further listed below:

(1) a combination of SEQ ID NOs: 4, 31, 7, and 82 (markers: hsa-miR-4294, hsa-miR-6085, hsa-miR-6836-3p, and hsa-miR-1202);

(2) a combination of SEQ ID NOs: 4, 31, 28, and 82 (markers: hsa-miR-4294, hsa-miR-6085, hsa-miR-6821-5p, and hsa-miR-1202);

(3) a combination of SEQ ID NOs: 4, 10, 7, and 82 (markers: hsa-miR-4294, hsa-miR-4530, hsa-miR-6836-3p, and hsa-miR-1202);

(4) a combination of SEQ ID NOs: 4, 7, 82, and 103 (markers: hsa-miR-4294, hsa-miR-6836-3p, hsa-miR-1202, and hsa-miR-4665-3p); and

(5) a combination of SEQ ID NOs: 4, 105, 10, and 6 (markers: hsa-miR-4294, hsa-miR-125a-3p, hsa-miR-4530, and hsa-miR-4476).

[0460] Non-limiting examples of the combination of the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 7 or a complementary sequence thereof, with polynucleotides consisting of nucleotide sequences represented by SEQ ID NOs of three polynucleotides selected from the cancer type-specific polynucleotide group 1 or complementary sequences thereof are further listed below:

(1) a combination of SEQ ID NOs: 4, 7, 82, and 101 (markers: hsa-miR-4294, hsa-miR-6836-3p, hsa-miR-1202, and hsa-miR-940);

(2) a combination of SEQ ID NOs: 4, 7, 38, and 82 (markers: hsa-miR-4294, hsa-miR-6836-3p, hsa-miR-1238-5p, and hsa-miR-1202);

(3) a combination of SEQ ID NOs: 6, 7, 61, and 68 (markers: hsa-miR-4476, hsa-miR-6836-3p, hsa-miR-6778-5p, and hsa-miR-760);

(4) a combination of SEQ ID NOs: 4, 7, 47, and 82 (markers: hsa-miR-4294, hsa-miR-6836-3p, hsa-miR-6805-5p, and hsa-miR-1202); and

(5) a combination of SEQ ID NOs: 4, 7, 82, and 103 (markers: hsa-miR-4294, hsa-miR-6836-3p, hsa-miR-1202, and hsa-miR-4665-3p).

[0461] 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 three polynucleotides selected from the cancer type-specific polynucleotide group 1 or complementary sequences thereof are further listed below:

(1) a combination of SEQ ID NOs: 10, 47, 90, and 101 (markers: hsa-miR-4530, hsa-miR-6805-5p, hsa-miR-3162-5p, and hsa-miR-940);

(2) a combination of SEQ ID NOs: 10, 30, 103, and 365 (markers: hsa-miR-4530, hsa-miR-5585-3p, hsa-miR-4665-3, and hsa-miR-3178);

(3) a combination of SEQ ID NOs: 9, 10, 61, and 68 (markers: hsa-miR-6799-5p, hsa-miR-4530, hsa-miR-6778-5p, and hsa-miR-760);

(4) a combination of SEQ ID NOs: 10, 48, 68, and 90 (markers: hsa-miR-4530, hsa-miR-6132, hsa-miR-760, and hsa-miR-3162-5p); and

(5) a combination of SEQ ID NOs: 10, 30, 68, and 365 (markers: hsa-miR-4530, hsa-miR-5585-3p, hsa-miR-760, and hsa-miR-3178).

[0462] Non-limiting examples of the combination of the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 25 or a complementary sequence thereof, with polynucleotides consisting of nucleotide sequences

represented by SEQ ID NOs of three polynucleotides selected from the cancer type-specific polynucleotide group 1 or complementary sequences thereof are further listed below:

(1) a combination of SEQ ID NOs: 7, 25, 466, and 47 (markers: hsa-miR-6836-3p, hsa-miR-6880-5p, hsa-miR-4258, and hsa-miR-6805-5p);

(2) a combination of SEQ ID NOs: 7, 25, 48, and 466 (markers: hsa-miR-6836-3p, hsa-miR-6880-5p, hsa-miR-6132, and hsa-miR-4258);

(3) a combination of SEQ ID NOs: 7, 25, 28, and 466 (markers: hsa-miR-6836-3p, hsa-miR-6880-5p, hsa-miR-6821-5p, and hsa-miR-4258);

(4) a combination of SEQ ID NOs: 7, 25, 30, and 466 (markers: hsa-miR-6836-3p, hsa-miR-6880-5p, hsa-miR-5585-3p, and hsa-miR-4258); and

(5) a combination of SEQ ID NOs: 7, 25, 31, and 47 (markers: hsa-miR-6836-3p, hsa-miR-6880-5p, hsa-miR-6085, and hsa-miR-6805-5p).

[0463] The kit or the device of the present invention can also comprise a known polynucleotide(s) that enables detection of pancreatic cancer, or a polynucleotide(s) that will be found in the future, in addition to the polynucleotide(s) (which may include a variant(s), a fragment(s), and a derivative(s)) as described above according to the present invention.

[0464] The kit of the present invention can also comprise an antibody for measuring a marker or markers for pancreatic cancer examination known in the art, such as CEA, CA19-9, SPan-1, DUPAN-2, CA50, CA242, TAG-72, urinary fucose, POA, and TPS, in addition to the polynucleotide(s) according to the present invention as described above, and a variant or variants thereof or a fragment or fragments thereof.

[0465] These polynucleotides and variants thereof or fragments thereof contained in the kit of the present invention may be packaged in different containers either individually or in any combination.

[0466] The kit of the present invention may comprise a kit for extracting nucleic acids (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.

[0467] 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, variants thereof, derivatives thereof, or fragments thereof 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).

[0468] 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 target nucleic acids through the use of hybridization using this array.

[0469] 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 pancreatic 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 pancreatic 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 pancreatic cancer marker miRNAs, respectively, of the group 3 described above.

[0470] The kit or the device of the present invention can be used for detecting pancreatic cancer as described in Section 4 below.

4. Method for detecting pancreatic cancer

[0471] The present invention further provides a method for detecting pancreatic cancer, comprising using the kit or the device of the present invention (comprising the above-mentioned nucleic acid(s) that can be used in the present invention) as described in Section 3 above to measure expression levels of one or more pancreatic cancer-derived

genes represented by: an expression level(s) of pancreatic cancer-derived gene(s) selected from the following group of miRNAs, i.e., miR-6893-5p, miR-6075, miR-6820-5p, miR-4294, miR-6729-5p, miR-4476, miR-6836-3p, miR-6765-3p, miR-6799-5p, miR-4530, miR-7641, miR-4454, miR-615-5p, miR-8073, miR-663a, miR-4634, miR-4450, miR-4792, miR-665, miR-7975, miR-7109-5p, miR-6789-5p, miR-4497, miR-6877-5p, miR-6880-5p, miR-7977, miR-4734, miR-6821-5p, miR-8089, miR-5585-3p, miR-6085, miR-6845-5p, miR-4651, miR-4433-3p, miR-1231, miR-4665-5p, miR-7114-5p, miR-1238-5p, miR-8069, miR-4732-5p, miR-619-5p, miR-3622a-5p, miR-1260a, miR-6741-5p, miR-6781-5p, miR-6125, miR-6805-5p, miR-6132, miR-6872-3p, miR-6875-5p, miR-1908-3p, miR-4433b-3p, miR-4736, miR-5100, miR-6724-5p, miR-7107-5p, miR-6726-5p, miR-3185, miR-4638-5p, miR-1273g-3p, miR-6778-5p, miR-328-5p, miR-3679-3p, miR-1228-3p, miR-6779-5p, miR-4723-5p, miR-6850-5p, miR-760, miR-7704, miR-8072, miR-4486, miR-1913, miR-4656, miR-1260b, miR-7106-5p, miR-6889-5p, miR-6780b-5p, miR-6090, miR-4534, miR-4449, miR-5195-3p, miR-1202, miR-4467, miR-6515-3p, miR-4281, miR-4505, miR-4484, miR-6805-3p, miR-3135b, miR-3162-5p, miR-6768-5p, miR-6721-5p, miR-1227-5p, miR-6722-3p, miR-4286, miR-4746-3p, miR-6727-5p, miR-6816-5p, miR-4741, miR-4508, miR-940, miR-4327, miR-4665-3p and miR-718, miR-1203, miR-663b, miR-4258, miR-4649-5p, miR-4516, miR-3619-3p, miR-6826-5p, miR-6757-5p, miR-3131, miR-1343-3p, miR-6775-5p, miR-6813-5p, and miR-3940-5p; and optionally an expression level(s) of pancreatic cancer-derived gene(s) selected from the following group of miRNA: i.e., miR-125a-3p, miR-204-3p, miR-1469, miR-575, miR-150-3p, miR-423-5p, miR-564, miR-3188, miR-1246, miR-602, miR-1290, miR-16-5p, miR-451a, miR-24-3p, miR-187-5p, miR-1908-5p, miR-371a-5p, and miR-550a-5p; and optionally an expression level(s) of pancreatic cancer-derived gene(s) selected from the following group of miRNAs, i.e., miR-4417, miR-4707-5p, miR-7847-3p, miR-2861, miR-4513, miR-7111-5p, miR-6777-5p, miR-7113-3p, miR-4648, miR-3184-5p, miR-4271, miR-6791-5p, miR-642a-3p, miR-7108-5p, miR-128-1-5p, miR-5196-5p, miR-3178, miR-3656, miR-92a-2-5p, miR-6769b-5p, miR-4689, miR-6076, miR-92b-5p, miR-6774-5p, miR-486-3p, miR-6806-5p, miR-6842-5p, miR-6716-5p, miR-557, miR-4673, miR-4674, miR-4442, miR-1915-3p, miR-4687-3p, and miR-92b-3p, in a sample *in vitro*, further comparing, for example, the expression level(s) of the gene(s) in the sample (e.g., blood, serum, or plasma) collected from a subject suspected of having pancreatic cancer, with a control expression level(s) in the sample(s) collected from a healthy subject(s) (including a non-pancreatic cancer patient(s)), and evaluating the subject as having pancreatic cancer when the expression level(s) of the target nucleic acid(s) is statistically significantly different between the samples.

[0472] This method of the present invention enables a limitedly invasive, early diagnosis of the cancer with high sensitivity and high 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.

[0473] The method for extracting the pancreatic cancer-derived gene(s) 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^(TM) RNA extraction reagent from liquid sample kit (Toray Industries, Inc.). A general acidic phenol method (acid guanidinium-phenol-chloroform (AGPC)) may be used, or Trizol^(TM) (Life Technologies Corp.) may be used. The pancreatic cancer-derived gene(s) 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., Japan). Alternatively, a kit such as miRNeasy^(TM) Mini Kit (Qiagen N.V.) may be used, though the method is not limited thereto.

[0474] The present invention also provides use of the kit or the device of the present invention for detecting *in vitro* an expression product(s) of a pancreatic cancer-derived miRNA gene(s) in a sample derived from a subject.

[0475] In the method of the present invention, the kit or the device described above comprises a single polynucleotide or any possible combination of polynucleotides that can be used in the present invention as described above.

[0476] In the detection or (genetic) diagnosis of pancreatic 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^(TM) 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.

[0477] 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.

[0478] The kit or the device of the present invention is useful for the diagnosis of pancreatic cancer or the detection of the presence or absence of pancreatic cancer. Specifically, the detection of pancreatic cancer using the kit or the device can be performed by detecting *in vitro* an expression level(s) of a gene(s) using the nucleic acid probe(s) or the primer(s) contained in the kit or the device, in a sample such as blood, serum, plasma, or urine from a subject suspected of having pancreatic cancer. The subject suspected of having pancreatic cancer can be evaluated as having pancreatic cancer when the expression level(s) of a target miRNA marker(s) measured using polynucleotide(s) (including a variant(s),

a fragment(s), and a derivative(s) thereof) consisting of a nucleotide sequence(s) represented by at least one or more of SEQ ID NOs: 1 to 104, 464 to 473, and 492 to 494 or a complementary sequence(s) thereof, and optionally a nucleotide sequence(s) represented by one or more of SEQ ID NOs: 105 to 122 or a complementary sequence(s) thereof, and optionally a nucleotide sequence(s) represented by one or more of SEQ ID NOs: 349 to 383 or a complementary sequence(s) thereof, in the sample such as blood, serum, plasma, or urine of the subject, has a statistically significant difference compared to an expression level(s) thereof in the sample such as blood, serum, or plasma, or urine of a healthy subject.

[0479] The method of the present invention can be combined with a diagnostic imaging method such as abdominal ultrasonography, CT scanning, endoscopic retrograde cholangiopancreatography, or endoscopic ultrasonography. The method of the present invention is capable of specifically detecting pancreatic cancer and can substantially discriminate pancreatic cancer from the other cancers. Particularly, for bile duct cancer, some miRNA markers for pancreatic cancer can be commonly used. However, pancreatic cancer can be discriminated from bile duct cancer by a way of determining a discriminant boundary according to a discriminant. Alternatively, pancreatic cancer can be discriminated therefrom by combination with an additional diagnostic method such as the diagnostic imaging method as described above.

[0480] The method for detecting the absence of an expression product(s) of a pancreatic cancer-derived gene(s) or the presence of the expression product(s) of a pancreatic cancer-derived gene(s) 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 of a subject, and measuring the expression level(s) of the target gene(s) contained therein using one or more polynucleotides (including a variant(s), a fragment(s), or a derivative(s)) selected from the groups of polynucleotides of the present invention, to evaluate the presence or absence of pancreatic cancer or to detect pancreatic cancer. The method for detecting pancreatic cancer according to the present invention can also evaluate or diagnose, for example, the presence or absence of amelioration of the disease or the degree of amelioration thereof in a pancreatic cancer patient in the case that a therapeutic drug is administered to the patient for amelioration of the disease.

[0481] The method of the present invention can comprise, for example, the following steps (a), (b), and (c):

(a) a step of contacting *in vitro* a sample from a subject with a polynucleotide(s) contained in the kit or the device of the present invention;

(b) a step of measuring an expression level(s) of the target nucleic acid(s) in the sample using the polynucleotide(s) as a nucleic acid probe(s) or primer(s); and

(c) a step of evaluating the presence or absence of pancreatic cancer (cells) in the subject on the basis of the measurement results in the step (b).

[0482] Specifically, the present invention provides a method for detecting pancreatic cancer, comprising: measuring an expression level(s) of a target nucleic acid(s) in a sample of a subject using a nucleic acid(s) capable of specifically binding to at least one or more (preferably at least two or more) polynucleotides selected from the following miRNAs: miR-6893-5p, miR-6075, miR-6820-5p, miR-4294, miR-6729-5p, miR-4476, miR-6836-3p, miR-6765-3p, miR-6799-5p, miR-4530, miR-7641, miR-4454, miR-615-5p, miR-8073, miR-663a, miR-4634, miR-4450, miR-4792, miR-665, miR-7975, miR-7109-5p, miR-6789-5p, miR-4497, miR-6877-5p, miR-6880-5p, miR-7977, miR-4734, miR-6821-5p, miR-8089, miR-5585-3p, miR-6085, miR-6845-5p, miR-4651, miR-4433-3p, miR-1231, miR-4665-5p, miR-7114-5p, miR-1238-5p, miR-8069, miR-4732-5p, miR-619-5p, miR-3622a-5p, miR-1260a, miR-6741-5p, miR-6781-5p, miR-6125, miR-6805-5p, miR-6132, miR-6872-3p, miR-6875-5p, miR-1908-3p, miR-4433b-3p, miR-4736, miR-5100, miR-6724-5p, miR-7107-5p, miR-6726-5p, miR-3185, miR-4638-5p, miR-1273g-3p, miR-6778-5p, miR-328-5p, miR-3679-3p, miR-1228-3p, miR-6779-5p, miR-4723-5p, miR-6850-5p, miR-760, miR-7704, miR-8072, miR-4486, miR-1913, miR-4656, miR-1260b, miR-7106-5p, miR-6889-5p, miR-6780b-5p, miR-6090, miR-4534, miR-4449, miR-5195-3p, miR-1202, miR-4467, miR-6515-3p, miR-4281, miR-4505, miR-4484, miR-6805-3p, miR-3135b, miR-3162-5p, miR-6768-5p, miR-6721-5p, miR-1227-5p, miR-6722-3p, miR-4286, miR-4746-3p, miR-6727-5p, miR-6816-5p, miR-4741, miR-4508, miR-940, miR-4327, miR-4665-3p and miR-718, miR-1203, miR-663b, miR-4258, miR-4649-5p, miR-4516, miR-3619-3p, miR-6826-5p, miR-6757-5p, miR-3131, miR-1343-3p, miR-6775-5p, miR-6813-5p, and miR-3940-5p; and evaluating *in vitro* whether or not the subject has pancreatic cancer subject using the above-measured expression levels and control expression levels of a healthy subject(s) measured in the same way as above.

[0483] As used herein, the term "evaluation" is evaluation support based on results of *in vitro* examination, not physician's judgment.

[0484] As described above, in the method of the present invention, specifically, miR-6893-5p is hsa-miR-6893-5p, miR-6075 is hsa-miR-6075, miR-6820-5p is hsa-miR-6820-5p, miR-4294 is hsa-miR-4294, miR-6729-5p is hsa-miR-6729-5p, miR-4476 is hsa-miR-4476, miR-6836-3p is hsa-miR-6836-3p, miR-6765-3p is hsa-miR-6765-3p, miR-6799-5p is hsa-miR-6799-5p, miR-4530 is hsa-miR-4530, miR-7641 is hsa-miR-7641, miR-4454 is hsa-miR-4454, miR-615-5p is hsa-miR-615-5p, miR-8073 is hsa-miR-8073, miR-663a is hsa-miR-663a, miR-4634 is hsa-miR-4634, miR-4450 is hsa-miR-4450, miR-4792 is hsa-miR-4792, miR-665 is hsa-miR-665, miR-7975 is hsa-miR-7975, miR-7109-5p is hsa-

miR-7109-5p, miR-6789-5p is hsa-miR-6789-5p, miR-4497 is hsa-miR-4497, miR-6877-5p is hsa-miR-6877-5p, miR-6880-5p is hsa-miR-6880-5p, miR-7977 is hsa-miR-7977, miR-4734 is hsa-miR-4734, miR-6821-5p is hsa-miR-6821-5p, miR-8089 is hsa-miR-8089, miR-5585-3p is hsa-miR-5585-3p, miR-6085 is hsa-miR-6085, miR-6845-5p is hsa-miR-6845-5p, miR-4651 is hsa-miR-4651, miR-4433-3p is hsa-miR-4433-3p, miR-1231 is hsa-miR-1231, miR-4665-5p is hsa-miR-4665-5p, miR-7114-5p is hsa-miR-7114-5p, miR-1238-5p is hsa-miR-1238-5p, miR-8069 is hsa-miR-8069, miR-4732-5p is hsa-miR-4732-5p, miR-619-5p is hsa-miR-619-5p, miR-3622a-5p is hsa-miR-3622a-5p, miR-1260a is hsa-miR-1260a, miR-6741-5p is hsa-miR-6741-5p, miR-6781-5p is hsa-miR-6781-5p, miR-6125 is hsa-miR-6125, miR-6805-5p is hsa-miR-6805-5p, miR-6132 is hsa-miR-6132, miR-6872-3p is hsa-miR-6872-3p, miR-6875-5p is hsa-miR-6875-5p, miR-1908-3p is hsa-miR-1908-3p, miR-4433b-3p is hsa-miR-4433b-3p, miR-4736 is hsa-miR-4736, miR-5100 is hsa-miR-5100, miR-6724-5p is hsa-miR-6724-5p, miR-7107-5p is hsa-miR-7107-5p, miR-6726-5p is hsa-miR-6726-5p, miR-3185 is hsa-miR-3185, miR-4638-5p is hsa-miR-4638-5p, miR-1273g-3p is hsa-miR-1273g-3p, miR-6778-5p is hsa-miR-6778-5p, miR-328-5p is hsa-miR-328-5p, miR-3679-3p is hsa-miR-3679-3p, miR-1228-3p is hsa-miR-1228-3p, miR-6779-5p is hsa-miR-6779-5p, miR-4723-5p is hsa-miR-4723-5p, miR-6850-5p is hsa-miR-6850-5p, miR-760 is hsa-miR-760, miR-7704 is hsa-miR-7704, miR-8072 is hsa-miR-8072, miR-4486 is hsa-miR-4486, miR-1913 is hsa-miR-1913, miR-4656 is hsa-miR-4656, miR-1260b is hsa-miR-1260b, miR-7106-5p is hsa-miR-7106-5p, miR-6889-5p is hsa-miR-6889-5p, miR-6780b-5p is hsa-miR-6780b-5p, miR-6090 is hsa-miR-6090, miR-4534 is hsa-miR-4534, miR-4449 is hsa-miR-4449, miR-5195-3p is hsa-miR-5195-3p, miR-1202 is hsa-miR-1202, miR-4467 is hsa-miR-4467, miR-6515-3p is hsa-miR-6515-3p, miR-4281 is hsa-miR-4281, miR-4505 is hsa-miR-4505, miR-4484 is hsa-miR-4484, miR-6805-3p is hsa-miR-6805-3p, miR-3135b is hsa-miR-3135b, miR-3162-5p is hsa-miR-3162-5p, miR-6768-5p is hsa-miR-6768-5p, miR-6721-5p is hsa-miR-6721-5p, miR-1227-5p is hsa-miR-1227-5p, miR-6722-3p is hsa-miR-6722-3p, miR-4286 is hsa-miR-4286, miR-4746-3p is hsa-miR-4746-3p, miR-6727-5p is hsa-miR-6727-5p, miR-6816-5p is hsa-miR-6816-5p, miR-4741 is hsa-miR-4741, miR-4508 is hsa-miR-4508, miR-940 is hsa-miR-940, miR-4327 is hsa-miR-4327, miR-4665-3p is hsa-miR-4665-3p, miR-718 is hsa-miR-718, miR-1203 is hsa-miR-1203, miR-663b is hsa-miR-663b, miR-4258 is hsa-miR-4258, miR-4649-5p is hsa-miR-4649-5p, miR-4516 is hsa-miR-4516, miR-3619-3p is hsa-miR-3619-3p, miR-6826-5p is hsa-miR-6826-5p, miR-6757-5p is hsa-miR-6757-5p, miR-3131 is hsa-miR-3131, miR-1343-3p is hsa-miR-1343-3p, miR-6775-5p is hsa-miR-6775-5p, miR-6813-5p is hsa-miR-6813-5p, and miR-3940-5p is hsa-miR-3940-5p.

[0485] In the method of the present invention, specifically, the nucleic acid(s) (specifically, probe(s) or primer(s)) is 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: 1 to 104, 464 to 473, and 492 to 494 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: 1 to 104, 464 to 473, and 492 to 494;

(c) a polynucleotide consisting of a nucleotide sequence complementary to a nucleotide sequence represented by any of SEQ ID NOs: 1 to 104, 464 to 473, and 492 to 494 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: 1 to 104, 464 to 473, and 492 to 494 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).

[0486] The nucleic acid(s) further used in the method of the present invention can comprise a nucleic acid(s) capable of specifically binding to at least one or more polynucleotides selected from the following miRNAs: miR-125a-3p, miR-204-3p, miR-1469, miR-575, miR-150-3p, miR-423-5p, miR-564, miR-3188, miR-1246, miR-602, miR-1290, miR-16-5p, miR-451a, miR-24-3p, miR-187-5p, miR-1908-5p, miR-371a-5p, and miR-550a-5p

[0487] Specifically, miR-125a-3p is hsa-miR-125a-3p, miR-204-3p is hsa-miR-204-3p, miR-1469 is hsa-miR-1469, miR-575 is hsa-miR-575, miR-150-3p is hsa-miR-150-3p, miR-423-5p is hsa-miR-423-5p, miR-564 is hsa-miR-564, miR-3188 is hsa-miR-3188, miR-1246 is hsa-miR-1246, miR-602 is hsa-miR-602, miR-1290 is hsa-miR-1290, miR-16-5p is hsa-miR-16-5p, miR-451a is hsa-miR-451a, miR-24-3p is hsa-miR-24-3p, miR-187-5p is hsa-miR-187-5p, miR-1908-5p is hsa-miR-1908-5p, miR-371a-5p is hsa-miR-371a-5p, and miR-550a-5p is hsa-miR-550a-5p.

[0488] Specifically, the nucleic acid(s) is further 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: 105 to 122 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: 105 to 122;
- (h) a polynucleotide consisting of a nucleotide sequence complementary to a nucleotide sequence represented by any of SEQ ID NOs: 105 to 122 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: 105 to 122 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).

[0489] The nucleic acid(s) further used can comprise a nucleic acid capable of specifically binding to at least one or more polynucleotides selected from the following miRNAs: miR-4417, miR-4707-5p, miR-7847-3p, miR-2861, miR-4513, miR-7111-5p, miR-6777-5p, miR-7113-3p, miR-4648, miR-3184-5p, miR-4271, miR-6791-5p, miR-642a-3p, miR-7108-5p, miR-128-1-5p, miR-5196-5p, miR-3178, miR-3656, miR-92a-2-5p, miR-6769b-5p, miR-4689, miR-6076, miR-92b-5p, miR-6774-5p, miR-486-3p, miR-6806-5p, miR-6842-5p, miR-6716-5p, miR-557, miR-4673, miR-4674, miR-4442, miR-1915-3p, miR-4687-3p, and miR-92b-3p.

[0490] Specifically, miR-4417 is hsa-miR-4417, miR-4707-5p is hsa-miR-4707-5p, miR-7847-3p is hsa-miR-7847-3p, miR-2861 is hsa-miR-2861, miR-4513 is hsa-miR-4513, miR-7111-5p is hsa-miR-7111-5p, miR-6777-5p is hsa-miR-6777-5p, miR-7113-3p is hsa-miR-7113-3p, miR-4648 is hsa-miR-4648, miR-3184-5p is hsa-miR-3184-5p, miR-4271 is hsa-miR-4271, miR-6791-5p is hsa-miR-6791-5p, miR-642a-3p is hsa-miR-642a-3p, miR-7108-5p is hsa-miR-7108-5p, miR-128-1-5p is hsa-miR-128-1-5p, miR-5196-5p is hsa-miR-5196-5p, miR-3178 is hsa-miR-3178, miR-3656 is hsa-miR-3656, miR-92a-2-5p is hsa-miR-92a-2-5p, miR-6769b-5p is hsa-miR-6769b-5p, miR-4689 is hsa-miR-4689, miR-6076 is hsa-miR-6076, miR-92b-5p is hsa-miR-92b-5p, miR-6774-5p is hsa-miR-6774-5p, miR-486-3p is hsa-miR-486-3p, miR-6806-5p is hsa-miR-6806-5p, miR-6842-5p is hsa-miR-6842-5p, miR-6716-5p is hsa-miR-6716-5p, miR-557 is hsa-miR-557, miR-4673 is hsa-miR-4673, miR-4674 is hsa-miR-4674, miR-4442 is hsa-miR-4442, miR-1915-3p is hsa-miR-1915-3p, miR-4687-3p is hsa-miR-4687-3p, and miR-92b-3p is hsa-miR-92b-3p.

[0491] Specifically, the nucleic acid(s) further used is a polynucleotide(s) 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: 349 to 383 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: 349 to 383;
- (m) a polynucleotide consisting of a nucleotide sequence complementary to a nucleotide sequence represented by any of SEQ ID NOs: 349 to 383 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: 349 to 383 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).

[0492] Examples of the sample used in the method of the present invention can include samples prepared from living tissues (preferably pancreatic tissues) or body fluids such as blood, serum, plasma, and urine from subjects. 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.

[0493] As used herein, the subject refers to a mammal, for example, a primate such as a human or a monkey, a rodent such as a mouse or a rat, a pet animal such as a dog or a cat, and an athletic animal such as a horse without any limitation, and is preferably a human.

[0494] The steps of the method of the present invention can be changed according to the type of the sample to be assayed.

[0495] In the case of using RNA as an analyte, the detection of pancreatic cancer (cells) can comprise, for example, the following steps (a), (b), and (c):

- (a) a step of binding RNA prepared from a sample from a subject or complementary polynucleotides (cDNAs) transcribed from the RNA to a polynucleotide(s) in the kit or the device of the present invention;
- (b) a step of measuring the sample-derived RNA or the cDNAs synthesized from the RNA, which is/are bound to

the polynucleotide(s), by hybridization using the polynucleotide(s) as a nucleic acid probe(s) or by quantitative RT-PCR using the polynucleotide(s) as a primer(s); and
(c) a step of evaluating the presence or absence of pancreatic cancer (or pancreatic cancer-derived gene expression) on the basis of the measurement results of the step (b).

5

[0496] For example, various hybridization methods can be used for detecting, examining, evaluating, or diagnosing pancreatic cancer (or pancreatic 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.

10 **[0497]** 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(s) that can be used in the present invention. Specific examples thereof can include a method which comprises labeling the nucleic acid probe (or a complementary strand) with a radioisotope (^{32}P , ^{33}P , ^{35}S , etc.), a fluorescent material, or the like, hybridizing the labeled product with the tissue-derived RNA from a subject, which is 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., Japan)) or a fluorescence detector (examples thereof can include STORM 865 (GE Healthcare Japan Corp.)).

15 **[0498]** 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 comprises preparing cDNAs from the 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) prepared from the composition for detection 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.

20 **[0499]** In the case of using the nucleic acid array analysis, an RNA chip or a DNA chip in which the composition for detection of the present invention is attached as nucleic acid probes (single-stranded or double-stranded) 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 group of genes 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. In the present specification, the term "chip" includes these arrays. 3D-Gene^(TM) Human miRNA Oligo chip (Toray Industries, Inc.) can be used as the DNA chip, though the DNA chip is not limited thereto.

25 **[0500]** 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 composition for detection using an image detector (examples thereof can include Typhoon 9410 (GE Healthcare) and 3D-Gene^(TM) scanner (Toray Industries, Inc.)).

30 **[0501]** The "stringent conditions" used herein are, as mentioned above, conditions under which a nucleic acid probe hybridizes to its target sequence to a detectably 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.

35 **[0502]** The stringent conditions are defined by hybridization and subsequent washing. Examples of the hybridization conditions include, but not limited to, 30°C to 60°C for 1 to 24 hours in a solution containing SSC, a surfactant, formamide, dextran sulfate, a blocking agent(s), etc. In this context, 1 \times 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 comprise 3-10 \times SSC and 0.1-1% SDS. Examples of the conditions for the washing, following the hybridization, which is another condition to define the stringent conditions, can include conditions comprising continuous washing at 30°C in a solution containing 0.5 \times SSC and 0.1% SDS, at 30°C in a solution containing 0.2 \times SSC and 0.1% SDS, and at 30°C in a 0.05 \times 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.

40 **[0503]** 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.

[0504] Examples of the conditions for carrying out PCR using polynucleotide fragments in the kit of the present invention as primers include treatment for approximately 15 seconds to 1 minute at 5 to 10°C plus a T_m value calculated from the sequences of the primers, using a PCR buffer having composition such as 10 mM Tris-HCL (pH 8.3), 50 mM KCL, and 1 to 2 mM MgCl₂. Examples of the method for calculating such a T_m value include T_m value = 2 x (the number of adenine residues + the number of thymine residues) + 4 x (the number of guanine residues + the number of cytosine residues).

[0505] In the case of using the quantitative RT-PCR, a commercially available kit for measurement specially designed for quantitatively measuring miRNA, such as TaqMan^(TM) MicroRNA Assays (Life Technologies Corp.), LNA^(TM)-based MicroRNA PCR (Exiqon), or Ncode^(TM) miRNA qRT-PCT kit (Invitrogen Corp.) may be used.

[0506] 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 2⁶, preferably 2⁸, more preferably 2¹⁰ 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).

[0507] The present invention also provides a method comprising measuring target genes or gene expression levels in a sample from a subject using the polynucleotides, the kit, or the device (e.g., chip) for diagnosis of the present invention, or a combination thereof, preparing a discriminant (discriminant function) with gene expression levels in a sample from a pancreatic cancer patient and a sample from a healthy subject as supervising samples, and determining or evaluating the presence and/or absence of the pancreatic cancer-derived genes in the sample.

[0508] Specifically, the present invention further provides the method comprising: a first step of measuring *in vitro* expression levels of target genes in a plurality of samples known to determine or evaluate the presence and/or absence of the pancreatic cancer-derived genes in the samples, using the polynucleotides, the kit, or the device (e.g., chip) for diagnosis of the present invention, or a combination thereof; a second step of preparing a discriminant with the measurement values of the expression levels of the target genes obtained in the first step as supervising samples; a third step of measuring *in vitro* expression levels of the target genes in a sample derived from a subject in the same way as in the first step; and a fourth step of assigning the measurement values of the expression levels of the target genes obtained in the third step to the discriminant obtained in the second step, and determining or evaluating the presence and/or absence of the pancreatic cancer-derived genes in the sample on the basis of the results obtained from the discriminant, wherein the target genes can be detected using the polynucleotides or using polynucleotides, variants thereof, or fragments thereof contained in 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.

[0509] When a clustering boundary is a straight line or a hyperplane, the linear discriminant analysis is a method for determining the belonging 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.

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

[0510] 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.

[0511] 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 the 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 discriminant analysis,

direction w of projection is determined so as to maximize Formula 2. In this formula, μ represents an average input, n_g represents the number of data belonging to class g , and μ_g represents an average input of the data belonging to class g . The numerator and the denominator are the interclass variance and the intraclass variance, respectively, when each data is projected in the direction of the vector w . Discriminant coefficient w_i is determined by maximizing this ratio (Takafumi Kanamori et al., "Pattern Recognition", Kyoritsu Shuppan Co., Ltd., Tokyo, Japan (2009); and Richard O. et al., Pattern Classification Second Edition., Wiley-Interscience, 2000).

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

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

[0512] The Mahalanobis' distance is calculated according to Formula 3 in consideration of data correlation and can be used as nonlinear discriminant analysis for determining a cluster in which a data point belongs to, based on a short Mahalanobis' distance from the data point to that cluster. In 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.

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

[0513] SVM is a discriminant analysis method devised by V. Vapnik (The Nature of Statistical Learning 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 result of the discriminant analysis may be classes, may be a probability of being 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 analysis 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, Tokyo, Japan (2004); Nello Cristianini et al., Introduction to SVM, Kyoritsu Shuppan Co., Ltd., Tokyo, Japan (2008)).

[0514] C-support vector classification (C-SVC), one type of SVM, comprises preparing a hyperplane by supervising a data set 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).

[0515] 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 pancreatic cancer patient group and a healthy subject group. For example, pancreatic tissue examination can be used for a reference under which each subject is confirmed either as a pancreatic cancer patient or as a healthy subject.

[0516] 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 found to differ clearly in their gene expression levels between the two groups as explanatory variables and 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.

$$\min_a \frac{1}{2} a^T Q a - e^T a$$

Formula 4

5

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

[0517] Formula 5 is a finally obtained discriminant, and a group in which the data point belongs to 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 belonging of a group, a represents the corresponding coefficient, b represents a constant term, and K represents a kernel function.

10

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

Formula 5

15

[0518] 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.

20

$$K(x_i, x_j) = \exp \left(-r \|x_i - x_j\|^2 \right) \quad r < 0$$

Formula 6

25

[0519] 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 pancreatic cancer-derived target gene(s) in a sample derived from a subject, or for evaluating the expression level thereof by comparison with a control derived from a healthy subject.

[0520] The method of the present invention can comprise, for example, the following steps (a), (b), and (c):

30

(a) a step of measuring an expression level(s) of a target gene(s) in tissues containing pancreatic cancer-derived genes derived from pancreatic cancer patients and/or samples already known to be tissues containing no pancreatic cancer-derived gene(s) derived from healthy subjects, using the polynucleotide(s), the kit, or the device (e.g., DNA chip) for detection according to the present invention;

35

(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

40

(c) a step of measuring an expression level(s) of the target gene(s) in a sample derived from a subject using the polynucleotide(s), the kit, or the device (e.g., DNA chip) for diagnosis (detection) according to the present invention, assigning the obtained measurement value(s) to the discriminants prepared in the step (b), and determining or evaluating the presence and/or absence of expression of the pancreatic cancer-derived target genes in the sample, or evaluating the expression levels thereof by comparison with a healthy subject-derived control, on the basis of the obtained results.

45

[0521] 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(s) selected from the polynucleotides described in Section 2 above, or any fragment thereof. Specifically, the explanatory variable for discriminating a pancreatic cancer patient from a healthy subject according to the present invention is a gene expression level(s) selected from, for example, the following expression levels (1) to (3):

50

(1) a gene expression level(s) in the serum of a pancreatic cancer patient or a healthy subject measured by any RNA or DNA comprising 15 or more consecutive nucleotides in a nucleotide sequence represented by any of SEQ ID NOs: 1 to 104, 464 to 473, and 492 to 494 or a complementary sequence thereof, or nucleotides derived from the nucleotides by the replacement of u with t;

55

(2) a gene expression level(s) in the serum of a pancreatic cancer patient or a healthy subject measured by any RNA or DNA comprising 15 or more consecutive nucleotides in a nucleotide sequence represented by any of SEQ ID NOs: 105 to 122 or a complementary sequence thereof, or nucleotides derived from the nucleotides by the replacement of u with t; and

(3) a gene expression level(s) in the serum of a pancreatic cancer patient or a healthy subject measured by any RNA or DNA comprising 15 or more consecutive nucleotides in a nucleotide sequence represented by any of SEQ

ID NOs: 349 to 383 or a complementary sequence thereof, or nucleotides derived from the nucleotides by the replacement of u with t.

5 **[0522]** As described above, for the method for determining or evaluating the presence and/or absence of a pancreatic cancer-derived gene(s) in a sample derived from a subject, the preparation of a discriminant requires a discriminant prepared from a training cohort. For enhancing the accuracy of the discriminant, it is necessary to use genes having clear difference between two groups in the training cohort when preparing the discriminant.

10 **[0523]** Each gene that is used for an explanatory variable in a discriminant is preferably determined as follows. First, comprehensive gene expression levels of a pancreatic cancer patient group and comprehensive gene expression levels of a healthy subject group, both of which are 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.

15 **[0524]** The gene can be regarded as being statistically significant when the critical rate (significance level) as the P value obtained by the test is smaller than, for example, 5%, 1%, or 0.01%.

20 **[0525]** 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.

25 **[0526]** Instead of the 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 pancreatic 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 pancreatic 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.

30 **[0527]** 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 discrimination accuracy include a method of constructing a discriminant in every combination of genes that satisfy the significance level being P value, and a method of repetitively evaluating the genes for use in the preparation of a discriminant while increasing the number of genes 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 pancreatic cancer patient or healthy subject is assigned as an explanatory variable to this discriminant to calculate discrimination results of the group to which this independent pancreatic cancer patient or healthy subject belongs. Specifically, the found gene set for diagnosis and the discriminant constructed using the gene set for diagnosis can be evaluated in an independent sample cohort to find a more universal gene set for diagnosis capable of detecting pancreatic cancer and a more universal method for discriminating pancreatic cancer.

35 **[0528]** Split-sample method is preferably used for evaluating the 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 using the training cohort. Accuracy, sensitivity, and specificity are calculated using a result of discriminating a validation cohort according to the discriminant, and a true group to which the validation cohort belongs, to evaluate the performance of the discriminant. On the other hand, instead of dividing a data set, the 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 analysis using a newly prepared sample cohort for evaluation of the performance of the discriminant.

40 **[0529]** The present invention provides polynucleotides for disease diagnosis useful in the diagnosis and treatment of pancreatic cancer, a method for detecting pancreatic cancer using the polynucleotide(s), and a kit and a device for the detection of pancreatic cancer, comprising the polynucleotide(s). Particularly, in order to select a gene(s) for diagnosis and prepare a discriminant so as to exhibit accuracy beyond the pancreatic cancer diagnosis methods using the existing tumor markers CEA and CA19-9, a gene set for diagnosis and a discriminant for the method of the present invention can be constructed, which exhibit accuracy beyond CEA and CA19-9, for example, by comparing expressed genes in serum from a patient confirmed to be negative using CEA and CA19-9 but finally found to have pancreatic cancer by detailed examination such as computed tomography using a contrast medium, with genes expressed in serum from a patient having no pancreatic cancer.

45 **[0530]** 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 any of SEQ ID NOs: 1 to 104, 464 to 473, and 492 to 494 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, or a complementary

sequence thereof as described above; and optionally one or two or more of the polynucleotides based on a nucleotide sequence represented by any of SEQ ID NOs: 105 to 122 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, 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: 349 to 383 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, or a complementary sequence thereof. Further, a discriminant is constructed using expression levels of the gene set for diagnosis in samples from class I pancreatic cancer patients as a result of tissue diagnosis and samples from class II healthy subjects as a result of tissue diagnosis. As a result, the presence or absence of pancreatic 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 an unknown sample.

EXAMPLES

[0531] 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 of pancreatic cancer patient and healthy subject>

[0532] Sera were collected using VENOJECT II vacuum blood collecting tube VP-AS109K60 (Terumo Corp., Japan) from 100 healthy subjects and 67 pancreatic cancer patients (1 case with stage IB, 10 cases with stage IIB, 17 cases with stage III, and 39 cases with stage IV) confirmed to have no cancer in organs other than the pancreas after obtainment of informed consent, and used as a training cohort. Likewise, sera were collected using VENOJECT II vacuum blood collecting tube VP-AS109K60 (Terumo Corp.) from 50 healthy subjects and 33 pancreatic cancer patients (1 case with stage IB, 2 cases with stage IIA, 4 cases with stage IIB, 11 cases with stage III, and 15 cases with stage IV) confirmed to have no cancer in organs other than the pancreas after obtainment of informed consent, and used as a validation cohort.

<Extraction of total RNA>

[0533] Total RNA was obtained using a reagent for RNA extraction in 3D-Gene^(TM) RNA extraction reagent from liquid sample kit (Toray Industries, Inc., Japan) according to the protocol provided by the manufacturer from 300 μ L of the serum sample obtained from each of 250 persons in total of 150 healthy subjects and 100 pancreatic cancer patients included in the training cohort and the validation cohort.

<Measurement of gene expression level>

[0534] miRNAs in the total RNA obtained from the serum samples of each of 250 persons in total of 150 healthy subjects and 100 pancreatic cancer patients included in the training cohort and the validation cohort were fluorescently labeled using 3D-Gene^(TM) 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^(TM) 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 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^(TM) scanner (Toray Industries, Inc.) to obtain images. Fluorescence intensity was digitized using 3D-Gene^(TM) 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 sera were obtained for the 100 pancreatic 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 of other cancers and benign diseases>

5 **[0535]** Sera were collected using VENOJECT II vacuum blood collecting tube VP-AS109K60 (Terumo Corp.) from each of 35 colorectal cancer patients, 37 stomach cancer patients, 32 esophageal cancer patients, 38 liver cancer patients, and 13 benign pancreaticobiliary disease patients confirmed to have no cancer in other organs after obtainment of informed consent, and used as a training cohort together with the samples of 67 pancreatic cancer patients (1 case with stage IIA, 11 cases with stage IIB, 17 cases with stage III, and 38 cases with stage IV) and 93 healthy subjects of Reference Example 1. Likewise, sera were collected using VENOJECT II vacuum blood collecting tube VP-AS109K60 (Terumo Corp.) from each of 15 colorectal cancer patients, 13 stomach cancer patients, 18 esophageal cancer patients, 12 liver cancer patients, and 8 benign pancreaticobiliary disease patients confirmed to have no cancer in other organs after obtainment of informed consent, and used as a validation cohort together with the samples of 33 pancreatic cancer patients (2 cases with stage IB, 1 case with stage IIA, 3 cases with stage IIB, 11 cases with stage III, and 16 cases with stage IV) and 57 healthy subjects of Reference Example 1. Subsequent extraction of total RNA and measurement and analysis of gene expression levels were conducted in the same way as in Reference Example 1.

[Example 1]

20 <Selection of gene markers using the training cohort, and method for evaluating pancreatic cancer discriminant performance of the single gene marker using the validation cohort>

[0536] In this Example, a gene marker for discriminating a pancreatic cancer patient from a healthy subject was selected from the training cohort and studied in the validation cohort independent of the training cohort.

25 **[0537]** Specifically, first, the miRNA expression levels of the training cohort and the validation cohort obtained in the preceding Reference Examples were combined and normalized by quantile normalization.

[0538] Next, genes for diagnosis were selected using the training cohort. Here, in order to acquire diagnostic markers with higher reliability, only genes having the expression level of 2⁶ or higher in 50% or more of the samples in either of the pancreatic cancer patient group of the training cohort or the healthy subject group of the training cohort were selected. In order to further acquire statistically significant genes for discriminating a pancreatic cancer patient group from a healthy subject group, the P value obtained by two-tailed 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 and described in Table 2.

30 **[0539]** In this way, hsa-miR-6893-5p, hsa-miR-6075, hsa-miR-6820-5p, hsa-miR-4294, hsa-miR-6729-5p, hsa-miR-4476, hsa-miR-6836-3p, hsa-miR-6765-3p, hsa-miR-6799-5p, hsa-miR-4530, hsa-miR-7641, hsa-miR-4454, hsa-miR-615-5p, hsa-miR-8073, hsa-miR-663a, hsa-miR-4634, hsa-miR-4450, hsa-miR-4792, hsa-miR-665, hsa-miR-7975, hsa-miR-7109-5p, hsa-miR-6789-5p, hsa-miR-4497, hsa-miR-6877-5p, hsa-miR-6880-5p, hsa-miR-7977, hsa-miR-4734, hsa-miR-6821-5p, hsa-miR-8089, hsa-miR-5585-3p, hsa-miR-6085, hsa-miR-6845-5p, hsa-miR-4651, hsa-miR-4433-3p, hsa-miR-1231, hsa-miR-4665-5p, hsa-miR-7114-5p, hsa-miR-1238-5p, hsa-miR-8069, hsa-miR-4732-5p, hsa-miR-619-5p, hsa-miR-3622a-5p, hsa-miR-1260a, hsa-miR-6741-5p, hsa-miR-6781-5p, hsa-miR-6125, hsa-miR-6805-5p, hsa-miR-6132, hsa-miR-6872-3p, hsa-miR-6875-5p, hsa-miR-1908-3p, hsa-miR-4433b-3p, hsa-miR-4736, hsa-miR-5100, hsa-miR-6724-5p, hsa-miR-7107-5p, hsa-miR-6726-5p, hsa-miR-3185, hsa-miR-4638-5p, hsa-miR-1273g-3p, hsa-miR-6778-5p, hsa-miR-328-5p, hsa-miR-3679-3p, hsa-miR-1228-3p, hsa-miR-6779-5p, hsa-miR-4723-5p, hsa-miR-6850-5p, hsa-miR-760, hsa-miR-7704, hsa-miR-8072, hsa-miR-4486, hsa-miR-1913, hsa-miR-4656, hsa-miR-1260b, hsa-miR-7106-5p, hsa-miR-6889-5p, hsa-miR-6780b-5p, hsa-miR-6090, hsa-miR-4534, hsa-miR-4449, hsa-miR-5195-3p, hsa-miR-1202, hsa-miR-4467, hsa-miR-6515-3p, hsa-miR-4281, hsa-miR-4505, hsa-miR-4484, hsa-miR-6805-3p, hsa-miR-3135b, hsa-miR-3162-5p, hsa-miR-6768-5p, hsa-miR-6721-5p, hsa-miR-1227-5p, hsa-miR-6722-3p, hsa-miR-4286, hsa-miR-4746-3p, hsa-miR-6727-5p, hsa-miR-6816-5p, hsa-miR-4741, hsa-miR-4508, hsa-miR-940, hsa-miR-4327, hsa-miR-4665-3p, hsa-miR-718, hsa-miR-125a-3p, hsa-miR-204-3p, hsa-miR-1469, hsa-miR-575, hsa-miR-150-3p, hsa-miR-423-5p, hsa-miR-564, hsa-miR-3188, hsa-miR-1246, hsa-miR-602, hsa-miR-1290, hsa-miR-16-5p, hsa-miR-451a, hsa-miR-24-3p, hsa-miR-187-5p, hsa-miR-1908-5p, hsa-miR-371a-5p, and hsa-miR-550a-5p genes, and the nucleotide sequences of SEQ ID NOs: 1 to 122 related thereto were found.

45 **[0540]** A discriminant for determining the presence or absence of pancreatic cancer was further prepared by Fisher's discriminant analysis with the expression levels of these genes as indicators. Specifically, any newly found polynucleotide consisting of a nucleotide sequence represented by any of SEQ ID NOs: 1 to 104 among the 122 genes selected in the training cohort was input to Formula 2 above to prepare a discriminant. Calculated accuracy, sensitivity, and specificity are shown in Table 3. In this respect, a discriminant coefficient and a constant term are shown in Table 4.

[0541] 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 independent samples (Table 3). For example, the expression level measurement value of the nucleotide sequence represented by SEQ ID NO: 1 was compared between the healthy subjects (50 persons) and the pancreatic cancer patients (33 persons) in the validation cohort. As a result, the gene expression level measurement values in the training cohort were found to be significantly lower in the pancreatic cancer patient group than in the healthy subject group (see the left diagram of Figure 2). These results were also reproducible in the validation cohort (see the right diagram of Figure 2). Likewise, the results obtained about the other polynucleotides shown in SEQ ID NOs: 1 to 122 showed that the gene expression level measurement values were significantly lower (-) or higher (+) in the pancreatic cancer patient group than in the healthy subject group (Table 2). 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 correctly or incorrectly identified samples in the detection of pancreatic cancer was calculated using the threshold (8.02) that was set in the training cohort and discriminated between the two groups. As a result, 30 true positives, 49 true negatives, 1 false positive, and 3 false negatives were obtained. From these values, 95% accuracy, 91% sensitivity, and 98% specificity were obtained as the detection performance. In this way, the detection performance was calculated as to all of the polynucleotides shown in SEQ ID NOs: 1 to 122, and described in Table 3. Among the polynucleotides consisting of the nucleotide sequences represented by SEQ ID NOs: 1 to 104 shown in Table 2, for example, 14 polynucleotides consisting of the nucleotide sequences represented by SEQ ID NOs: 1, 2, 4, 5, 7, 9, 11, 18, 21, 22, 24, 25, 35, and 46 exhibited sensitivity of 87.9%, 90.9%, 87.9%, 81.8%, 90.9%, 78.8%, 78.8%, 78.8%, 84.8%, 78.8%, 81.8%, 81.8%, 93.9%, and 81.8%, respectively, in the validation cohort (Table 3). Also, these polynucleotides were able to correctly identify one stage 1 pancreatic cancer sample contained in the validation cohort as a pancreatic cancer sample. Furthermore, these polynucleotides were able to correctly discriminate pancreatic cancer as to any of the tumors occupying the head, the body, and the tail of the pancreas in the validation cohort, and, particularly, were able to detect tumors even in the tail of the pancreas, which are prone to delayed diagnosis. As seen from Comparative Example mentioned later, the existing markers CEA and CA19-9 had sensitivity of 45.5% and 75.8%, respectively, in the validation cohort (Table 5), demonstrating that, for example, the 14 polynucleotides consisting of the nucleotide sequences represented by SEQ ID Nos: 1, 2, 4, 5, 7, 9, 11, 18, 21, 22, 24, 25, 35, and 46 can discriminate, each alone, pancreatic cancer in the validation cohort with sensitivity beyond CA19-9.

[Example 2]

<Method A for evaluating pancreatic cancer discriminant performance by combination of plurality of gene markers using samples in the validation cohort>

[0542] In this Example, a method for evaluating pancreatic cancer discriminant performance by a combination of the gene markers selected in Example 1 was studied.

[0543] Specifically, Fisher's discriminant analysis was conducted as to 7,228 combinations of two expression level measurement values comprising at least one or more of the expression level measurement values of the newly found polynucleotides consisting of the nucleotide sequences represented by SEQ ID NOs: 1 to 104 among the polynucleotides consisting of the nucleotide sequences represented by SEQ ID NOs: 1 to 122 selected in Example 1, to construct a discriminant for determining the presence or absence of pancreatic 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 independent samples. 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 (50 persons) and the pancreatic cancer patients (33 persons) in the validation cohort. As a result, a scatter diagram that significantly separated the expression level measurement values of the pancreatic cancer patient group from those of the healthy subject group was obtained in the training cohort (see the left diagram of Figure 3). These results were also reproducible 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 pancreatic 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 the newly found polynucleotides consisting of the nucleotide sequences represented by SEQ ID NOs: 1 to 104 among the polynucleotides consisting of the nucleotide sequences represented by SEQ ID NOs: 1 to 122. 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 were correctly or incorrectly identified pancreatic cancer was calculated using the threshold ($0 = 1.74x + y + 5.14$) that was set in the training cohort and discriminated between the two groups. As a result, 30 true positives, 49 true negatives, 1 false positive, and 3 false negatives were obtained. From these values, 95% accuracy, 91% sensitivity, and 98% specificity were obtained as the detection performance. In this way, the detection performance was calculated for the combinations of two expression level measurement values comprising at least one or more of the expression level measurement values of the newly found polynucleotides consisting of the nucleotide sequences rep-

EP 3 150 707 A1

resented by SEQ ID NOs: 1 to 104 among the polynucleotides consisting of the nucleotide sequences represented by SEQ ID NOs: 1 to 122, and the 2,619 combinations that showed sensitivity better than the sensitivity (75.8%) of the existing marker in the validation cohort, were described in Table 6.

[0544] The discriminant analysis for pancreatic cancer in the validation cohort was performed using the 7,228 combinations of the expression level measurement values of the polynucleotides. As a result, for example, the combinations of the expression level measurement values of the polynucleotides consisting of the nucleotide sequences represented by SEQ ID NOs: 2 and 105, SEQ ID NOs: 18 and 105, SEQ ID NOs: 46 and 105, and SEQ ID NOs: 55 and 105 exhibited sensitivity of 100%, 100%, and 100%, respectively, in the validation cohort. In this way, the 2,691 combinations of the expression level measurement values of the polynucleotides having sensitivity beyond the existing marker CA19-9 (Table 5) were obtained in the validation cohort. All of the nucleotide sequences 1 to 122 described in Table 2 obtained in Example 1 were employed at least once in these combinations. These results demonstrated that the combinations of two 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 122 can detect pancreatic cancer with sensitivity beyond CA19-9 in the validation cohort.

[0545] Thus, markers capable of detecting pancreatic cancer with excellent sensitivity are obtained even if 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 122 are combined. For example, the polynucleotides consisting of the nucleotide sequences represented by SEQ ID NOs: 1 to 122 selected in Example 1 were ranked in the descending order of their P values which indicate statistical significance, and detection performance was calculated using combinations of one or more miRNAs to which the miRNAs were added one by one from the top to the bottom according to the rank. As a result, the sensitivity in the validation cohort was 87.9% for 2 miRNAs, 90.9% for 3 miRNAs, 100% for 5 miRNAs, 100% for 10 miRNAs, 100% for 20 miRNAs, 100% for 50 miRNAs, 100% for 100 miRNAs, and 100% for 122 miRNAs. These values of the sensitivity were higher than the sensitivity of the existing tumor marker in blood, demonstrating that even combinations of a plurality of the miRNAs can serve as excellent markers for the detection of pancreatic cancer. In this context, the combinations of a plurality of the miRNAs are not limited to the combinations of the miRNAs added in the order of statistically significant difference as described above, and any combination of a plurality of the miRNAs can be used in the detection of pancreatic cancer.

[0546] From these results, it can be concluded that all of the polynucleotides consisting of the nucleotide sequences represented by SEQ ID NOs: 1 to 122 serve as excellent diagnostic markers.

[0547] Tables 2, 3, 4, 5, and 6 mentioned above are as follows.

[Table 2]

SEQ ID NO:	Gene name	P value after Bonferroni correction	Expression level in pancreatic cancer patient relative to healthy subject
1	hsa-miR-6893-5p	7.19E-46	-
2	hsa-miR-6075	1.91E-29	+
3	hsa-miR-6820-5p	1.78E-27	-
4	hsa-miR-4294	3.27E-27	-
5	hsa-miR-6729-5p	6.76E-26	+
6	hsa-miR-4476	8.49E-25	-
7	hsa-miR-6836-3p	1.97E-22	+
8	hsa-miR-6765-3p	4.75E-22	-
9	hsa-miR-6799-5p	5.00E-19	-
10	hsa-miR-4530	9.09E-19	-
11	hsa-miR-7641	7.84E-18	-
12	hsa-miR-4454	1.29E-17	-
13	hsa-miR-615-5p	3.14E-17	-
14	hsa-miR-8073	3.61E-17	+
15	hsa-miR-663a	1.72E-16	+
16	hsa-miR-4634	2.55E-16	+

EP 3 150 707 A1

(continued)

SEQIDNO:	Gene name	P value after Bonferroni correction	Expression level in pancreatic cancer patient relative to healthy subject	
5	17	hsa-miR-4450	3.14E-16	-
	18	hsa-miR-4792	3.80E-16	+
	19	hsa-miR-665	7.86E-16	+
10	20	hsa-miR-7975	8.48E-15	-
	21	hsa-miR-7109-5p	3.23E-14	-
	22	hsa-miR-6789-5p	4.58E-13	+
	23	hsa-miR-4497	5.38E-13	-
15	24	hsa-miR-6877-5p	5.58E-13	-
	25	hsa-miR-6880-5p	6.14E-13	-
	26	hsa-miR-7977	6.28E-13	-
20	27	hsa-miR-4734	6.79E-13	+
	28	hsa-miR-6821-5p	8.22E-13	-
	29	hsa-miR-8089	9.61E-13	-
	30	hsa-miR-5585-3p	1.38E-12	+
25	31	hsa-miR-6085	4.32E-12	-
	32	hsa-miR-6845-5p	1.41E-11	+
	33	hsa-miR-4651	1.53E-11	-
30	34	hsa-miR-4433-3p	5.65E-11	+
	35	hsa-miR-1231	1.38E-10	+
	36	hsa-miR-4665-5p	2.54E-10	-
	37	hsa-miR-7114-5p	5.73E-10	-
35	38	hsa-miR-1238-5p	6.26E-10	+
	39	hsa-miR-8069	7.39E-10	+
	40	hsa-miR-4732-5p	8.03E-10	+
40	41	hsa-miR-619-5p	2.23E-09	+
	42	hsa-miR-3622a-5p	2.53E-09	-
	43	hsa-miR-1260a	3.84E-09	-
	44	hsa-miR-6741-5p	6.57E-09	-
45	45	hsa-miR-6781-5p	6.86E-09	+
	46	hsa-miR-6125	7.51E-09	+
	47	hsa-miR-6805-5p	8.71E-09	+
50	48	hsa-miR-6132	1.71E-08	-
	49	hsa-miR-6872-3p	1.74E-08	-
	50	hsa-miR-6875-5p	2.76E-08	+
	51	hsa-miR-1908-3p	2.77E-08	+
55	52	hsa-miR-4433b-3p	5.12E-08	+
	53	hsa-miR-4736	5.45E-08	+

EP 3 150 707 A1

(continued)

SEQIDNO:	Gene name	P value after Bonferroni correction	Expression level in pancreatic cancer patient relative to healthy subject
5	54	7.94E-08	-
	55	9.14E-08	+
	56	9.80E-08	-
10	57	2.49E-07	-
	58	2.57E-07	+
	59	6.78E-07	-
	60	6.87E-07	+
15	61	6.95E-07	+
	62	7.01E-07	-
	63	7.68E-07	+
20	64	9.27E-07	+
	65	1.28E-06	-
	66	1.35E-06	-
	67	1.68E-06	+
25	68	1.69E-06	-
	69	1.82E-06	-
	70	5.28E-06	+
30	71	8.48E-06	+
	72	1.02E-05	+
	73	1.36E-05	+
	74	3.21E-05	-
35	75	3.55E-05	-
	76	4.00E-05	-
	77	4.32E-05	+
40	78	5.02E-05	+
	79	1.36E-04	-
	80	1.63E-04	+
	81	1.70E-04	-
45	82	1.83E-04	-
	83	7.51E-04	+
	84	8.23E-04	+
50	85	8.83E-04	-
	86	8.88E-04	-
	87	9.98E-04	+
	88	1.04E-03	+
55	89	1.11E-03	-
	90	1.26E-03	-

EP 3 150 707 A1

(continued)

SEQIDNO:	Gene name	P value after Bonferroni correction	Expression level in pancreatic cancer patient relative to healthy subject
5	91	1.45E-03	-
	92	1.57E-03	+
	93	1.65E-03	+
10	94	1.66E-03	+
	95	1.73E-03	-
	96	1.83E-03	+
	97	3.32E-03	-
15	98	4.09E-03	+
	99	4.57E-03	+
	100	6.50E-03	+
20	101	7.02E-03	-
	102	7.54E-03	-
	103	7.88E-03	+
	104	9.73E-03	+
25	105	2.01E-50	-
	106	1.58E-30	-
	107	1.67E-28	+
30	108	1.50E-26	-
	109	7.09E-23	-
	110	4.74E-21	-
	111	2.56E-10	-
35	112	2.93E-09	+
	113	3.33E-08	+
	114	1.67E-06	+
40	115	3.00E-06	+
	116	3.74E-06	-
	117	1.28E-05	-
	118	4.71E-05	-
45	119	1.11E-04	-
	120	4.29E-04	+
	121	1.56E-03	-
50	122	8.60E-03	+

[Table 3]

SEQ ID NO:	Training cohort			Validation cohort		
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
1	95.8	94	97	92.8	87.9	96

EP 3 150 707 A1

(continued)

	Training cohort			Validation cohort			
SEQ ID NO:	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)	
5	2	88.6	74.6	98	96.4	90.9	100
	3	90.4	85.1	94	78.3	66.7	86
	4	86.8	74.6	95	88	87.9	88
10	5	88	85.1	90	84.3	81.8	86
	6	86.2	73.1	95	81.9	69.7	90
	7	91.6	86.6	95	92.8	90.9	94
15	8	85	73.1	93	84.3	69.7	94
	9	85	80.6	88	83.1	78.8	86
	10	83.2	77.6	87	79.5	75.8	82
	11	79	68.7	86	81.9	78.8	84
20	12	81.9	71.2	89	80.7	66.7	90
	13	82	77.6	85	81.9	72.7	88
	14	82	65.7	93	78.3	54.5	94
25	15	83.2	64.2	96	85.5	66.7	98
	16	80.8	73.1	86	74.7	63.6	82
	17	83.8	65.7	96	81.9	72.7	88
30	18	85	77.6	90	89.2	78.8	96
	19	79.6	64.2	90	81.9	63.6	94
	20	75.4	64.2	83	73.5	51.5	88
	21	76.6	70.1	81	81.9	84.8	80
35	22	77.8	62.7	88	83.1	78.8	86
	23	75.4	58.2	87	65.9	46.9	78
	24	76	59.7	87	83.1	81.8	84
40	25	80.8	67.2	90	86.7	81.8	90
	26	76.6	61.2	87	73.5	48.5	90
	27	77.2	62.7	87	75.9	51.5	92
	28	76	65.7	83	71.1	69.7	72
45	29	76	62.7	85	74.7	63.6	82
	30	79.6	68.7	87	83.1	63.6	96
	31	76	62.7	85	74.7	72.7	76
	32	79	64.2	89	71.1	48.5	86
50	33	78.4	58.2	92	80.7	60.6	94
	34	79	74.6	82	75.9	66.7	82
	35	77.8	61.2	89	88	93.9	84
55	36	76	59.7	87	69.9	51.5	82
	37	74.9	61.2	84	79.5	63.6	90
	38	77.8	52.2	95	78.3	51.5	96

EP 3 150 707 A1

(continued)

	Training cohort			Validation cohort			
SEQ ID NO:	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)	
5	39	74.9	52.2	90	83.1	66.7	94
	40	79.6	56.7	95	75.9	54.5	90
	41	76	56.7	89	75.9	45.5	96
10	42	78.4	53.7	95	78.3	66.7	86
	43	75.4	61.2	85	68.7	36.4	90
	44	77.8	61.2	89	75.9	57.6	88
15	45	71.9	59.7	80	69.9	54.5	80
	46	75.4	62.7	84	84.3	81.8	86
	47	71.3	50.7	85	68.7	45.5	84
	48	75.4	56.7	88	73.5	48.5	90
20	49	72.5	53.7	85	66.3	39.4	84
	50	68.9	49.3	82	75.6	68.8	80
	51	77.2	62.7	87	78.3	66.7	86
25	52	78.4	70.1	84	72.3	63.6	78
	53	74.9	55.2	88	73.5	51.5	88
	54	74.9	53.7	89	72.3	51.5	86
30	55	73.7	56.7	85	74.7	63.6	82
	56	72.5	56.7	83	67.5	54.5	76
	57	74.9	47.8	93	78.3	54.5	94
	58	75.4	56.7	88	81.9	72.7	88
35	59	75.4	55.2	89	75.9	57.6	88
	60	74.3	46.3	93	71.1	39.4	92
	61	74.3	52.2	89	72.3	42.4	92
40	62	71.3	64.2	76	69.9	57.6	78
	63	67.1	47.8	80	61.4	42.4	74
	64	74.3	59.7	84	74.7	66.7	80
	65	71.9	55.2	83	79.5	66.7	88
45	66	77.8	64.2	87	81.9	75.8	86
	67	70.1	47.8	85	75.9	69.7	80
	68	69.5	46.3	85	68.7	45.5	84
50	69	74.9	62.7	83	63.9	54.5	70
	70	77.2	59.7	89	71.1	60.6	78
	71	70.7	46.3	87	72.3	42.4	92
	72	70.7	50.7	84	65.9	39.4	83.7
55	73	72.5	47.8	89	69.9	33.3	94
	74	71.3	44.8	89	71.1	45.5	88
	75	71.9	50.7	86	78.3	69.7	84

EP 3 150 707 A1

(continued)

	Training cohort			Validation cohort			
SEQ ID NO:	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)	
5	76	65.3	37.3	84	65.1	30.3	88
	77	71.9	50.7	86	75.3	58.1	86
	78	68.3	56.7	76	68.7	66.7	70
10	79	74.9	53.7	89	79.5	69.7	86
	80	70.1	43.3	88	75.9	54.5	90
	81	71.7	51.5	85	75.9	57.6	88
15	82	65.3	40.3	82	74.7	60.6	84
	83	65.9	38.8	84	77.1	63.6	86
	84	66.5	43.3	82	60.2	36.4	76
	85	66.5	46.3	80	74.7	45.5	94
20	86	71.9	44.8	90	67.5	36.4	88
	87	64.7	41.8	80	65.1	36.4	84
	88	64.7	40.3	81	67.5	45.5	82
25	89	71.9	47.8	88	77.1	57.6	90
	90	70.7	41.8	90	72.3	45.5	90
	91	70.7	43.3	89	69.9	42.4	88
	92	68.9	50.7	81	68.7	57.6	76
30	93	62.9	38.8	79	69.9	51.5	82
	94	68.3	35.8	90	78.3	63.6	88
	95	66.5	41.8	83	60.2	27.3	82
35	96	70.1	44.8	87	79.5	60.6	78
	97	73.7	49.3	90	69.9	45.5	84
	98	75.3	57.6	87	77.1	60.6	86
	99	67.7	43.3	84	73.5	54.5	82
40	100	64.1	28.4	88	63.9	39.4	90
	101	62.9	31.3	84	62.7	27.3	94
	102	68.9	43.3	86	66.3	24.2	84
45	103	72.5	46.3	90	74.7	63.6	82
	104	70.1	44.8	87	68.7	45.5	86

[Table 4]

SEQ ID NO:	Discriminant coefficient	Constant term	
50	1	2.460	19.714
	2	2.382	21.068
55	3	3.095	21.899
	4	2.352	23.243

EP 3 150 707 A1

(continued)

SEQ ID NO:	Discriminant coefficient	Constant term
5	7.904	99.660
6	1.427	9.523
7	2.999	26.661
8	1.567	13.180
10	4.320	34.683
10	2.347	21.497
11	1.240	8.775
12	2.099	24.008
13	2.507	16.240
14	2.542	16.656
15	3.003	30.919
20	5.690	56.064
16	1.236	6.777
17	1.762	12.038
18	2.603	19.023
20	1.993	19.451
21	5.292	39.055
22	4.377	43.459
23	2.108	26.455
24	3.957	28.165
25	2.128	15.182
26	1.961	18.889
27	4.907	58.675
28	4.501	38.362
29	3.320	21.613
30	1.615	9.456
31	5.158	53.443
32	3.419	32.836
33	4.112	44.623
34	3.556	26.261
35	3.089	20.506
36	2.763	26.001
37	4.150	28.312
38	2.643	17.528
39	5.818	74.782
40	1.432	9.710
41	1.548	12.083
42	3.016	17.886

EP 3 150 707 A1

(continued)

SEQ ID NO:	Discriminant coefficient	Constant term	
5	43	2.295	15.780
	44	3.562	24.535
	45	4.999	52.068
	46	4.621	55.322
10	47	5.752	65.582
	48	3.690	28.014
	49	2.300	13.896
15	50	3.446	30.899
	51	2.754	19.334
	52	3.342	26.922
	53	2.877	17.377
20	54	2.361	24.174
	55	3.775	37.577
	56	4.572	35.653
25	57	2.278	22.355
	58	1.996	14.097
	59	1.651	10.003
30	60	2.120	16.586
	61	2.027	16.365
	62	4.550	49.932
	63	3.688	22.416
35	64	4.384	27.791
	65	5.587	39.777
	66	2.642	23.269
40	67	4.993	56.756
	68	2.773	24.275
	69	6.973	96.404
	70	4.314	53.140
45	71	2.482	17.866
	72	3.669	22.882
	73	3.449	25.517
50	74	2.141	18.183
	75	2.787	16.795
	76	2.574	18.040
	77	3.025	26.735
55	78	6.736	87.662
	79	2.855	19.214
	80	3.280	21.398

EP 3 150 707 A1

(continued)

SEQ ID NO:	Discriminant coefficient	Constant term
81	3.072	21.250
82	3.225	21.272
83	1.954	19.003
84	4.310	29.038
85	3.905	45.270
86	4.055	33.489
87	2.767	31.507
88	2.531	18.803
89	2.479	19.469
90	2.939	21.665
91	3.025	28.509
92	3.753	28.267
93	6.207	58.913
94	5.548	47.238
95	2.358	17.589
96	2.487	16.190
97	5.449	69.434
98	3.843	38.475
99	3.266	32.112
100	6.751	87.358
101	3.318	20.579
102	4.434	37.869
103	3.950	23.214
104	3.491	23.806

[Table 5-1]

Training cohort			
Sample name	Cancer stage	CEA(ng/mL)	CA19-9(U/mL)
P01	III	5.6(+)	202.7(+)
P05	IV	7.9(+)	2535(+)
P06	IV	5.7(+)	2381(+)
P07	IB	0.7(-)	81.9(+)
P09	IV	1(-)	48.6(+)
P10	IIB	3.3(-)	85.4(+)
P11	IV	1.4(-)	8.4(-)
P12	IV	23.6(+)	0.5(-)
P13	IV	3.8(-)	21.5(-)

EP 3 150 707 A1

(continued)

5
10
15
20
25
30
35
40
45
50
55

Training cohort			
Sample name	Cancer stage	CEA(ng/mL)	CA19-9(U/mL)
P14	IV	39.2(+)	248000(+)
P17	IV	282.1(+)	77700(+)
P18	IV	14.8(+)	7580(+)
P19	IIB	6.1(+)	562(+)
P21	III	1.4(-)	4690(+)
P25	IV	255.7(+)	302.9(+)
P26	IIB	3.9(-)	0.1(-)
P27	III	1(-)	1304(+)
P29	III	5.9(+)	883(+)
P33	IV	3.6(-)	3.7(-)
P35	IV	3.8(-)	8600(+)
P38	IV	26.7(+)	9080(+)
P39	IV	31.2(+)	299000(+)
P42	IV	4.8(-)	14.1(-)
P43	IV	188.2(+)	119700(+)
P44	IV	55.3(+)	38620(+)
P46	IV	20.7(+)	10.6(-)
P47	IV	5.6(+)	107.9(+)
P48	III	3.4(-)	285.6(+)
P49	IIB	3.6(-)	338.8(+)
P50	III	11(+)	2760(+)
P52	IV	13.6(+)	9850(+)
P53	III	8.8(+)	891(+)
P54	III	8.4(+)	0.5(-)
P55	IV	8.1(+)	8799(+)
P56	IV	202(+)	337900(+)
P57	IV	1.8(-)	110.7(+)
P59	IV	64.3(+)	223.9(+)
P60	IIB	2.8(-)	270.2(+)
P61	IIB	1(-)	29.5(-)
P62	III	32.2(+)	1490(+)
P66	IIB	1.5(-)	0.1(-)
P68	III	5.7(+)	236.9(+)
P71	IIB	6.2(+)	742(+)
P72	IIB	3.2(-)	81.4(+)
P73	IV	4.4(-)	970(+)
P75	III	1.4(-)	580(+)

EP 3 150 707 A1

(continued)

5
10
15
20
25
30
35

Training cohort			
Sample name	Cancer stage	CEA(ng/mL)	CA19-9(U/mL)
P76	III	59.9(+)	1279(+)
P79	IV	2.6(-)	1297(+)
P80	IV	8.4(+)	0.9(-)
P81	IV	4.1(-)	882(+)
P83	IV	8.6(+)	2.2(-)
P84	IV	2(-)	1375(+)
P86	III	4.3(-)	17640(+)
P87	III	6.6(+)	374.3(+)
P88	IV	147.4(+)	2695(+)
P89	IV	2.9(-)	2274(+)
P90	IV	7.4(+)	1986(+)
P93	IV	17.8(+)	2771(+)
P94	III	2(-)	116.1(+)
P95	III	3.5(-)	132.9(+)
P96	IV	1.2(-)	2.3(-)
P97	IV	338.1(+)	42990(+)
P98	IV	1.5(-)	57500(+)
P99	IV	74.1(+)	89700(+)
B38	IIB	0.9(-)	19(-)
B87	III	5.7(+)	0.1(-)
P101	IV	43.2(+)	91500(+)
	Sensitivity (%)	55.2	77.6

[Table 5-2]

40
45
50
55

Validation cohort			
Sample name	Cancer stage	CEA(ng/mL)	CA19-9(U/mL)
P02	IV	1.5(-)	569(+)
P03	III	4(-)	1116(+)
P04	IV	4.6(-)	5.8(-)
P08	III	3.3(-)	81.4(+)
P15	IV	12.8(+)	47.1(+)
P16	IV	5.1(+)	181.4(+)
P20	III	0.9(-)	13.6(-)
P22	III	0.7(-)	31.4(-)
P23	IV	7.7(+)	17080(+)
P24	III	1.7(-)	72.9(+)

EP 3 150 707 A1

(continued)

5
10
15
20
25
30
35
40

Validation cohort			
Sample name	Cancer stage	CEA(ng/mL)	CA19-9(U/mL)
P28	IV	25.1(+)	2995(+)
P30	IV	4.3(-)	5.7(-)
P31	IV	2.9(-)	3375(+)
P32	III	12.2(+)	2955(+)
P34	IIA	1.3(-)	66(+)
P36	III	2.7(-)	32.2(-)
P37	III	2(-)	858(+)
P40	III	65.6(+)	9.6(-)
P41	IV	11.4(+)	128080(+)
P45	III	2(-)	410.8(+)
P51	IV	26.1(+)	5880(+)
P58	IV	80.3(+)	6510(+)
P63	IIB	4.4(-)	5490(+)
P65	IB	7(+)	55.3(+)
P67	IIB	2.5(-)	28.7(-)
P69	IIB	4.2(-)	832(+)
P70	IIB	1.6(-)	71.3(+)
P74	IIA	3.2(-)	36.8(-)
P77	IV	9.5(+)	6110(+)
P78	IV	417(+)	971000(+)
P82	III	6.7(+)	3730(+)
P85	IV	5.4(+)	6960(+)
P100	IV	240(+)	68500(+)
	Sensitivity (%)	45.5	75.8

For CEA, 5 ng/ml or lower was indicated as "-", and, for CA19-9, 37 U/ml or lower was indicated as "-", while values exceeding these were indicated as "+".

[Table 6]

45
50
55

SEQ ID NO:	Training cohort			Validation cohort		
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
2_105	96.4	94	98	100	100	100
18_105	98.8	97	100	100	100	100
46_105	97.6	95.5	99	100	100	100
55_105	98.2	97	99	100	100	100
58_105	98.2	95.5	100	100	100	100
66_105	96.4	92.5	99	100	100	100
71_105	98.2	97	99	100	100	100

EP 3 150 707 A1

(continued)

SEQ ID NO:	Training cohort			Validation cohort		
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
77_105	98.8	97	100	100	100	100
83_105	97	95.5	98	100	100	100
99_105	97	94	99	100	100	100
10_18	96.4	91	100	100	100	100
52_105	96.4	94	98	98.8	100	98
18_109	97.6	95.5	99	98.8	100	98
18_25	88.6	79.1	95	97.6	100	96
25_112	89.2	80.6	95	97.6	100	96
8_109	95.8	94	97	96.4	100	94
25_58	87.4	74.6	96	95.2	100	92
5_105	98.2	97	99	98.8	97	100
8_105	97.6	95.5	99	98.8	97	100
13_105	98.2	95.5	100	98.8	97	100
35_105	97.6	95.5	99	98.8	97	100
70_105	97	94	99	98.8	97	100
74_105	97	95.5	98	98.8	97	100
79_105	97.6	95.5	99	98.8	97	100
89_105	97	94	99	98.8	97	100
93_105	97	94	99	98.8	97	100
96_105	97	94	99	98.8	97	100
97_105	97.6	94	100	98.8	97	100
18_107	97	94	99	98.8	97	100
18_108	97.6	94	100	98.8	97	100
6_18	97.6	95.5	99	98.8	97	100
4_105	97	94	99	97.6	97	98
14_105	97.6	95.5	99	97.6	97	98
21_105	97	94	99	97.6	97	98
39_105	98.2	97	99	97.6	97	98
56_105	97	95.5	98	97.6	97	98
68_105	97.6	95.5	99	97.6	97	98
94_105	97	94	99	97.6	97	98
2_16	92.2	83.6	98	97.6	97	98
4_119	88	80.6	93	97.6	97	98
12_108	93.4	89.4	96	97.6	97	98
83_108	92.2	83.6	98	97.6	97	98
5_33	93.4	89.6	96	97.6	97	98
13_22	91.6	88.1	94	97.6	97	98

EP 3 150 707 A1

(continued)

SEQ ID NO:	Training cohort			Validation cohort		
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
22_105	97	94	99	96.4	97	96
2_10	92.2	83.6	98	96.4	97	96
2_22	90.4	82.1	96	96.4	97	96
34_108	95.2	89.6	99	96.4	97	96
4_45	89.8	83.6	94	95.2	97	94
37_108	91.6	86.6	95	95.2	97	94
12_109	93.4	90.9	95	95.2	97	94
13_24	91.6	92.5	91	95.2	97	94
18_70	88	77.6	95	95.2	97	94
25_83	83.8	74.6	90	95.2	97	94
35_113	88.6	76.1	97	95.2	97	94
35_87	80.8	73.1	86	95.2	97	94
2_109	91.6	83.6	97	94	97	92
93_108	86.8	79.1	92	94	97	92
24_71	80.2	70.1	87	94	97	92
24_35	84.4	73.1	92	92.8	97	90
4_98	86.7	75.8	94	91.6	97	88
13_25	91	89.6	92	91.6	97	88
35_44	83.8	73.1	91	91.6	97	88
35_99	77.2	65.7	85	91.6	97	88
4_58	88	77.6	95	90.4	97	86
25_35	82	68.7	91	89.2	97	84
35_63	80.8	71.6	87	89.2	97	84
35_97	79.6	68.7	87	89.2	97	84
35_66	81.4	67.2	91	88	97	82
35_121	81.4	67.2	91	88	97	82
35_94	77.8	61.2	89	86.7	97	80
66_109	88	80.6	93	85.5	97	78
66_100	80.2	64.2	91	85.5	97	78
50_105	97	95.5	98	98.8	96.9	100
23_105	97	94	99	97.6	96.9	98
35_50	80.2	67.2	89	89	96.9	84
1_77	95.8	91	99	96.3	96.8	96
6_105	96.4	94	98	97.6	93.9	100
7_105	97	94	99	97.6	93.9	100
12_105	97.6	97	98	97.6	93.9	100
15_105	96.4	94	98	97.6	93.9	100

EP 3 150 707 A1

(continued)

SEQ ID NO:	Training cohort			Validation cohort			
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)	
5	17_105	97	94	99	97.6	93.9	100
	20_105	97.6	97	98	97.6	93.9	100
	25_105	96.4	94	98	97.6	93.9	100
10	26_105	97.6	97	98	97.6	93.9	100
	27_105	97	94	99	97.6	93.9	100
	31_105	96.4	92.5	99	97.6	93.9	100
15	33_105	97	94	99	97.6	93.9	100
	34_105	95.8	92.5	98	97.6	93.9	100
	40_105	96.4	94	98	97.6	93.9	100
	49_105	97	97	97	97.6	93.9	100
20	57_105	97	94	99	97.6	93.9	100
	67_105	96.4	94	98	97.6	93.9	100
	81_105	97.6	95.5	99	97.6	93.9	100
25	88_105	97	94	99	97.6	93.9	100
	90_105	97.6	95.5	99	97.6	93.9	100
	98_105	96.4	93.9	98	97.6	93.9	100
30	1_119	97	95.5	98	97.6	93.9	100
	2_108	95.2	88.1	100	97.6	93.9	100
	2_13	91.6	82.1	98	97.6	93.9	100
	2_18	91	77.6	100	97.6	93.9	100
35	2_34	90.4	79.1	98	97.6	93.9	100
	2_35	88.6	74.6	98	97.6	93.9	100
	2_37	89.8	77.6	98	97.6	93.9	100
	2_52	89.8	77.6	98	97.6	93.9	100
40	2_58	89.2	76.1	98	97.6	93.9	100
	2_62	91	80.6	98	97.6	93.9	100
	2_65	89.8	79.1	97	97.6	93.9	100
45	2_71	89.2	76.1	98	97.6	93.9	100
	2_119	90.4	80.6	97	97.6	93.9	100
	2_120	88	76.1	96	97.6	93.9	100
	2_121	88	74.6	97	97.6	93.9	100
50	2_94	88.6	76.1	97	97.6	93.9	100
	2_98	89.2	77.3	97	97.6	93.9	100
	2_99	88.6	74.6	98	97.6	93.9	100
55	4_13	95.2	89.6	99	97.6	93.9	100
	58_108	95.2	88.1	100	97.6	93.9	100
	6_8	94.6	91	97	97.6	93.9	100

EP 3 150 707 A1

(continued)

SEQ ID NO:	Training cohort			Validation cohort			
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)	
5	9_105	97	94	99	96.4	93.9	98
	24_105	97	94	99	96.4	93.9	98
	28_105	97	94	99	96.4	93.9	98
10	29_105	97	94	99	96.4	93.9	98
	36_105	97	94	99	96.4	93.9	98
	37_105	97.6	95.5	99	96.4	93.9	98
15	38_105	97	94	99	96.4	93.9	98
	43_105	97	95.5	98	96.4	93.9	98
	45_105	97	94	99	96.4	93.9	98
	47_105	96.4	94	98	96.4	93.9	98
20	62_105	96.4	94	98	96.4	93.9	98
	65_105	97.6	95.5	99	96.4	93.9	98
	80_105	97	94	99	96.4	93.9	98
25	82_105	97	94	99	96.4	93.9	98
	84_105	97	94	99	96.4	93.9	98
	85_105	96.4	94	98	96.4	93.9	98
	86_105	97	94	99	96.4	93.9	98
30	92_105	95.8	92.5	98	96.4	93.9	98
	102_105	97	94	99	96.4	93.9	98
	1_20	95.2	92.5	97	96.4	93.9	98
35	2_6	93.4	88.1	97	96.4	93.9	98
	2_112	87.4	74.6	96	96.4	93.9	98
	2_45	90.4	79.1	98	96.4	93.9	98
	2_80	88.6	74.6	98	96.4	93.9	98
40	2_81	88.6	75.8	97	96.4	93.9	98
	2_88	90.4	79.1	98	96.4	93.9	98
	13_107	96.4	91	100	96.4	93.9	98
45	4_18	89.8	77.6	98	96.4	93.9	98
	5_19	92.2	85.1	97	96.4	93.9	98
	7_34	91.6	83.6	97	96.4	93.9	98
	16_105	97.6	95.5	99	95.2	93.9	96
50	51_105	97	94	99	95.2	93.9	96
	75_105	97.6	95.5	99	95.2	93.9	96
	78_105	97	94	99	95.2	93.9	96
55	100_105	97.6	95.5	99	95.2	93.9	96
	104_105	97	94	99	95.2	93.9	96
	1_2	96.4	92.5	99	95.2	93.9	96

EP 3 150 707 A1

(continued)

SEQ ID NO:	Training cohort			Validation cohort		
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
1_12	95.8	92.4	98	95.2	93.9	96
1_37	95.2	94	96	95.2	93.9	96
2_21	90.4	77.6	99	95.2	93.9	96
2_67	89.2	77.6	97	95.2	93.9	96
2_78	89.2	79.1	96	95.2	93.9	96
2_103	89.8	77.6	98	95.2	93.9	96
37_107	92.2	86.6	96	95.2	93.9	96
35_108	92.2	82.1	99	95.2	93.9	96
71_108	94.6	89.6	98	95.2	93.9	96
5_44	91	86.6	94	95.2	93.9	96
5_57	91.6	83.6	97	95.2	93.9	96
7_12	91.6	87.9	94	95.2	93.9	96
7_94	92.2	83.6	98	95.2	93.9	96
18_24	88.6	80.6	94	95.2	93.9	96
25_98	84.3	75.8	90	95.2	93.9	96
30_35	86.2	80.6	90	95.2	93.9	96
3_105	95.8	94	97	94	93.9	94
2_54	89.2	77.6	97	94	93.9	94
5_107	94	91	96	94	93.9	94
4_112	88.6	76.1	97	94	93.9	94
74_108	91.6	86.6	95	94	93.9	94
5_18	91	80.6	98	94	93.9	94
5_30	95.8	94	97	94	93.9	94
7_18	93.4	86.6	98	94	93.9	94
7_37	90.4	83.6	95	94	93.9	94
13_42	89.8	85.1	93	94	93.9	94
22_24	86.8	82.1	90	94	93.9	94
35_115	82.6	70.1	91	94	93.9	94
12_107	95.2	93.9	96	92.8	93.9	92
4_12	91	84.8	95	92.8	93.9	92
4_44	88	76.1	96	92.8	93.9	92
4_75	84.4	73.1	92	92.8	93.9	92
4_120	86.8	76.1	94	92.8	93.9	92
4_97	89.2	82.1	94	92.8	93.9	92
13_108	93.4	89.6	96	92.8	93.9	92
97_108	95.2	94	96	92.8	93.9	92
5_31	91.6	88.1	94	92.8	93.9	92

EP 3 150 707 A1

(continued)

SEQ ID NO:	Training cohort			Validation cohort		
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
5_66	91	86.6	94	92.8	93.9	92
5_80	86.8	73.1	96	92.8	93.9	92
6_112	93.4	91	95	92.8	93.9	92
7_119	91.6	86.6	95	92.8	93.9	92
9_35	83.8	73.1	91	92.8	93.9	92
10_13	90.4	88.1	92	92.8	93.9	92
18_35	84.4	73.1	92	92.8	93.9	92
22_120	83.8	73.1	91	92.8	93.9	92
25_81	81.9	71.2	89	92.8	93.9	92
35_112	79	65.7	88	92.8	93.9	92
4_26	88.6	79.1	95	91.6	93.9	90
4_49	90.4	82.1	96	91.6	93.9	90
4_63	88.6	80.6	94	91.6	93.9	90
4_71	88.6	79.1	95	91.6	93.9	90
37_109	89.2	80.6	95	91.6	93.9	90
7_13	93.4	92.5	94	91.6	93.9	90
10_112	94	89.6	97	91.6	93.9	90
13_35	88.6	82.1	93	91.6	93.9	90
18_22	87.4	82.1	91	91.6	93.9	90
22_98	84.9	77.3	90	91.6	93.9	90
24_93	82	73.1	88	91.6	93.9	90
25_120	88.6	83.6	92	91.6	93.9	90
35_47	80.2	70.1	87	91.6	93.9	90
35_65	80.2	70.1	87	91.6	93.9	90
34_107	91.6	91	92	90.4	93.9	88
4_20	91	83.6	96	90.4	93.9	88
4_34	87.4	80.6	92	90.4	93.9	88
4_46	88	76.1	96	90.4	93.9	88
4_65	89.8	82.1	95	90.4	93.9	88
4_89	89.8	80.6	96	90.4	93.9	88
13_66	86.8	82.1	90	90.4	93.9	88
24_112	87.4	80.6	92	90.4	93.9	88
24_83	80.2	67.2	89	90.4	93.9	88
24_96	82.6	73.1	89	90.4	93.9	88
25_119	84.4	79.1	88	90.4	93.9	88
25_96	82.6	68.7	92	90.4	93.9	88
31_119	84.4	76.1	90	90.4	93.9	88

EP 3 150 707 A1

(continued)

SEQ ID NO:	Training cohort			Validation cohort		
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
35_53	79.6	64.2	90	90.4	93.9	88
35_55	79.6	59.7	93	90.4	93.9	88
35_119	80.8	68.7	89	90.4	93.9	88
35_98	82.5	69.7	91	90.4	93.9	88
4_109	88	77.6	95	89.2	93.9	86
20_109	94.6	92.5	96	89.2	93.9	86
22_35	83.2	74.6	89	89.2	93.9	86
22_58	83.2	71.6	91	89.2	93.9	86
22_100	83.2	74.6	89	89.2	93.9	86
35_89	82.6	70.1	91	89.2	93.9	86
35_92	80.8	64.2	92	89.2	93.9	86
4_52	86.8	76.1	94	88	93.9	84
10_35	89.8	83.6	94	88	93.9	84
25_52	88	79.1	94	88	93.9	84
35_80	80.8	65.7	91	88	93.9	84
35_83	77.8	59.7	90	88	93.9	84
35_72	80.2	65.7	90	87.8	93.9	83.7
26_109	92.8	89.6	95	86.7	93.9	82
22_83	82	70.1	90	86.7	93.9	82
25_99	83.2	71.6	91	86.7	93.9	82
35_79	79	64.2	89	86.7	93.9	82
10_52	90.4	86.6	93	85.5	93.9	80
25_79	81.4	68.7	90	85.5	93.9	80
1_23	97	95.5	98	96.3	93.8	98
4_50	86.2	73.1	95	90.2	93.8	88
3_77	92.2	83.6	98	95.1	93.5	96
11_105	97	94	99	96.4	90.9	100
19_105	95.8	94	97	96.4	90.9	100
30_105	97.6	95.5	99	96.4	90.9	100
41_105	96.4	94	98	96.4	90.9	100
44_105	97	94	99	96.4	90.9	100
48_105	97	94	99	96.4	90.9	100
60_105	97	94	99	96.4	90.9	100
73_105	96.4	94	98	96.4	90.9	100
87_105	97	94	99	96.4	90.9	100
1_13	97	94	99	96.4	90.9	100
1_61	97	95.5	98	96.4	90.9	100

EP 3 150 707 A1

(continued)

SEQ ID NO:	Training cohort			Validation cohort		
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
2_7	92.8	83.6	99	96.4	90.9	100
2_15	94	86.6	99	96.4	90.9	100
2_19	92.2	83.6	98	96.4	90.9	100
2_24	91	82.1	97	96.4	90.9	100
2_25	90.4	80.6	97	96.4	90.9	100
2_30	90.4	82.1	96	96.4	90.9	100
2_44	89.8	79.1	97	96.4	90.9	100
2_46	88.6	74.6	98	96.4	90.9	100
2_53	91.6	80.6	99	96.4	90.9	100
2_55	88.6	74.6	98	96.4	90.9	100
2_63	91	80.6	98	96.4	90.9	100
2_66	88.6	74.6	98	96.4	90.9	100
2_70	88.6	74.6	98	96.4	90.9	100
2_73	90.4	80.6	97	96.4	90.9	100
2_74	89.2	77.6	97	96.4	90.9	100
2_118	89.2	77.6	97	96.4	90.9	100
2_85	88	74.6	97	96.4	90.9	100
2_87	89.8	80.6	96	96.4	90.9	100
2_89	89.8	77.6	98	96.4	90.9	100
2_90	89.2	76.1	98	96.4	90.9	100
2_92	88.6	74.6	98	96.4	90.9	100
2_93	88.6	74.6	98	96.4	90.9	100
2_96	88.6	76.1	97	96.4	90.9	100
2_100	88	74.6	97	96.4	90.9	100
32_105	95.8	92.5	98	95.2	90.9	98
42_105	97	94	99	95.2	90.9	98
53_105	96.4	94	98	95.2	90.9	98
54_105	96.4	94	98	95.2	90.9	98
63_105	97	94	99	95.2	90.9	98
64_105	96.4	94	98	95.2	90.9	98
69_105	97	94	99	95.2	90.9	98
76_105	97	94	99	95.2	90.9	98
91_105	97	94	99	95.2	90.9	98
103_105	97	94	99	95.2	90.9	98
1_108	97	95.5	98	95.2	90.9	98
1_18	97	92.5	100	95.2	90.9	98
1_30	95.2	91	98	95.2	90.9	98

EP 3 150 707 A1

(continued)

SEQ ID NO:	Training cohort			Validation cohort			
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)	
5	1_36	96.4	94	98	95.2	90.9	98
	1_120	96.4	94	98	95.2	90.9	98
	2_5	91	80.6	98	95.2	90.9	98
10	2_14	92.8	83.6	99	95.2	90.9	98
	2_28	93.4	85.1	99	95.2	90.9	98
	2_41	91	82.1	97	95.2	90.9	98
15	2_116	89.2	77.6	97	95.2	90.9	98
	2_117	89.2	77.6	97	95.2	90.9	98
	2_82	90.4	77.6	99	95.2	90.9	98
	2_84	91	80.6	98	95.2	90.9	98
20	2_104	91	80.6	98	95.2	90.9	98
	4_30	88.6	77.6	96	95.2	90.9	98
	4_87	91	79.1	99	95.2	90.9	98
25	8_108	96.4	92.5	99	95.2	90.9	98
	98_108	95.2	87.9	100	95.2	90.9	98
	5_13	92.2	86.6	96	95.2	90.9	98
	7_52	91	82.1	97	95.2	90.9	98
30	8_10	94.6	89.6	98	95.2	90.9	98
	18_110	95.8	94	97	95.2	90.9	98
	18_111	89.2	79.1	96	95.2	90.9	98
35	19_35	86.8	77.6	93	95.2	90.9	98
	19_58	89.8	83.6	94	95.2	90.9	98
	72_105	96.4	94	98	95.1	90.9	98
40	1_4	95.8	94	97	94	90.9	96
	1_8	96.4	94	98	94	90.9	96
	1_110	96.4	94	98	94	90.9	96
	1_14	97	94	99	94	90.9	96
45	1_22	95.8	95.5	96	94	90.9	96
	1_25	95.8	94	97	94	90.9	96
	1_26	94.6	91	97	94	90.9	96
	1_35	97	95.5	98	94	90.9	96
50	1_40	96.4	94	98	94	90.9	96
	1_112	95.8	91	99	94	90.9	96
	1_43	95.2	91	98	94	90.9	96
55	1_49	95.8	92.5	98	94	90.9	96
	1_113	95.8	92.5	98	94	90.9	96
	1_52	97	94	99	94	90.9	96

EP 3 150 707 A1

(continued)

SEQ ID NO:	Training cohort			Validation cohort			
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)	
5	1_55	96.4	94	98	94	90.9	96
	1_56	96.4	95.5	97	94	90.9	96
	1_58	95.8	92.5	98	94	90.9	96
10	1_65	96.4	94	98	94	90.9	96
	1_66	94.6	91	97	94	90.9	96
	1_69	97	94	99	94	90.9	96
15	1_71	98.2	98.5	98	94	90.9	96
	1_74	95.8	92.5	98	94	90.9	96
	1_79	96.4	95.5	97	94	90.9	96
	1_81	97	93.9	99	94	90.9	96
20	1_83	96.4	94	98	94	90.9	96
	1_99	97	94	99	94	90.9	96
	1_102	97	95.5	98	94	90.9	96
25	8_106	94.6	88.1	99	94	90.9	96
	2_107	93.4	86.6	98	94	90.9	96
	2_4	89.2	79.1	96	94	90.9	96
	2_9	92.8	85.1	98	94	90.9	96
30	2_12	91.6	81.8	98	94	90.9	96
	2_111	92.2	83.6	98	94	90.9	96
	2_39	88.6	74.6	98	94	90.9	96
35	2_114	89.2	74.6	99	94	90.9	96
	2_69	90.4	80.6	97	94	90.9	96
	2_95	89.2	77.6	97	94	90.9	96
	4_7	92.2	83.6	98	94	90.9	96
40	4_41	88	77.6	95	94	90.9	96
	5_108	95.2	91	98	94	90.9	96
	21_108	92.2	85.1	97	94	90.9	96
45	49_108	92.8	86.6	97	94	90.9	96
	65_108	91.6	88.1	94	94	90.9	96
	96_108	93.4	88.1	97	94	90.9	96
	99_108	94	86.6	99	94	90.9	96
50	13_109	94.6	89.6	98	94	90.9	96
	7_67	91	83.6	96	94	90.9	96
	7_70	92.8	86.6	97	94	90.9	96
55	9_119	87.4	83.6	90	94	90.9	96
	10_12	91.6	89.4	93	94	90.9	96
	13_16	94.6	98.5	92	94	90.9	96

EP 3 150 707 A1

(continued)

SEQ ID NO:	Training cohort			Validation cohort		
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
14_18	94	88.1	98	94	90.9	96
35_41	83.2	73.1	90	94	90.9	96
66_85	83.2	68.7	93	94	90.9	96
1_21	96.4	95.5	97	92.8	90.9	94
1_29	96.4	94	98	92.8	90.9	94
1_39	97.6	97	98	92.8	90.9	94
1_70	97	94	99	92.8	90.9	94
1_75	97	94	99	92.8	90.9	94
4_107	90.4	85.1	94	92.8	90.9	94
14_107	92.2	80.6	100	92.8	90.9	94
58_107	92.8	88.1	96	92.8	90.9	94
66_107	90.4	80.6	97	92.8	90.9	94
94_107	90.4	83.6	95	92.8	90.9	94
99_107	89.8	80.6	96	92.8	90.9	94
3_119	91	89.6	92	92.8	90.9	94
4_14	90.4	82.1	96	92.8	90.9	94
4_113	90.4	80.6	97	92.8	90.9	94
4_115	89.8	79.1	97	92.8	90.9	94
43_108	93.4	91	95	92.8	90.9	94
5_7	95.2	94	96	92.8	90.9	94
5_12	91.6	84.8	96	92.8	90.9	94
5_24	93.4	91	95	92.8	90.9	94
5_112	87.4	79.1	93	92.8	90.9	94
5_89	90.4	83.6	95	92.8	90.9	94
7_9	90.4	89.6	91	92.8	90.9	94
7_16	90.4	88.1	92	92.8	90.9	94
7_22	91	83.6	96	92.8	90.9	94
7_51	91	85.1	95	92.8	90.9	94
7_62	91.6	85.1	96	92.8	90.9	94
7_114	89.8	83.6	94	92.8	90.9	94
7_80	92.2	85.1	97	92.8	90.9	94
7_83	91	80.6	98	92.8	90.9	94
7_103	91.6	86.6	95	92.8	90.9	94
10_20	89.8	85.1	93	92.8	90.9	94
10_58	94.6	91	97	92.8	90.9	94
13_27	91	86.6	94	92.8	90.9	94
18_30	86.8	80.6	91	92.8	90.9	94

EP 3 150 707 A1

(continued)

SEQ ID NO:	Training cohort			Validation cohort		
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
18_41	85	77.6	90	92.8	90.9	94
18_66	85	74.6	92	92.8	90.9	94
22_85	86.2	77.6	92	92.8	90.9	94
24_37	85	74.6	92	92.8	90.9	94
24_119	82.6	76.1	87	92.8	90.9	94
25_39	86.2	74.6	94	92.8	90.9	94
25_45	88.6	76.1	97	92.8	90.9	94
25_46	85	73.1	93	92.8	90.9	94
1_121	98.2	97	99	91.6	90.9	92
20_107	95.2	92.5	97	91.6	90.9	92
26_107	95.8	94	97	91.6	90.9	92
49_107	94	91	96	91.6	90.9	92
3_58	94.6	91	97	91.6	90.9	92
4_5	91	83.6	96	91.6	90.9	92
4_6	90.4	80.6	97	91.6	90.9	92
4_10	91.6	86.6	95	91.6	90.9	92
4_24	87.4	76.1	95	91.6	90.9	92
4_48	89.2	79.1	96	91.6	90.9	92
4_55	88.6	79.1	95	91.6	90.9	92
4_88	86.2	77.6	92	91.6	90.9	92
4_102	89.2	80.6	95	91.6	90.9	92
55_108	91.6	83.6	97	91.6	90.9	92
5_25	91	86.6	94	91.6	90.9	92
5_42	91.6	86.6	95	91.6	90.9	92
5_56	91.6	88.1	94	91.6	90.9	92
7_21	90.4	85.1	94	91.6	90.9	92
7_35	89.8	79.1	97	91.6	90.9	92
7_112	93.4	86.6	98	91.6	90.9	92
7_65	91	86.6	94	91.6	90.9	92
7_66	91	85.1	95	91.6	90.9	92
7_79	89.8	83.6	94	91.6	90.9	92
7_120	91	83.6	96	91.6	90.9	92
7_87	91.6	85.1	96	91.6	90.9	92
7_88	90.4	86.6	93	91.6	90.9	92
7_104	91	86.6	94	91.6	90.9	92
10_120	91.6	85.1	96	91.6	90.9	92
13_21	89.8	86.6	92	91.6	90.9	92

EP 3 150 707 A1

(continued)

SEQ ID NO:	Training cohort			Validation cohort		
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
5 18_46	83.2	74.6	89	91.6	90.9	92
22_96	80.8	70.1	88	91.6	90.9	92
24_79	82	68.7	91	91.6	90.9	92
10 25_94	82.6	68.7	92	91.6	90.9	92
35_90	79.6	65.7	89	91.6	90.9	92
54_107	92.2	88.1	95	90.4	90.9	90
15 3_21	91	88.1	93	90.4	90.9	90
3_35	94.6	95.5	94	90.4	90.9	90
4_9	88	77.6	95	90.4	90.9	90
4_37	85.6	74.6	93	90.4	90.9	90
20 4_43	86.8	74.6	95	90.4	90.9	90
4_47	89.2	79.1	96	90.4	90.9	90
4_56	88.6	79.1	95	90.4	90.9	90
25 4_74	86.8	74.6	95	90.4	90.9	90
47_108	91.6	83.6	97	90.4	90.9	90
94_108	91.6	82.1	98	90.4	90.9	90
5_11	91.6	86.6	95	90.4	90.9	90
30 5_21	91.6	85.1	96	90.4	90.9	90
5_75	88.6	83.6	92	90.4	90.9	90
7_109	93.4	86.6	98	90.4	90.9	90
35 7_44	92.2	85.1	97	90.4	90.9	90
7_58	89.8	77.6	98	90.4	90.9	90
7_71	89.2	82.1	94	90.4	90.9	90
7_121	91	88.1	93	90.4	90.9	90
40 7_99	88.6	80.6	94	90.4	90.9	90
9_24	89.2	83.6	93	90.4	90.9	90
9_58	88	80.6	93	90.4	90.9	90
45 10_34	91.6	88.1	94	90.4	90.9	90
10_119	91	88.1	93	90.4	90.9	90
18_67	88.6	80.6	94	90.4	90.9	90
18_79	85.6	76.1	92	90.4	90.9	90
50 21_25	84.4	73.1	92	90.4	90.9	90
22_46	83.2	73.1	90	90.4	90.9	90
22_88	83.8	77.6	88	90.4	90.9	90
55 24_55	85	70.1	95	90.4	90.9	90
24_80	77.8	64.2	87	90.4	90.9	90
24_81	84.9	77.3	90	90.4	90.9	90

EP 3 150 707 A1

(continued)

SEQ ID NO:	Training cohort			Validation cohort		
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
24_90	83.2	71.6	91	90.4	90.9	90
25_34	89.8	80.6	96	90.4	90.9	90
35_37	79	68.7	86	90.4	90.9	90
66_98	79.5	63.6	90	90.4	90.9	90
52_107	92.2	89.6	94	89.2	90.9	88
4_25	88	79.1	94	89.2	90.9	88
4_80	86.8	74.6	95	89.2	90.9	88
4_81	86.7	75.8	94	89.2	90.9	88
4_82	86.8	74.6	95	89.2	90.9	88
4_83	86.8	74.6	95	89.2	90.9	88
4_85	88	76.1	96	89.2	90.9	88
4_90	87.4	76.1	95	89.2	90.9	88
4_91	85.6	73.1	94	89.2	90.9	88
4_94	87.4	74.6	96	89.2	90.9	88
49_109	89.8	89.6	90	89.2	90.9	88
10_81	89.2	81.8	94	89.2	90.9	88
10_83	89.2	82.1	94	89.2	90.9	88
10_121	89.2	83.6	93	89.2	90.9	88
22_80	83.2	74.6	89	89.2	90.9	88
24_31	83.2	68.7	93	89.2	90.9	88
24_118	83.2	74.6	89	89.2	90.9	88
25_66	80.8	67.2	90	89.2	90.9	88
25_70	82.6	68.7	92	89.2	90.9	88
25_75	82.6	73.1	89	89.2	90.9	88
25_80	84.4	73.1	92	89.2	90.9	88
28_35	82	71.6	89	89.2	90.9	88
4_11	86.8	79.1	92	88	90.9	86
4_16	88	77.6	95	88	90.9	86
4_21	87.4	76.1	95	88	90.9	86
4_39	89.2	79.1	96	88	90.9	86
4_76	86.8	73.1	96	88	90.9	86
4_92	85.6	73.1	94	88	90.9	86
4_96	88	76.1	96	88	90.9	86
4_99	85.6	71.6	95	88	90.9	86
9_109	88.6	79.1	95	88	90.9	86
54_109	88	83.6	91	88	90.9	86
9_46	88	85.1	90	88	90.9	86

EP 3 150 707 A1

(continued)

SEQ ID NO:	Training cohort			Validation cohort		
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
13_67	83.2	74.6	89	88	90.9	86
13_79	84.4	82.1	86	88	90.9	86
16_83	83.8	82.1	85	88	90.9	86
22_55	81.4	73.1	87	88	90.9	86
24_121	83.2	73.1	90	88	90.9	86
25_92	82.6	71.6	90	88	90.9	86
35_71	78.4	62.7	89	88	90.9	86
35_93	77.8	61.2	89	88	90.9	86
4_84	87.4	79.1	93	86.7	90.9	84
4_121	86.8	76.1	94	86.7	90.9	84
81_109	84.9	80.3	88	86.7	90.9	84
21_35	80.8	70.1	88	86.7	90.9	84
21_75	80.2	70.1	87	86.7	90.9	84
21_83	80.8	74.6	85	86.7	90.9	84
21_89	79	70.1	85	86.7	90.9	84
21_97	81.4	71.6	88	86.7	90.9	84
22_66	77.2	67.2	84	86.7	90.9	84
22_119	83.8	80.6	86	86.7	90.9	84
24_58	81.4	71.6	88	86.7	90.9	84
24_120	83.2	76.1	88	86.7	90.9	84
31_112	82.6	73.1	89	86.7	90.9	84
35_118	81.4	67.2	91	86.7	90.9	84
35_120	79	64.2	89	86.7	90.9	84
35_96	78.4	62.7	89	86.7	90.9	84
66_70	81.4	68.7	90	86.7	90.9	84
66_119	79	70.1	85	86.7	90.9	84
21_109	91	85.1	95	85.5	90.9	82
21_55	79.6	65.7	89	85.5	90.9	82
21_56	80.8	68.7	89	85.5	90.9	82
22_78	78.4	68.7	85	85.5	90.9	82
35_42	82.6	65.7	94	85.5	90.9	82
35_81	77.1	63.6	86	85.5	90.9	82
35_82	77.2	62.7	87	85.5	90.9	82
35_100	77.8	64.2	87	85.5	90.9	82
35_103	80.8	65.7	91	85.5	90.9	82
39_109	84.4	76.1	90	84.3	90.9	80
31_58	82.6	73.1	89	84.3	90.9	80

EP 3 150 707 A1

(continued)

SEQ ID NO:	Training cohort			Validation cohort		
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
35_75	77.8	59.7	90	84.3	90.9	80
9_100	88.6	91	87	83.1	90.9	78
10_94	85	79.1	89	83.1	90.9	78
21_71	80.8	71.6	87	83.1	90.9	78
79_109	85	73.1	93	81.9	90.9	76
99_109	85.6	80.6	89	81.9	90.9	76
31_109	85	73.1	93	80.7	90.9	74
2_50	91	79.1	99	96.3	90.6	100
1_50	96.4	94	98	93.9	90.6	96
7_50	91	83.6	96	93.9	90.6	96
2_23	91.6	82.1	98	92.7	90.6	94
18_23	89.8	82.1	95	92.7	90.6	94
5_50	91	83.6	96	91.5	90.6	92
24_50	81.4	74.6	86	91.5	90.6	92
4_23	86.8	74.6	95	87.8	90.6	86
22_50	83.2	76.1	88	87.8	90.6	86
50_109	88	82.1	92	80.5	90.6	74
2_77	88.6	74.6	98	96.3	90.3	100
7_77	88.6	82.1	93	95.1	90.3	98
4_77	88	76.1	96	92.6	90.3	94
21_77	80.8	76.1	84	87.7	90.3	86
1_105	97	94	99	95.2	87.9	100
61_105	97	94	99	95.2	87.9	100
1_19	95.2	91	98	95.2	87.9	100
1_87	98.2	97	99	95.2	87.9	100
13_106	94	85.1	100	95.2	87.9	100
2_11	91	82.1	97	95.2	87.9	100
2_17	92.2	83.6	98	95.2	87.9	100
2_29	91.6	82.1	98	95.2	87.9	100
2_33	92.8	85.1	98	95.2	87.9	100
2_38	92.8	85.1	98	95.2	87.9	100
2_47	88.6	76.1	97	95.2	87.9	100
2_49	88.6	77.6	96	95.2	87.9	100
2_113	91.6	82.1	98	95.2	87.9	100
2_56	91	82.1	97	95.2	87.9	100
2_57	88.6	76.1	97	95.2	87.9	100
2_60	90.4	80.6	97	95.2	87.9	100

EP 3 150 707 A1

(continued)

SEQ ID NO:	Training cohort			Validation cohort		
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
2_64	91	80.6	98	95.2	87.9	100
2_68	90.4	79.1	98	95.2	87.9	100
2_115	91	80.6	98	95.2	87.9	100
2_79	88.6	74.6	98	95.2	87.9	100
2_91	89.2	76.1	98	95.2	87.9	100
2_101	89.2	76.1	98	95.2	87.9	100
37_111	84.4	71.6	93	95.2	87.9	100
2_72	89.8	80.6	96	95.1	87.9	100
10_105	97.6	95.5	99	94	87.9	98
95_105	97	95.5	98	94	87.9	98
1_5	97.6	97	98	94	87.9	98
1_7	97.6	94	100	94	87.9	98
1_41	95.8	92.5	98	94	87.9	98
1_54	95.8	92.5	98	94	87.9	98
1_97	96.4	94	98	94	87.9	98
1_101	96.4	94	98	94	87.9	98
18_106	95.8	91	99	94	87.9	98
30_106	92.8	82.1	100	94	87.9	98
2_3	96.4	91	100	94	87.9	98
2_26	88.6	76.1	97	94	87.9	98
2_27	89.8	79.1	97	94	87.9	98
2_31	88.6	74.6	98	94	87.9	98
2_32	92.2	82.1	99	94	87.9	98
2_40	92.2	82.1	99	94	87.9	98
2_51	91	80.6	98	94	87.9	98
2_83	90.4	77.6	99	94	87.9	98
3_12	92.8	89.4	95	94	87.9	98
3_18	95.2	89.6	99	94	87.9	98
4_19	89.2	77.6	97	94	87.9	98
7_108	92.8	85.1	98	94	87.9	98
26_108	92.8	89.6	95	94	87.9	98
46_108	92.2	85.1	97	94	87.9	98
89_108	89.2	82.1	94	94	87.9	98
5_15	92.2	83.6	98	94	87.9	98
5_38	91.6	83.6	97	94	87.9	98
6_37	89.8	82.1	95	94	87.9	98
7_45	92.2	83.6	98	94	87.9	98

EP 3 150 707 A1

(continued)

SEQ ID NO:	Training cohort			Validation cohort		
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
5 7_74	93.4	89.6	96	94	87.9	98
7_85	92.8	85.1	98	94	87.9	98
7_96	91	80.6	98	94	87.9	98
10 18_38	89.8	80.6	96	94	87.9	98
18_59	92.2	85.1	97	94	87.9	98
19_46	90.4	85.1	94	94	87.9	98
15 59_105	97	95.5	98	92.8	87.9	96
101_105	97	95.5	98	92.8	87.9	96
1_106	95.8	94	97	92.8	87.9	96
1_3	96.4	94	98	92.8	87.9	96
20 1_6	95.8	94	97	92.8	87.9	96
1_9	96.4	94	98	92.8	87.9	96
1_10	97	94	99	92.8	87.9	96
25 1_11	95.8	94	97	92.8	87.9	96
1_16	97.6	97	98	92.8	87.9	96
1_17	95.8	94	97	92.8	87.9	96
1_24	97	95.5	98	92.8	87.9	96
30 1_28	96.4	94	98	92.8	87.9	96
1_31	97.6	95.5	99	92.8	87.9	96
1_32	96.4	94	98	92.8	87.9	96
35 1_33	95.8	94	97	92.8	87.9	96
1_34	97	94	99	92.8	87.9	96
1_38	95.8	92.5	98	92.8	87.9	96
1_42	95.8	94	97	92.8	87.9	96
40 1_44	95.8	94	97	92.8	87.9	96
1_45	96.4	92.5	99	92.8	87.9	96
1_46	96.4	92.5	99	92.8	87.9	96
45 1_47	97	97	97	92.8	87.9	96
1_48	97	94	99	92.8	87.9	96
1_51	95.8	94	97	92.8	87.9	96
1_53	95.2	92.5	97	92.8	87.9	96
50 1_57	95.8	94	97	92.8	87.9	96
1_60	95.8	94	97	92.8	87.9	96
1_62	96.4	94	98	92.8	87.9	96
55 1_63	95.8	94	97	92.8	87.9	96
1_64	95.8	94	97	92.8	87.9	96
1_114	95.2	91	98	92.8	87.9	96

EP 3 150 707 A1

(continued)

SEQ ID NO:	Training cohort			Validation cohort			
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)	
5	1_67	96.4	94	98	92.8	87.9	96
	1_68	95.8	94	97	92.8	87.9	96
	1_115	95.8	94	97	92.8	87.9	96
10	1_117	95.8	92.5	98	92.8	87.9	96
	1_73	97	95.5	98	92.8	87.9	96
	1_76	95.8	94	97	92.8	87.9	96
15	1_118	97.6	95.5	99	92.8	87.9	96
	1_78	95.8	94	97	92.8	87.9	96
	1_80	96.4	95.5	97	92.8	87.9	96
	1_84	95.8	94	97	92.8	87.9	96
20	1_85	95.8	94	97	92.8	87.9	96
	1_86	97	95.5	98	92.8	87.9	96
	1_88	95.8	92.5	98	92.8	87.9	96
25	1_89	97	94	99	92.8	87.9	96
	1_90	97	97	97	92.8	87.9	96
	1_91	95.8	94	97	92.8	87.9	96
	1_92	95.2	92.5	97	92.8	87.9	96
30	1_94	96.4	94	98	92.8	87.9	96
	1_95	96.4	94	98	92.8	87.9	96
	1_98	97	93.9	99	92.8	87.9	96
35	1_100	95.8	94	97	92.8	87.9	96
	1_103	96.4	95.5	97	92.8	87.9	96
	1_104	95.8	94	97	92.8	87.9	96
40	2_20	90.4	79.1	98	92.8	87.9	96
	2_36	91.6	82.1	98	92.8	87.9	96
	2_42	91.6	83.6	97	92.8	87.9	96
	2_59	91.6	82.1	98	92.8	87.9	96
45	35_107	88	79.1	94	92.8	87.9	96
	98_107	90.4	81.8	96	92.8	87.9	96
	3_13	92.8	88.1	96	92.8	87.9	96
	3_120	90.4	85.1	94	92.8	87.9	96
50	3_99	92.2	86.6	96	92.8	87.9	96
	5_17	91.6	86.6	95	92.8	87.9	96
	5_26	91	85.1	95	92.8	87.9	96
55	5_115	91.6	91	92	92.8	87.9	96
	5_97	91	83.6	96	92.8	87.9	96
	7_10	92.2	86.6	96	92.8	87.9	96

EP 3 150 707 A1

(continued)

SEQ ID NO:	Training cohort			Validation cohort		
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
7_20	91	86.6	94	92.8	87.9	96
7_24	92.8	88.1	96	92.8	87.9	96
7_54	88.6	82.1	93	92.8	87.9	96
7_76	89.8	83.6	94	92.8	87.9	96
7_118	93.4	86.6	98	92.8	87.9	96
7_91	91	83.6	96	92.8	87.9	96
7_102	92.8	88.1	96	92.8	87.9	96
9_18	91.6	85.1	96	92.8	87.9	96
9_120	83.2	79.1	86	92.8	87.9	96
11_18	88	83.6	91	92.8	87.9	96
12_24	86.1	80.3	90	92.8	87.9	96
13_30	89.2	89.6	89	92.8	87.9	96
13_53	85	85.1	85	92.8	87.9	96
13_60	86.8	79.1	92	92.8	87.9	96
14_24	88	77.6	95	92.8	87.9	96
18_19	88	80.6	93	92.8	87.9	96
42_119	79	65.7	88	92.8	87.9	96
1_72	95.8	94	97	92.7	87.9	95.9
1_109	97	95.5	98	91.6	87.9	94
1_59	95.2	91	98	91.6	87.9	94
1_116	95.8	92.5	98	91.6	87.9	94
1_93	97.6	95.5	99	91.6	87.9	94
2_106	93.4	85.1	99	91.6	87.9	94
9_106	92.2	83.6	98	91.6	87.9	94
9_107	93.4	86.6	98	91.6	87.9	94
39_107	91	85.1	95	91.6	87.9	94
44_107	95.2	91	98	91.6	87.9	94
55_107	92.8	85.1	98	91.6	87.9	94
3_5	97	95.5	98	91.6	87.9	94
3_71	98.2	98.5	98	91.6	87.9	94
4_108	93.4	88.1	97	91.6	87.9	94
4_8	92.8	85.1	98	91.6	87.9	94
20_108	93.4	89.6	96	91.6	87.9	94
70_108	90.4	79.1	98	91.6	87.9	94
81_108	92.2	84.8	97	91.6	87.9	94
87_108	88	83.6	91	91.6	87.9	94
5_20	92.2	88.1	95	91.6	87.9	94

EP 3 150 707 A1

(continued)

SEQ ID NO:	Training cohort			Validation cohort		
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
5_29	90.4	82.1	96	91.6	87.9	94
5_87	89.8	83.6	94	91.6	87.9	94
5_90	88	82.1	92	91.6	87.9	94
14_109	87.4	74.6	96	91.6	87.9	94
7_47	86.8	80.6	91	91.6	87.9	94
7_55	92.2	83.6	98	91.6	87.9	94
7_115	94	88.1	98	91.6	87.9	94
7_75	89.8	83.6	94	91.6	87.9	94
7_82	90.4	85.1	94	91.6	87.9	94
7_92	90.4	83.6	95	91.6	87.9	94
7_93	91	82.1	97	91.6	87.9	94
7_97	91	83.6	96	91.6	87.9	94
7_98	89.8	81.8	95	91.6	87.9	94
11_25	88	80.6	93	91.6	87.9	94
14_21	88.6	79.1	95	91.6	87.9	94
18_42	89.8	79.1	97	91.6	87.9	94
18_51	89.2	83.6	93	91.6	87.9	94
18_115	85.6	76.1	92	91.6	87.9	94
19_21	87.4	76.1	95	91.6	87.9	94
19_34	88.6	83.6	92	91.6	87.9	94
28_39	85.6	74.6	93	91.6	87.9	94
30_46	85	79.1	89	91.6	87.9	94
39_87	86.2	73.1	95	91.6	87.9	94
58_113	87.4	79.1	93	91.6	87.9	94
7_72	89.2	83.6	93	91.5	87.9	93.9
5_106	94	88.1	98	90.4	87.9	92
16_106	93.4	86.6	98	90.4	87.9	92
24_107	89.2	82.1	94	90.4	87.9	92
74_107	93.4	88.1	97	90.4	87.9	92
96_107	89.8	82.1	95	90.4	87.9	92
3_55	93.4	91	95	90.4	87.9	92
3_83	93.4	92.5	94	90.4	87.9	92
4_22	88	77.6	95	90.4	87.9	92
4_86	91	83.6	96	90.4	87.9	92
9_108	90.4	86.6	93	90.4	87.9	92
31_108	91	82.1	97	90.4	87.9	92
44_108	93.4	88.1	97	90.4	87.9	92

EP 3 150 707 A1

(continued)

SEQ ID NO:	Training cohort			Validation cohort		
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
52_108	95.2	88.1	100	90.4	87.9	92
80_108	91	88.1	93	90.4	87.9	92
7_28	92.2	91	93	90.4	87.9	92
7_117	93.4	88.1	97	90.4	87.9	92
7_78	92.8	86.6	97	90.4	87.9	92
7_81	90.4	83.3	95	90.4	87.9	92
7_90	91	85.1	95	90.4	87.9	92
8_21	86.2	76.1	93	90.4	87.9	92
9_13	92.2	94	91	90.4	87.9	92
10_37	88	82.1	92	90.4	87.9	92
10_66	87.4	76.1	95	90.4	87.9	92
13_31	87.4	82.1	91	90.4	87.9	92
13_114	86.2	85.1	87	90.4	87.9	92
13_103	85.6	82.1	88	90.4	87.9	92
16_119	86.2	80.6	90	90.4	87.9	92
18_27	89.2	83.6	93	90.4	87.9	92
18_47	83.8	76.1	89	90.4	87.9	92
18_113	90.4	83.6	95	90.4	87.9	92
18_56	87.4	79.1	93	90.4	87.9	92
22_45	87.4	79.1	93	90.4	87.9	92
22_97	83.2	79.1	86	90.4	87.9	92
24_32	84.4	77.6	89	90.4	87.9	92
24_74	80.2	76.1	83	90.4	87.9	92
24_99	83.2	74.6	89	90.4	87.9	92
30_34	84.4	77.6	89	90.4	87.9	92
35_39	78.4	61.2	90	90.4	87.9	92
66_112	83.8	71.6	92	90.4	87.9	92
51_58	85.6	74.6	93	90.4	87.9	92
65_107	92.8	85.1	98	89.2	87.9	90
92_107	92.8	89.6	95	89.2	87.9	90
3_4	93.4	88.1	97	89.2	87.9	90
4_32	90.4	83.6	95	89.2	87.9	90
4_53	86.2	73.1	95	89.2	87.9	90
4_69	87.4	79.1	93	89.2	87.9	90
4_117	88.6	77.6	96	89.2	87.9	90
4_79	86.8	74.6	95	89.2	87.9	90
4_101	86.8	77.6	93	89.2	87.9	90

EP 3 150 707 A1

(continued)

SEQ ID NO:	Training cohort			Validation cohort		
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
42_108	89.2	80.6	95	89.2	87.9	90
45_108	94.6	89.6	98	89.2	87.9	90
5_34	89.8	86.6	92	89.2	87.9	90
5_96	87.4	77.6	94	89.2	87.9	90
6_58	91.6	83.6	97	89.2	87.9	90
87_109	92.2	88.1	95	89.2	87.9	90
7_69	89.8	83.6	94	89.2	87.9	90
7_100	94	91	96	89.2	87.9	90
9_20	89.8	89.6	90	89.2	87.9	90
9_25	84.4	77.6	89	89.2	87.9	90
9_55	86.2	77.6	92	89.2	87.9	90
10_98	89.8	89.4	90	89.2	87.9	90
11_112	83.8	77.6	88	89.2	87.9	90
12_21	85.5	77.3	91	89.2	87.9	90
13_18	89.8	85.1	93	89.2	87.9	90
21_119	81.4	73.1	87	89.2	87.9	90
21_122	77.8	68.7	84	89.2	87.9	90
22_115	85	79.1	89	89.2	87.9	90
24_33	82	70.1	90	89.2	87.9	90
24_34	82.6	76.1	87	89.2	87.9	90
24_42	77.8	59.7	90	89.2	87.9	90
24_66	83.2	68.7	93	89.2	87.9	90
24_70	83.8	71.6	92	89.2	87.9	90
24_82	81.4	71.6	88	89.2	87.9	90
24_97	83.2	77.6	87	89.2	87.9	90
25_89	85	74.6	92	89.2	87.9	90
25_121	80.8	70.1	88	89.2	87.9	90
35_51	77.8	59.7	90	89.2	87.9	90
35_54	80.8	70.1	88	89.2	87.9	90
35_61	76	62.7	85	89.2	87.9	90
35_85	77.2	62.7	87	89.2	87.9	90
59_112	86.8	76.1	94	89.2	87.9	90
67_112	80.8	64.2	92	89.2	87.9	90
46_104	84.4	71.6	93	89.2	87.9	90
51_52	85	79.1	89	89.2	87.9	90
55_113	89.8	80.6	96	89.2	87.9	90
3_67	92.2	89.6	94	88	87.9	88

EP 3 150 707 A1

(continued)

SEQ ID NO:	Training cohort			Validation cohort		
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
3_94	91.6	86.6	95	88	87.9	88
4_31	86.2	73.1	95	88	87.9	88
4_35	86.8	74.6	95	88	87.9	88
4_51	86.8	74.6	95	88	87.9	88
4_59	86.2	73.1	95	88	87.9	88
4_62	88	74.6	97	88	87.9	88
4_114	87.4	74.6	96	88	87.9	88
4_68	86.2	73.1	95	88	87.9	88
4_116	88.6	77.6	96	88	87.9	88
4_78	86.2	74.6	94	88	87.9	88
4_93	86.8	76.1	94	88	87.9	88
4_103	86.8	74.6	95	88	87.9	88
4_104	86.8	74.6	95	88	87.9	88
75_108	91.6	82.1	98	88	87.9	88
5_35	89.2	80.6	95	88	87.9	88
6_21	89.8	79.1	97	88	87.9	88
9_70	86.8	79.1	92	88	87.9	88
9_85	83.2	79.1	86	88	87.9	88
10_79	85	74.6	92	88	87.9	88
11_55	81.4	71.6	88	88	87.9	88
16_112	88	83.6	91	88	87.9	88
18_21	86.8	77.6	93	88	87.9	88
19_75	88.6	80.6	94	88	87.9	88
21_22	80.2	71.6	86	88	87.9	88
21_111	83.8	73.1	91	88	87.9	88
21_45	85.6	83.6	87	88	87.9	88
21_115	80.2	70.1	87	88	87.9	88
22_112	87.4	76.1	95	88	87.9	88
22_62	83.2	70.1	92	88	87.9	88
22_118	83.2	73.1	90	88	87.9	88
24_64	77.2	62.7	87	88	87.9	88
24_65	83.2	76.1	88	88	87.9	88
24_75	81.4	70.1	89	88	87.9	88
25_93	83.2	73.1	90	88	87.9	88
27_120	82.6	77.6	86	88	87.9	88
35_46	78.4	62.7	89	88	87.9	88
35_91	80.2	67.2	89	88	87.9	88

EP 3 150 707 A1

(continued)

SEQ ID NO:	Training cohort			Validation cohort		
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
35_122	79	67.2	87	88	87.9	88
42_58	83.2	71.6	91	88	87.9	88
70_112	82	67.2	92	88	87.9	88
79_112	80.8	67.2	90	88	87.9	88
4_72	89.2	82.1	94	87.8	87.9	87.8
21_106	93.4	85.1	99	86.7	87.9	86
4_64	85.6	74.6	93	86.7	87.9	86
4_66	88	77.6	95	86.7	87.9	86
4_118	89.8	82.1	95	86.7	87.9	86
5_78	88.6	82.1	93	86.7	87.9	86
5_82	89.8	85.1	93	86.7	87.9	86
9_56	83.2	77.6	87	86.7	87.9	86
9_71	86.2	79.1	91	86.7	87.9	86
9_94	85.6	77.6	91	86.7	87.9	86
11_35	80.8	70.1	88	86.7	87.9	86
16_35	85.6	80.6	89	86.7	87.9	86
21_24	85	74.6	92	86.7	87.9	86
21_39	82.6	73.1	89	86.7	87.9	86
21_46	82.6	71.6	90	86.7	87.9	86
21_49	83.2	74.6	89	86.7	87.9	86
21_57	84.4	76.1	90	86.7	87.9	86
21_85	80.2	68.7	88	86.7	87.9	86
22_52	84.4	77.6	89	86.7	87.9	86
22_65	86.8	82.1	90	86.7	87.9	86
22_114	82	77.6	85	86.7	87.9	86
22_94	81.4	71.6	88	86.7	87.9	86
22_99	83.8	74.6	90	86.7	87.9	86
25_44	83.2	71.6	91	86.7	87.9	86
25_65	86.2	80.6	90	86.7	87.9	86
25_67	80.8	70.1	88	86.7	87.9	86
29_31	85	74.6	92	86.7	87.9	86
35_58	82	68.7	91	86.7	87.9	86
35_70	79.6	61.2	92	86.7	87.9	86
35_84	79.6	67.2	88	86.7	87.9	86
55_115	83.2	71.6	91	86.7	87.9	86
58_79	79	64.2	89	86.7	87.9	86
66_83	80.8	67.2	90	86.7	87.9	86

EP 3 150 707 A1

(continued)

SEQ ID NO:	Training cohort			Validation cohort		
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
5 67_80	76.6	65.7	84	86.7	87.9	86
79_98	77.1	60.6	88	86.7	87.9	86
83_104	79	64.2	89	86.7	87.9	86
10 4_36	87.4	76.1	95	85.5	87.9	84
4_100	86.8	74.6	95	85.5	87.9	84
5_109	93.4	89.6	96	85.5	87.9	84
15 16_109	90.4	86.6	93	85.5	87.9	84
25_109	85.6	76.1	92	85.5	87.9	84
58_110	88	83.6	91	85.5	87.9	84
11_71	80.8	74.6	85	85.5	87.9	84
20 21_65	79.6	70.1	86	85.5	87.9	84
21_68	81.4	70.1	89	85.5	87.9	84
21_74	83.2	71.6	91	85.5	87.9	84
25 21_118	84.4	79.1	88	85.5	87.9	84
21_90	77.2	71.6	81	85.5	87.9	84
22_104	79	73.1	83	85.5	87.9	84
24_52	81.4	71.6	88	85.5	87.9	84
30 24_67	82	73.1	88	85.5	87.9	84
24_92	80.2	70.1	87	85.5	87.9	84
34_75	80.2	76.1	83	85.5	87.9	84
35 35_104	79	62.7	90	85.5	87.9	84
81_104	80.1	65.2	90	85.5	87.9	84
35_109	85	73.1	93	84.3	87.9	82
104_109	88	80.6	93	84.3	87.9	82
40 10_99	88	82.1	92	84.3	87.9	82
21_31	78.4	65.7	87	84.3	87.9	82
21_98	78.9	69.7	85	84.3	87.9	82
45 24_98	84.9	77.3	90	84.3	87.9	82
24_100	77.2	61.2	88	84.3	87.9	82
25_100	82.6	71.6	90	84.3	87.9	82
31_34	84.4	76.1	90	84.3	87.9	82
50 31_120	82.6	74.6	88	84.3	87.9	82
35_52	79	65.7	88	84.3	87.9	82
35_114	79.6	65.7	89	84.3	87.9	82
55 35_69	83.8	73.1	91	84.3	87.9	82
58_67	79	58.2	93	84.3	87.9	82
65_78	74.9	65.7	81	84.3	87.9	82

EP 3 150 707 A1

(continued)

SEQ ID NO:	Training cohort			Validation cohort		
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
5 66_94	77.8	56.7	92	84.3	87.9	82
29_109	83.8	73.1	91	83.1	87.9	80
90_109	88	80.6	93	83.1	87.9	80
10 21_34	83.8	74.6	90	83.1	87.9	80
21_52	80.8	71.6	87	83.1	87.9	80
21_121	82	74.6	87	83.1	87.9	80
15 21_94	79.6	70.1	86	83.1	87.9	80
21_102	78.4	71.6	83	83.1	87.9	80
31_98	78.9	68.2	86	83.1	87.9	80
66_93	77.8	59.7	90	83.1	87.9	80
20 34_109	88.6	91	87	81.9	87.9	78
80_109	87.4	80.6	92	81.9	87.9	78
21_100	81.4	71.6	88	81.9	87.9	78
25 35_78	76.6	59.7	88	81.9	87.9	78
42_109	85	77.6	90	80.7	87.9	76
75_109	83.8	76.1	89	80.7	87.9	76
96_109	85	80.6	88	80.7	87.9	76
30 103_109	86.8	80.6	91	80.7	87.9	76
10_92	89.2	86.6	91	80.7	87.9	76
52_109	88	85.1	90	79.5	87.9	74
35 50_79	74.3	56.7	86	86.6	87.5	86
23_35	81.4	67.2	91	85.4	87.5	84
10_50	90.4	83.6	95	84.1	87.5	82
50_67	74.3	61.2	83	82.9	87.5	80
40 77_108	90.4	77.6	99	95.1	87.1	100
24_77	80.8	74.6	85	88.9	87.1	90
9_77	83.8	76.1	89	87.7	87.1	88
45 19_106	93.4	86.6	98	94	84.8	100
87_106	92.2	83.6	98	94	84.8	100
2_8	92.2	85.1	97	94	84.8	100
2_75	88.6	76.1	97	94	84.8	100
50 2_97	88	74.6	97	94	84.8	100
2_102	92.8	82.1	100	94	84.8	100
2_122	89.2	77.6	97	94	84.8	100
55 6_119	91.6	83.6	97	94	84.8	100
7_8	93.4	85.1	99	94	84.8	100
7_32	91	82.1	97	94	84.8	100

EP 3 150 707 A1

(continued)

SEQ ID NO:	Training cohort			Validation cohort		
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
8_17	90.4	79.1	98	94	84.8	100
12_15	92.8	86.4	97	94	84.8	100
17_18	91	82.1	97	94	84.8	100
1_107	95.8	92.5	98	92.8	84.8	98
1_122	96.4	94	98	92.8	84.8	98
2_110	92.2	85.1	97	92.8	84.8	98
2_48	91.6	80.6	99	92.8	84.8	98
2_61	89.8	76.1	99	92.8	84.8	98
2_76	91.6	80.6	99	92.8	84.8	98
8_107	97	94	99	92.8	84.8	98
3_66	92.8	86.6	97	92.8	84.8	98
90_108	88	80.6	93	92.8	84.8	98
5_113	93.4	94	93	92.8	84.8	98
5_53	91	85.1	95	92.8	84.8	98
6_12	92.2	83.3	98	92.8	84.8	98
6_13	94	86.6	99	92.8	84.8	98
6_20	91.6	86.6	95	92.8	84.8	98
6_26	91	83.6	96	92.8	84.8	98
7_111	88.6	77.6	96	92.8	84.8	98
7_57	89.8	79.1	97	92.8	84.8	98
7_101	91.6	88.1	94	92.8	84.8	98
8_9	92.2	89.6	94	92.8	84.8	98
13_17	89.2	79.1	96	92.8	84.8	98
14_55	92.8	82.1	100	92.8	84.8	98
17_20	89.2	79.1	96	92.8	84.8	98
18_69	86.8	76.1	94	92.8	84.8	98
1_15	96.4	94	98	91.6	84.8	96
1_27	97	95.5	98	91.6	84.8	96
1_111	96.4	95.5	97	91.6	84.8	96
1_82	96.4	95.5	97	91.6	84.8	96
1_96	95.8	92.5	98	91.6	84.8	96
49_106	91.6	83.6	97	91.6	84.8	96
7_107	94.6	88.1	99	91.6	84.8	96
16_107	93.4	91	95	91.6	84.8	96
22_107	89.8	83.6	94	91.6	84.8	96
83_107	89.2	80.6	95	91.6	84.8	96
85_107	87.4	77.6	94	91.6	84.8	96

EP 3 150 707 A1

(continued)

SEQ ID NO:	Training cohort			Validation cohort		
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
5 87_107	93.4	88.1	97	91.6	84.8	96
101_107	90.4	79.1	98	91.6	84.8	96
3_26	90.4	86.6	93	91.6	84.8	96
10 4_61	89.2	80.6	95	91.6	84.8	96
64_108	86.8	76.1	94	91.6	84.8	96
66_108	91.6	85.1	96	91.6	84.8	96
15 5_28	91.6	89.6	93	91.6	84.8	96
5_37	90.4	83.6	95	91.6	84.8	96
5_119	91	82.1	97	91.6	84.8	96
30_109	92.8	86.6	97	91.6	84.8	96
20 7_11	91.6	83.6	97	91.6	84.8	96
7_19	92.8	88.1	96	91.6	84.8	96
7_26	93.4	88.1	97	91.6	84.8	96
25 7_30	92.8	88.1	96	91.6	84.8	96
7_38	93.4	86.6	98	91.6	84.8	96
7_46	91	82.1	97	91.6	84.8	96
7_86	89.8	83.6	94	91.6	84.8	96
30 11_13	89.2	82.1	94	91.6	84.8	96
12_17	90.4	80.3	97	91.6	84.8	96
12_25	92.2	89.4	94	91.6	84.8	96
35 18_55	83.2	71.6	91	91.6	84.8	96
18_57	82.6	70.1	91	91.6	84.8	96
22_30	85	77.6	90	91.6	84.8	96
24_26	82.6	76.1	87	91.6	84.8	96
40 24_30	87.4	77.6	94	91.6	84.8	96
35_60	83.8	68.7	94	91.6	84.8	96
41_112	84.4	80.6	87	91.6	84.8	96
45 46_113	86.2	79.1	91	91.6	84.8	96
51_120	83.2	71.6	91	91.6	84.8	96
5_72	90.4	89.6	91	91.5	84.8	95.9
20_106	92.2	83.6	98	90.4	84.8	94
50 25_107	90.4	83.6	95	90.4	84.8	94
47_107	90.4	83.6	95	90.4	84.8	94
89_107	91	80.6	98	90.4	84.8	94
55 103_107	89.2	79.1	96	90.4	84.8	94
104_107	91	83.6	96	90.4	84.8	94
4_33	88	76.1	96	90.4	84.8	94

EP 3 150 707 A1

(continued)

SEQ ID NO:	Training cohort			Validation cohort			
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)	
5	4_38	86.2	74.6	94	90.4	84.8	94
	4_40	88.6	77.6	96	90.4	84.8	94
	19_108	91.6	83.6	97	90.4	84.8	94
10	24_108	89.8	83.6	94	90.4	84.8	94
	5_49	91	85.1	95	90.4	84.8	94
	5_68	89.2	83.6	93	90.4	84.8	94
15	5_74	89.2	82.1	94	90.4	84.8	94
	6_46	85.6	73.1	94	90.4	84.8	94
	7_25	91	86.6	94	90.4	84.8	94
	7_27	90.4	83.6	95	90.4	84.8	94
20	7_39	91	80.6	98	90.4	84.8	94
	7_53	91	86.6	94	90.4	84.8	94
	7_64	90.4	83.6	95	90.4	84.8	94
25	7_122	91.6	86.6	95	90.4	84.8	94
	9_117	85.6	79.1	90	90.4	84.8	94
	13_40	86.2	79.1	91	90.4	84.8	94
	14_35	88	79.1	94	90.4	84.8	94
30	18_40	89.2	77.6	97	90.4	84.8	94
	20_24	86.2	80.6	90	90.4	84.8	94
	22_34	87.4	82.1	91	90.4	84.8	94
35	22_44	85.6	77.6	91	90.4	84.8	94
	24_25	82	67.2	92	90.4	84.8	94
	24_40	82	73.1	88	90.4	84.8	94
	25_56	81.4	73.1	87	90.4	84.8	94
40	25_85	82	76.1	86	90.4	84.8	94
	27_112	86.2	80.6	90	90.4	84.8	94
	30_58	85	80.6	88	90.4	84.8	94
45	30_79	85	80.6	88	90.4	84.8	94
	30_81	82.5	72.7	89	90.4	84.8	94
	33_35	82.6	67.2	93	90.4	84.8	94
	35_40	84.4	68.7	95	90.4	84.8	94
50	35_86	84.4	76.1	90	90.4	84.8	94
	37_46	79.6	71.6	85	90.4	84.8	94
	38_112	86.8	77.6	93	90.4	84.8	94
55	41_58	85.6	80.6	89	90.4	84.8	94
	46_53	84.4	74.6	91	90.4	84.8	94
	46_115	82.6	73.1	89	90.4	84.8	94

EP 3 150 707 A1

(continued)

SEQ ID NO:	Training cohort			Validation cohort		
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
46_87	79.6	73.1	84	90.4	84.8	94
53_94	82	71.6	89	90.4	84.8	94
58_60	85	77.6	90	90.4	84.8	94
21_107	92.8	85.1	98	89.2	84.8	92
31_107	91	80.6	98	89.2	84.8	92
67_107	89.8	82.1	95	89.2	84.8	92
79_107	89.8	79.1	97	89.2	84.8	92
95_107	92.2	85.1	97	89.2	84.8	92
97_107	91	83.6	96	89.2	84.8	92
100_107	89.8	79.1	97	89.2	84.8	92
3_112	93.4	89.6	96	89.2	84.8	92
3_81	94.6	90.9	97	89.2	84.8	92
4_28	88	77.6	95	89.2	84.8	92
53_108	88	76.1	96	89.2	84.8	92
54_108	89.2	80.6	95	89.2	84.8	92
63_108	85.6	79.1	90	89.2	84.8	92
85_108	89.8	83.6	94	89.2	84.8	92
88_108	91	82.1	97	89.2	84.8	92
103_108	88.6	82.1	93	89.2	84.8	92
5_9	93.4	94	93	89.2	84.8	92
5_10	94	91	96	89.2	84.8	92
5_16	92.2	91	93	89.2	84.8	92
5_45	91	86.6	94	89.2	84.8	92
5_51	89.8	86.6	92	89.2	84.8	92
5_104	91	83.6	96	89.2	84.8	92
7_31	90.4	86.6	93	89.2	84.8	92
7_42	91	83.6	96	89.2	84.8	92
7_84	90.4	85.1	94	89.2	84.8	92
7_95	92.2	86.6	96	89.2	84.8	92
9_112	91	88.1	93	89.2	84.8	92
9_116	85	79.1	89	89.2	84.8	92
10_26	88.6	82.1	93	89.2	84.8	92
10_71	90.4	85.1	94	89.2	84.8	92
13_113	88	86.6	89	89.2	84.8	92
13_56	85.6	80.6	89	89.2	84.8	92
15_34	88	82.1	92	89.2	84.8	92
16_24	89.8	85.1	93	89.2	84.8	92

EP 3 150 707 A1

(continued)

SEQ ID NO:	Training cohort			Validation cohort		
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
17_35	85.6	70.1	96	89.2	84.8	92
17_112	90.4	82.1	96	89.2	84.8	92
18_31	86.2	76.1	93	89.2	84.8	92
18_53	87.4	79.1	93	89.2	84.8	92
18_68	88.6	79.1	95	89.2	84.8	92
18_100	86.2	77.6	92	89.2	84.8	92
21_37	81.4	70.1	89	89.2	84.8	92
24_103	80.2	67.2	89	89.2	84.8	92
25_111	86.2	76.1	93	89.2	84.8	92
25_117	85	74.6	92	89.2	84.8	92
25_90	80.2	67.2	89	89.2	84.8	92
29_35	86.2	73.1	95	89.2	84.8	92
37_55	79	68.7	86	89.2	84.8	92
38_99	86.2	76.1	93	89.2	84.8	92
58_115	84.4	73.1	92	89.2	84.8	92
45_107	91	83.6	96	88	84.8	90
3_108	91.6	85.1	96	88	84.8	90
3_39	93.4	89.6	96	88	84.8	90
4_27	88.6	77.6	96	88	84.8	90
4_54	88.6	77.6	96	88	84.8	90
4_95	85.6	73.1	94	88	84.8	90
4_122	85.6	71.6	95	88	84.8	90
25_108	90.4	83.6	95	88	84.8	90
48_108	87.4	77.6	94	88	84.8	90
59_108	88	82.1	92	88	84.8	90
62_108	89.2	80.6	95	88	84.8	90
86_108	86.8	73.1	96	88	84.8	90
5_22	91	86.6	94	88	84.8	90
5_36	91.6	88.1	94	88	84.8	90
5_111	91.6	86.6	95	88	84.8	90
5_39	89.2	80.6	95	88	84.8	90
5_52	90.4	82.1	96	88	84.8	90
5_79	88.6	83.6	92	88	84.8	90
9_12	91	87.9	93	88	84.8	90
9_21	84.4	77.6	89	88	84.8	90
9_22	83.8	79.1	87	88	84.8	90
9_89	87.4	82.1	91	88	84.8	90

EP 3 150 707 A1

(continued)

SEQ ID NO:	Training cohort			Validation cohort			
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)	
5	10_89	88	80.6	93	88	84.8	90
	11_37	86.2	82.1	89	88	84.8	90
	13_46	84.4	76.1	90	88	84.8	90
10	13_121	83.2	77.6	87	88	84.8	90
	16_18	88	83.6	91	88	84.8	90
	18_34	86.2	80.6	90	88	84.8	90
15	18_75	85.6	82.1	88	88	84.8	90
	18_81	85.5	78.8	90	88	84.8	90
	20_35	83.8	74.6	90	88	84.8	90
	21_41	81.4	73.1	87	88	84.8	90
20	21_113	82.6	73.1	89	88	84.8	90
	24_39	82.6	70.1	91	88	84.8	90
	28_46	86.8	77.6	93	88	84.8	90
25	34_41	83.2	79.1	86	88	84.8	90
	34_113	85	74.6	92	88	84.8	90
	35_48	86.8	79.1	92	88	84.8	90
	35_102	80.8	70.1	88	88	84.8	90
30	44_111	79.6	62.7	91	88	84.8	90
	46_112	76.6	62.7	86	88	84.8	90
	47_112	81.4	76.1	85	88	84.8	90
35	46_70	75.4	61.2	85	88	84.8	90
	46_89	78.4	65.7	87	88	84.8	90
	55_65	83.2	67.2	94	88	84.8	90
	58_70	77.8	62.7	88	88	84.8	90
40	66_75	78.4	62.7	89	88	84.8	90
	80_83	72.5	53.7	85	88	84.8	90
	25_106	88.6	79.1	95	86.7	84.8	88
45	34_106	89.2	80.6	95	86.7	84.8	88
	3_34	91.6	86.6	95	86.7	84.8	88
	3_121	94	92.5	95	86.7	84.8	88
	3_96	93.4	89.6	96	86.7	84.8	88
50	4_42	86.8	76.1	94	86.7	84.8	88
	4_57	88.6	79.1	95	86.7	84.8	88
	4_67	86.8	74.6	95	86.7	84.8	88
55	4_70	86.8	73.1	96	86.7	84.8	88
	79_108	90.4	79.1	98	86.7	84.8	88
	6_52	87.4	80.6	92	86.7	84.8	88

EP 3 150 707 A1

(continued)

SEQ ID NO:	Training cohort			Validation cohort		
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
5 6_99	86.8	79.1	92	86.7	84.8	88
40_109	86.8	77.6	93	86.7	84.8	88
9_11	88	80.6	93	86.7	84.8	88
10 9_37	85	79.1	89	86.7	84.8	88
9_45	86.8	83.6	89	86.7	84.8	88
9_98	84.3	80.3	87	86.7	84.8	88
15 10_22	84.4	77.6	89	86.7	84.8	88
10_55	86.8	83.6	89	86.7	84.8	88
11_39	79.6	71.6	85	86.7	84.8	88
11_46	79	68.7	86	86.7	84.8	88
20 11_75	81.4	73.1	87	86.7	84.8	88
13_63	88.6	91	87	86.7	84.8	88
13_81	84.3	81.8	86	86.7	84.8	88
25 16_46	84.4	82.1	86	86.7	84.8	88
16_58	84.4	82.1	86	86.7	84.8	88
16_120	84.4	77.6	89	86.7	84.8	88
17_34	84.4	73.1	92	86.7	84.8	88
30 18_78	82.6	76.1	87	86.7	84.8	88
18_84	88.6	79.1	95	86.7	84.8	88
21_26	83.2	70.1	92	86.7	84.8	88
35 21_33	82.6	74.6	88	86.7	84.8	88
21_42	85	71.6	94	86.7	84.8	88
21_43	82.6	71.6	90	86.7	84.8	88
22_25	82	76.1	86	86.7	84.8	88
40 22_75	80.2	68.7	88	86.7	84.8	88
22_89	82.6	76.1	87	86.7	84.8	88
22_121	82	70.1	90	86.7	84.8	88
45 24_44	81.4	70.1	89	86.7	84.8	88
24_46	82.6	74.6	88	86.7	84.8	88
25_118	84.4	74.6	91	86.7	84.8	88
34_35	79.6	70.1	86	86.7	84.8	88
50 35_49	84.4	77.6	89	86.7	84.8	88
51_83	82	67.2	92	86.7	84.8	88
56_66	83.8	74.6	90	86.7	84.8	88
55 58_66	83.8	68.7	94	86.7	84.8	88
70_104	79.6	67.2	88	86.7	84.8	88
24_72	79	65.7	88	86.6	84.8	87.8

EP 3 150 707 A1

(continued)

SEQ ID NO:	Training cohort			Validation cohort		
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
31_106	89.8	77.6	98	85.5	84.8	86
71_106	89.8	79.1	97	85.5	84.8	86
99_106	89.8	77.6	98	85.5	84.8	86
76_108	85.6	79.1	90	85.5	84.8	86
21_110	89.2	85.1	92	85.5	84.8	86
9_34	86.8	80.6	91	85.5	84.8	86
9_83	83.8	74.6	90	85.5	84.8	86
9_102	86.2	80.6	90	85.5	84.8	86
10_39	91	86.6	94	85.5	84.8	86
11_24	83.2	76.1	88	85.5	84.8	86
11_31	83.8	73.1	91	85.5	84.8	86
11_66	80.8	68.7	89	85.5	84.8	86
11_85	79.6	70.1	86	85.5	84.8	86
11_88	77.2	71.6	81	85.5	84.8	86
13_47	89.8	85.1	93	85.5	84.8	86
16_89	85	79.1	89	85.5	84.8	86
21_48	82.6	74.6	88	85.5	84.8	86
22_39	83.2	73.1	90	85.5	84.8	86
22_51	82	76.1	86	85.5	84.8	86
22_67	79	64.2	89	85.5	84.8	86
22_71	81.4	70.1	89	85.5	84.8	86
22_103	78.4	70.1	84	85.5	84.8	86
24_45	84.4	74.6	91	85.5	84.8	86
24_85	76.6	64.2	85	85.5	84.8	86
24_89	83.2	80.6	85	85.5	84.8	86
25_55	85	71.6	94	85.5	84.8	86
25_57	86.2	77.6	92	85.5	84.8	86
25_71	83.2	70.1	92	85.5	84.8	86
25_104	81.4	71.6	88	85.5	84.8	86
28_71	86.8	80.6	91	85.5	84.8	86
31_39	82	70.1	90	85.5	84.8	86
34_111	80.8	73.1	86	85.5	84.8	86
35_117	77.8	58.2	91	85.5	84.8	86
35_76	81.4	65.7	92	85.5	84.8	86
44_46	79	68.7	86	85.5	84.8	86
46_80	78.4	61.2	90	85.5	84.8	86
66_78	76	61.2	86	85.5	84.8	86

EP 3 150 707 A1

(continued)

SEQ ID NO:	Training cohort			Validation cohort		
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
5 66_88	79	65.7	88	85.5	84.8	86
70_119	75.4	62.7	84	85.5	84.8	86
70_98	80.7	63.6	92	85.5	84.8	86
10 79_89	80.8	65.7	91	85.5	84.8	86
103_106	89.2	79.1	96	84.3	84.8	84
3_78	88.6	83.6	92	84.3	84.8	84
15 32_109	87.4	77.6	94	84.3	84.8	84
35_110	85.6	74.6	93	84.3	84.8	84
9_75	83.8	76.1	89	84.3	84.8	84
10_74	86.2	80.6	90	84.3	84.8	84
20 11_79	80.2	70.1	87	84.3	84.8	84
11_98	81.9	74.2	87	84.3	84.8	84
16_21	85	77.6	90	84.3	84.8	84
25 20_67	84.4	77.6	89	84.3	84.8	84
21_59	82	74.6	87	84.3	84.8	84
21_120	79.6	71.6	85	84.3	84.8	84
21_86	79.6	73.1	84	84.3	84.8	84
30 21_96	77.2	68.7	83	84.3	84.8	84
21_99	82.6	77.6	86	84.3	84.8	84
22_92	86.2	82.1	89	84.3	84.8	84
35 22_93	82	68.7	91	84.3	84.8	84
24_94	79	62.7	90	84.3	84.8	84
31_35	77.2	61.2	88	84.3	84.8	84
32_35	84.4	74.6	91	84.3	84.8	84
40 34_42	79	70.1	85	84.3	84.8	84
35_57	79	58.2	93	84.3	84.8	84
42_94	77.8	55.2	93	84.3	84.8	84
45 44_70	83.8	73.1	91	84.3	84.8	84
55_67	81.4	64.2	93	84.3	84.8	84
66_99	75.4	58.2	87	84.3	84.8	84
79_94	76.6	59.7	88	84.3	84.8	84
50 82_83	72.5	52.2	86	84.3	84.8	84
93_106	89.2	76.1	98	83.1	84.8	82
51_109	86.8	76.1	94	83.1	84.8	82
55 53_109	91.6	88.1	94	83.1	84.8	82
58_109	86.2	80.6	90	83.1	84.8	82
10_44	87.4	82.1	91	83.1	84.8	82

EP 3 150 707 A1

(continued)

SEQ ID NO:	Training cohort			Validation cohort		
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
10_96	90.4	88.1	92	83.1	84.8	82
11_21	81.4	74.6	86	83.1	84.8	82
11_70	79.6	68.7	87	83.1	84.8	82
11_83	79	68.7	86	83.1	84.8	82
21_44	82	71.6	89	83.1	84.8	82
21_58	81.4	70.1	89	83.1	84.8	82
21_70	80.8	68.7	89	83.1	84.8	82
24_56	81.4	77.6	84	83.1	84.8	82
25_31	80.8	65.7	91	83.1	84.8	82
25_103	82	70.1	90	83.1	84.8	82
27_34	83.8	77.6	88	83.1	84.8	82
35_64	79	65.7	88	83.1	84.8	82
44_79	82.6	65.7	94	83.1	84.8	82
55_79	78.4	62.7	89	83.1	84.8	82
55_103	77.2	64.2	86	83.1	84.8	82
67_89	73.1	52.2	87	83.1	84.8	82
70_94	76	61.2	86	83.1	84.8	82
79_119	75.4	64.2	83	83.1	84.8	82
83_103	71.3	50.7	85	83.1	84.8	82
3_109	92.2	89.6	94	81.9	84.8	80
100_108	89.8	83.6	94	81.9	84.8	80
22_109	86.2	77.6	92	81.9	84.8	80
24_109	84.4	79.1	88	81.9	84.8	80
46_109	83.8	73.1	91	81.9	84.8	80
55_109	83.8	76.1	89	81.9	84.8	80
85_109	83.2	77.6	87	81.9	84.8	80
11_16	89.2	83.6	93	81.9	84.8	80
11_78	79.6	71.6	85	81.9	84.8	80
11_121	80.2	70.1	87	81.9	84.8	80
11_92	78.4	68.7	85	81.9	84.8	80
11_103	79.6	67.2	88	81.9	84.8	80
21_63	83.2	74.6	89	81.9	84.8	80
21_67	81.4	68.7	90	81.9	84.8	80
21_79	80.2	73.1	85	81.9	84.8	80
21_81	80.1	72.7	85	81.9	84.8	80
21_84	83.2	73.1	90	81.9	84.8	80
21_92	80.2	71.6	86	81.9	84.8	80

EP 3 150 707 A1

(continued)

SEQ ID NO:	Training cohort			Validation cohort		
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
21_93	78.4	71.6	83	81.9	84.8	80
28_75	81.4	73.1	87	81.9	84.8	80
42_52	79	59.7	92	81.9	84.8	80
81_94	75.9	57.6	88	81.9	84.8	80
94_121	72.5	53.7	85	81.9	84.8	80
21_72	79.6	70.1	86	81.7	84.8	79.6
47_109	85.6	79.1	90	80.7	84.8	78
56_109	82.6	76.1	87	80.7	84.8	78
62_109	86.8	77.6	93	80.7	84.8	78
82_109	85.6	76.1	92	80.7	84.8	78
88_109	85.6	83.6	87	80.7	84.8	78
89_109	85	77.6	90	80.7	84.8	78
13_104	88.6	89.6	88	80.7	84.8	78
29_75	82	74.6	87	80.7	84.8	78
29_79	83.2	74.6	89	80.7	84.8	78
31_45	85.6	79.1	90	80.7	84.8	78
79_99	74.3	55.2	87	80.7	84.8	78
104_121	77.8	67.2	85	80.7	84.8	78
67_109	84.4	74.6	91	79.5	84.8	76
94_109	82.6	76.1	87	79.5	84.8	76
98_109	88	84.8	90	79.5	84.8	76
31_78	80.2	67.2	89	79.5	84.8	76
83_109	83.8	76.1	89	78.3	84.8	74
79_80	75.4	58.2	87	78.3	84.8	74
92_109	85.6	83.6	87	77.1	84.8	72
31_100	79.6	70.1	86	77.1	84.8	72
25_50	85.6	74.6	93	91.5	84.4	96
23_107	88	77.6	95	90.2	84.4	94
7_23	91	85.1	95	90.2	84.4	94
14_50	86.2	73.1	95	90.2	84.4	94
50_108	89.8	80.6	96	87.8	84.4	90
50_107	89.8	80.6	96	86.6	84.4	88
5_23	91	86.6	94	85.4	84.4	86
50_112	76	62.7	85	85.4	84.4	86
50_71	77.2	65.7	85	85.4	84.4	86
16_50	84.4	79.1	88	84.1	84.4	84
21_50	82	74.6	87	84.1	84.4	84

EP 3 150 707 A1

(continued)

SEQ ID NO:	Training cohort			Validation cohort		
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
50_100	74.9	59.7	85	82.9	84.4	82
50_70	77.2	62.7	87	81.7	84.4	80
50_55	78.4	62.7	89	80.5	84.4	78
10_77	89.8	79.1	97	92.6	83.9	98
77_106	92.2	82.1	99	91.4	83.9	96
22_77	85.6	77.6	91	90.1	83.9	94
25_77	85	73.1	93	90.1	83.9	94
35_77	77.2	64.2	86	88.9	83.9	92
77_109	86.2	82.1	89	86.4	83.9	88
28_77	82.6	76.1	87	86.4	83.9	88
5_77	88	85.1	90	85.2	83.9	86
6_7	91.6	82.1	98	92.8	81.8	100
6_49	89.8	86.6	92	92.8	81.8	100
7_17	89.8	77.6	98	92.8	81.8	100
8_111	90.4	79.1	98	92.8	81.8	100
13_15	88.6	82.1	93	92.8	81.8	100
15_20	88.6	83.6	92	92.8	81.8	100
15_112	89.8	82.1	95	92.8	81.8	100
17_119	87.4	74.6	96	92.8	81.8	100
17_87	86.2	71.6	96	92.8	81.8	100
2_43	88.6	77.6	96	91.6	81.8	98
5_14	93.4	88.1	97	91.6	81.8	98
7_14	93.4	88.1	97	91.6	81.8	98
7_33	91	82.1	97	91.6	81.8	98
7_48	90.4	85.1	94	91.6	81.8	98
7_59	90.4	82.1	96	91.6	81.8	98
7_89	91.6	83.6	97	91.6	81.8	98
8_110	93.4	89.6	96	91.6	81.8	98
8_14	89.8	77.6	98	91.6	81.8	98
11_87	86.8	74.6	95	91.6	81.8	98
13_19	90.4	88.1	92	91.6	81.8	98
13_96	86.2	74.6	94	91.6	81.8	98
14_66	82.6	65.7	94	91.6	81.8	98
14_80	85	68.7	96	91.6	81.8	98
14_96	86.8	77.6	93	91.6	81.8	98
15_25	87.4	73.1	97	91.6	81.8	98
15_65	86.2	76.1	93	91.6	81.8	98

EP 3 150 707 A1

(continued)

SEQ ID NO:	Training cohort			Validation cohort		
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
17_26	88.6	79.1	95	91.6	81.8	98
18_76	92.8	91	94	91.6	81.8	98
19_45	85	71.6	94	91.6	81.8	98
19_70	88	82.1	92	91.6	81.8	98
19_83	86.2	82.1	89	91.6	81.8	98
24_117	83.8	67.2	95	91.6	81.8	98
12_106	94	86.4	99	90.4	81.8	96
38_106	90.4	80.6	97	90.4	81.8	96
28_107	93.4	86.6	98	90.4	81.8	96
36_107	88	76.1	96	90.4	81.8	96
38_107	91.6	82.1	98	90.4	81.8	96
41_107	91	83.6	96	90.4	81.8	96
51_107	88.6	77.6	96	90.4	81.8	96
59_107	88.6	77.6	96	90.4	81.8	96
68_107	88	76.1	96	90.4	81.8	96
70_107	88	76.1	96	90.4	81.8	96
75_107	89.8	77.6	98	90.4	81.8	96
82_107	89.2	79.1	96	90.4	81.8	96
3_8	94.6	92.5	96	90.4	81.8	96
3_20	91	86.6	94	90.4	81.8	96
14_108	88.6	77.6	96	90.4	81.8	96
39_108	94	89.6	97	90.4	81.8	96
5_40	91.6	88.1	94	90.4	81.8	96
5_41	94	89.6	97	90.4	81.8	96
5_60	92.2	89.6	94	90.4	81.8	96
6_16	88.6	82.1	93	90.4	81.8	96
6_38	88.6	74.6	98	90.4	81.8	96
6_74	87.4	76.1	95	90.4	81.8	96
6_120	88	79.1	94	90.4	81.8	96
7_29	92.8	85.1	98	90.4	81.8	96
7_43	92.8	89.6	95	90.4	81.8	96
7_113	94.6	89.6	98	90.4	81.8	96
7_73	91	85.1	95	90.4	81.8	96
8_25	92.2	83.6	98	90.4	81.8	96
8_59	91	82.1	97	90.4	81.8	96
10_30	87.4	76.1	95	90.4	81.8	96
11_30	88	80.6	93	90.4	81.8	96

EP 3 150 707 A1

(continued)

SEQ ID NO:	Training cohort			Validation cohort		
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
11_119	82.6	73.1	89	90.4	81.8	96
13_111	85.6	73.1	94	90.4	81.8	96
14_42	87.4	71.6	98	90.4	81.8	96
14_46	86.2	73.1	95	90.4	81.8	96
15_31	83.8	68.7	94	90.4	81.8	96
15_35	86.2	73.1	95	90.4	81.8	96
15_94	85	73.1	93	90.4	81.8	96
17_37	85.6	73.1	94	90.4	81.8	96
18_48	88.6	79.1	95	90.4	81.8	96
18_89	85.6	79.1	90	90.4	81.8	96
19_39	92.2	83.6	98	90.4	81.8	96
19_93	85	74.6	92	90.4	81.8	96
19_96	87.4	80.6	92	90.4	81.8	96
24_60	79.6	62.7	91	90.4	81.8	96
30_120	83.2	76.1	88	90.4	81.8	96
26_106	91.6	83.6	97	89.2	81.8	94
40_106	90.4	77.6	99	89.2	81.8	94
53_106	92.2	83.6	98	89.2	81.8	94
10_107	88.6	77.6	96	89.2	81.8	94
15_107	90.4	77.6	99	89.2	81.8	94
17_107	88.6	76.1	97	89.2	81.8	94
29_107	89.2	79.1	96	89.2	81.8	94
40_107	91.6	80.6	99	89.2	81.8	94
43_107	92.8	89.6	95	89.2	81.8	94
46_107	89.8	77.6	98	89.2	81.8	94
56_107	89.2	79.1	96	89.2	81.8	94
60_107	90.4	79.1	98	89.2	81.8	94
62_107	91.6	83.6	97	89.2	81.8	94
64_107	91	85.1	95	89.2	81.8	94
71_107	90.4	83.6	95	89.2	81.8	94
76_107	88.6	77.6	96	89.2	81.8	94
80_107	89.2	79.1	96	89.2	81.8	94
81_107	92.8	86.4	97	89.2	81.8	94
84_107	89.2	80.6	95	89.2	81.8	94
86_107	90.4	79.1	98	89.2	81.8	94
93_107	89.8	79.1	97	89.2	81.8	94
11_108	90.4	77.6	99	89.2	81.8	94

EP 3 150 707 A1

(continued)

SEQ ID NO:	Training cohort			Validation cohort		
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
29_108	91	80.6	98	89.2	81.8	94
38_108	86.2	71.6	96	89.2	81.8	94
56_108	90.4	80.6	97	89.2	81.8	94
102_108	89.2	79.1	96	89.2	81.8	94
5_63	91	86.6	94	89.2	81.8	94
6_54	90.4	83.6	95	89.2	81.8	94
6_55	86.8	74.6	95	89.2	81.8	94
6_71	87.4	77.6	94	89.2	81.8	94
6_80	86.2	73.1	95	89.2	81.8	94
7_41	91.6	89.6	93	89.2	81.8	94
7_49	91	85.1	95	89.2	81.8	94
7_56	91.6	86.6	95	89.2	81.8	94
7_63	93.4	88.1	97	89.2	81.8	94
7_68	91.6	83.6	97	89.2	81.8	94
9_30	87.4	82.1	91	89.2	81.8	94
13_38	86.2	82.1	89	89.2	81.8	94
13_112	85.6	83.6	87	89.2	81.8	94
13_71	88	82.1	92	89.2	81.8	94
13_90	86.2	82.1	89	89.2	81.8	94
14_29	90.4	76.1	100	89.2	81.8	94
14_83	83.8	68.7	94	89.2	81.8	94
15_58	88	79.1	94	89.2	81.8	94
17_25	87.4	74.6	96	89.2	81.8	94
17_90	84.4	71.6	93	89.2	81.8	94
18_39	84.4	71.6	93	89.2	81.8	94
18_60	88.6	77.6	96	89.2	81.8	94
18_62	86.8	76.1	94	89.2	81.8	94
18_82	86.2	82.1	89	89.2	81.8	94
18_91	89.2	80.6	95	89.2	81.8	94
18_94	84.4	77.6	89	89.2	81.8	94
18_104	83.2	73.1	90	89.2	81.8	94
19_79	85	76.1	91	89.2	81.8	94
24_61	83.2	71.6	91	89.2	81.8	94
25_30	88.6	77.6	96	89.2	81.8	94
35_38	83.2	70.1	92	89.2	81.8	94
37_42	84.4	74.6	91	89.2	81.8	94
37_67	79.6	68.7	87	89.2	81.8	94

EP 3 150 707 A1

(continued)

SEQ ID NO:	Training cohort			Validation cohort		
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
38_58	83.2	70.1	92	89.2	81.8	94
55_112	80.8	65.7	91	89.2	81.8	94
46_60	85.6	74.6	93	89.2	81.8	94
51_97	89.2	82.1	94	89.2	81.8	94
83_113	85	76.1	91	89.2	81.8	94
4_106	89.2	77.6	97	88	81.8	92
54_106	91.6	80.6	99	88	81.8	92
32_107	91	79.1	99	88	81.8	92
42_107	86.8	74.6	95	88	81.8	92
63_107	92.2	85.1	97	88	81.8	92
78_107	88	76.1	96	88	81.8	92
88_107	91	80.6	98	88	81.8	92
90_107	89.8	80.6	96	88	81.8	92
3_70	94	88.1	98	88	81.8	92
3_75	92.8	89.6	95	88	81.8	92
4_73	87.4	77.6	94	88	81.8	92
22_108	88	80.6	93	88	81.8	92
36_108	86.8	73.1	96	88	81.8	92
40_108	89.8	79.1	97	88	81.8	92
5_6	95.2	94	96	88	81.8	92
5_43	87.4	82.1	91	88	81.8	92
5_48	94	89.6	97	88	81.8	92
5_62	89.2	85.1	92	88	81.8	92
5_64	89.8	82.1	95	88	81.8	92
5_65	88	79.1	94	88	81.8	92
5_114	89.8	82.1	95	88	81.8	92
5_73	92.2	89.6	94	88	81.8	92
5_88	91	82.1	97	88	81.8	92
6_96	88.6	83.6	92	88	81.8	92
7_40	95.2	89.6	99	88	81.8	92
7_61	92.2	88.1	95	88	81.8	92
7_116	91	85.1	95	88	81.8	92
8_11	91.6	88.1	94	88	81.8	92
37_110	88	83.6	91	88	81.8	92
9_17	83.8	73.1	91	88	81.8	92
9_39	85	76.1	91	88	81.8	92
9_44	88	82.1	92	88	81.8	92

EP 3 150 707 A1

(continued)

SEQ ID NO:	Training cohort			Validation cohort			
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)	
5	9_114	83.2	77.6	87	88	81.8	92
	9_87	82.6	80.6	84	88	81.8	92
	10_49	91	89.6	92	88	81.8	92
10	10_65	88	83.6	91	88	81.8	92
	10_87	86.8	82.1	90	88	81.8	92
	10_90	86.2	83.6	88	88	81.8	92
15	11_38	85.6	76.1	92	88	81.8	92
	13_37	90.4	89.6	91	88	81.8	92
	13_44	88	86.6	89	88	81.8	92
	13_51	88.6	85.1	91	88	81.8	92
20	13_59	86.8	79.1	92	88	81.8	92
	14_20	91	82.1	97	88	81.8	92
	14_58	89.2	82.1	94	88	81.8	92
25	18_36	88.6	82.1	93	88	81.8	92
	19_25	83.8	70.1	93	88	81.8	92
	19_55	89.2	82.1	94	88	81.8	92
	19_67	86.8	77.6	93	88	81.8	92
30	21_38	86.8	77.6	93	88	81.8	92
	22_29	88	82.1	92	88	81.8	92
	22_111	83.2	67.2	94	88	81.8	92
35	25_62	80.8	74.6	85	88	81.8	92
	29_55	83.2	74.6	89	88	81.8	92
	29_66	82.6	70.1	91	88	81.8	92
40	34_51	86.2	82.1	89	88	81.8	92
	34_60	84.4	77.6	89	88	81.8	92
	35_73	81.4	71.6	88	88	81.8	92
45	58_111	79	64.2	89	88	81.8	92
	37_112	84.4	74.6	91	88	81.8	92
	51_112	86.8	80.6	91	88	81.8	92
	46_51	84.4	73.1	92	88	81.8	92
	51_75	80.8	68.7	89	88	81.8	92
50	51_119	80.8	70.1	88	88	81.8	92
	51_96	82	70.1	90	88	81.8	92
	98_113	86.7	75.8	94	88	81.8	92
55	90_94	75.4	56.7	88	88	81.8	92
	72_108	89.2	79.1	96	87.8	81.8	91.8
	39_106	89.8	79.1	97	86.7	81.8	90

EP 3 150 707 A1

(continued)

SEQ ID NO:	Training cohort			Validation cohort		
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
44_106	91	80.6	98	86.7	81.8	90
47_106	89.2	79.1	96	86.7	81.8	90
64_106	89.8	80.6	96	86.7	81.8	90
66_106	89.8	76.1	99	86.7	81.8	90
97_106	89.8	82.1	95	86.7	81.8	90
98_106	89.8	80.3	96	86.7	81.8	90
91_107	90.4	79.1	98	86.7	81.8	90
3_93	94.6	91	97	86.7	81.8	90
4_15	89.2	82.1	94	86.7	81.8	90
4_17	87.4	73.1	97	86.7	81.8	90
4_29	89.2	79.1	96	86.7	81.8	90
4_60	86.8	73.1	96	86.7	81.8	90
10_108	86.2	74.6	94	86.7	81.8	90
16_108	90.4	86.6	93	86.7	81.8	90
28_108	87.4	80.6	92	86.7	81.8	90
51_108	86.8	74.6	95	86.7	81.8	90
67_108	88.6	79.1	95	86.7	81.8	90
69_108	86.8	77.6	93	86.7	81.8	90
82_108	86.8	76.1	94	86.7	81.8	90
91_108	86.8	77.6	93	86.7	81.8	90
5_59	91	86.6	94	86.7	81.8	90
5_118	89.2	83.6	93	86.7	81.8	90
5_85	87.4	83.6	90	86.7	81.8	90
5_86	92.8	89.6	95	86.7	81.8	90
6_34	89.2	82.1	94	86.7	81.8	90
6_35	88.6	76.1	97	86.7	81.8	90
6_66	88.6	76.1	97	86.7	81.8	90
15_109	86.2	73.1	95	86.7	81.8	90
9_26	89.2	86.6	91	86.7	81.8	90
9_54	86.8	82.1	90	86.7	81.8	90
9_66	83.8	77.6	88	86.7	81.8	90
9_80	84.4	80.6	87	86.7	81.8	90
9_97	87.4	85.1	89	86.7	81.8	90
10_46	90.4	80.6	97	86.7	81.8	90
10_56	83.8	74.6	90	86.7	81.8	90
10_117	85	74.6	92	86.7	81.8	90
10_75	86.2	76.1	93	86.7	81.8	90

EP 3 150 707 A1

(continued)

SEQ ID NO:	Training cohort			Validation cohort		
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
12_42	84.9	72.7	93	86.7	81.8	90
12_67	86.7	78.8	92	86.7	81.8	90
13_14	86.2	79.1	91	86.7	81.8	90
13_65	86.8	83.6	89	86.7	81.8	90
17_21	85.6	73.1	94	86.7	81.8	90
17_24	83.8	73.1	91	86.7	81.8	90
17_31	85.6	70.1	96	86.7	81.8	90
17_42	83.8	64.2	97	86.7	81.8	90
17_66	85.6	67.2	98	86.7	81.8	90
18_73	85	76.1	91	86.7	81.8	90
18_90	83.2	71.6	91	86.7	81.8	90
21_62	78.4	62.7	89	86.7	81.8	90
22_26	86.2	77.6	92	86.7	81.8	90
22_37	81.4	73.1	87	86.7	81.8	90
22_56	82	73.1	88	86.7	81.8	90
24_43	83.8	80.6	86	86.7	81.8	90
24_114	83.2	71.6	91	86.7	81.8	90
24_95	79.6	73.1	84	86.7	81.8	90
25_29	86.2	74.6	94	86.7	81.8	90
25_97	79.6	65.7	89	86.7	81.8	90
26_31	86.8	76.1	94	86.7	81.8	90
26_35	86.2	77.6	92	86.7	81.8	90
27_119	83.2	77.6	87	86.7	81.8	90
27_98	80.1	71.2	86	86.7	81.8	90
28_83	84.4	77.6	89	86.7	81.8	90
29_71	85.6	79.1	90	86.7	81.8	90
30_67	85.6	74.6	93	86.7	81.8	90
35_101	77.8	67.2	85	86.7	81.8	90
66_111	83.2	64.2	96	86.7	81.8	90
39_42	83.2	70.1	92	86.7	81.8	90
39_51	86.2	77.6	92	86.7	81.8	90
40_55	85.6	70.1	96	86.7	81.8	90
65_112	83.8	74.6	90	86.7	81.8	90
44_67	80.2	71.6	86	86.7	81.8	90
47_66	78.4	65.7	87	86.7	81.8	90
61_67	79	67.2	87	86.7	81.8	90
66_118	80.8	65.7	91	86.7	81.8	90

EP 3 150 707 A1

(continued)

SEQ ID NO:	Training cohort			Validation cohort		
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
5 67_120	75.4	61.2	85	86.7	81.8	90
79_115	80.8	67.2	90	86.7	81.8	90
83_99	70.7	53.7	82	86.7	81.8	90
10 24_106	90.4	82.1	96	85.5	81.8	88
29_106	89.2	79.1	96	85.5	81.8	88
35_106	87.4	73.1	97	85.5	81.8	88
15 46_106	88.6	74.6	98	85.5	81.8	88
58_106	90.4	79.1	98	85.5	81.8	88
80_106	88.6	76.1	97	85.5	81.8	88
82_106	88.6	76.1	97	85.5	81.8	88
20 83_106	88.6	74.6	98	85.5	81.8	88
88_106	92.2	82.1	99	85.5	81.8	88
104_106	89.8	79.1	97	85.5	81.8	88
25 3_22	94	91	96	85.5	81.8	88
3_31	95.2	91	98	85.5	81.8	88
3_79	94	91	96	85.5	81.8	88
4_111	85.6	71.6	95	85.5	81.8	88
30 32_108	88.6	82.1	93	85.5	81.8	88
78_108	90.4	80.6	97	85.5	81.8	88
84_108	85.6	76.1	92	85.5	81.8	88
35 92_108	89.8	85.1	93	85.5	81.8	88
5_55	89.8	82.1	95	85.5	81.8	88
5_71	88	83.6	91	85.5	81.8	88
5_91	88.6	82.1	93	85.5	81.8	88
40 5_94	88.6	82.1	93	85.5	81.8	88
5_100	88	82.1	92	85.5	81.8	88
5_103	89.8	82.1	95	85.5	81.8	88
45 6_31	85.6	71.6	95	85.5	81.8	88
6_89	86.8	77.6	93	85.5	81.8	88
28_109	91	86.6	94	85.5	81.8	88
38_109	85	73.1	93	85.5	81.8	88
50 9_110	89.2	82.1	94	85.5	81.8	88
9_42	85	79.1	89	85.5	81.8	88
9_47	82.6	77.6	86	85.5	81.8	88
55 9_62	80.2	74.6	84	85.5	81.8	88
9_74	86.8	80.6	91	85.5	81.8	88
10_24	88	82.1	92	85.5	81.8	88

EP 3 150 707 A1

(continued)

SEQ ID NO:	Training cohort			Validation cohort		
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
10_116	85.6	76.1	92	85.5	81.8	88
10_118	86.8	80.6	91	85.5	81.8	88
10_80	83.8	76.1	89	85.5	81.8	88
11_20	88	83.6	91	85.5	81.8	88
11_56	82.6	73.1	89	85.5	81.8	88
11_62	83.8	71.6	92	85.5	81.8	88
11_114	82.6	68.7	92	85.5	81.8	88
11_102	82	73.1	88	85.5	81.8	88
12_14	92.2	84.8	97	85.5	81.8	88
12_35	84.9	74.2	92	85.5	81.8	88
12_51	86.7	80.3	91	85.5	81.8	88
13_78	84.4	79.1	88	85.5	81.8	88
13_82	82.6	77.6	86	85.5	81.8	88
13_94	85.6	82.1	88	85.5	81.8	88
13_100	83.2	80.6	85	85.5	81.8	88
16_45	85	80.6	88	85.5	81.8	88
16_98	84.9	81.8	87	85.5	81.8	88
17_96	85	70.1	95	85.5	81.8	88
18_83	82	73.1	88	85.5	81.8	88
20_21	83.2	74.6	89	85.5	81.8	88
20_42	83.8	71.6	92	85.5	81.8	88
21_30	85	79.1	89	85.5	81.8	88
21_40	83.2	65.7	95	85.5	81.8	88
21_51	76	64.2	84	85.5	81.8	88
21_61	81.4	71.6	88	85.5	81.8	88
21_117	79	70.1	85	85.5	81.8	88
21_87	80.2	71.6	86	85.5	81.8	88
24_57	82.6	73.1	89	85.5	81.8	88
24_63	80.2	71.6	86	85.5	81.8	88
25_82	83.2	74.6	89	85.5	81.8	88
27_58	79	70.1	85	85.5	81.8	88
31_47	78.4	67.2	86	85.5	81.8	88
35_36	80.2	67.2	89	85.5	81.8	88
35_56	80.2	67.2	89	85.5	81.8	88
35_62	80.2	70.1	87	85.5	81.8	88
35_74	79	65.7	88	85.5	81.8	88
40_67	80.2	65.7	90	85.5	81.8	88

EP 3 150 707 A1

(continued)

SEQ ID NO:	Training cohort			Validation cohort		
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
42_55	83.8	71.6	92	85.5	81.8	88
42_120	79	68.7	86	85.5	81.8	88
42_98	81.3	63.6	93	85.5	81.8	88
75_112	79.6	71.6	85	85.5	81.8	88
44_71	77.2	64.2	86	85.5	81.8	88
46_119	76	62.7	85	85.5	81.8	88
46_96	74.9	62.7	83	85.5	81.8	88
51_93	81.4	68.7	90	85.5	81.8	88
75_113	88	82.1	92	85.5	81.8	88
53_58	82.6	74.6	88	85.5	81.8	88
66_80	78.4	58.2	92	85.5	81.8	88
66_120	77.8	61.2	89	85.5	81.8	88
45_106	90.4	79.1	98	84.3	81.8	86
55_106	89.2	77.6	97	84.3	81.8	86
59_106	88	74.6	97	84.3	81.8	86
63_106	89.8	80.6	96	84.3	81.8	86
67_106	88	74.6	97	84.3	81.8	86
79_106	87.4	73.1	97	84.3	81.8	86
89_106	88	76.1	96	84.3	81.8	86
96_106	88	76.1	96	84.3	81.8	86
5_46	88	85.1	90	84.3	81.8	86
5_81	87.3	83.3	90	84.3	81.8	86
5_120	88	85.1	90	84.3	81.8	86
5_121	88	85.1	90	84.3	81.8	86
5_93	88	85.1	90	84.3	81.8	86
5_98	87.3	83.3	90	84.3	81.8	86
5_99	86.2	80.6	90	84.3	81.8	86
6_79	88.6	77.6	96	84.3	81.8	86
34_110	86.2	86.6	86	84.3	81.8	86
9_65	83.8	79.1	87	84.3	81.8	86
9_67	82	76.1	86	84.3	81.8	86
9_90	82.6	76.1	87	84.3	81.8	86
9_121	83.8	77.6	88	84.3	81.8	86
10_47	84.4	74.6	91	84.3	81.8	86
10_97	86.8	85.1	88	84.3	81.8	86
11_22	85.6	76.1	92	84.3	81.8	86
11_44	83.8	79.1	87	84.3	81.8	86

EP 3 150 707 A1

(continued)

SEQ ID NO:	Training cohort			Validation cohort		
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
11_65	86.2	77.6	92	84.3	81.8	86
11_80	80.8	67.2	90	84.3	81.8	86
11_81	79.5	69.7	86	84.3	81.8	86
11_97	81.4	74.6	86	84.3	81.8	86
11_99	82.6	77.6	86	84.3	81.8	86
13_69	88	82.1	92	84.3	81.8	86
13_70	85.6	79.1	90	84.3	81.8	86
16_93	83.2	77.6	87	84.3	81.8	86
17_56	82.6	62.7	96	84.3	81.8	86
18_63	86.8	77.6	93	84.3	81.8	86
20_31	88	77.6	95	84.3	81.8	86
21_27	82	71.6	89	84.3	81.8	86
21_53	82	76.1	86	84.3	81.8	86
21_116	80.2	70.1	87	84.3	81.8	86
22_28	81.4	76.1	85	84.3	81.8	86
22_42	82.6	68.7	92	84.3	81.8	86
22_47	82.6	71.6	90	84.3	81.8	86
22_69	82	74.6	87	84.3	81.8	86
22_70	83.2	73.1	90	84.3	81.8	86
22_81	81.9	68.2	91	84.3	81.8	86
24_27	84.4	73.1	92	84.3	81.8	86
24_36	77.2	62.7	87	84.3	81.8	86
24_88	80.8	76.1	84	84.3	81.8	86
25_114	83.2	70.1	92	84.3	81.8	86
25_78	82.6	70.1	91	84.3	81.8	86
25_88	85	77.6	90	84.3	81.8	86
28_98	84.3	71.2	93	84.3	81.8	86
29_93	83.8	73.1	91	84.3	81.8	86
30_75	87.4	80.6	92	84.3	81.8	86
31_89	82.6	73.1	89	84.3	81.8	86
35_45	82.6	70.1	91	84.3	81.8	86
40_58	86.2	73.1	95	84.3	81.8	86
42_83	78.4	62.7	89	84.3	81.8	86
42_96	78.4	62.7	89	84.3	81.8	86
56_112	83.2	74.6	89	84.3	81.8	86
46_66	81.4	67.2	91	84.3	81.8	86
46_83	75.4	62.7	84	84.3	81.8	86

EP 3 150 707 A1

(continued)

SEQ ID NO:	Training cohort			Validation cohort		
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
46_90	76.6	65.7	84	84.3	81.8	86
46_92	76	62.7	85	84.3	81.8	86
46_99	73.1	62.7	80	84.3	81.8	86
58_100	73.7	59.7	83	84.3	81.8	86
65_66	80.8	70.1	88	84.3	81.8	86
65_94	78.4	65.7	87	84.3	81.8	86
71_114	82	67.2	92	84.3	81.8	86
70_80	79.6	62.7	91	84.3	81.8	86
75_98	77.1	63.6	86	84.3	81.8	86
13_72	87.4	85.1	89	84.1	81.8	85.7
92_106	89.2	79.1	96	83.1	81.8	84
94_106	88	76.1	96	83.1	81.8	84
3_52	90.4	85.1	94	83.1	81.8	84
33_109	86.8	77.6	93	83.1	81.8	84
73_109	86.8	82.1	90	83.1	81.8	84
66_110	86.2	74.6	94	83.1	81.8	84
9_52	85	80.6	88	83.1	81.8	84
9_78	82.6	74.6	88	83.1	81.8	84
9_96	85	76.1	91	83.1	81.8	84
9_99	86.2	82.1	89	83.1	81.8	84
11_63	81.4	73.1	87	83.1	81.8	84
11_64	79.6	73.1	84	83.1	81.8	84
11_93	79	70.1	85	83.1	81.8	84
11_96	80.2	70.1	87	83.1	81.8	84
11_104	83.2	70.1	92	83.1	81.8	84
13_75	86.8	85.1	88	83.1	81.8	84
16_25	85	80.6	88	83.1	81.8	84
16_70	83.8	80.6	86	83.1	81.8	84
21_112	85.6	79.1	90	83.1	81.8	84
21_47	85	76.1	91	83.1	81.8	84
21_91	80.8	71.6	87	83.1	81.8	84
21_101	79	70.1	85	83.1	81.8	84
22_82	80.8	70.1	88	83.1	81.8	84
25_84	82	73.1	88	83.1	81.8	84
29_47	82	70.1	90	83.1	81.8	84
29_58	80.2	71.6	86	83.1	81.8	84
31_44	83.8	73.1	91	83.1	81.8	84

EP 3 150 707 A1

(continued)

SEQ ID NO:	Training cohort			Validation cohort		
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
31_99	78.4	67.2	86	83.1	81.8	84
34_70	82.6	77.6	86	83.1	81.8	84
35_88	76.6	67.2	83	83.1	81.8	84
35_95	79	65.7	88	83.1	81.8	84
42_46	82	70.1	90	83.1	81.8	84
42_99	79	58.2	93	83.1	81.8	84
46_114	82	71.6	89	83.1	81.8	84
46_79	77.2	64.2	86	83.1	81.8	84
46_94	74.9	59.7	85	83.1	81.8	84
46_98	75.9	62.1	85	83.1	81.8	84
55_66	76.6	64.2	85	83.1	81.8	84
55_82	80.8	65.7	91	83.1	81.8	84
65_119	77.2	68.7	83	83.1	81.8	84
65_80	80.2	71.6	86	83.1	81.8	84
66_114	81.4	65.7	92	83.1	81.8	84
66_67	77.2	56.7	91	83.1	81.8	84
66_79	79	64.2	89	83.1	81.8	84
93_114	77.8	62.7	88	83.1	81.8	84
67_119	79	62.7	90	83.1	81.8	84
79_85	74.9	58.2	86	83.1	81.8	84
99_104	76	59.7	87	83.1	81.8	84
52_106	89.8	80.6	96	81.9	81.8	82
27_109	84.4	76.1	90	81.9	81.8	82
43_109	89.2	80.6	95	81.9	81.8	82
44_109	89.2	85.1	92	81.9	81.8	82
45_109	87.4	82.1	91	81.9	81.8	82
63_109	86.2	82.1	89	81.9	81.8	82
31_110	88	79.1	94	81.9	81.8	82
9_16	82.6	79.1	85	81.9	81.8	82
9_63	84.4	79.1	88	81.9	81.8	82
9_92	82.6	76.1	87	81.9	81.8	82
10_45	92.2	88.1	95	81.9	81.8	82
11_67	80.2	70.1	87	81.9	81.8	82
11_118	82	79.1	84	81.9	81.8	82
16_80	82.6	77.6	86	81.9	81.8	82
16_94	85.6	83.6	87	81.9	81.8	82
16_99	82	79.1	84	81.9	81.8	82

EP 3 150 707 A1

(continued)

SEQ ID NO:	Training cohort			Validation cohort		
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
21_64	80.2	67.2	89	81.9	81.8	82
21_114	79.6	68.7	87	81.9	81.8	82
22_79	81.4	71.6	88	81.9	81.8	82
25_69	83.8	73.1	91	81.9	81.8	82
28_47	85	80.6	88	81.9	81.8	82
31_92	80.8	67.2	90	81.9	81.8	82
34_67	78.4	70.1	84	81.9	81.8	82
35_67	78.4	64.2	88	81.9	81.8	82
36_99	79	70.1	85	81.9	81.8	82
42_67	79.6	64.2	90	81.9	81.8	82
42_79	80.8	62.7	93	81.9	81.8	82
42_93	81.4	65.7	92	81.9	81.8	82
46_58	76	62.7	85	81.9	81.8	82
46_103	75.4	61.2	85	81.9	81.8	82
55_78	74.3	65.7	80	81.9	81.8	82
66_87	73.7	59.7	83	81.9	81.8	82
67_83	72.5	58.2	82	81.9	81.8	82
75_115	79.6	67.2	88	81.9	81.8	82
57_109	85.6	76.1	92	80.7	81.8	80
97_109	85	82.1	87	80.7	81.8	80
11_69	81.4	71.6	88	80.7	81.8	80
21_66	77.8	70.1	83	80.7	81.8	80
21_78	77.2	65.7	85	80.7	81.8	80
21_80	77.2	67.2	84	80.7	81.8	80
21_82	78.4	73.1	82	80.7	81.8	80
21_88	79	70.1	85	80.7	81.8	80
21_103	77.8	68.7	84	80.7	81.8	80
21_104	76	68.7	81	80.7	81.8	80
28_93	80.8	76.1	84	80.7	81.8	80
31_52	85	73.1	93	80.7	81.8	80
34_79	82	76.1	86	80.7	81.8	80
35_59	80.8	65.7	91	80.7	81.8	80
52_111	82	71.6	89	80.7	81.8	80
66_69	83.8	70.1	93	80.7	81.8	80
65_109	86.2	79.1	91	79.5	81.8	78
68_109	82.6	73.1	89	79.5	81.8	78
71_109	84.4	77.6	89	79.5	81.8	78

EP 3 150 707 A1

(continued)

SEQ ID NO:	Training cohort			Validation cohort		
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
21_69	81.4	73.1	87	79.5	81.8	78
28_119	80.2	79.1	81	79.5	81.8	78
67_97	74.9	59.7	85	79.5	81.8	78
71_78	73.1	61.2	81	79.5	81.8	78
11_109	86.2	77.6	92	78.3	81.8	76
17_109	83.8	74.6	90	78.3	81.8	76
11_94	79.6	71.6	85	78.3	81.8	76
65_100	77.2	65.7	85	78.3	81.8	76
79_104	73.7	59.7	83	78.3	81.8	76
83_100	64.7	40.3	81	78.3	81.8	76
69_109	82.6	76.1	87	77.1	81.8	74
78_109	84.4	77.6	89	77.1	81.8	74
84_109	84.4	74.6	91	77.1	81.8	74
93_109	82.6	74.6	88	77.1	81.8	74
31_65	81.4	76.1	85	77.1	81.8	74
100_109	82	77.6	85	75.9	81.8	72
28_100	80.2	73.1	85	75.9	81.8	72
64_79	77.8	67.2	85	75.9	81.8	72
70_100	75.4	59.7	86	75.9	81.8	72
10_100	86.2	80.6	90	74.7	81.8	70
67_69	79.6	71.6	85	74.7	81.8	70
13_50	85	79.1	89	87.8	81.2	92
18_50	83.8	73.1	91	87.8	81.2	92
50_106	89.8	77.6	98	85.4	81.2	88
40_50	81.4	67.2	91	85.4	81.2	88
50_114	80.2	65.7	90	85.4	81.2	88
9_50	84.4	77.6	89	84.1	81.2	86
50_66	74.9	56.7	87	82.9	81.2	84
50_81	74.1	57.6	85	82.9	81.2	84
11_50	77.8	68.7	84	81.7	81.2	82
50_58	76	59.7	87	81.7	81.2	82
50_83	70.7	52.2	83	81.7	81.2	82
23_109	83.2	71.6	91	75.6	81.2	72
6_77	89.2	80.6	95	91.4	80.6	98
77_107	90.4	85.1	94	88.9	80.6	94
19_77	82.6	71.6	90	88.9	80.6	94
42_77	78.4	62.7	89	87.7	80.6	92

EP 3 150 707 A1

(continued)

SEQ ID NO:	Training cohort			Validation cohort		
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
51_77	80.2	62.7	92	87.7	80.6	92
6_28	91.6	85.1	96	91.6	78.8	100
6_43	86.2	76.1	93	91.6	78.8	100
6_87	90.4	82.1	96	91.6	78.8	100
7_15	91	82.1	97	91.6	78.8	100
8_15	89.8	85.1	93	91.6	78.8	100
10_41	86.8	74.6	95	91.6	78.8	100
15_18	90.4	86.6	93	91.6	78.8	100
18_33	86.2	74.6	94	91.6	78.8	100
14_106	91	79.1	99	90.4	78.8	98
41_106	91.6	82.1	98	90.4	78.8	98
2_86	91	80.6	98	90.4	78.8	98
30_107	92.2	85.1	97	90.4	78.8	98
6_108	89.8	80.6	96	90.4	78.8	98
15_108	88	76.1	96	90.4	78.8	98
30_108	92.8	85.1	98	90.4	78.8	98
41_108	91	82.1	97	90.4	78.8	98
68_108	87.4	76.1	95	90.4	78.8	98
6_14	91	80.6	98	90.4	78.8	98
7_110	91.6	82.1	98	90.4	78.8	98
9_19	88	82.1	92	90.4	78.8	98
13_80	85	82.1	87	90.4	78.8	98
14_112	91.6	80.6	99	90.4	78.8	98
15_39	89.2	79.1	96	90.4	78.8	98
18_32	89.2	80.6	95	90.4	78.8	98
18_118	85.6	76.1	92	90.4	78.8	98
24_41	82.6	68.7	92	90.4	78.8	98
30_31	84.4	73.1	92	90.4	78.8	98
33_112	85.6	71.6	95	90.4	78.8	98
87_111	83.2	67.2	94	90.4	78.8	98
7_106	92.2	82.1	99	89.2	78.8	96
28_106	93.4	85.1	99	89.2	78.8	96
61_106	91.6	80.6	99	89.2	78.8	96
19_107	94	88.1	98	89.2	78.8	96
3_7	95.2	89.6	99	89.2	78.8	96
3_30	91	85.1	95	89.2	78.8	96
17_108	87.4	71.6	98	89.2	78.8	96

EP 3 150 707 A1

(continued)

SEQ ID NO:	Training cohort			Validation cohort		
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
5_8	95.2	91	98	89.2	78.8	96
5_122	90.4	85.1	94	89.2	78.8	96
6_22	85.6	74.6	93	89.2	78.8	96
6_90	87.4	80.6	92	89.2	78.8	96
7_36	91.6	82.1	98	89.2	78.8	96
9_41	87.4	82.1	91	89.2	78.8	96
12_111	88	78.8	94	89.2	78.8	96
12_56	87.3	83.3	90	89.2	78.8	96
13_36	89.8	83.6	94	89.2	78.8	96
13_41	85.6	85.1	86	89.2	78.8	96
14_34	89.8	82.1	95	89.2	78.8	96
14_37	89.8	79.1	97	89.2	78.8	96
14_44	89.8	76.1	99	89.2	78.8	96
14_75	86.2	73.1	95	89.2	78.8	96
14_89	86.2	71.6	96	89.2	78.8	96
15_21	84.4	71.6	93	89.2	78.8	96
15_44	85	71.6	94	89.2	78.8	96
18_112	84.4	76.1	90	89.2	78.8	96
18_44	85.6	74.6	93	89.2	78.8	96
18_117	85	73.1	93	89.2	78.8	96
18_119	84.4	76.1	90	89.2	78.8	96
18_80	83.8	76.1	89	89.2	78.8	96
18_120	84.4	76.1	90	89.2	78.8	96
18_98	84.3	75.8	90	89.2	78.8	96
18_122	84.4	76.1	90	89.2	78.8	96
19_26	83.2	73.1	90	89.2	78.8	96
19_31	87.4	76.1	95	89.2	78.8	96
19_52	86.8	80.6	91	89.2	78.8	96
20_33	88	79.1	94	89.2	78.8	96
20_111	88.6	77.6	96	89.2	78.8	96
24_38	84.4	71.6	93	89.2	78.8	96
25_38	85	67.2	97	89.2	78.8	96
30_112	85	79.1	89	89.2	78.8	96
30_94	82.6	73.1	89	89.2	78.8	96
33_71	82.6	73.1	89	89.2	78.8	96
33_99	83.8	68.7	94	89.2	78.8	96
98_111	77.7	56.1	92	89.2	78.8	96

EP 3 150 707 A1

(continued)

SEQ ID NO:	Training cohort			Validation cohort		
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
37_70	79	71.6	84	89.2	78.8	96
38_46	87.4	76.1	95	89.2	78.8	96
40_42	82.6	61.2	97	89.2	78.8	96
41_120	80.8	73.1	86	89.2	78.8	96
96_113	85	74.6	92	89.2	78.8	96
36_106	91	79.1	99	88	78.8	94
37_106	91	80.6	98	88	78.8	94
60_106	91.6	82.1	98	88	78.8	94
62_106	91	80.6	98	88	78.8	94
74_106	91	80.6	98	88	78.8	94
90_106	89.8	77.6	98	88	78.8	94
3_107	92.8	86.6	97	88	78.8	94
6_107	88	76.1	96	88	78.8	94
27_107	91	83.6	96	88	78.8	94
48_107	91	82.1	97	88	78.8	94
57_107	91	82.1	97	88	78.8	94
73_107	91	80.6	98	88	78.8	94
102_107	90.4	79.1	98	88	78.8	94
3_37	91.6	88.1	94	88	78.8	94
27_108	90.4	79.1	98	88	78.8	94
33_108	86.8	73.1	96	88	78.8	94
57_108	87.4	71.6	98	88	78.8	94
6_9	88.6	79.1	95	88	78.8	94
6_25	86.2	74.6	94	88	78.8	94
6_85	86.2	79.1	91	88	78.8	94
6_98	86.7	77.3	93	88	78.8	94
7_60	92.8	89.6	95	88	78.8	94
8_31	89.2	82.1	94	88	78.8	94
8_42	89.8	79.1	97	88	78.8	94
26_110	91	86.6	94	88	78.8	94
9_38	83.2	76.1	88	88	78.8	94
10_19	88.6	79.1	95	88	78.8	94
10_43	88	83.6	91	88	78.8	94
12_13	92.2	89.4	94	88	78.8	94
13_29	89.2	82.1	94	88	78.8	94
13_39	86.8	74.6	95	88	78.8	94
14_52	89.2	79.1	96	88	78.8	94

EP 3 150 707 A1

(continued)

SEQ ID NO:	Training cohort			Validation cohort		
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
15_119	85	77.6	90	88	78.8	94
17_54	87.4	71.6	98	88	78.8	94
17_64	85	68.7	96	88	78.8	94
17_120	84.4	68.7	95	88	78.8	94
18_29	85	74.6	92	88	78.8	94
18_114	85	74.6	92	88	78.8	94
18_71	80.2	70.1	87	88	78.8	94
18_86	86.2	77.6	92	88	78.8	94
18_92	84.4	76.1	90	88	78.8	94
18_99	83.8	74.6	90	88	78.8	94
20_25	89.8	83.6	94	88	78.8	94
24_49	83.8	79.1	87	88	78.8	94
24_116	82.6	67.2	93	88	78.8	94
24_87	82.6	68.7	92	88	78.8	94
30_39	89.8	82.1	95	88	78.8	94
30_70	85.6	74.6	93	88	78.8	94
34_38	85	74.6	92	88	78.8	94
38_98	82.5	65.2	94	88	78.8	94
39_113	87.4	76.1	95	88	78.8	94
39_60	88	74.6	97	88	78.8	94
40_46	85	74.6	92	88	78.8	94
41_66	79.6	62.7	91	88	78.8	94
41_83	79	65.7	88	88	78.8	94
71_112	79.6	65.7	89	88	78.8	94
83_112	77.2	64.2	86	88	78.8	94
46_62	80.2	70.1	87	88	78.8	94
58_73	80.8	71.6	87	88	78.8	94
59_119	82	64.2	94	88	78.8	94
67_115	78.4	68.7	85	88	78.8	94
83_115	83.8	73.1	91	88	78.8	94
70_120	76	59.7	87	88	78.8	94
72_107	89.2	79.1	96	87.8	78.8	93.9
22_106	89.2	79.1	96	86.7	78.8	92
32_106	91	77.6	100	86.7	78.8	92
33_106	90.4	80.6	97	86.7	78.8	92
11_107	89.8	80.6	96	86.7	78.8	92
3_98	90.4	86.4	93	86.7	78.8	92

EP 3 150 707 A1

(continued)

SEQ ID NO:	Training cohort			Validation cohort		
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
5_61	89.8	86.6	92	86.7	78.8	92
5_70	87.4	80.6	92	86.7	78.8	92
5_101	87.4	80.6	92	86.7	78.8	92
6_83	85.6	76.1	92	86.7	78.8	92
41_109	89.2	83.6	93	86.7	78.8	92
9_111	83.8	71.6	92	86.7	78.8	92
9_43	88.6	85.1	91	86.7	78.8	92
9_113	86.8	79.1	92	86.7	78.8	92
9_115	85	79.1	89	86.7	78.8	92
10_14	87.4	76.1	95	86.7	78.8	92
10_21	89.8	82.1	95	86.7	78.8	92
10_33	85	73.1	93	86.7	78.8	92
11_28	86.8	76.1	94	86.7	78.8	92
11_113	86.8	77.6	93	86.7	78.8	92
13_58	85	76.1	91	86.7	78.8	92
13_68	87.4	79.1	93	86.7	78.8	92
13_115	85.6	82.1	88	86.7	78.8	92
14_26	89.2	76.1	98	86.7	78.8	92
14_31	84.4	70.1	94	86.7	78.8	92
14_119	88	76.1	96	86.7	78.8	92
15_42	85	68.7	96	86.7	78.8	92
17_22	85	71.6	94	86.7	78.8	92
17_46	84.4	71.6	93	86.7	78.8	92
17_55	88	74.6	97	86.7	78.8	92
17_58	85	73.1	93	86.7	78.8	92
17_65	85	70.1	95	86.7	78.8	92
17_94	83.2	68.7	93	86.7	78.8	92
18_28	89.8	82.1	95	86.7	78.8	92
18_61	85.6	76.1	92	86.7	78.8	92
18_121	83.8	77.6	88	86.7	78.8	92
19_81	86.1	80.3	90	86.7	78.8	92
22_113	87.4	80.6	92	86.7	78.8	92
24_113	83.2	73.1	90	86.7	78.8	92
25_40	86.2	73.1	95	86.7	78.8	92
25_42	84.4	71.6	93	86.7	78.8	92
25_116	84.4	74.6	91	86.7	78.8	92
26_29	85	74.6	92	86.7	78.8	92

EP 3 150 707 A1

(continued)

SEQ ID NO:	Training cohort			Validation cohort		
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
29_70	82	71.6	89	86.7	78.8	92
30_119	80.2	74.6	84	86.7	78.8	92
33_55	83.2	67.2	94	86.7	78.8	92
36_119	80.8	71.6	87	86.7	78.8	92
55_111	81.4	67.2	91	86.7	78.8	92
37_66	79	68.7	86	86.7	78.8	92
39_46	77.8	65.7	86	86.7	78.8	92
39_70	78.4	64.2	88	86.7	78.8	92
39_75	77.8	65.7	86	86.7	78.8	92
40_112	86.8	74.6	95	86.7	78.8	92
41_67	80.2	64.2	91	86.7	78.8	92
91_112	82.6	65.7	94	86.7	78.8	92
93_112	77.8	65.7	86	86.7	78.8	92
46_55	79	64.2	89	86.7	78.8	92
66_113	83.8	68.7	94	86.7	78.8	92
79_113	84.4	73.1	92	86.7	78.8	92
52_53	84.4	79.1	88	86.7	78.8	92
58_119	75.4	62.7	84	86.7	78.8	92
58_87	82	74.6	87	86.7	78.8	92
98_115	81.9	65.2	93	86.7	78.8	92
15_106	89.8	77.6	98	85.5	78.8	90
65_106	93.4	86.6	98	85.5	78.8	90
81_106	91	80.3	98	85.5	78.8	90
85_106	88.6	79.1	95	85.5	78.8	90
69_107	87.4	77.6	94	85.5	78.8	90
3_9	93.4	88.1	97	85.5	78.8	90
3_45	92.8	86.6	97	85.5	78.8	90
3_46	93.4	88.1	97	85.5	78.8	90
61_108	91.6	86.6	95	85.5	78.8	90
73_108	86.2	73.1	95	85.5	78.8	90
5_58	86.8	77.6	93	85.5	78.8	90
5_69	90.4	83.6	95	85.5	78.8	90
5_76	90.4	83.6	95	85.5	78.8	90
5_84	89.2	85.1	92	85.5	78.8	90
5_92	88.6	85.1	91	85.5	78.8	90
5_95	89.8	83.6	94	85.5	78.8	90
6_11	85.6	74.6	93	85.5	78.8	90

EP 3 150 707 A1

(continued)

SEQ ID NO:	Training cohort			Validation cohort			
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)	
5	8_35	89.2	82.1	94	85.5	78.8	90
	8_40	87.4	76.1	95	85.5	78.8	90
	9_10	86.8	82.1	90	85.5	78.8	90
10	9_32	84.4	79.1	88	85.5	78.8	90
	9_48	84.4	80.6	87	85.5	78.8	90
	10_25	82.6	73.1	89	85.5	78.8	90
15	10_70	88	77.6	95	85.5	78.8	90
	12_66	82.5	72.7	89	85.5	78.8	90
	12_95	85.5	78.8	90	85.5	78.8	90
	13_34	91	85.1	95	85.5	78.8	90
20	13_52	89.2	82.1	94	85.5	78.8	90
	13_99	84.4	80.6	87	85.5	78.8	90
	15_52	88	82.1	92	85.5	78.8	90
25	16_55	84.4	79.1	88	85.5	78.8	90
	17_45	85.6	73.1	94	85.5	78.8	90
	17_118	83.8	70.1	93	85.5	78.8	90
	17_83	83.2	67.2	94	85.5	78.8	90
30	17_85	83.8	67.2	95	85.5	78.8	90
	17_88	82	67.2	92	85.5	78.8	90
	17_97	83.2	70.1	92	85.5	78.8	90
35	18_65	86.2	76.1	93	85.5	78.8	90
	21_32	84.4	80.6	87	85.5	78.8	90
	21_73	79.6	76.1	82	85.5	78.8	90
40	22_40	87.4	76.1	95	85.5	78.8	90
	22_57	86.8	79.1	92	85.5	78.8	90
	22_76	77.8	64.2	87	85.5	78.8	90
	24_28	85	79.1	89	85.5	78.8	90
45	24_111	83.8	73.1	91	85.5	78.8	90
	24_47	77.8	65.7	86	85.5	78.8	90
	24_62	82.6	68.7	92	85.5	78.8	90
	25_43	85	76.1	91	85.5	78.8	90
50	25_51	83.2	71.6	91	85.5	78.8	90
	25_113	83.2	68.7	93	85.5	78.8	90
	25_115	82.6	68.7	92	85.5	78.8	90
55	28_55	87.4	76.1	95	85.5	78.8	90
	28_58	87.4	79.1	93	85.5	78.8	90
	29_119	83.8	80.6	86	85.5	78.8	90

EP 3 150 707 A1

(continued)

SEQ ID NO:	Training cohort			Validation cohort		
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
34_115	82.6	73.1	89	85.5	78.8	90
99_111	81.4	62.7	94	85.5	78.8	90
38_55	88	73.1	98	85.5	78.8	90
39_104	80.2	65.7	90	85.5	78.8	90
40_81	80.7	68.2	89	85.5	78.8	90
41_79	81.4	68.7	90	85.5	78.8	90
42_112	82	67.2	92	85.5	78.8	90
42_56	82	71.6	89	85.5	78.8	90
68_112	82.6	70.1	91	85.5	78.8	90
45_66	79	68.7	86	85.5	78.8	90
51_81	77.7	66.7	85	85.5	78.8	90
51_98	80.7	72.7	86	85.5	78.8	90
94_113	84.4	70.1	94	85.5	78.8	90
58_117	78.4	61.2	90	85.5	78.8	90
58_80	78.4	62.7	89	85.5	78.8	90
58_99	76.6	61.2	87	85.5	78.8	90
62_66	79	64.2	89	85.5	78.8	90
99_114	79	67.2	87	85.5	78.8	90
81_115	78.3	66.7	86	85.5	78.8	90
76_98	80.7	69.7	88	85.5	78.8	90
27_106	89.2	76.1	98	84.3	78.8	88
68_106	89.8	79.1	97	84.3	78.8	88
75_106	88	74.6	97	84.3	78.8	88
84_106	89.2	79.1	96	84.3	78.8	88
91_106	89.8	79.1	97	84.3	78.8	88
3_111	88.6	79.1	95	84.3	78.8	88
3_103	91.6	86.6	95	84.3	78.8	88
4_110	91	86.6	94	84.3	78.8	88
95_108	89.8	85.1	93	84.3	78.8	88
104_108	88	79.1	94	84.3	78.8	88
5_110	95.2	91	98	84.3	78.8	88
5_27	88.6	83.6	92	84.3	78.8	88
6_39	89.8	85.1	93	84.3	78.8	88
6_45	90.4	80.6	97	84.3	78.8	88
6_67	87.4	74.6	96	84.3	78.8	88
6_93	87.4	76.1	95	84.3	78.8	88
9_59	86.8	79.1	92	84.3	78.8	88

EP 3 150 707 A1

(continued)

SEQ ID NO:	Training cohort			Validation cohort			
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)	
5	9_86	85.6	80.6	89	84.3	78.8	88
	9_88	83.8	79.1	87	84.3	78.8	88
	9_103	82.6	74.6	88	84.3	78.8	88
10	9_104	81.4	76.1	85	84.3	78.8	88
	10_60	83.8	71.6	92	84.3	78.8	88
	11_47	83.8	74.6	90	84.3	78.8	88
15	11_76	82	71.6	89	84.3	78.8	88
	11_120	79.6	68.7	87	84.3	78.8	88
	12_16	88	89.4	87	84.3	78.8	88
	12_31	87.3	80.3	92	84.3	78.8	88
20	12_78	85.5	80.3	89	84.3	78.8	88
	13_62	83.2	82.1	84	84.3	78.8	88
	13_93	83.8	82.1	85	84.3	78.8	88
25	14_100	85.6	71.6	95	84.3	78.8	88
	16_34	88	85.1	90	84.3	78.8	88
	16_39	89.2	86.6	91	84.3	78.8	88
	16_97	84.4	85.1	84	84.3	78.8	88
30	17_27	85	70.1	95	84.3	78.8	88
	17_39	84.4	74.6	91	84.3	78.8	88
	17_44	85	70.1	95	84.3	78.8	88
35	17_121	83.2	67.2	94	84.3	78.8	88
	22_74	83.2	77.6	87	84.3	78.8	88
	24_84	79.6	68.7	87	84.3	78.8	88
	25_32	84.4	73.1	92	84.3	78.8	88
40	25_74	83.8	74.6	90	84.3	78.8	88
	25_76	80.8	67.2	90	84.3	78.8	88
	25_91	81.4	67.2	91	84.3	78.8	88
45	27_28	83.2	74.6	89	84.3	78.8	88
	28_94	82	73.1	88	84.3	78.8	88
	28_96	86.2	76.1	93	84.3	78.8	88
	29_42	80.2	64.2	91	84.3	78.8	88
50	29_96	78.4	70.1	84	84.3	78.8	88
	31_115	80.8	67.2	90	84.3	78.8	88
	32_46	85	77.6	90	84.3	78.8	88
55	32_55	86.8	82.1	90	84.3	78.8	88
	35_111	82	65.7	93	84.3	78.8	88
	35_68	78.4	64.2	88	84.3	78.8	88

EP 3 150 707 A1

(continued)

SEQ ID NO:	Training cohort			Validation cohort		
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
37_100	79	67.2	87	84.3	78.8	88
39_44	80.2	67.2	89	84.3	78.8	88
40_66	81.4	61.2	95	84.3	78.8	88
42_66	80.2	59.7	94	84.3	78.8	88
76_112	88	80.6	93	84.3	78.8	88
78_112	77.2	61.2	88	84.3	78.8	88
81_112	77.7	62.1	88	84.3	78.8	88
44_78	79.6	68.7	87	84.3	78.8	88
46_75	75.4	67.2	81	84.3	78.8	88
46_85	76.6	61.2	87	84.3	78.8	88
46_93	74.9	59.7	85	84.3	78.8	88
51_55	79	67.2	87	84.3	78.8	88
53_67	77.2	67.2	84	84.3	78.8	88
53_75	81.4	70.1	89	84.3	78.8	88
53_83	76.6	62.7	86	84.3	78.8	88
55_62	83.8	70.1	93	84.3	78.8	88
56_58	79	64.2	89	84.3	78.8	88
56_114	79	70.1	85	84.3	78.8	88
56_119	77.8	65.7	86	84.3	78.8	88
62_70	80.2	64.2	91	84.3	78.8	88
65_70	83.2	70.1	92	84.3	78.8	88
65_98	76.5	62.1	86	84.3	78.8	88
66_71	80.2	67.2	89	84.3	78.8	88
66_74	80.8	67.2	90	84.3	78.8	88
66_81	77.7	62.1	88	84.3	78.8	88
66_89	80.2	68.7	88	84.3	78.8	88
75_114	81.4	70.1	89	84.3	78.8	88
71_104	80.8	65.7	91	84.3	78.8	88
81_89	77.1	62.1	87	84.3	78.8	88
90_98	74.1	57.6	85	84.3	78.8	88
72_106	89.2	79.1	96	84.1	78.8	87.8
9_72	85	79.1	89	84.1	78.8	87.8
18_72	87.4	80.6	92	84.1	78.8	87.8
6_106	89.8	79.1	97	83.1	78.8	86
10_106	88	76.1	96	83.1	78.8	86
11_106	89.2	77.6	97	83.1	78.8	86
42_106	89.2	77.6	97	83.1	78.8	86

EP 3 150 707 A1

(continued)

SEQ ID NO:	Training cohort			Validation cohort		
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
57_106	89.2	76.1	98	83.1	78.8	86
69_106	89.2	77.6	97	83.1	78.8	86
76_106	89.2	77.6	97	83.1	78.8	86
3_56	91.6	85.1	96	83.1	78.8	86
5_67	87.4	82.1	91	83.1	78.8	86
6_121	86.8	76.1	94	83.1	78.8	86
46_110	83.8	77.6	88	83.1	78.8	86
9_28	86.2	86.6	86	83.1	78.8	86
9_64	82.6	74.6	88	83.1	78.8	86
9_76	83.8	77.6	88	83.1	78.8	86
9_79	85.6	79.1	90	83.1	78.8	86
9_82	84.4	79.1	88	83.1	78.8	86
9_95	86.8	80.6	91	83.1	78.8	86
9_101	85.6	83.6	87	83.1	78.8	86
10_11	85.6	74.6	93	83.1	78.8	86
10_111	82	68.7	91	83.1	78.8	86
10_40	85.6	74.6	93	83.1	78.8	86
11_59	80.8	73.1	86	83.1	78.8	86
11_68	79	71.6	84	83.1	78.8	86
11_117	80.2	70.1	87	83.1	78.8	86
11_74	81.4	74.6	86	83.1	78.8	86
11_90	79.6	73.1	84	83.1	78.8	86
13_55	90.4	83.6	95	83.1	78.8	86
16_44	82.6	76.1	87	83.1	78.8	86
16_65	82.6	80.6	84	83.1	78.8	86
16_66	80.8	73.1	86	83.1	78.8	86
16_71	83.8	77.6	88	83.1	78.8	86
17_52	84.4	71.6	93	83.1	78.8	86
17_98	84.3	68.2	95	83.1	78.8	86
21_76	79	73.1	83	83.1	78.8	86
22_31	80.2	68.7	88	83.1	78.8	86
22_43	86.2	76.1	93	83.1	78.8	86
22_90	79.6	70.1	86	83.1	78.8	86
22_91	77.8	67.2	85	83.1	78.8	86
26_67	83.2	74.6	89	83.1	78.8	86
28_34	88.6	79.1	95	83.1	78.8	86
28_52	87.4	80.6	92	83.1	78.8	86

EP 3 150 707 A1

(continued)

SEQ ID NO:	Training cohort			Validation cohort		
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
29_111	80.2	65.7	90	83.1	78.8	86
29_112	83.8	73.1	91	83.1	78.8	86
29_45	85	79.1	89	83.1	78.8	86
29_46	81.4	73.1	87	83.1	78.8	86
31_40	82	67.2	92	83.1	78.8	86
31_46	77.8	65.7	86	83.1	78.8	86
32_66	82.6	71.6	90	83.1	78.8	86
32_98	86.1	80.3	90	83.1	78.8	86
34_66	83.2	74.6	89	83.1	78.8	86
35_116	77.2	59.7	89	83.1	78.8	86
39_66	78.4	64.2	88	83.1	78.8	86
42_71	81.4	65.7	92	83.1	78.8	86
42_81	84.3	72.7	92	83.1	78.8	86
44_83	76.6	61.2	87	83.1	78.8	86
44_93	77.8	67.2	85	83.1	78.8	86
46_120	73.7	59.7	83	83.1	78.8	86
51_65	82	74.6	87	83.1	78.8	86
51_66	79.6	64.2	90	83.1	78.8	86
51_94	80.2	67.2	89	83.1	78.8	86
54_56	85.6	83.6	87	83.1	78.8	86
55_75	77.8	62.7	88	83.1	78.8	86
55_94	75.4	59.7	86	83.1	78.8	86
55_98	73.5	56.1	85	83.1	78.8	86
58_82	77.2	59.7	89	83.1	78.8	86
58_93	74.9	58.2	86	83.1	78.8	86
62_81	70.5	57.6	79	83.1	78.8	86
64_67	82.6	73.1	89	83.1	78.8	86
66_96	77.2	61.2	88	83.1	78.8	86
67_98	76.5	60.6	87	83.1	78.8	86
17_106	89.8	79.1	97	81.9	78.8	84
70_106	88.6	74.6	98	81.9	78.8	84
64_109	86.2	80.6	90	81.9	78.8	84
39_110	87.4	83.6	90	81.9	78.8	84
9_31	83.8	76.1	89	81.9	78.8	84
9_81	85.5	80.3	89	81.9	78.8	84
10_31	85.6	79.1	90	81.9	78.8	84
10_63	83.8	79.1	87	81.9	78.8	84

EP 3 150 707 A1

(continued)

SEQ ID NO:	Training cohort			Validation cohort		
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
10_114	87.4	77.6	94	81.9	78.8	84
10_67	84.4	76.1	90	81.9	78.8	84
10_88	88.6	79.1	95	81.9	78.8	84
11_36	79.6	70.1	86	81.9	78.8	84
11_57	79	68.7	86	81.9	78.8	84
11_58	80.8	71.6	87	81.9	78.8	84
11_82	80.8	68.7	89	81.9	78.8	84
11_89	80.2	70.1	87	81.9	78.8	84
11_91	79.6	68.7	87	81.9	78.8	84
12_22	90.4	84.8	94	81.9	78.8	84
16_22	82	76.1	86	81.9	78.8	84
16_96	80.8	73.1	86	81.9	78.8	84
17_75	83.8	67.2	95	81.9	78.8	84
17_100	83.2	71.6	91	81.9	78.8	84
22_54	84.4	77.6	89	81.9	78.8	84
27_29	83.8	74.6	90	81.9	78.8	84
28_66	83.2	76.1	88	81.9	78.8	84
28_70	83.8	74.6	90	81.9	78.8	84
28_120	85	76.1	91	81.9	78.8	84
29_34	81.4	74.6	86	81.9	78.8	84
31_32	86.2	79.1	91	81.9	78.8	84
31_66	76	64.2	84	81.9	78.8	84
31_85	77.2	67.2	84	81.9	78.8	84
31_87	79	71.6	84	81.9	78.8	84
31_94	79	65.7	88	81.9	78.8	84
31_96	80.2	71.6	86	81.9	78.8	84
34_82	79	74.6	82	81.9	78.8	84
44_99	76	58.2	88	81.9	78.8	84
44_103	81.4	64.2	93	81.9	78.8	84
45_46	77.2	67.2	84	81.9	78.8	84
46_82	73.7	61.2	82	81.9	78.8	84
47_51	80.2	67.2	89	81.9	78.8	84
47_120	76.6	68.7	82	81.9	78.8	84
51_71	82.6	73.1	89	81.9	78.8	84
55_117	78.4	59.7	91	81.9	78.8	84
55_99	77.8	65.7	86	81.9	78.8	84
58_75	76	64.2	84	81.9	78.8	84

EP 3 150 707 A1

(continued)

SEQ ID NO:	Training cohort			Validation cohort		
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
58_94	76.6	58.2	89	81.9	78.8	84
83_114	82.6	65.7	94	81.9	78.8	84
94_114	78.4	64.2	88	81.9	78.8	84
67_118	73.7	52.2	88	81.9	78.8	84
67_121	75.4	64.2	83	81.9	78.8	84
78_119	73.1	56.7	84	81.9	78.8	84
81_98	74.5	60	84	81.9	78.8	84
93_98	74.1	56.1	86	81.9	78.8	84
78_106	89.2	77.6	97	80.7	78.8	82
100_106	89.2	80.6	95	80.7	78.8	82
10_109	86.2	77.6	92	80.7	78.8	82
74_109	89.2	82.1	94	80.7	78.8	82
102_109	84.4	73.1	92	80.7	78.8	82
79_110	86.8	76.1	94	80.7	78.8	82
96_110	86.2	85.1	87	80.7	78.8	82
9_69	82.6	80.6	84	80.7	78.8	82
9_84	82	77.6	85	80.7	78.8	82
9_93	82.6	74.6	88	80.7	78.8	82
10_78	85.6	77.6	91	80.7	78.8	82
10_93	83.8	77.6	88	80.7	78.8	82
10_103	85	77.6	90	80.7	78.8	82
11_42	83.2	76.1	88	80.7	78.8	82
11_95	78.4	68.7	85	80.7	78.8	82
11_100	78.4	68.7	85	80.7	78.8	82
24_78	79	64.2	89	80.7	78.8	82
25_28	82	74.6	87	80.7	78.8	82
25_63	83.8	76.1	89	80.7	78.8	82
28_42	82	70.1	90	80.7	78.8	82
29_56	80.2	70.1	87	80.7	78.8	82
31_111	81.4	65.7	92	80.7	78.8	82
32_79	81.4	73.1	87	80.7	78.8	82
92_111	77.2	62.7	87	80.7	78.8	82
39_100	74.9	61.2	84	80.7	78.8	82
42_57	79	58.2	93	80.7	78.8	82
42_121	81.4	70.1	89	80.7	78.8	82
44_100	76	61.2	86	80.7	78.8	82
100_113	84.4	74.6	91	80.7	78.8	82

EP 3 150 707 A1

(continued)

SEQ ID NO:	Training cohort			Validation cohort		
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
55_118	82	67.2	92	80.7	78.8	82
55_81	76.5	54.5	91	80.7	78.8	82
55_87	77.2	65.7	85	80.7	78.8	82
62_93	77.2	65.7	85	80.7	78.8	82
78_114	77.2	65.7	85	80.7	78.8	82
70_96	74.3	62.7	82	80.7	78.8	82
70_103	80.2	65.7	90	80.7	78.8	82
78_80	74.9	59.7	85	80.7	78.8	82
46_72	79	71.6	84	80.5	78.8	81.6
101_109	86.8	79.1	92	79.5	78.8	80
10_95	82.6	74.6	88	79.5	78.8	80
16_78	82	76.1	86	79.5	78.8	80
21_29	82	73.1	88	79.5	78.8	80
21_95	81.4	67.2	91	79.5	78.8	80
27_45	83.2	80.6	85	79.5	78.8	80
28_45	89.2	86.6	91	79.5	78.8	80
31_114	81.4	68.7	90	79.5	78.8	80
31_80	79.6	62.7	91	79.5	78.8	80
31_88	79.6	71.6	85	79.5	78.8	80
31_97	82	73.1	88	79.5	78.8	80
42_100	77.8	56.7	92	79.5	78.8	80
45_79	78.4	67.2	86	79.5	78.8	80
46_121	75.4	61.2	85	79.5	78.8	80
46_100	74.9	64.2	82	79.5	78.8	80
55_100	76.6	59.7	88	79.5	78.8	80
56_98	74.7	60.6	84	79.5	78.8	80
58_78	76	62.7	85	79.5	78.8	80
65_79	79	62.7	90	79.5	78.8	80
65_104	77.8	67.2	85	79.5	78.8	80
67_99	74.9	58.2	86	79.5	78.8	80
78_81	72.3	59.1	81	79.5	78.8	80
78_90	74.3	61.2	83	79.5	78.8	80
79_96	76	62.7	85	79.5	78.8	80
80_121	74.9	62.7	83	79.5	78.8	80
94_99	71.9	53.7	84	79.5	78.8	80
3_92	92.8	89.6	95	78.3	78.8	78
6_109	86.2	77.6	92	78.3	78.8	78

EP 3 150 707 A1

(continued)

SEQ ID NO:	Training cohort			Validation cohort		
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
52_110	85.6	85.1	86	78.3	78.8	78
10_42	84.4	76.1	90	78.3	78.8	78
29_67	82.6	73.1	89	78.3	78.8	78
31_83	78.4	64.2	88	78.3	78.8	78
46_52	79	70.1	85	78.3	78.8	78
67_79	74.9	56.7	87	78.3	78.8	78
67_93	73.1	53.7	86	78.3	78.8	78
67_103	76	58.2	88	78.3	78.8	78
70_92	75.4	62.7	84	78.3	78.8	78
59_109	83.8	74.6	90	77.1	78.8	76
70_109	83.2	74.6	89	77.1	78.8	76
76_109	82.6	73.1	89	77.1	78.8	76
95_109	86.2	79.1	91	77.1	78.8	76
31_42	81.4	67.2	91	77.1	78.8	76
31_55	83.2	70.1	92	77.1	78.8	76
34_55	80.2	73.1	85	77.1	78.8	76
42_78	76	59.7	87	77.1	78.8	76
67_85	71.3	56.7	81	77.1	78.8	76
78_85	72.5	55.2	84	77.1	78.8	76
79_92	72.5	52.2	86	77.1	78.8	76
94_103	73.7	50.7	89	77.1	78.8	76
99_100	71.9	52.2	85	77.1	78.8	76
36_109	83.8	74.6	90	75.9	78.8	74
91_109	84.4	76.1	90	75.9	78.8	74
46_78	76	62.7	85	75.9	78.8	74
52_67	76	65.7	83	75.9	78.8	74
63_78	78.4	74.6	81	75.9	78.8	74
67_70	77.8	61.2	89	75.9	78.8	74
69_79	80.2	71.6	86	75.9	78.8	74
31_104	77.8	65.7	86	74.7	78.8	72
63_79	79	68.7	86	74.7	78.8	72
67_92	73.1	56.7	84	74.7	78.8	72
75_78	76.6	65.7	84	74.7	78.8	72
69_78	74.9	61.2	84	73.5	78.8	70
79_100	74.3	59.7	84	73.5	78.8	70
13_23	91	82.1	97	90.2	78.1	98
23_108	89.2	80.6	95	87.8	78.1	94

EP 3 150 707 A1

(continued)

SEQ ID NO:	Training cohort			Validation cohort		
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
8_23	88.6	79.1	95	87.8	78.1	94
41_50	81.4	67.2	91	86.6	78.1	92
50_51	79	64.2	89	85.4	78.1	90
50_87	78.4	62.7	89	85.4	78.1	90
37_50	82.6	71.6	90	84.1	78.1	88
9_23	87.4	82.1	91	82.9	78.1	86
50_68	79.6	64.2	90	82.9	78.1	86
23_106	89.2	76.1	98	81.7	78.1	84
46_50	76.6	67.2	83	81.7	78.1	84
50_75	76	64.2	84	81.7	78.1	84
50_111	79	61.2	91	80.5	78.1	82
31_50	82.6	70.1	91	78	78.1	78
50_78	73.7	62.7	81	74.4	78.1	72
77_110	84.4	76.1	90	88.9	77.4	96
18_77	83.2	74.6	89	86.4	77.4	92
77_115	79	67.2	87	86.4	77.4	92
16_77	85.6	82.1	88	85.2	77.4	90
29_77	83.2	76.1	88	85.2	77.4	90
58_77	74.3	56.7	86	85.2	77.4	90
66_77	76.6	59.7	88	85.2	77.4	90
77_104	79.6	62.7	91	84	77.4	88
11_77	80.2	71.6	86	82.7	77.4	86

[Example 3]

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

[0548] In this Example, the samples of 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 pancreatic cancer discriminant performance were conducted using all of the samples.

[0549] Specifically, the miRNA expression levels in the sera of the 100 pancreatic cancer patients and the 150 healthy subjects obtained in the preceding Reference Examples were normalized by quantile normalization. In order to acquire diagnosis markers with higher reliability, only genes having a gene expression level of 2⁶ or higher in 50% or more of the samples in either of the pancreatic 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 pancreatic cancer patient group from a healthy subject group, the P value obtained by two-tailed 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 and described in Table 7. In this way, hsa-miR-4417, hsa-miR-4707-5p, hsa-miR-7847-3p, hsa-miR-2861, hsa-miR-4513, hsa-miR-7111-5p, hsa-miR-6777-5p, hsa-miR-7113-3p, hsa-miR-4648, hsa-miR-3184-5p, hsa-miR-4271, hsa-miR-6791-5p, hsa-miR-642a-3p, hsa-miR-7108-5p, hsa-miR-128-1-5p, hsa-miR-5196-5p, hsa-miR-3178, hsa-miR-3656, hsa-miR-92a-2-5p, hsa-miR-6769b-5p, hsa-miR-4689, hsa-miR-6076, hsa-miR-92b-5p, hsa-miR-6774-5p, hsa-miR-486-3p, hsa-miR-6806-5p, hsa-miR-6842-5p, hsa-miR-6716-5p, hsa-miR-557,

EP 3 150 707 A1

hsa-miR-4673, hsa-miR-4674, hsa-miR-4442, hsa-miR-1915-3p, hsa-miR-4687-3p, and hsa-miR-92b-3p genes, and the nucleotide sequences of SEQ ID NOs: 349 to 383 related thereto were found in addition to the genes described in Table 2. As with the nucleotide sequences of SEQ ID NOs: 1 to 122, the results obtained about the polynucleotides shown in SEQ ID NOs: 349 to 383 also showed that the measurement values were significantly lower (-) or higher (+) in the pancreatic 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 pancreatic cancer in the newly obtained samples can be determined by the methods described in Examples 1 and 2 by using, alone or in combination, the gene expression level measurement values described in Table 7.

[Table 7]

SEQ ID NO:	Name	p. value	Expression level in pancreatic cancer patient relative to healthy subject
105	hsa-miR-125a-3p	7.05E-72	-
1	hsa-miR-6893-5p	4.14E-64	-
2	hsa-miR-6075	1.06E-49	+
4	hsa-miR-4294	5.56E-43	-
107	hsa-miR-1469	1.06E-42	+
106	hsa-miR-204-3p	6.17E-42	-
108	hsa-miR-575	1.26E-39	-
5	hsa-miR-6729-5p	1.24E-38	+
6	hsa-miR-4476	2.46E-36	-
3	hsa-miR-6820-5p	1.80E-34	-
8	hsa-miR-6765-3p	3.08E-32	-
109	hsa-miR-150-3p	7.57E-31	-
7	hsa-miR-6836-3p	1.12E-29	+
18	hsa-miR-4792	4.50E-29	+
9	hsa-miR-6799-5p	3.91E-28	-
10	hsa-miR-4530	6.27E-27	-
13	hsa-miR-615-5p	2.79E-26	-
12	hsa-miR-4454	4.13E-26	-
17	hsa-miR-4450	6.27E-26	-
11	hsa-miR-7641	1.99E-25	-
110	hsa-miR-423-5p	3.69E-25	-
24	hsa-miR-6877-5p	4.17E-25	-
19	hsa-miR-665	6.54E-25	+
14	hsa-miR-8073	3.32E-24	+
35	hsa-miR-1231	4.73E-23	+
25	hsa-miR-6880-5p	4.77E-23	-
22	hsa-miR-6789-5p	1.52E-22	+
16	hsa-miR-4634	3.85E-22	+
30	hsa-miR-5585-3p	8.16E-22	+
20	hsa-miR-7975	1.73E-20	-
33	hsa-miR-4651	3.57E-19	-

EP 3 150 707 A1

(continued)

SEQ ID NO:	Name	p. value	Expression level in pancreatic cancer patient relative to healthy subject	
5	31	hsa-miR-6085	3.92E-19	-
	26	hsa-miR-7977	4.07E-19	-
	29	hsa-miR-8089	2.29E-18	-
10	112	hsa-miR-3188	3.55E-18	+
	34	hsa-miR-4433-3p	6.97E-18	+
	27	hsa-miR-4734	8.43E-18	+
	111	hsa-miR-564	8.77E-18	-
15	46	hsa-miR-6125	4.60E-17	+
	21	hsa-miR-7109-5p	4.84E-17	-
	23	hsa-miR-4497	1.63E-16	-
20	41	hsa-miR-619-5p	2.74E-16	+
	37	hsa-miR-7114-5p	2.89E-16	-
	42	hsa-miR-3622a-5p	4.11E-16	-
	39	hsa-miR-8069	1.67E-15	+
25	58	hsa-miR-3185	2.47E-15	+
	66	hsa-miR-4723-5p	2.57E-15	-
	38	hsa-miR-1238-5p	2.84E-15	+
30	44	hsa-miR-6741-5p	3.06E-15	-
	40	hsa-miR-4732-5p	4.29E-15	+
	32	hsa-miR-6845-5p	1.09E-14	+
	55	hsa-miR-6724-5p	1.51E-14	+
35	28	hsa-miR-6821-5p	2.47E-14	-
	50	hsa-miR-6875-5p	7.80E-14	+
	113	hsa-miR-1246	1.34E-13	+
40	53	hsa-miR-4736	2.22E-13	+
	47	hsa-miR-6805-5p	2.32E-13	+
	36	hsa-miR-4665-5p	5.61E-13	-
	114	hsa-miR-602	7.01E-13	+
45	45	hsa-miR-6781-5p	1.70E-12	+
	15	hsa-miR-663a	1.70E-12	+
	57	hsa-miR-6726-5p	2.61E-12	-
50	67	hsa-miR-6850-5p	4.31E-12	+
	56	hsa-miR-7107-5p	7.43E-12	-
	52	hsa-miR-4433b-3p	7.79E-12	+
	71	hsa-miR-4486	8.29E-12	+
55	65	hsa-miR-6779-5p	1.76E-11	-
	115	hsa-miR-1290	1.99E-11	+

EP 3 150 707 A1

(continued)

SEQ ID NO:	Name	p. value	Expression level in pancreatic cancer patient relative to healthy subject
51	hsa-miR-1908-3p	2.20E-11	+
70	hsa-miR-8072	2.98E-11	+
60	hsa-miR-1273g-3p	6.69E-11	+
43	hsa-miR-1260a	1.14E-10	-
79	hsa-miR-4534	2.20E-10	-
80	hsa-miR-4449	2.54E-10	+
77	hsa-miR-6780b-5p	2.77E-10	+
49	hsa-miR-6872-3p	3.55E-10	-
119	hsa-miR-187-5p	3.74E-10	-
75	hsa-miR-7106-5p	4.23E-10	-
54	hsa-miR-5100	5.83E-10	-
83	hsa-miR-4467	6.44E-10	+
59	hsa-miR-4638-5p	9.61E-10	-
81	hsa-miR-5195-3p	1.12E-09	-
62	hsa-miR-328-5p	1.36E-09	-
68	hsa-miR-760	2.30E-09	-
78	hsa-miR-6090	2.36E-09	+
90	hsa-miR-3162-5p	3.27E-09	-
48	hsa-miR-6132	4.46E-09	-
120	hsa-miR-1908-5p	4.47E-09	+
61	hsa-miR-6778-5p	6.12E-09	+
98	hsa-miR-6816-5p	9.29E-09	+
94	hsa-miR-6722-3p	9.46E-09	+
82	hsa-miR-1202	1.14E-08	-
117	hsa-miR-451a	2.71E-08	-
118	hsa-miR-24-3p	3.63E-08	-
74	hsa-miR-1260b	6.21E-08	-
73	hsa-miR-4656	6.81E-08	+
85	hsa-miR-4281	6.81E-08	-
99	hsa-miR-4741	9.33E-08	+
116	hsa-miR-16-5p	9.82E-08	-
121	hsa-miR-371a-5p	1.38E-07	-
93	hsa-miR-1227-5p	1.43E-07	+
63	hsa-miR-3679-3p	1.83E-07	+
72	hsa-miR-1913	3.84E-07	+
69	hsa-miR-7704	1.35E-06	-
87	hsa-miR-4484	1.46E-06	+

EP 3 150 707 A1

(continued)

SEQ ID NO:	Name	p. value	Expression level in pancreatic cancer patient relative to healthy subject
5	89	1.72E-06	-
	103	3.01E-06	+
	349	3.10E-06	+
10	350	3.58E-06	+
	88	4.95E-06	+
	351	5.06E-06	-
	352	6.22E-06	-
15	104	7.23E-06	+
	353	7.71E-06	-
	76	1.88E-05	-
20	92	2.26E-05	+
	354	2.67E-05	-
	355	3.00E-05	-
	91	3.39E-05	-
25	356	3.47E-05	+
	97	3.73E-05	-
	357	4.03E-05	+
30	100	4.48E-05	+
	358	4.67E-05	+
	359	4.87E-05	-
	96	4.91E-05	+
35	360	7.71E-05	+
	361	2.26E-04	-
	362	2.56E-04	+
40	363	2.70E-04	+
	364	2.85E-04	-
	365	6.64E-04	+
	366	7.51E-04	+
45	367	1.04E-03	-
	368	1.06E-03	-
	369	1.17E-03	-
50	370	1.29E-03	-
	371	1.68E-03	+
	122	1.80E-03	+
	372	1.81E-03	+
55	373	2.00E-03	+
	374	2.02E-03	+

EP 3 150 707 A1

(continued)

SEQ ID NO:	Name	p. value	Expression level in pancreatic cancer patient relative to healthy subject
64	hsa-miR-1228-3p	2.28E-03	+
375	hsa-miR-6842-5p	2.35E-03	+
102	hsa-miR-4327	2.57E-03	-
376	hsa-miR-6716-5p	2.70E-03	+
377	hsa-miR-557	2.87E-03	+
378	hsa-miR-4673	3.26E-03	+
379	hsa-miR-4674	3.91E-03	+
95	hsa-miR-4286	4.47E-03	-
86	hsa-miR-4505	5.22E-03	-
380	hsa-miR-4442	5.97E-03	-
381	hsa-miR-1915-3p	6.28E-03	+
382	hsa-miR-4687-3p	6.36E-03	-
383	hsa-miR-92b-3p	7.44E-03	+

[Example 4]

<Method for evaluating pancreatic cancer-specific discriminant performance by combination of plurality of gene markers using samples of validation cohort>

[0550] In this Example, gene expression levels of miRNAs in sera were compared between pancreatic cancer patients and a control group consisting of healthy subjects, colorectal cancer patients, stomach cancer patients, esophageal cancer patients, liver cancer patients, and benign pancreaticobiliary disease patients in the same way as the method described in Example 1 with respect to the training cohort as the sample group described in Reference Example 2 to select an additional gene marker for diagnosis. The additional gene marker for diagnosis (at least one of SEQ ID NOs: 464 to 473 and 492 to 494) thus selected was combined with the gene markers selected in Example 1 to study a method for evaluating pancreatic cancer-specific discriminant performance.

[0551] Specifically, first, the miRNA expression levels of 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 newly found polynucleotides consisting of the nucleotide sequences represented by SEQ ID NOs: 1 to 104, 349 to 383, 464 to 473, and 492 to 494 among the polynucleotides consisting of the nucleotide sequences represented by SEQ ID NOs: 1 to 122, 349 to 383, 464 to 473, and 492 to 494, and the polynucleotides consisting of the nucleotide sequences represented by SEQ ID NOs: 105 and 108, to construct a discriminant for determining the presence or absence of pancreatic cancer. Next, accuracy, sensitivity, and specificity in the validation cohort were calculated using the discriminant thus prepared, with the pancreatic cancer patient group as a positive sample group and the healthy subject group, the colorectal cancer patient group, the stomach cancer patient group, the esophageal cancer patient group, the liver cancer patient group, and the benign pancreaticobiliary disease patient group as negative sample groups. The discriminant performance of the selected polynucleotides was validated using independent samples.

[0552] Most of polynucleotides consisting of the nucleotide sequences represented by these SEQ ID NOs (SEQ ID NOs: 1 to 122, 349 to 383, 464 to 473, and 492 to 494 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 pancreatic cancer, and furthermore, were able to specifically discriminate pancreatic 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: 2, 4, 6, 7, 9, 10, 25, 28, 30, 31, 38, 48, 82, 103, 105, 108, and 464 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 polynucleotides preferably selected from the group consisting of polynucleotides con-

sisting of the nucleotide sequences represented by SEQ ID NOs: 2, 4, 7, 10, and 25 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 pancreatic cancer from the other cancers with high accuracy.

5 **[0553]** The number of the polynucleotides with cancer type specificity in the combination mentioned above 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 discrimination accuracy of 80% or higher.

[0554] The probes used in the measurement were the above-defined nucleic acids capable of specifically binding to each polynucleotide as a target marker.

10 **[0555]** Specifically, the following results were obtained as the discrimination accuracy of the measurement using the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 2 or a complementary sequence thereof as a target marker.

15 **[0556]** 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 91.1% in the training cohort and the highest accuracy of 85.3% in the validation cohort (Table 8). 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 the highest accuracy of 93.0% in the training cohort and the highest accuracy of 91.7% in the validation cohort (Table 9). 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 the highest accuracy of 92.7% in the training cohort and the highest accuracy of 93.6% in the validation cohort (Table 10). 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 the highest accuracy of 93.3% in the training cohort and the highest accuracy of 96.2% in the validation cohort (Table 11).

25 **[0557]** Specifically, the following results were obtained as the discrimination accuracy of the measurement using the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 4 or a complementary sequence thereof as a target marker.

30 **[0558]** The measurement using the combination of one polynucleotide comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 4 or a complementary sequence thereof exhibited accuracy of 77.1% in the training cohort and the highest accuracy of 78.8% in the validation cohort (Table 8). 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: 4 or a complementary sequence thereof exhibited the highest accuracy of 89.8% in the training cohort and the highest accuracy of 88.5% in the validation cohort (Table 9). 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: 4 or a complementary sequence thereof exhibited the highest accuracy of 92.7% in the training cohort and the highest accuracy of 91.7% in the validation cohort (Table 10). 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: 4 or a complementary sequence thereof exhibited the highest accuracy of 92.7% in the training cohort and the highest accuracy of 93.6% in the validation cohort (Table 11).

35 **[0559]** Specifically, the following results were obtained as the discrimination accuracy of the measurement using the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 7 or a complementary sequence thereof as a target marker.

40 **[0560]** The measurement using the combination of one polynucleotide comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 7 or a complementary sequence thereof exhibited accuracy of 86.7% in the training cohort and the highest accuracy of 82.1% in the validation cohort (Table 8). 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: 7 or a complementary sequence thereof exhibited the highest accuracy of 90.2% in the training cohort and the highest accuracy of 89.1% in the validation cohort (Table 9). 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: 7 or a complementary sequence thereof exhibited the highest accuracy of 92.7% in the training cohort and the highest accuracy of 93.6% in the validation cohort (Table 10). 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: 7 or a complementary sequence thereof exhibited the highest accuracy of 93.3% in the training cohort and the highest accuracy of 96.2% in the validation cohort (Table 11).

55 **[0561]** Specifically, the following results were obtained as the discrimination accuracy of the measurement using the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 10 or a complementary sequence

thereof as a target marker.

[0562] 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 77.1% in the training cohort and the highest accuracy of 68.6% in the validation cohort (Table 8). 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 the highest accuracy of 90.8% in the training cohort and the highest accuracy of 89.7% in the validation cohort (Table 9). 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 the highest accuracy of 93.0% in the training cohort and the highest accuracy of 91.7% in the validation cohort (Table 10). 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 the highest accuracy of 93.7% in the training cohort and the highest accuracy of 93.6% in the validation cohort (Table 11).

[0563] Specifically, the following results were obtained as the discrimination accuracy of the measurement using the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 25 or a complementary sequence thereof as a target marker.

[0564] The measurement using the combination of one polynucleotide comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 25 or a complementary sequence thereof exhibited accuracy of 82.2% in the training cohort and the highest accuracy of 75.6% in the validation cohort (Table 8). 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: 25 or a complementary sequence thereof exhibited the highest accuracy of 90.8% in the training cohort and the highest accuracy of 87.8% in the validation cohort (Table 9). 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: 25 or a complementary sequence thereof exhibited the highest accuracy of 91.1% in the training cohort and the highest accuracy of 91.0% in the validation cohort (Table 10). 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: 25 or a complementary sequence thereof exhibited the highest accuracy of 92.7% in the training cohort and the highest accuracy of 93.6% in the validation cohort (Table 11).

[0565] The expression level measurement values of the nucleotide sequences represented by SEQ ID NOs: 2, 7, 9, and 105 were compared among 67 pancreatic cancer patients, 93 healthy subjects, 35 colorectal cancer patients, 37 stomach cancer patients, 32 esophageal cancer patients, 38 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 pancreatic cancer patient group from the other discriminant scores was obtained in the training cohort (see the upper diagram of Figure 4). These results were also reproducible in the validation cohort (see the lower diagram of Figure 4).

[0566] Tables 8, 9, 10, and 11 mentioned above are as follows.

[Table 8]

SEQ ID NO:	Training cohort			Validation cohort		
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
2	91.1	83.6	93.1	85.3	69.7	89.4
4	77.1	77.6	77	78.8	81.8	78
6	81	76.1	82.3	75	60.6	78.9
7	86.7	89.6	85.9	82.1	87.9	80.5
9	78.4	85.1	76.6	75	90.9	70.7
10	77.1	82.1	75.8	68.6	75.8	66.7
25	82.2	86.6	81	75.6	72.7	76.4
28	68.9	74.6	67.3	67.9	69.7	67.5
30	70.2	70.1	70.2	76.3	72.7	77.2
31	75.6	68.7	77.4	74.4	69.7	75.6

EP 3 150 707 A1

(continued)

5

	Training cohort			Validation cohort		
SEQ ID NO:	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
38	77.1	67.2	79.8	73.7	63.6	76.4
48	74	77.6	73	74.4	66.7	76.4
82	57.5	59.7	56.9	62.2	63.6	61.8
103	58.1	49.3	60.5	52.6	48.5	53.7
108	74.6	70.1	75.8	71.2	69.7	71.5
464	68.3	53.7	72.2	67.3	57.6	69.9

15

[Table 9]

20

	Training cohort			Validation cohort		
SEQ IDNO:	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
2_48	93	83.6	95.6	91.7	81.8	94.3
2_10	90.8	86.6	91.9	89.7	87.9	90.2
2_465	89.5	83.6	91.1	89.7	87.9	90.2
2_9	90.5	85.1	91.9	89.7	84.8	91.1
2_30	91.7	85.1	93.5	89.7	81.8	91.9
2_61	89.8	79.1	92.7	89.7	81.8	91.9
2_101	90.5	82.1	92.7	89.7	78.8	92.7
2_7	90.2	80.6	92.7	89.1	84.8	90.2
2_28	90.5	83.6	92.3	89.1	84.8	90.2
2_4	89.8	83.6	91.5	88.5	81.8	90.2
2_68	90.8	85.1	92.3	88.5	81.8	90.2
2_25	90.8	86.6	91.9	87.8	81.8	89.4

40

[Table 10]

45

	Training cohort			Validation cohort		
SEQ ID NO:	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
2_7_101	92.7	86.6	94.4	93.6	93.9	93.5
2_48_68	93.7	83.6	96.4	93.6	78.8	97.6
2_7_82	92.7	82.1	95.6	92.9	87.9	94.3
2_6_48	93.7	85.1	96	92.9	87.9	94.3
2_48_17	92.7	83.6	95.2	92.9	84.8	95.1
2_48_101	93.3	85.1	95.6	92.9	84.8	95.1
2_465_467	90.8	82.1	93.1	92.3	93.9	91.9
2_7_48	92.4	83.6	94.8	92.3	84.8	94.3
2_48_38	92.7	82.1	95.6	92.3	84.8	94.3
2_48_22	92.7	85.1	94.8	92.3	84.8	94.3

55

EP 3 150 707 A1

(continued)

	Training cohort			Validation cohort			
SEQ ID NO:	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)	
5	2_48_30	94.3	88.1	96	92.3	84.8	94.3
	2_48_53	93.3	83.6	96	92.3	84.8	94.3
	2_48_47	93	85.1	95.2	92.3	84.8	94.3
10	2_48_365	93	85.1	95.2	92.3	84.8	94.3
	2_38_101	91.4	85.1	93.1	92.3	84.8	94.3
	2_31_101	91.7	82.1	94.4	92.3	81.8	95.1
15	2_48_82	93	83.6	95.6	92.3	81.8	95.1
	2_9_103	91.4	83.6	93.5	91.7	93.9	91.1
	2_9_469	90.2	85.1	91.5	91.7	93.9	91.1
	2_38_465	91.7	85.1	93.5	91.7	87.9	92.7
20	2_465_373	89.8	83.6	91.5	91.7	87.9	92.7
	2_61_365	88.9	79.1	91.5	91.7	87.9	92.7
	2_31_48	93.7	86.6	95.6	91.7	84.8	93.5
25	2_6_101	91.7	85.1	93.5	91.7	84.8	93.5
	2_48_103	93.3	85.1	95.6	91.7	84.8	93.5
	2_68_101	91.7	85.1	93.5	91.7	84.8	93.5
	2_465_101	90.8	82.1	93.1	91.7	84.8	93.5
30	2_61_101	90.5	80.6	93.1	91.7	84.8	93.5
	2_4_48	92.7	82.1	95.6	91.7	81.8	94.3
	2_10_48	93	85.1	95.2	91.7	81.8	94.3
35	2_9_48	93.3	85.1	95.6	91.7	81.8	94.3
	2_48_51	93	83.6	95.6	91.7	81.8	94.3
	2_48_465	93	83.6	95.6	91.7	81.8	94.3
	2_48_108	93	82.1	96	91.7	81.8	94.3
40	2_48_28	93	83.6	95.6	91.7	81.8	94.3
	2_48_373	93	80.6	96.4	91.7	81.8	94.3
	2_48_466	92.7	82.1	95.6	91.7	81.8	94.3
45	2_48_61	93	83.6	95.6	91.7	81.8	94.3
	2_48_467	93.3	82.1	96.4	91.7	81.8	94.3
	2_48_464	93	83.6	95.6	91.7	81.8	94.3
	2_48_382	92.7	83.3	95.2	91.7	81.8	94.3
50	2_48_370	93	82.1	96	91.7	81.8	94.3
	2_101_365	90.5	79.1	93.5	91.7	81.8	94.3
	2_10_365	89.5	83.6	91.1	91	93.9	90.2
55	2_7_465	91.1	82.1	93.5	91	90.9	91.1
	2_7_61	90.2	82.1	92.3	91	90.9	91.1
	2_9_467	90.5	85.1	91.9	91	90.9	91.1

EP 3 150 707 A1

(continued)

	Training cohort			Validation cohort		
SEQ ID NO:	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
5 2_465_469	89.2	83.6	90.7	91	90.9	91.1
2_25_30	91.1	86.6	92.3	91	87.9	91.9
2_7_466	90.2	80.6	92.7	91	87.9	91.9
10 2_7_47	89.8	82.1	91.9	91	87.9	91.9
2_10_82	90.8	88.1	91.5	91	87.9	91.9
2_9_47	90.8	85.1	92.3	91	87.9	91.9
15 2_7_68	92.4	85.1	94.4	91	84.8	92.7
2_7_22	91.7	83.6	94	91	84.8	92.7
2_7_100	90.2	80.6	92.7	91	84.8	92.7
2_10_101	92.7	86.6	94.4	91	84.8	92.7
20 2_9_101	92.4	85.1	94.4	91	84.8	92.7
2_48_359	93	82.1	96	91	84.8	92.7
2_38_103	91.4	85.1	93.1	91	84.8	92.7
25 2_465_82	90.5	85.1	91.9	91	84.8	92.7
2_28_382	91.1	83.3	93.1	91	84.8	92.7
2_28_82	91.7	85.1	93.5	91	84.8	92.7
2_30_101	92.1	83.6	94.4	91	84.8	92.7
30 2_25_48	93	85.1	95.2	91	81.8	93.5
2_48_90	94	88.1	95.6	91	81.8	93.5
2_48_468	93	83.6	95.6	91	81.8	93.5
35 2_48_118	92.4	85.1	94.4	91	81.8	93.5
2_51_101	90.8	83.6	92.7	91	81.8	93.5
2_38_30	90.8	82.1	93.1	91	81.8	93.5
2_61_469	90.5	80.6	93.1	91	81.8	93.5
40 2_53_101	91.1	83.6	93.1	91	81.8	93.5
2_101_464	90.2	80.6	92.7	91	81.8	93.5
2_101_118	90.2	82.1	92.3	91	81.8	93.5
45 2_101_469	90.5	82.1	92.7	91	81.8	93.5
2_101_47	91.4	83.6	93.5	91	78.8	94.3
2_101_100	90.5	82.1	92.7	91	78.8	94.3
2_465_365	88.9	82.1	90.7	90.4	93.9	89.4
50 2_7_9	91.4	83.6	93.5	90.4	90.9	90.2
2_7_28	91.1	82.1	93.5	90.4	90.9	90.2
2_7_53	91.1	83.6	93.1	90.4	90.9	90.2
55 2_7_365	89.8	80.6	92.3	90.4	90.9	90.2
2_10_9	91.1	86.6	92.3	90.4	90.9	90.2
2_9_365	89.5	83.6	91.1	90.4	90.9	90.2

EP 3 150 707 A1

(continued)

	Training cohort			Validation cohort			
SEQ ID NO:	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)	
5	2_9_82	92.1	86.6	93.5	90.4	90.9	90.2
	2_465_47	89.8	83.6	91.5	90.4	90.9	90.2
	2_25_61	91.1	85.1	92.7	90.4	87.9	91.1
10	2_7_17	90.5	80.6	93.1	90.4	87.9	91.1
	2_7_464	89.2	79.1	91.9	90.4	87.9	91.1
	2_7_103	92.4	85.1	94.4	90.4	87.9	91.1
15	2_7_469	90.2	80.6	92.7	90.4	87.9	91.1
	2_10_30	91.7	88.1	92.7	90.4	87.9	91.1
	2_10_61	90.5	85.1	91.9	90.4	87.9	91.1
	2_9_31	90.2	85.1	91.5	90.4	87.9	91.1
20	2_9_28	91.1	83.6	93.1	90.4	87.9	91.1
	2_9_468	90.2	85.1	91.5	90.4	87.9	91.1
	2_9_370	90.8	85.1	92.3	90.4	87.9	91.1
25	2_9_100	89.8	85.1	91.1	90.4	87.9	91.1
	2_38_61	90.8	83.6	92.7	90.4	87.9	91.1
	2_7_382	92	81.8	94.8	90.4	84.8	91.9
	2_9_61	90.5	83.6	92.3	90.4	84.8	91.9
30	2_48_100	93.7	85.1	96	90.4	84.8	91.9
	2_48_469	93	82.1	96	90.4	84.8	91.9
	2_51_30	91.7	86.6	93.1	90.4	84.8	91.9
35	2_68_28	92.1	83.6	94.4	90.4	84.8	91.9
	2_465_30	91.1	85.1	92.7	90.4	84.8	91.9
	2_465_61	90.8	85.1	92.3	90.4	84.8	91.9
	2_28_30	92.4	85.1	94.4	90.4	84.8	91.9
40	2_28_47	90.2	83.6	91.9	90.4	84.8	91.9
	2_28_370	91.1	83.6	93.1	90.4	84.8	91.9
	2_22_61	90.5	80.6	93.1	90.4	84.8	91.9
45	2_30_365	90.5	82.1	92.7	90.4	84.8	91.9
	2_30_100	91.4	85.1	93.1	90.4	84.8	91.9
	2_61_467	89.5	80.6	91.9	90.4	84.8	91.9
	2_61_464	89.5	77.6	92.7	90.4	84.8	91.9
50	2_25_101	91.1	85.1	92.7	90.4	81.8	92.7
	2_4_101	90.5	80.6	93.1	90.4	81.8	92.7
	2_28_101	91.7	83.6	94	90.4	81.8	92.7
55	2_22_101	90.2	80.6	92.7	90.4	81.8	92.7
	2_30_53	90.8	82.1	93.1	90.4	81.8	92.7
	2_61_47	88.9	80.6	91.1	90.4	81.8	92.7

EP 3 150 707 A1

(continued)

	Training cohort			Validation cohort		
SEQ ID NO:	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
5 2_108_101	91.1	82.1	93.5	90.4	78.8	93.5
2_28_17	92.1	85.1	94	90.4	78.8	93.5
2_373_101	90.5	82.1	92.7	90.4	78.8	93.5
10 2_466_101	90.8	82.1	93.1	90.4	78.8	93.5
2_101_468	90.5	82.1	92.7	90.4	78.8	93.5
2_101_370	89.8	79.1	92.7	90.4	78.8	93.5
15 2_101_82	91.1	82.1	93.5	90.4	78.8	93.5
2_7_10	91.7	85.1	93.5	89.7	90.9	89.4
2_9_38	91.7	86.6	93.1	89.7	90.9	89.4
2_25_465	89.2	85.1	90.3	89.7	87.9	90.2
20 2_25_28	90.8	85.1	92.3	89.7	87.9	90.2
2_7_38	92.4	82.1	95.2	89.7	87.9	90.2
2_7_108	90.2	80.6	92.7	89.7	87.9	90.2
25 2_7_118	89.5	83.6	91.1	89.7	87.9	90.2
2_4_465	89.5	83.6	91.1	89.7	87.9	90.2
2_10_465	91.7	86.6	93.1	89.7	87.9	90.2
2_10_28	91.1	86.6	92.3	89.7	87.9	90.2
30 2_10_466	90.8	86.6	91.9	89.7	87.9	90.2
2_10_370	91.1	86.6	92.3	89.7	87.9	90.2
2_10_359	90.8	86.6	91.9	89.7	87.9	90.2
35 2_10_469	91.7	86.6	93.1	89.7	87.9	90.2
2_9_6	89.8	86.6	90.7	89.7	87.9	90.2
2_9_465	90.5	83.6	92.3	89.7	87.9	90.2
2_9_382	90.8	84.8	92.3	89.7	87.9	90.2
40 2_6_365	89.5	83.6	91.1	89.7	87.9	90.2
2_51_465	89.5	83.6	91.1	89.7	87.9	90.2
2_465_108	89.8	83.6	91.5	89.7	87.9	90.2
45 2_465_28	90.8	85.1	92.3	89.7	87.9	90.2
2_465_22	89.2	83.6	90.7	89.7	87.9	90.2
2_465_17	89.5	83.6	91.1	89.7	87.9	90.2
2_465_466	89.8	83.6	91.5	89.7	87.9	90.2
50 2_465_464	89.8	85.1	91.1	89.7	87.9	90.2
2_465_368	89.5	83.6	91.1	89.7	87.9	90.2
2_465_359	89.5	83.6	91.1	89.7	87.9	90.2
55 2_465_100	89.8	85.1	91.1	89.7	87.9	90.2
2_25_47	89.8	85.1	91.1	89.7	84.8	91.1
2_7_4	90.2	80.6	92.7	89.7	84.8	91.1

EP 3 150 707 A1

(continued)

	Training cohort			Validation cohort			
SEQ ID NO:	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)	
5	2_7_31	90.2	80.6	92.7	89.7	84.8	91.1
	2_7_373	89.8	79.1	92.7	89.7	84.8	91.1
	2_7_370	90.5	80.6	93.1	89.7	84.8	91.1
10	2_4_61	89.8	80.6	92.3	89.7	84.8	91.1
	2_10_108	90.8	86.6	91.9	89.7	84.8	91.1
	2_10_118	90.5	86.6	91.5	89.7	84.8	91.1
15	2_9_108	90.5	85.1	91.9	89.7	84.8	91.1
	2_9_22	90.5	85.1	91.9	89.7	84.8	91.1
	2_9_30	91.7	85.1	93.5	89.7	84.8	91.1
	2_9_466	90.5	85.1	91.9	89.7	84.8	91.1
20	2_9_368	90.5	85.1	91.9	89.7	84.8	91.1
	2_51_61	90.8	83.6	92.7	89.7	84.8	91.1
	2_38_382	91.1	84.8	92.7	89.7	84.8	91.1
25	2_465_53	90.5	85.1	91.9	89.7	84.8	91.1
	2_108_61	89.8	82.1	91.9	89.7	84.8	91.1
	2_28_467	91.4	85.1	93.1	89.7	84.8	91.1
	2_28_468	91.4	85.1	93.1	89.7	84.8	91.1
30	2_28_469	91.1	83.6	93.1	89.7	84.8	91.1
	2_22_103	89.8	83.6	91.5	89.7	84.8	91.1
	2_466_61	90.5	82.1	92.7	89.7	84.8	91.1
35	2_7_30	92.1	88.1	93.1	89.7	81.8	91.9
	2_4_30	91.1	82.1	93.5	89.7	81.8	91.9
	2_9_373	90.2	85.1	91.5	89.7	81.8	91.9
	2_9_464	90.5	85.1	91.9	89.7	81.8	91.9
40	2_31_465	89.8	83.6	91.5	89.7	81.8	91.9
	2_31_61	89.8	79.1	92.7	89.7	81.8	91.9
	2_68_38	92.1	85.1	94	89.7	81.8	91.9
45	2_465_103	91.1	83.6	93.1	89.7	81.8	91.9
	2_28_373	91.7	85.1	93.5	89.7	81.8	91.9
	2_28_61	90.8	85.1	92.3	89.7	81.8	91.9
	2_28_368	91.4	85.1	93.1	89.7	81.8	91.9
50	2_28_118	90.2	85.1	91.5	89.7	81.8	91.9
	2_373_61	90.2	80.6	92.7	89.7	81.8	91.9
	2_22_30	91.4	85.1	93.1	89.7	81.8	91.9
55	2_30_17	91.7	85.1	93.5	89.7	81.8	91.9
	2_30_61	91.7	85.1	93.5	89.7	81.8	91.9
	2_30_368	91.4	83.6	93.5	89.7	81.8	91.9

EP 3 150 707 A1

(continued)

	Training cohort			Validation cohort			
SEQ ID NO:	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)	
5	2_30_118	92.1	85.1	94	89.7	81.8	91.9
	2_30_359	91.7	85.1	93.5	89.7	81.8	91.9
	2_30_103	92.4	83.6	94.8	89.7	81.8	91.9
10	2_17_61	89.8	79.1	92.7	89.7	81.8	91.9
	2_61_370	89.8	79.1	92.7	89.7	81.8	91.9
	2_61_368	89.8	77.6	93.1	89.7	81.8	91.9
15	2_61_118	90.2	80.6	92.7	89.7	81.8	91.9
	2_61_82	89.8	76.1	93.5	89.7	81.8	91.9
	2_17_101	90.5	82.1	92.7	89.7	78.8	92.7
	2_467_101	90.5	82.1	92.7	89.7	78.8	92.7
20	2_101_382	91.1	81.8	93.5	89.7	78.8	92.7
	2_101_368	90.5	82.1	92.7	89.7	78.8	92.7
	2_101_359	90.5	82.1	92.7	89.7	78.8	92.7
25	2_101_103	90.5	82.1	92.7	89.7	78.8	92.7
	2_90_101	90.8	82.1	93.1	89.7	75.8	93.5
	2_25_9	90.2	85.1	91.5	89.1	87.9	89.4
	2_25_53	89.8	85.1	91.1	89.1	87.9	89.4
30	2_7_6	90.8	85.1	92.3	89.1	87.9	89.4
	2_10_22	90.8	86.6	91.9	89.1	87.9	89.4
	2_10_53	90.8	86.6	91.9	89.1	87.9	89.4
35	2_10_47	89.8	86.6	90.7	89.1	87.9	89.4
	2_9_51	90.5	85.1	91.9	89.1	87.9	89.4
	2_25_7	91.4	83.6	93.5	89.1	84.8	90.2
	2_25_68	91.4	86.6	92.7	89.1	84.8	90.2
40	2_25_17	90.5	86.6	91.5	89.1	84.8	90.2
	2_25_365	89.5	83.6	91.1	89.1	84.8	90.2
	2_7_467	90.8	80.6	93.5	89.1	84.8	90.2
45	2_7_468	90.5	80.6	93.1	89.1	84.8	90.2
	2_7_368	90.2	80.6	92.7	89.1	84.8	90.2
	2_7_359	90.8	83.6	92.7	89.1	84.8	90.2
	2_4_10	90.8	86.6	91.9	89.1	84.8	90.2
50	2_4_9	90.5	85.1	91.9	89.1	84.8	90.2
	2_4_28	90.5	83.6	92.3	89.1	84.8	90.2
	2_4_90	90.5	82.1	92.7	89.1	84.8	90.2
55	2_10_31	91.1	86.6	92.3	89.1	84.8	90.2
	2_10_51	90.8	86.6	91.9	89.1	84.8	90.2
	2_10_382	90.4	86.4	91.5	89.1	84.8	90.2

EP 3 150 707 A1

(continued)

	Training cohort			Validation cohort			
SEQ ID NO:	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)	
5	2_9_53	91.1	85.1	92.7	89.1	84.8	90.2
	2_9_359	90.5	85.1	91.9	89.1	84.8	90.2
	2_51_28	90.8	83.6	92.7	89.1	84.8	90.2
10	2_51_90	90.8	80.6	93.5	89.1	84.8	90.2
	2_68_61	91.4	82.1	94	89.1	84.8	90.2
	2_38_28	90.8	85.1	92.3	89.1	84.8	90.2
15	2_108_30	91.7	88.1	92.7	89.1	84.8	90.2
	2_28_466	90.5	83.6	92.3	89.1	84.8	90.2
	2_28_359	90.8	83.6	92.7	89.1	84.8	90.2
	2_28_100	90.8	85.1	92.3	89.1	84.8	90.2
20	2_30_464	91.4	82.1	94	89.1	84.8	90.2
	2_468_365	88.9	80.6	91.1	89.1	84.8	90.2
	2_25_82	90.8	86.6	91.9	89.1	81.8	91.1
25	2_7_51	89.2	77.6	92.3	89.1	81.8	91.1
	2_4_103	91.1	82.1	93.5	89.1	81.8	91.1
	2_31_68	90.2	83.6	91.9	89.1	81.8	91.1
	2_31_30	91.1	82.1	93.5	89.1	81.8	91.1
30	2_6_30	91.7	88.1	92.7	89.1	81.8	91.1
	2_48_368	93	85.1	95.2	89.1	81.8	91.1
	2_51_373	89.8	83.6	91.5	89.1	81.8	91.1
35	2_68_47	90.5	85.1	91.9	89.1	81.8	91.1
	2_68_368	91.4	85.1	93.1	89.1	81.8	91.1
	2_68_100	91.1	85.1	92.7	89.1	81.8	91.1
	2_68_103	90.8	85.1	92.3	89.1	81.8	91.1
40	2_38_82	90.5	85.1	91.9	89.1	81.8	91.1
	2_108_28	91.1	83.6	93.1	89.1	81.8	91.1
	2_108_17	91.4	83.6	93.5	89.1	81.8	91.1
45	2_373_30	92.4	86.6	94	89.1	81.8	91.1
	2_30_466	90.8	85.1	92.3	89.1	81.8	91.1
	2_30_370	91.7	85.1	93.5	89.1	81.8	91.1
	2_30_82	91.4	85.1	93.1	89.1	81.8	91.1
50	2_466_103	91.4	85.1	93.1	89.1	81.8	91.1
	2_61_53	91.1	82.1	93.5	89.1	81.8	91.1
	2_61_468	89.8	79.1	92.7	89.1	81.8	91.1
55	2_61_359	89.8	79.1	92.7	89.1	81.8	91.1
	2_9_17	90.5	85.1	91.9	89.1	78.8	91.9
	2_28_103	91.4	83.6	93.5	89.1	78.8	91.9

EP 3 150 707 A1

(continued)

	Training cohort			Validation cohort			
SEQ ID NO:	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)	
5	2_90_100	90.5	80.6	93.1	89.1	78.8	91.9
	2_61_382	90.1	80.3	92.7	89.1	78.8	91.9
	2_100_103	90.8	83.6	92.7	89.1	75.8	92.7
10	2_25_10	90.2	88.1	90.7	88.5	84.8	89.4
	2_25_464	90.5	86.6	91.5	88.5	84.8	89.4
	2_4_82	90.5	85.1	91.9	88.5	84.8	89.4
15	2_10_467	90.8	86.6	91.9	88.5	84.8	89.4
	2_10_464	91.1	86.6	92.3	88.5	84.8	89.4
	2_10_368	90.8	86.6	91.9	88.5	84.8	89.4
	2_9_68	92.1	86.6	93.5	88.5	84.8	89.4
20	2_6_51	89.8	85.1	91.1	88.5	84.8	89.4
	2_6_61	88.9	83.6	90.3	88.5	84.8	89.4
	2_6_464	89.5	85.1	90.7	88.5	84.8	89.4
25	2_6_100	90.2	85.1	91.5	88.5	84.8	89.4
	2_51_365	89.5	83.6	91.1	88.5	84.8	89.4
	2_38_90	90.8	80.6	93.5	88.5	84.8	89.4
	2_38_365	88.6	82.1	90.3	88.5	84.8	89.4
30	2_108_365	89.2	83.6	90.7	88.5	84.8	89.4
	2_108_82	91.1	85.1	92.7	88.5	84.8	89.4
	2_28_365	89.2	83.6	90.7	88.5	84.8	89.4
35	2_22_467	89.8	85.1	91.1	88.5	84.8	89.4
	2_22_382	89.8	83.3	91.5	88.5	84.8	89.4
	2_22_82	90.5	85.1	91.9	88.5	84.8	89.4
	2_466_365	89.2	83.6	90.7	88.5	84.8	89.4
40	2_25_38	91.4	86.6	92.7	88.5	81.8	90.2
	2_25_373	90.5	86.6	91.5	88.5	81.8	90.2
	2_25_468	90.8	85.1	92.3	88.5	81.8	90.2
45	2_4_464	90.2	83.6	91.9	88.5	81.8	90.2
	2_4_468	89.8	83.6	91.5	88.5	81.8	90.2
	2_4_47	90.2	83.6	91.9	88.5	81.8	90.2
	2_10_373	90.2	86.6	91.1	88.5	81.8	90.2
50	2_10_468	90.8	86.6	91.9	88.5	81.8	90.2
	2_9_90	90.5	82.1	92.7	88.5	81.8	90.2
	2_9_118	90.5	85.1	91.9	88.5	81.8	90.2
55	2_31_38	90.2	85.1	91.5	88.5	81.8	90.2
	2_6_68	91.7	85.1	93.5	88.5	81.8	90.2
	2_51_82	90.2	83.6	91.9	88.5	81.8	90.2

EP 3 150 707 A1

(continued)

	Training cohort			Validation cohort			
SEQ ID NO:	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)	
5	2_68_373	90.8	85.1	92.3	88.5	81.8	90.2
	2_68_464	89.8	83.6	91.5	88.5	81.8	90.2
	2_38_464	90.2	85.1	91.5	88.5	81.8	90.2
10	2_38_359	91.4	85.1	93.1	88.5	81.8	90.2
	2_465_90	90.2	80.6	92.7	88.5	81.8	90.2
	2_465_468	90.2	83.6	91.9	88.5	81.8	90.2
15	2_465_370	89.8	82.1	91.9	88.5	81.8	90.2
	2_465_118	90.8	86.6	91.9	88.5	81.8	90.2
	2_28_464	91.1	85.1	92.7	88.5	81.8	90.2
	2_22_90	90.2	80.6	92.7	88.5	81.8	90.2
20	2_22_118	90.8	83.6	92.7	88.5	81.8	90.2
	2_30_467	91.7	85.1	93.5	88.5	81.8	90.2
	2_30_468	92.1	85.1	94	88.5	81.8	90.2
25	2_30_47	92.1	86.6	93.5	88.5	81.8	90.2
	2_61_103	90.2	77.6	93.5	88.5	81.8	90.2
	2_467_365	87.9	80.6	89.9	88.5	81.8	90.2
	2_53_365	88.9	80.6	91.1	88.5	81.8	90.2
30	2_53_103	91.1	82.1	93.5	88.5	81.8	90.2
	2_31_382	89.5	80.3	91.9	88.5	78.8	91.1
	2_31_103	89.5	79.1	92.3	88.5	78.8	91.1
35	2_68_30	92.4	85.1	94.4	88.5	78.8	91.1
	2_68_370	90.2	83.6	91.9	88.5	78.8	91.1
	2_68_82	91.4	85.1	93.1	88.5	78.8	91.1
40	2_38_17	90.5	85.1	91.9	88.5	78.8	91.1
	2_38_100	90.2	85.1	91.5	88.5	78.8	91.1
	2_90_61	90.5	79.1	93.5	88.5	78.8	91.1
	2_90_464	90.5	80.6	93.1	88.5	78.8	91.1
45	2_90_370	90.8	80.6	93.5	88.5	78.8	91.1
	2_30_382	91.1	81.8	93.5	88.5	78.8	91.1
	2_30_469	91.1	83.6	93.1	88.5	78.8	91.1
	2_61_100	89.8	80.6	92.3	88.5	78.8	91.1
50	2_368_82	90.8	83.6	92.7	88.5	78.8	91.1
	2_100_82	90.2	83.6	91.9	88.5	78.8	91.1
	2_90_368	90.8	80.6	93.5	88.5	75.8	91.9
55	2_90_118	90.2	80.6	92.7	88.5	75.8	91.9
	7_4_82	90.2	85.1	91.5	90.4	90.9	90.2
	7_68_61	89.8	88.1	90.3	89.7	87.9	90.2

EP 3 150 707 A1

(continued)

	Training cohort			Validation cohort		
SEQ ID NO:	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
7_38_101	90.2	86.6	91.1	89.7	87.9	90.2
7_30_101	87.6	89.6	87.1	89.1	90.9	88.6
7_30_82	87.9	89.6	87.5	89.1	87.9	89.4
2_25_7	91.4	83.6	93.5	89.1	84.8	90.2
7_68_28	89.2	85.1	90.3	89.1	84.8	90.2
7_4_103	88.9	88.1	89.1	88.5	87.9	88.6
7_10_31	86.3	79.1	88.3	88.5	87.9	88.6
7_68_38	90.5	86.6	91.5	88.5	84.8	89.4
7_68_47	88.6	85.1	89.5	88.5	84.8	89.4
7_30_103	87.9	89.6	87.5	88.5	81.8	90.2
25_7_47	87.9	86.6	88.3	90.4	87.9	91.1
25_7_373	89.2	91	88.7	89.1	93.9	87.8
25_7_61	87.6	89.6	87.1	89.1	93.9	87.8
25_7_48	89.2	88.1	89.5	89.1	87.9	89.4
25_7_467	89.2	89.6	89.1	88.5	90.9	87.8
25_7_464	87.9	91	87.1	88.5	90.9	87.8
25_7_118	88.9	91	88.3	88.5	90.9	87.8

[Table 11]

	Training cohort			Validation cohort		
SEQ ID NO:	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
2_7_61_82	93.3	85.1	95.6	96.2	97	95.9
2_7_82_103	93	83.6	95.6	95.5	87.9	97.6
2_7_47_82	92.4	83.6	94.8	94.9	93.9	95.1
2_7_82_101	94.6	88.1	96.4	94.9	87.9	96.7
2_7_9_101	92.7	86.6	94.4	94.2	93.9	94.3
2_7_31_101	93	86.6	94.8	94.2	93.9	94.3
2_7_51_101	92.4	83.6	94.8	94.2	93.9	94.3
2_38_53_465	92.1	85.1	94	94.2	93.9	94.3
2_7_9_82	93	85.1	95.2	94.2	90.9	95.1
2_7_48_103	93.7	85.1	96	94.2	90.9	95.1
2_7_101_466	92.1	82.1	94.8	94.2	90.9	95.1
2_7_47_101	92.4	85.1	94.4	94.2	90.9	95.1
2_7_48_51	93	86.6	94.8	94.2	87.9	95.9
2_7_48_469	92.7	83.6	95.2	94.2	87.9	95.9
2_38_82_101	91.4	83.6	93.5	94.2	87.9	95.9

EP 3 150 707 A1

(continued)

		Training cohort			Validation cohort		
	SEQ ID NO:	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
5	2_7_48_82	94	83.6	96.8	94.2	84.8	96.7
	2_48_68_467	94	85.1	96.4	94.2	81.8	97.6
	2_48_68_370	93.3	83.6	96	94.2	81.8	97.6
10	2_7_25_101	92.7	86.6	94.4	93.6	93.9	93.5
	2_7_101_465	92.7	86.6	94.4	93.6	93.9	93.5
	2_7_61_101	92.7	86.6	94.4	93.6	93.9	93.5
15	2_7_61_103	92.7	83.6	95.2	93.6	93.9	93.5
	2_7_101_368	92.4	85.1	94.4	93.6	93.9	93.5
	2_7_101_365	92.7	85.1	94.8	93.6	93.9	93.5
	2_38_51_465	91.1	85.1	92.7	93.6	93.9	93.5
20	2_28_465_467	92.7	86.6	94.4	93.6	93.9	93.5
	2_365_373_465	90.2	83.6	91.9	93.6	93.9	93.5
	2_100_465_467	91.4	85.1	93.1	93.6	93.9	93.5
25	2_7_10_82	93.7	83.6	96.4	93.6	90.9	94.3
	2_7_38_48	93.3	83.6	96	93.6	90.9	94.3
	2_7_48_359	93.3	83.6	96	93.6	90.9	94.3
	2_7_101_373	92.7	85.1	94.8	93.6	90.9	94.3
30	2_7_82_118	92.4	83.6	94.8	93.6	90.9	94.3
	2_7_82_365	92.1	80.6	95.2	93.6	90.9	94.3
	2_6_48_359	93.7	83.6	96.4	93.6	90.9	94.3
35	2_38_82_465	92.1	85.1	94	93.6	90.9	94.3
	2_38_101_365	92.1	83.6	94.4	93.6	90.9	94.3
	2_7_25_82	93.7	85.1	96	93.6	87.9	95.1
	2_7_48_466	92.4	85.1	94.4	93.6	87.9	95.1
40	2_7_48_467	93	83.6	95.6	93.6	87.9	95.1
	2_7_82_465	92.7	82.1	95.6	93.6	87.9	95.1
	2_7_30_82	93	85.1	95.2	93.6	87.9	95.1
45	2_7_101_382	93.3	84.8	95.6	93.6	87.9	95.1
	2_30_31_48	94.6	89.6	96	93.6	87.9	95.1
	2_31_48_53	93.7	86.6	95.6	93.6	87.9	95.1
	2_31_48_82	93.3	86.6	95.2	93.6	87.9	95.1
50	2_31_53_101	91.4	80.6	94.4	93.6	87.9	95.1
	2_38_48_101	92.7	83.6	95.2	93.6	87.9	95.1
	2_48_465_467	93.3	83.6	96	93.6	87.9	95.1
55	2_17_48_365	92.7	83.6	95.2	93.6	87.9	95.1
	2_28_68_101	93.3	86.6	95.2	93.6	87.9	95.1
	2_30_38_101	93	86.6	94.8	93.6	87.9	95.1

EP 3 150 707 A1

(continued)

		Training cohort			Validation cohort		
	SEQ ID NO:	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
5	2_17_25_48	92.7	83.6	95.2	93.6	84.8	95.9
	2_7_47_68	91.7	83.6	94	93.6	84.8	95.9
	2_7_28_82	93.7	85.1	96	93.6	84.8	95.9
10	2_7_382_82	92.7	81.8	95.6	93.6	84.8	95.9
	2_4_38_48	92.7	82.1	95.6	93.6	84.8	95.9
	2_48_465_466	93	83.6	95.6	93.6	84.8	95.9
15	2_48_101_108	93	83.6	95.6	93.6	84.8	95.9
	2_22_48_82	92.4	85.1	94.4	93.6	84.8	95.9
	2_30_48_467	93.3	82.1	96.4	93.6	84.8	95.9
	2_30_48_82	94.6	89.6	96	93.6	84.8	95.9
20	2_17_48_101	92.7	83.6	95.2	93.6	84.8	95.9
	2_48_82_101	93.3	85.1	95.6	93.6	84.8	95.9
	2_38_101_359	91.7	85.1	93.5	93.6	84.8	95.9
25	2_82_101_108	91.4	82.1	94	93.6	84.8	95.9
	2_31_48_68	94	86.6	96	93.6	81.8	96.7
	2_6_48_68	94.3	85.1	96.8	93.6	81.8	96.7
	2_38_48_68	93.3	83.6	96	93.6	81.8	96.7
30	2_48_68_90	94	86.6	96	93.6	81.8	96.7
	2_25_48_68	93.7	83.6	96.4	93.6	78.8	97.6
	2_4_48_68	93.7	83.6	96.4	93.6	78.8	97.6
35	2_48_51_68	93.7	83.6	96.4	93.6	78.8	97.6
	2_48_68_465	93.7	83.6	96.4	93.6	78.8	97.6
	2_48_68_108	93.7	83.6	96.4	93.6	78.8	97.6
	2_48_68_373	94	83.6	96.8	93.6	78.8	97.6
40	2_48_68_466	93.7	83.6	96.4	93.6	78.8	97.6
	2_48_68_101	94	85.1	96.4	93.6	78.8	97.6
	2_48_68_103	93.7	83.6	96.4	93.6	78.8	97.6
45	2_7_61_365	89.8	79.1	92.7	92.9	97	91.9
	2_10_82_365	91.1	85.1	92.7	92.9	97	91.9
	2_9_82_467	92.7	88.1	94	92.9	97	91.9
	2_7_10_101	93.3	86.6	95.2	92.9	93.9	92.7
50	2_7_38_101	93.3	86.6	95.2	92.9	93.9	92.7
	2_7_61_466	90.5	80.6	93.1	92.9	93.9	92.7
	2_51_465_467	90.8	82.1	93.1	92.9	93.9	92.7
55	2_38_465_466	91.4	83.6	93.5	92.9	93.9	92.7
	2_38_365_465	91.1	83.6	93.1	92.9	93.9	92.7
	2_47_465_467	90.8	80.6	93.5	92.9	93.9	92.7

EP 3 150 707 A1

(continued)

		Training cohort			Validation cohort		
	SEQ ID NO:	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
5	2_368_465_467	90.8	82.1	93.1	92.9	93.9	92.7
	2_25_61_101	90.8	82.1	93.1	92.9	90.9	93.5
	2_7_47_465	90.2	82.1	92.3	92.9	90.9	93.5
10	2_7_28_47	90.8	82.1	93.1	92.9	90.9	93.5
	2_7_30_101	93.3	88.1	94.8	92.9	90.9	93.5
	2_7_53_101	93	88.1	94.4	92.9	90.9	93.5
15	2_7_101_359	92.7	85.1	94.8	92.9	90.9	93.5
	2_10_82_90	94	89.6	95.2	92.9	90.9	93.5
	2_9_31_101	91.4	82.1	94	92.9	90.9	93.5
	2_31_38_48	93	85.1	95.2	92.9	84.8	95.1
20	2_28_31_48	93.7	86.6	95.6	92.3	87.9	93.5
	4_7_82_101	92.4	91	92.7	92.3	93.9	91.9
	4_7_38_82	91.1	85.1	92.7	92.3	90.9	92.7
25	6_7_61_68	92.1	89.6	92.7	92.3	84.8	94.3
	7_25_47_466	87.3	83.6	88.3	92.3	87.9	93.5
	7_25_48_466	89.8	85.1	91.1	92.3	84.8	94.3
	4_7_82_103	92.4	89.6	93.1	91.7	90.9	91.9
30	4_7_47_82	89.2	86.6	89.9	91.7	90.9	91.9
	7_25_28_466	91.7	86.6	93.1	91.7	90.9	91.9
	7_25_30_466	89.2	89.6	89.1	91.7	90.9	91.9
35	7_25_31_47	88.9	89.6	88.7	91.7	90.9	91.9
	4_7_31_82	88.6	83.6	89.9	91	87.9	91.9
	2_7_9_105	91.4	83.6	93.5	90.4	90.9	90.2
	2_7_108_464	89.2	80.6	91.5	90.4	87.9	91.1
40	2_10_25_105	90.2	88.1	90.7	89.1	87.9	89.4
	4_28_31_82	87.6	82.1	89.1	89.1	87.9	89.4
	10_47_90_101	91.1	92.5	90.7	88.5	90.9	87.8
45	10_30_103_365	86.3	85.1	86.7	88.5	84.8	89.4
	9_10_61_68	90.5	86.6	91.5	88.5	78.8	91.1
	10_48_68_90	93.7	89.6	94.8	88.5	75.8	91.9
	10_30_68_365	91.1	82.1	93.5	88.5	75.8	91.9
50	4_7_10_82	88.9	86.6	89.5	87.8	84.8	88.6
	4_6_10_105	81	83.6	80.2	78.8	78.8	78.9

55

[Example 5]

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

5

[0567] Example 2 showed that discriminant performance was improved by using a combination of the multiple gene markers selected in Example 1, as compared with using one of the gene marker. Thus, in this Example, even the gene markers that were not selected in Example 1 were studied as to whether high pancreatic cancer discriminant performance is obtained by combinations with the gene markers selected in Example 1.

10

[0568] Specifically, among the genes having a gene expression level of 2^6 or higher in 50% or more of the samples in either of the pancreatic cancer patient group in the training cohort or the healthy subject group in the training cohort, genes that showed statistical significance for discriminating a pancreatic cancer patient group from a healthy subject group with the P value smaller than 0.5 calculated by two-tailed t-test assuming equal variance as to each gene expression level and corrected by the Bonferroni method, were examined. As a result, 161 genes containing the 122 genes selected in Example 1 were found. Fisher's discriminant analysis was conducted as to 13,042 combinations using one or two of these 161 genes, to construct a discriminant for determining the presence or absence of pancreatic cancer. The discriminant performance of the selected combinations of 1 or 2 of the genes was validated in the same way as the method of Example 2.

15

[0569] As a result, some combinations of these genes exhibited accuracy of 85% or higher in both of the training cohort and the validation cohort and are shown in Table 12. For example, the newly found polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 492, 493, or 494 discriminated the pancreatic cancer patients from the healthy subjects with high discriminant performance when used in combination of two polynucleotides comprising any of the polynucleotides consisting of the nucleotide sequences represented by SEQ ID NOs: 1 to 122. More specifically, the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 492, 493, or 494 was able to exhibit discrimination accuracy of 85% or higher between the pancreatic cancer patients and the healthy subjects in both of the training cohort and the validation cohort when used in combination of two polynucleotides comprising any of the polynucleotides consisting of the nucleotide sequences represented by SEQ ID NOs: 1, 2, 4, 7, 15, 24, 105, 107, and 108. Examples of such combinations of two genes include combinations of SEQ ID NOs: 105 and 492, SEQ ID NOs: 105 and 493, SEQ ID NOs: 1 and 492, SEQ ID NOs: 105 and 494, SEQ ID NOs: 1 and 493, SEQ ID NOs: 1 and 494, SEQ ID NOs: 107 and 493, SEQ ID NOs: 2 and 493, SEQ ID NOs: 7 and 493, SEQ ID NOs: 4 and 493, SEQ ID NOs: 2 and 492, SEQ ID NOs: 108 and 492, SEQ ID NOs: 2 and 494, SEQ ID NOs: 7 and 492, SEQ ID NOs: 7 and 494, SEQ ID NOs: 108 and 494, SEQ ID NOs: 4 and 492, SEQ ID NOs: 107 and 492, SEQ ID NOs: 107 and 494, SEQ ID NOs: 108 and 493, SEQ ID NOs: 15 and 492, SEQ ID NOs: 24 and 493, and SEQ ID NOs: 15 and 494.

20

25

30

[0570] As one example, an attempt was made to discriminate the pancreatic cancer patients from the healthy subjects using the expression level measurement values of the nucleotide sequences represented by SEQ ID NO: 105 and SEQ ID NO: 492. As a result, discriminant performance as high as 97.6% accuracy, 95.5% sensitivity, and 99.0% specificity in the training cohort and 96.4% accuracy, 93.9% sensitivity, and 98.0% specificity in the validation cohort was obtained.

35

[0571] From these results, it can be concluded that all of the polynucleotides consisting of the nucleotide sequences represented by SEQ ID NOs: 492 to 493 are also excellent diagnostic markers.

40

[0572] Table 12 mentioned above is as follows.

[Table 12]

SEQ IDNO:	Training cohort			Validation cohort		
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
105_492	97.6	95.5	99.0	96.4	93.9	98.0
105_493	97.6	95.5	99.0	96.4	93.9	98.0
1_492	97.6	97.0	98.0	94.0	90.9	96.0
105_494	96.4	94.0	98.0	96.4	93.9	98.0
1_493	95.8	92.5	98.0	92.8	87.9	96.0
1_494	95.8	94.0	97.0	92.8	87.9	96.0
107_493	94.0	88.1	98.0	89.2	84.8	92.0
2_493	92.2	83.6	98.0	95.2	90.9	98.0
7_493	91.0	89.6	92.0	90.4	90.9	90.0

45

50

55

(continued)

	Training cohort			Validation cohort		
SEQ IDNO:	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
4_493	91.0	85.1	95.0	88.0	87.9	88.0
2_492	90.4	79.1	98.0	96.4	93.9	98.0
108_492	89.8	86.6	92.0	89.2	87.9	90.0
2_494	89.2	79.1	96.0	95.2	93.9	96.0
7_492	88.6	89.6	88.0	86.7	90.9	84.0
7_494	88.6	85.1	91.0	90.4	90.9	90.0
108_494	88.6	83.6	92.0	88.0	87.9	88.0
4_492	88.0	79.1	94.0	89.2	90.9	88.0
107_492	88.0	83.6	91.0	85.5	84.8	86.0
107_494	87.4	83.6	90.0	86.7	84.8	88.0
108_493	86.8	83.6	89.0	86.7	84.8	88.0
15_492	85.6	76.1	92.0	88.0	84.8	90.0
24_493	85.6	83.6	87.0	86.7	84.8	88.0
15_494	85.6	74.6	93.0	86.7	78.8	92.0

[Comparative Example 1]

<Pancreatic cancer discriminant performance of existing tumor markers in blood>

[0573] The concentrations of the existing tumor markers CEA and CA19-9 in blood were measured in the training cohort and the validation cohort obtained in the preceding Reference Examples. When the concentrations of these tumor markers in blood are higher than the reference values described in Non-Patent Literature 3 above (CEA: 5 ng/mL, CA19-9: 37 U/mL), subjects are usually suspected of having cancer. Thus, whether or not the concentrations of CEA and CA19-9 in blood exceeded their reference values was confirmed for each sample to assess the ability of these tumor markers to detect cancer in pancreatic cancer patients. The sensitivity of each existing marker in the training cohort and the validation cohort was calculated. The results are shown in Table 5. The sensitivity of CEA and CA19-9 was as low as 55.2% and 77.6%, respectively, in the training cohort, and was as low as 45.5% and 75.8%, respectively, in the validation cohort, demonstrating that neither of the markers are useful in the detection of pancreatic cancer (Table 5).

[0574] On the other hand, as shown above in Tables 3 and 6 of Examples 1 and 2, it can be concluded that in all of the polynucleotides consisting of the nucleotide sequences represented by SEQ ID NOs: 1 to 122, combinations of 1, 2 or more polynucleotides exhibiting sensitivity beyond the existing pancreatic cancer markers are present, and thus such polynucleotides serve as excellent diagnosis markers.

[0575] As shown in these Examples and Comparative Example, the kit and the method of the present invention can detect pancreatic cancer with higher sensitivity than the existing tumor markers and therefore permit early decision to carry out the surgical resection of a cancer site. As a result, improvement in 5-year survival rate and reduction in the rate of recurrence can be achieved.

INDUSTRIAL APPLICABILITY

[0576] According to the present invention, pancreatic cancer can be effectively detected by a simple and inexpensive method. This enables early detection, diagnosis and treatment of pancreatic cancer. The method of the present invention can detect pancreatic cancer with limited invasiveness using the blood of a patient and therefore allows pancreatic cancer to be detected conveniently and rapidly.

[0577] All publications, patents, and patent applications cited herein are incorporated herein by reference in their entirety.

EP 3 150 707 A1

SEQUENCE LISTING

5 <110> Toray Industries, Inc.
 National Cancer Center
 <120> Kit or device and method for detecting pancreatic cancer
 <130> PH-6231-PCT
 10 <150> JP 2014-113523
 <151> 2014-05-30
 <150> JP 2014-185730
 <151> 2014-09-11
 15 <160> 499
 <170> PatentIn version 3.5
 <210> 1
 <211> 21
 20 <212> RNA
 <213> Homo sapiens
 <400> 1
 caggcaggug uaggguggag c 21
 25
 <210> 2
 <211> 21
 <212> RNA
 30 <213> Homo sapiens
 <400> 2
 acggcccagg cggcauuggu g 21
 35
 <210> 3
 <211> 19
 <212> RNA
 <213> Homo sapiens
 <400> 3
 40 ugccgcagag cugggguca 19
 <210> 4
 <211> 17
 <212> RNA
 45 <213> Homo sapiens
 <400> 4
 gggagucuac agcaggg 17
 50
 <210> 5
 <211> 22
 <212> RNA
 <213> Homo sapiens
 55 <400> 5
 ugggcgaggg cggcugagcg gc 22

EP 3 150 707 A1

	<210> 6		
	<211> 22		
	<212> RNA		
	<213> Homo sapiens		
5	<400> 6		
	caggaaggau uuagggacag gc		22
10	<210> 7		
	<211> 21		
	<212> RNA		
	<213> Homo sapiens		
15	<400> 7		
	augccucccc cggccccgca g		21
20	<210> 8		
	<211> 21		
	<212> RNA		
	<213> Homo sapiens		
25	<400> 8		
	ucaccuggcu ggcccccca g		21
30	<210> 9		
	<211> 20		
	<212> RNA		
	<213> Homo sapiens		
35	<400> 9		
	ggggaggugu gcagggcugg		20
40	<210> 10		
	<211> 18		
	<212> RNA		
	<213> Homo sapiens		
45	<400> 10		
	cccagcagga cgggagcg		18
50	<210> 11		
	<211> 19		
	<212> RNA		
	<213> Homo sapiens		
55	<400> 11		
	uugaucucgg aagcuaagc		19
60	<210> 12		
	<211> 20		
	<212> RNA		
	<213> Homo sapiens		
65	<400> 12		
	ggauccgagu cacggacca		20

EP 3 150 707 A1

<210> 13
 <211> 22
 <212> RNA
 <213> Homo sapiens
 5
 <400> 13
 ggggggucccc ggugcucgga uc 22

<210> 14
 <211> 22
 <212> RNA
 <213> Homo sapiens
 10
 <400> 14
 15 accuggcagc agggagcguc gu 22

<210> 15
 <211> 22
 <212> RNA
 <213> Homo sapiens
 20
 <400> 15
 aggcggggcg cgcgggacc gc 22

<210> 16
 <211> 19
 <212> RNA
 <213> Homo sapiens
 25
 <400> 16
 30 cggcgcgacc ggcccgggg 19

<210> 17
 <211> 22
 <212> RNA
 <213> Homo sapiens
 35
 <400> 17
 40 uggggauuug gagaaguggu ga 22

<210> 18
 <211> 18
 <212> RNA
 <213> Homo sapiens
 45
 <400> 18
 cggugagcgc ucgcuggc 18

<210> 19
 <211> 20
 <212> RNA
 <213> Homo sapiens
 50
 <400> 19
 55 accaggaggc ugaggcccu 20

EP 3 150 707 A1

<210> 20
 <211> 18
 <212> RNA
 <213> Homo sapiens
 5
 <400> 20
 auccuaguca cggcacca 18

 <210> 21
 <211> 21
 <212> RNA
 <213> Homo sapiens
 10
 <400> 21
 cuggggggag gagaccugc u 21

 <210> 22
 <211> 24
 <212> RNA
 <213> Homo sapiens
 20
 <400> 22
 guaggggcg cccgggcg cggg 24

 <210> 23
 <211> 17
 <212> RNA
 <213> Homo sapiens
 25
 <400> 23
 cuccgggacg gcugggc 17

 <210> 24
 <211> 22
 <212> RNA
 <213> Homo sapiens
 30
 <400> 24
 agggccgaag gguggaagcu gc 22

 <210> 25
 <211> 22
 <212> RNA
 <213> Homo sapiens
 35
 <400> 25
 ugguggagga agaggcagc uc 22

 <210> 26
 <211> 18
 <212> RNA
 <213> Homo sapiens
 40
 <400> 26
 uucccagcca acgcacca 18
 55

EP 3 150 707 A1

	<210> 27	
	<211> 22	
	<212> RNA	
	<213> Homo sapiens	
5	<400> 27	
	gcugcgggcu gcggucaggg cg	22
10	<210> 28	
	<211> 23	
	<212> RNA	
	<213> Homo sapiens	
15	<400> 28	
	gugcguggug gcucgagggc ggg	23
20	<210> 29	
	<211> 24	
	<212> RNA	
	<213> Homo sapiens	
25	<400> 29	
	ccuggggaca ggggauuggg gcag	24
30	<210> 30	
	<211> 22	
	<212> RNA	
	<213> Homo sapiens	
35	<400> 30	
	cugaauagcu gggacuacag gu	22
40	<210> 31	
	<211> 19	
	<212> RNA	
	<213> Homo sapiens	
45	<400> 31	
	aaggggcugg gggagcaca	19
50	<210> 32	
	<211> 19	
	<212> RNA	
	<213> Homo sapiens	
55	<400> 32	
	cggggccaga gcagagagc	19
50	<210> 33	
	<211> 20	
	<212> RNA	
	<213> Homo sapiens	
55	<400> 33	
	cggggugggu gaggucgggc	20

EP 3 150 707 A1

	<210> 34		
	<211> 21		
	<212> RNA		
	<213> Homo sapiens		
5	<400> 34		
	acaggagugg gggugggaca u		21
10	<210> 35		
	<211> 20		
	<212> RNA		
	<213> Homo sapiens		
15	<400> 35		
	gugucugggc ggacagcugc		20
20	<210> 36		
	<211> 23		
	<212> RNA		
	<213> Homo sapiens		
25	<400> 36		
	cugggggacg cgugagcgcg agc		23
30	<210> 37		
	<211> 21		
	<212> RNA		
	<213> Homo sapiens		
35	<400> 37		
	ucuguggagu ggggugccug u		21
40	<210> 38		
	<211> 23		
	<212> RNA		
	<213> Homo sapiens		
45	<400> 38		
	gugaguggga gccccagugu gug		23
50	<210> 39		
	<211> 23		
	<212> RNA		
	<213> Homo sapiens		
55	<400> 39		
	ggaugguugg gggcggucgg cgu		23
60	<210> 40		
	<211> 23		
	<212> RNA		
	<213> Homo sapiens		
65	<400> 40		
	uguagagcag ggagcaggaa gcu		23

EP 3 150 707 A1

	<210> 41		
	<211> 22		
	<212> RNA		
	<213> Homo sapiens		
5	<400> 41		
	gcugggauua caggcaugag cc		22
10	<210> 42		
	<211> 22		
	<212> RNA		
	<213> Homo sapiens		
15	<400> 42		
	caggcacggg agcucaggug ag		22
20	<210> 43		
	<211> 18		
	<212> RNA		
	<213> Homo sapiens		
25	<400> 43		
	aucccaccuc ugccacca		18
30	<210> 44		
	<211> 22		
	<212> RNA		
	<213> Homo sapiens		
35	<400> 44		
	gugggugcug gugggagccg ug		22
40	<210> 45		
	<211> 21		
	<212> RNA		
	<213> Homo sapiens		
45	<400> 45		
	cgggccggag gucaagggcg u		21
50	<210> 46		
	<211> 20		
	<212> RNA		
	<213> Homo sapiens		
55	<400> 46		
	gcggaaggcg gagcggcgga		20
60	<210> 47		
	<211> 22		
	<212> RNA		
	<213> Homo sapiens		
65	<400> 47		
	uagggggcg cuuguggagu gu		22

EP 3 150 707 A1

	<210> 48		
	<211> 19		
	<212> RNA		
	<213> Homo sapiens		
5	<400> 48		
	agcagggcug gggauugca		19
10	<210> 49		
	<211> 21		
	<212> RNA		
	<213> Homo sapiens		
15	<400> 49		
	cccaugccuc cugccgcggu c		21
20	<210> 50		
	<211> 21		
	<212> RNA		
	<213> Homo sapiens		
25	<400> 50		
	ugagggaccc aggacaggag a		21
30	<210> 51		
	<211> 21		
	<212> RNA		
	<213> Homo sapiens		
35	<400> 51		
	ccggccgccg gcuccgcccc g		21
40	<210> 52		
	<211> 21		
	<212> RNA		
	<213> Homo sapiens		
45	<400> 52		
	caggaguggg gggugggacg u		21
50	<210> 53		
	<211> 19		
	<212> RNA		
	<213> Homo sapiens		
55	<400> 53		
	aggcagguua ucugggcug		19
50	<210> 54		
	<211> 22		
	<212> RNA		
	<213> Homo sapiens		
55	<400> 54		
	uucagaucce agcggugccu cu		22

EP 3 150 707 A1

	<210> 55		
	<211> 23		
	<212> RNA		
	<213> Homo sapiens		
5			
	<400> 55		
	cugggcccgc ggcgggcgug ggg		23
10			
	<210> 56		
	<211> 22		
	<212> RNA		
	<213> Homo sapiens		
15			
	<400> 56		
	ucggccuggg gaggaggaag gg		22
20			
	<210> 57		
	<211> 21		
	<212> RNA		
	<213> Homo sapiens		
25			
	<400> 57		
	cgggagcugg ggucugcagg u		21
30			
	<210> 58		
	<211> 23		
	<212> RNA		
	<213> Homo sapiens		
35			
	<400> 58		
	agaagaaggc ggucggucug cgg		23
40			
	<210> 59		
	<211> 21		
	<212> RNA		
	<213> Homo sapiens		
45			
	<400> 59		
	acucggcugc gguggacaag u		21
50			
	<210> 60		
	<211> 21		
	<212> RNA		
	<213> Homo sapiens		
55			
	<400> 60		
	accacugcac uccagccuga g		21
55			
	<210> 61		
	<211> 22		
	<212> RNA		
	<213> Homo sapiens		
55			
	<400> 61		
	agugggagga caggaggcag gu		22

EP 3 150 707 A1

	<210> 62		
	<211> 23		
	<212> RNA		
	<213> Homo sapiens		
5	<400> 62		
	gggggggag gaggggcuca ggg		23
10	<210> 63		
	<211> 22		
	<212> RNA		
	<213> Homo sapiens		
15	<400> 63		
	cucccccca gaaucuuca uc		22
20	<210> 64		
	<211> 20		
	<212> RNA		
	<213> Homo sapiens		
25	<400> 64		
	ucacaccugc cugcccccc		20
30	<210> 65		
	<211> 21		
	<212> RNA		
	<213> Homo sapiens		
35	<400> 65		
	cugggagggg cuggguugg c		21
40	<210> 66		
	<211> 24		
	<212> RNA		
	<213> Homo sapiens		
45	<400> 66		
	ugggggagcc augagauaag agca		24
50	<210> 67		
	<211> 22		
	<212> RNA		
	<213> Homo sapiens		
55	<400> 67		
	gugcggaacg cuggccgggg cg		22
60	<210> 68		
	<211> 20		
	<212> RNA		
	<213> Homo sapiens		
65	<400> 68		
	cggcucuggg ucugugggga		20

EP 3 150 707 A1

	<210> 69		
	<211> 19		
	<212> RNA		
	<213> Homo sapiens		
5	<400> 69		
	cggggucggc ggcgacgug		19
10	<210> 70		
	<211> 20		
	<212> RNA		
	<213> Homo sapiens		
15	<400> 70		
	ggcggcgggg agguaggcag		20
20	<210> 71		
	<211> 17		
	<212> RNA		
	<213> Homo sapiens		
25	<400> 71		
	gcugggagcag gcuggca		17
30	<210> 72		
	<211> 22		
	<212> RNA		
	<213> Homo sapiens		
35	<400> 72		
	ucugcccccuc cgcugcugc ca		22
40	<210> 73		
	<211> 23		
	<212> RNA		
	<213> Homo sapiens		
45	<400> 73		
	ugggcugagg gcaggaggcc ugu		23
50	<210> 74		
	<211> 19		
	<212> RNA		
	<213> Homo sapiens		
55	<400> 74		
	aucccaccac ugccaccau		19
60	<210> 75		
	<211> 20		
	<212> RNA		
	<213> Homo sapiens		
65	<400> 75		
	ugggaggagg ggaucuuggg		20

EP 3 150 707 A1

	<210> 76	
	<211> 23	
	<212> RNA	
	<213> Homo sapiens	
5		
	<400> 76	
	ucggggaguc ugggguccgg aau	23
10		
	<210> 77	
	<211> 23	
	<212> RNA	
	<213> Homo sapiens	
15		
	<400> 77	
	uggggaaggc uggcagggga aga	23
20		
	<210> 78	
	<211> 19	
	<212> RNA	
	<213> Homo sapiens	
25		
	<400> 78	
	ggggagcgag gggcggggc	19
30		
	<210> 79	
	<211> 17	
	<212> RNA	
	<213> Homo sapiens	
35		
	<400> 79	
	ggauggagga ggggucu	17
40		
	<210> 80	
	<211> 22	
	<212> RNA	
	<213> Homo sapiens	
45		
	<400> 80	
	cgucccgggg cugcgcgagg ca	22
50		
	<210> 81	
	<211> 21	
	<212> RNA	
	<213> Homo sapiens	
55		
	<400> 81	
	auccaguucu cugagggggc u	21
55		
	<210> 82	
	<211> 21	
	<212> RNA	
	<213> Homo sapiens	
55		
	<400> 82	
	gugccagcug caguggggga g	21

EP 3 150 707 A1

	<210> 83		
	<211> 22		
	<212> RNA		
	<213> Homo sapiens		
5			
	<400> 83		
	uggcggcggu aguuaugggc uu		22
10			
	<210> 84		
	<211> 20		
	<212> RNA		
	<213> Homo sapiens		
15			
	<400> 84		
	ucucuucauc uacccccag		20
20			
	<210> 85		
	<211> 18		
	<212> RNA		
	<213> Homo sapiens		
25			
	<400> 85		
	gggucccggg gagggggg		18
30			
	<210> 86		
	<211> 18		
	<212> RNA		
	<213> Homo sapiens		
35			
	<400> 86		
	aggcugggcu gggacgga		18
40			
	<210> 87		
	<211> 20		
	<212> RNA		
	<213> Homo sapiens		
45			
	<400> 87		
	aaaaggcggg agaagcccca		20
50			
	<210> 88		
	<211> 23		
	<212> RNA		
	<213> Homo sapiens		
55			
	<400> 88		
	uugcucugcu cccccgccc cag		23
60			
	<210> 89		
	<211> 22		
	<212> RNA		
	<213> Homo sapiens		
65			
	<400> 89		
	ggcuggagcg agugcagugg ug		22

EP 3 150 707 A1

	<210> 90	
	<211> 23	
	<212> RNA	
	<213> Homo sapiens	
5		
	<400> 90	
	uuagggagua gaaggguggg gag	23
10		
	<210> 91	
	<211> 23	
	<212> RNA	
	<213> Homo sapiens	
15		
	<400> 91	
	cacacaggaa aagcggggcc cug	23
20		
	<210> 92	
	<211> 23	
	<212> RNA	
	<213> Homo sapiens	
25		
	<400> 92	
	ugggcagggg cuuauuguag gag	23
30		
	<210> 93	
	<211> 17	
	<212> RNA	
	<213> Homo sapiens	
35		
	<400> 93	
	guggggccag gcggugg	17
40		
	<210> 94	
	<211> 22	
	<212> RNA	
	<213> Homo sapiens	
45		
	<400> 94	
	ugcagggguc gggugggcca gg	22
50		
	<210> 95	
	<211> 17	
	<212> RNA	
	<213> Homo sapiens	
55		
	<400> 95	
	acccacucc ugguacc	17
60		
	<210> 96	
	<211> 21	
	<212> RNA	
	<213> Homo sapiens	
65		
	<400> 96	
	agcggugcuc cugcgggccg a	21

EP 3 150 707 A1

<210> 97
 <211> 23
 <212> RNA
 <213> Homo sapiens
 5
 <400> 97
 cucggggcag gcggcuggga gcg 23

<210> 98
 <211> 21
 <212> RNA
 <213> Homo sapiens
 10
 <400> 98
 15 uggggcgggg cagguccug c 21

<210> 99
 <211> 23
 <212> RNA
 <213> Homo sapiens
 20
 <400> 99
 25 cgggcugucc ggaggggucg gcu 23

<210> 100
 <211> 17
 <212> RNA
 <213> Homo sapiens
 30
 <400> 100
 gcggggcugg gcgcgcg 17

<210> 101
 <211> 21
 <212> RNA
 <213> Homo sapiens
 35
 <400> 101
 40 aaggcagggc ccccgucucc c 21

<210> 102
 <211> 19
 <212> RNA
 <213> Homo sapiens
 45
 <400> 102
 ggcuugcaug ggggacugg 19

<210> 103
 <211> 26
 <212> RNA
 <213> Homo sapiens
 50
 <400> 103
 55 cucggccgcg gcgcuagcc cccgcc 26

EP 3 150 707 A1

	<210> 104	
	<211> 21	
	<212> RNA	
	<213> Homo sapiens	
5	<400> 104	
	cuuccgcccc gccgggcguc g	21
10	<210> 105	
	<211> 22	
	<212> RNA	
	<213> Homo sapiens	
15	<400> 105	
	acaggugagg uucuugggag cc	22
20	<210> 106	
	<211> 21	
	<212> RNA	
	<213> Homo sapiens	
25	<400> 106	
	gcugggaagg caaagggacg u	21
30	<210> 107	
	<211> 22	
	<212> RNA	
	<213> Homo sapiens	
35	<400> 107	
	cucggcgcgg ggcgcgggcu cc	22
40	<210> 108	
	<211> 19	
	<212> RNA	
	<213> Homo sapiens	
45	<400> 108	
	gagccaguug gacaggagc	19
50	<210> 109	
	<211> 22	
	<212> RNA	
	<213> Homo sapiens	
55	<400> 109	
	cugguacagg ccugggggac ag	22
60	<210> 110	
	<211> 23	
	<212> RNA	
	<213> Homo sapiens	
65	<400> 110	
	ugaggggacag agagcgagac uuu	23

EP 3 150 707 A1

	<210> 111	
	<211> 19	
	<212> RNA	
	<213> Homo sapiens	
5		
	<400> 111	
	aggcacggug ucagcaggc	19
10		
	<210> 112	
	<211> 23	
	<212> RNA	
	<213> Homo sapiens	
15		
	<400> 112	
	agaggcuuug ugcggauacg ggg	23
20		
	<210> 113	
	<211> 19	
	<212> RNA	
	<213> Homo sapiens	
25		
	<400> 113	
	aauggauuuu uggagcagg	19
30		
	<210> 114	
	<211> 23	
	<212> RNA	
	<213> Homo sapiens	
35		
	<400> 114	
	gacacgggcg acagcugcgg ccc	23
40		
	<210> 115	
	<211> 19	
	<212> RNA	
	<213> Homo sapiens	
45		
	<400> 115	
	uggauuuuug gaucagggga	19
50		
	<210> 116	
	<211> 22	
	<212> RNA	
	<213> Homo sapiens	
55		
	<400> 116	
	uagcagcacg uaaauauugg cg	22
50		
	<210> 117	
	<211> 22	
	<212> RNA	
	<213> Homo sapiens	
55		
	<400> 117	
	aaaccguuac cauuacugag uu	22

EP 3 150 707 A1

<210> 118
 <211> 22
 <212> RNA
 <213> Homo sapiens
 5
 <400> 118
 uggcucaguu cagcaggaac ag 22

<210> 119
 <211> 22
 <212> RNA
 <213> Homo sapiens
 10
 <400> 119
 15 ggcuacaaca caggacccgg gc 22

<210> 120
 <211> 21
 <212> RNA
 <213> Homo sapiens
 20
 <400> 120
 cggcggggac ggcgauuggu c 21

<210> 121
 <211> 20
 <212> RNA
 <213> Homo sapiens
 25
 <400> 121
 30 acucaaacug ugggggcacu 20

<210> 122
 <211> 23
 <212> RNA
 <213> Homo sapiens
 35
 <400> 122
 40 agugccugag ggaguaagag ccc 23

<210> 123
 <211> 69
 <212> RNA
 <213> Homo sapiens
 45
 <400> 123
 ccgggcaggc agguguaggg uggagcccac uguggcuccu gacucagccc ugcugccuuc 60
 50 accugccag 69

<210> 124
 <211> 95
 <212> RNA
 <213> Homo sapiens
 55
 <400> 124

EP 3 150 707 A1

	gacaccacau gcuccuccag gccugccugc ccuccagguc auguuccagu gucccacaga	60
	ugcagcacca cggcccaggc ggcauuggug ucacc	95
5	<210> 125 <211> 62 <212> RNA <213> Homo sapiens	
10	<400> 125 ccuucugcgg cagagcuggg gucaccagcc cucauguacu ugugacuucu cccugccac	60
	ag	62
15	<210> 126 <211> 76 <212> RNA <213> Homo sapiens	
20	<400> 126 ccgaugccuc gggagucuc agcagggcca ugucugugag ggccaaggg ugcauguguc	60
	ucccagguuu cggugc	76
25	<210> 127 <211> 65 <212> RNA <213> Homo sapiens	
30	<400> 127 gagggugggc gagggcggcu gagcggcucc aucccccggc cugcucaucc cccucgcccu	60
	cucag	65
35	<210> 128 <211> 70 <212> RNA <213> Homo sapiens	
40	<400> 128 aaaagccugu cccuaagucc cucccagccu uccagaguug gugccaggaa ggauuuaggg	60
	acaggcuuug	70
45	<210> 129 <211> 63 <212> RNA <213> Homo sapiens	
50	<400> 129 ggcuccgcag ggcccuggcg caggcaucca gacagcgggc gaaugccucc cccggccccg	60
	cag	63
55	<210> 130 <211> 87 <212> RNA	

EP 3 150 707 A1

<213> Homo sapiens
 <400> 130
 5 gugagggcggg gccaggaggg uguguggcgu gggugcugcg gggccgucag ggugccugcg 60
 ggacgcucac cuggcuggcc cgcccag 87
 <210> 131
 <211> 69
 10 <212> RNA
 <213> Homo sapiens
 <400> 131
 15 gaggagggga ggugugcagg gcugggguca cugacucugc uccccugcc cugcauggug 60
 uccccacag 69
 <210> 132
 <211> 56
 20 <212> RNA
 <213> Homo sapiens
 <400> 132
 25 cgaccgcacc cgcccgaagc ugguucaagg agcccagcag gacgggagcg cggcgc 56
 <210> 133
 <211> 61
 <212> RNA
 <213> Homo sapiens
 30 <400> 133
 ucucguuuga ucucggaagc uaagcagggg ugggccuggu uaguacuugg augggaaacu 60
 u 61
 35 <210> 134
 <211> 53
 <212> RNA
 <213> Homo sapiens
 40 <400> 134
 guuugaucuc ggaagcuaag cagggucggg ccugguuagu acuuggaugg gag 53
 <210> 135
 <211> 55
 <212> RNA
 <213> Homo sapiens
 45 <400> 135
 50 ccggauccga gucacggcac caaauucau gcguguccgu gugaagagac cacca 55
 <210> 136
 <211> 96
 <212> RNA
 <213> Homo sapiens
 55 <400> 136

EP 3 150 707 A1

	cucgggaggg gcgggagggg ggucggcggu gcucggaucu cgaggggugcu uauuguucgg	60
	uccgagccug ggucuccuc uccccccaa ccccc	96
5	<210> 137 <211> 72 <212> RNA <213> Homo sapiens	
10	<400> 137 gauuucagug accuggcagc agggagcguc gucaguguuu gacuguuuau gguaugucag	60
	ggagcugguu cc	72
15	<210> 138 <211> 93 <212> RNA <213> Homo sapiens	
20	<400> 138 ccuuccggcg ucccaggcgg ggcgccggg gaccgccuc gugucugugg cggugggauc	60
	ccgcgccgu guuuuccugg uggcccggcc aug	93
25	<210> 139 <211> 54 <212> RNA <213> Homo sapiens	
30	<400> 139 ggacaagggc ggcgcgaccg gcccggggcu cuugggcggc cgcguuucc cucc	54
35	<210> 140 <211> 65 <212> RNA <213> Homo sapiens	
40	<400> 140 ugucugggga uuuggagaag uggugagcgc aggucuuugg caccaucucc ccugguccu	60
	uggcu	65
45	<210> 141 <211> 74 <212> RNA <213> Homo sapiens	
50	<400> 141 gcagcccggg gagcgcucgc uggccuggca gugcgcgga agaacagggc ggguggggcc	60
	gcgcacaucu cugc	74
55	<210> 142 <211> 72 <212> RNA <213> Homo sapiens	

EP 3 150 707 A1

	<400> 142		
	ucuccucgag gggucucugc cucuaccag gacucuuuca ugaccaggag gcugaggccc	60	
	cucacaggcg gc	72	
5			
	<210> 143		
	<211> 68		
	<212> RNA		
	<213> Homo sapiens		
10			
	<400> 143		
	gugcaaagag caggaggaca ggggauuuau cucccaaggg aggucccccug auccuaguca	60	
	cggcacca	68	
15			
	<210> 144		
	<211> 65		
	<212> RNA		
	<213> Homo sapiens		
20			
	<400> 144		
	gucuccuggg gggaggagac ccugcucucc cuggcagcaa gccucuccug cccuuccaga	60	
	uuagc	65	
25			
	<210> 145		
	<211> 98		
	<212> RNA		
	<213> Homo sapiens		
30			
	<400> 145		
	cgagguaggg gcgucuccggg cgcgcggggc ggucccaggc ugggcccuc ggaggccggg	60	
	ugcucacugc cccgucuccg cgcguguc uccuccag	98	
35			
	<210> 146		
	<211> 89		
	<212> RNA		
	<213> Homo sapiens		
40			
	<400> 146		
	accuccggga cggcugggcg ccggcggccg ggagaucg cguuccugaa ucccggccgg	60	
	cccggccggc gcccguccgc ccgcccggc	89	
45			
	<210> 147		
	<211> 64		
	<212> RNA		
	<213> Homo sapiens		
50			
	<400> 147		
	aguucagggc cgaagggugg aagcugcugg ugcucaucuc agccucugcc cuuggccucc	60	
	ccag	64	
55			
	<210> 148		
	<211> 62		

EP 3 150 707 A1

<212> RNA
 <213> Homo sapiens

 <400> 148
 5 gaggguggug gaggaagagg gcagcucca ugacugccug accgccuucu cuccucctcc 60
 ag 62

 <210> 149
 10 <211> 49
 <212> RNA
 <213> Homo sapiens

 <400> 149
 15 uucccagcca acgcaccaa aaugauaugg gucuguuguc uggagaaac 49

 <210> 150
 <211> 70
 <212> RNA
 20 <213> Homo sapiens

 <400> 150
 cucgggcccg accgcgccg cccgcaccuc ccggcccga gcugcgggcu gcggucaggg 60
 25 cgaucctcggg 70

 <210> 151
 <211> 74
 <212> RNA
 30 <213> Homo sapiens

 <400> 151
 gugcguggug gcucgagggc gggguggggg ccucgccug cuugggccc cccugaccuc 60
 35 uccgcuccgc acag 74

 <210> 152
 <211> 82
 <212> RNA
 40 <213> Homo sapiens

 <400> 152
 aaggagcacu cacuccaauu uccugggacu gggggcaggc ugccaccucc uggggacagg 60
 45 ggauuggggc aggauguucc ag 82

 <210> 153
 <211> 59
 <212> RNA
 50 <213> Homo sapiens

 <400> 153
 ugaaguacca gcuacucgag agguacagagg auugcuccug aauagcuggg acuacaggu 59

 <210> 154
 <211> 110
 <212> RNA
 55

EP 3 150 707 A1

<213> Homo sapiens

<400> 154
5 gucuaccagg ugugggcca gcuuacaua guucaugcug aggccgggau uucaugcaga 60
aaacugguug caaaaggugc ugaaggggcu gggggagcac aagggagaag 110

<210> 155
10 <211> 61
<212> RNA
<213> Homo sapiens

<400> 155
15 aacugcgggg ccagagcaga gagcccuugc acaccaccag ccucuccucc cugugcccca 60
g 61

<210> 156
20 <211> 73
<212> RNA
<213> Homo sapiens

<400> 156
25 cggcgacggc ggggugggug aggucgggcc ccaagacucg ggguuugccg ggcgccucag 60
uucaccgagg ccg 73

<210> 157
30 <211> 81
<212> RNA
<213> Homo sapiens

<400> 157
35 cauccuccuu acgucccacc cccacuccu guuucuggug aaauaucaa acaggagugg 60
gggugggaca uaaggaggau a 81

<210> 158
40 <211> 92
<212> RNA
<213> Homo sapiens

<400> 158
45 gucagugucu gggcggacag cugcaggaaa ggaagacca aggcucugcug ucuguccagu 60
cugccaccu acccugucug uucugccac ag 92

<210> 159
50 <211> 79
<212> RNA
<213> Homo sapiens

<400> 159
55 cucgaggugc ugsgggacgc gugagcgcga gccgcuuccu cacggcucgg ccgcggcgcg 60
uagccccgc cacaucggg 79

EP 3 150 707 A1

<210> 160
 <211> 61
 <212> RNA
 <213> Homo sapiens
 5
 <400> 160
 uccgcucugu ggaguggggu gccugucucc ugccacuggg ugacccaccc cucuccacca 60
 g 61
 10
 <210> 161
 <211> 83
 <212> RNA
 <213> Homo sapiens
 15
 <400> 161
 gugaguggga gccccagugu gugguugggg ccauggcggg ugggcagccc agccucugag 60
 ccuuccucgu cugucugccc cag 83
 20
 <210> 162
 <211> 86
 <212> RNA
 <213> Homo sapiens
 25
 <400> 162
 cgccugagcg ugcagcagga caucuuccug accugguaau aauuagguga gaaggauggu 60
 ugggggcggu cggcguaacu cagggga 86
 30
 <210> 163
 <211> 76
 <212> RNA
 <213> Homo sapiens
 35
 <400> 163
 gagggagcug uagagcaggg agcaggaagc uguguguguc cagcccugac cuguccuguu 60
 cugcccccag ccccuc 76
 40
 <210> 164
 <211> 99
 <212> RNA
 <213> Homo sapiens
 45
 <400> 164
 cgcccaccuc agccucccaa aaugcuggga uuacaggcau gagccacugc ggucgaccu 60
 gaccuggaca uguuugugcc caguacuguc aguuugcag 99
 50
 <210> 165
 <211> 83
 <212> RNA
 <213> Homo sapiens
 55
 <400> 165
 aauagagggg gcacaggcac gggagcucag gugaggcagg gagcugagcu caccugaccu 60

EP 3 150 707 A1

cccaugccug ugcacccucu auu 83

 5 <210> 166
 <211> 73
 <212> RNA
 <213> Homo sapiens

 <400> 166
 10 accuuuccag cucauccac cucugccacc aaaacacuca ucgcgggguc agagggagug 60
 ccaaaaaagg uaa 73

 15 <210> 167
 <211> 63
 <212> RNA
 <213> Homo sapiens

 <400> 167
 20 aauggguggg ugcugguggg agccgugccc uggccacuca uucggcucuc ucccucaccc 60
 uag 63

 25 <210> 168
 <211> 64
 <212> RNA
 <213> Homo sapiens

 <400> 168
 30 aacccggggc cggaggucuaa gggcgucgcu ucuccuaau guugccucuu uccacggcc 60
 ucag 64

 35 <210> 169
 <211> 96
 <212> RNA
 <213> Homo sapiens

 <400> 169
 40 gcucuggggc gugccggccg cgcugcugcc accuccccua ccgcuagugg aagaagaugg 60
 cggaaggcgg agcggcggau cuggacaccc agcggg 96

 45 <210> 170
 <211> 62
 <212> RNA
 <213> Homo sapiens

 <400> 170
 50 uggccuaggg ggcggcuugu ggaguguaug ggcugagccu ugcucugcuc ccccgcccc 60
 ag 62

 55 <210> 171
 <211> 109
 <212> RNA
 <213> Homo sapiens

EP 3 150 707 A1

	<400> 171		
	ugcuauuguc uuacugcuac agcagggcug gggauugcag uauccgcugu ugcugcugcu	60	
5	cccaguccug ccccugcugc uaccuagucc agccucaccg caucccaga	109	
	<210> 172		
	<211> 62		
	<212> RNA		
10	<213> Homo sapiens		
	<400> 172		
	gugggucucg caucaggagg caaggccagg acccgugac ccaugccucc ugccgcgguc	60	
	ag	62	
15			
	<210> 173		
	<211> 72		
	<212> RNA		
20	<213> Homo sapiens		
	<400> 173		
	gagucugagg gaccaggac aggagaaggc cuauggugau uugcauucuu ccugcccugg	60	
	cuccauccuc ag	72	
25			
	<210> 174		
	<211> 80		
	<212> RNA		
30	<213> Homo sapiens		
	<400> 174		
	cgggaaugcc gcggcgggga cggcgauugg uccguaugug uggugccacc ggccgccggc	60	
	uccgccccgg cccccgcccc	80	
35			
	<210> 175		
	<211> 102		
	<212> RNA		
40	<213> Homo sapiens		
	<400> 175		
	uguguucccu auccuccua ugucccacc ccacuccugu uugaauuuu caccagaaac	60	
	aggagugggg ggugggacgu aaggaggau ggggaaagaa ca	102	
45			
	<210> 176		
	<211> 47		
	<212> RNA		
50	<213> Homo sapiens		
	<400> 176		
	aggcagguua ucugggcugc caucuccac uggcugcuug ccugccu	47	
55			
	<210> 177		
	<211> 119		
	<212> RNA		
	<213> Homo sapiens		

EP 3 150 707 A1

<400> 177
 ccaugaggag cuggcagugg gauggccugg ggguaaggagc guggcuucug gagcuagacc 60
 acauggguuc agaucccagc ggugccucua acuggccaca ggaccuuggg cagucagcu 119
 5
 <210> 178
 <211> 92
 <212> RNA
 <213> Homo sapiens
 10
 <400> 178
 cgcugcgcuu cugggcccg cggcggcgug gggcugcccg ggccggucga ccagcgcgcc 60
 guagcucccg aggcccagc cgcgaccgc gg 92
 15
 <210> 179
 <211> 80
 <212> RNA
 <213> Homo sapiens
 20
 <400> 179
 ugccgucggc cuggggagga ggaagggcaa guccaaaggu auacaguugg ucugucauu 60
 cucucuuuuu ggccuacaag 80
 25
 <210> 180
 <211> 61
 <212> RNA
 <213> Homo sapiens
 30
 <400> 180
 gggggcgggg gcuggggucu gcagguucgc acugaugccu gcucgcccug ucucccgcu 60
 g 61
 35
 <210> 181
 <211> 68
 <212> RNA
 <213> Homo sapiens
 40
 <400> 181
 gaauggaaga agaaggcggc cggucugcgg gagccaggcc gcagagccau ccgccuucug 60
 uccauguc 68
 45
 <210> 182
 <211> 68
 <212> RNA
 <213> Homo sapiens
 50
 <400> 182
 gacucggcug cgguggacaa guccggcucc agaaccugga caccgcucag ccggccgagg 60
 cagggguc 68
 55
 <210> 183

EP 3 150 707 A1

<211> 100
 <212> RNA
 <213> Homo sapiens

5
 <400> 183
 gagguugggag gauugcuuga gucagggugg uugaggcugc aguaaguugu gaucauacca 60
 cugcacucca gccugaguga cagagcaaga ccuugucuca 100

10
 <210> 184
 <211> 73
 <212> RNA
 <213> Homo sapiens

15
 <400> 184
 guucaagugg gaggacagga ggcaggugug guuggaggaa gcagccugaa ccugccuccc 60
 ugacauucca cag 73

20
 <210> 185
 <211> 75
 <212> RNA
 <213> Homo sapiens

25
 <400> 185
 uggagugggg ggcagggagg ggcucagggg gaaagugcau acagccccug gccucucug 60
 ccuuccguc ccug 75

30
 <210> 186
 <211> 68
 <212> RNA
 <213> Homo sapiens

35
 <400> 186
 cguggugagg auauggcagg gaaggggagu uucccucua ucccuucccc ccaguaaucu 60
 ucaucaug 68

40
 <210> 187
 <211> 73
 <212> RNA
 <213> Homo sapiens

45
 <400> 187
 gugggcgggg gcaggugugu gguggguggu ggccugcggu gagcagggcc cucacaccug 60
 ccugcggccc cag 73

50
 <210> 188
 <211> 64
 <212> RNA
 <213> Homo sapiens

55
 <400> 188
 gagcucuggg aggggcuggg uuuggcagga caguuccaa gccucuguc cucccaucuu 60
 ccag 64

EP 3 150 707 A1

<210> 189
 <211> 81
 <212> RNA
 <213> Homo sapiens
 5
 <400> 189
 aguuggguggg ggagccauga gauaagagca ccuccuagag aauguugaac uaaaggugcc 60
 10 cucucuggcu ccucccaaaa g 81
 <210> 190
 <211> 61
 <212> RNA
 <213> Homo sapiens
 15
 <400> 190
 gugcgggaacg cuggccgggg cgggagggga agggacgccc ggccggaacg ccgcacucac 60
 20 g 61
 <210> 191
 <211> 80
 <212> RNA
 <213> Homo sapiens
 25
 <400> 191
 ggcgcgucgc cccccucagu ccaccagagc ccggauaccu cagaaauucg gcucuggguc 60
 30 uguggggagc gaaaugcaac 80
 <210> 192
 <211> 59
 <212> RNA
 <213> Homo sapiens
 35
 <400> 192
 cggggucggc ggcgacgugc ucagcuuggc acccaaguuc ugccgcuccg acgcccggc 59
 40
 <210> 193
 <211> 80
 <212> RNA
 <213> Homo sapiens
 45
 <400> 193
 gcgucaagau ggcggcgggg agguaggcag agcaggacgc cgcugcugcc gccgccaccg 60
 cccgccuccg uccagucgcc 80
 50
 <210> 194
 <211> 63
 <212> RNA
 <213> Homo sapiens
 55
 <400> 194
 gcaugcuggg cgaggcuggc aucuagcaca ggcgguagau gcuugcucuu gccauugcaa 60

EP 3 150 707 A1

	uga	63
5	<210> 195 <211> 80 <212> RNA <213> Homo sapiens	
10	<400> 195 accucuaccu cccggcagag gaggcugcag aggcuggcu uccaaaacuc ugccccucc gcugcugcca aguggcuggu	60 80
15	<210> 196 <211> 75 <212> RNA <213> Homo sapiens	
20	<400> 196 aggcuggcgu gggcugaggg caggaggccu guggccgguc ccaggccucc ugcuuccugg gcucaggcuc gguuu	60 75
25	<210> 197 <211> 89 <212> RNA <213> Homo sapiens	
30	<400> 197 ucuccguuua ucccaccacu gccaccaua uugcuacugu ucagcaggug cugcuggugg ugauggugau agucuggugg gggcggugg	60 89
35	<210> 198 <211> 65 <212> RNA <213> Homo sapiens	
40	<400> 198 gcuucuggga ggaggggauc uugggaguga ucccaacagc ugagcuccu gaaucccugu cccag	60 65
45	<210> 199 <211> 59 <212> RNA <213> Homo sapiens	
50	<400> 199 cugugucggg gagucuggg uccggaauc uccagagccu cugugccccu acuucccag	59
55	<210> 200 <211> 79 <212> RNA <213> Homo sapiens	
	<400> 200 cagccugggg aagguuggc agggaagaca caugagcagu gccuccacu cagccucuc	60

EP 3 150 707 A1

ccuugucucc uuucccuag 79

5 <210> 201
 <211> 60
 <212> RNA
 <213> Homo sapiens

10 <400> 201
 cgcuggggucc gcgcgcccug ggccgggcca uguccgcuug ggggagcgag gggcggggcg 60

15 <210> 202
 <211> 60
 <212> RNA
 <213> Homo sapiens

20 <400> 202
 ugugaaugac ccccuuccag agccaaaauc accagggaug gaggaggggu cuuggguacu 60

25 <210> 203
 <211> 66
 <212> RNA
 <213> Homo sapiens

30 <400> 203
 agcagcccuc ggcggcccgg ggggcgggcg gcggugcccg ucccggggcu gcgcgaggca 60
 caggcg 66

35 <210> 204
 <211> 115
 <212> RNA
 <213> Homo sapiens

40 <400> 204
 gagcaaaaac cagagaacaa caugggagcg uuccuaacct cuaaggcaac uggaugggag 60
 accugacca uccaguucuc ugagggggcu cuuguguguu cuacaagguu guuca 115

45 <210> 205
 <211> 83
 <212> RNA
 <213> Homo sapiens

50 <400> 205
 ccugcugcag aggugccagc ugcagugggg gaggcacugc cagggcugcc cacucugcuu 60
 agccagcagg ugccaagaac agg 83

55 <210> 206
 <211> 63
 <212> RNA
 <213> Homo sapiens

60 <400> 206
 ugguggcggc gguaguuaug ggcuucucu ucucaccagc agccccuggg ccgccgccuc 60

EP 3 150 707 A1

	ccu		63
5	<210> 207 <211> 57 <212> RNA <213> Homo sapiens		
10	<400> 207 cauuggaggg uguggaagac aucugggcca acucugaucu cuucaucuaac cccccag		57
15	<210> 208 <211> 62 <212> RNA <213> Homo sapiens		
20	<400> 208 gcugggggguc cccccacagu guggagcugg ggccgggucc cggggagggg gguucugggc		60
25	ag		62
30	<210> 209 <211> 73 <212> RNA <213> Homo sapiens		
35	<400> 209 ggaggcuggg cugggacgga cccccggccu ccacuuucug uggcagguac cuccucaug		60
40	ucggcccgcc uug		73
45	<210> 210 <211> 83 <212> RNA <213> Homo sapiens		
50	<400> 210 ggguuuccuc ugccuuuuuu uccaaugaaa auaacgaaac cuguuuuuuc ccuugaggg		60
55	ggaaaaaggc ggagaagcc cca		83
60	<210> 211 <211> 62 <212> RNA <213> Homo sapiens		
65	<400> 211 uggccuaggg ggcggcuugu ggaguguaug ggcugagccu ugcucugcuc ccccgcccc		60
70	ag		62
75	<210> 212 <211> 68 <212> RNA <213> Homo sapiens		
80	<400> 212 ugcccaggcu ggagcgagug caguggugca gucaguccua gcucacugca gccucgaacu		60

EP 3 150 707 A1

ccugggcu 68

5 <210> 213
 <211> 82
 <212> RNA
 <213> Homo sapiens

10 <400> 213
 cugacuuuuu uagggaguag aagggugggg agcaugaaca auguuucuca cucccuaccc 60
 cuccacuccc caaaaaaguc ag 82

15 <210> 214
 <211> 72
 <212> RNA
 <213> Homo sapiens

20 <400> 214
 ccaggcacac aggaaaagcg gggcccuggg uucggcugcu accccaaagc ccacauucuc 60
 cugugcacac ag 72

25 <210> 215
 <211> 87
 <212> RNA
 <213> Homo sapiens

30 <400> 215
 cccucaucuc ugggcagggg cuuauuguag gagucucuga agagagcugu ggacugaccu 60
 gcuuuuaccc uuccccaggu ucccuu 87

35 <210> 216
 <211> 88
 <212> RNA
 <213> Homo sapiens

40 <400> 216
 guggggccag gggguggugg gcacugcugg ggugggcaca gcagccaugc agagcgggca 60
 uuugaccccg ugccacccuu uuccccag 88

45 <210> 217
 <211> 78
 <212> RNA
 <213> Homo sapiens

50 <400> 217
 ggccucaggc aggcgcaccc gaccacaugc auggcuggug gcggcgugca ggggucgggu 60
 gggccaggcu guggggcg 78

55 <210> 218
 <211> 93
 <212> RNA
 <213> Homo sapiens

EP 3 150 707 A1

	<400> 218		
	uacuuauaggc accccacucc ugguaccaua gucauaaguu aggagauguu agagcuguga	60	
5	guaccaugac uuaagugugg uggcuuaaac aug	93	
	<210> 219		
	<211> 71		
	<212> RNA		
10	<213> Homo sapiens		
	<400> 219		
	gugucugugc cggucccagg agaaccugca gaggcaucgg gucagcggug cuccugcggg	60	
15	ccgacacuca c	71	
	<210> 220		
	<211> 65		
	<212> RNA		
20	<213> Homo sapiens		
	<400> 220		
	gggugcucgg ggcagggcggc ugggagcggc ccucacauug auggcuccug ccaccuccuc	60	
25	cgcag	65	
	<210> 221		
	<211> 66		
	<212> RNA		
30	<213> Homo sapiens		
	<400> 221		
	ccgagugggg cggggcaggu ccugcaggg acugugacac ugaaggaccu gcaccuucgc	60	
35	ccacag	66	
	<210> 222		
	<211> 90		
	<212> RNA		
40	<213> Homo sapiens		
	<400> 222		
	cgggcggggc ggguccggcc gccuccgagc ccggccggca gccccggcc uaaagcgcg	60	
45	ggcuguccgg aggggucggc uuucccaccg	90	
	<210> 223		
	<211> 70		
	<212> RNA		
50	<213> Homo sapiens		
	<400> 223		
	aggaccagc ggggucgggc gcgcggagca gcgcugggug cagcggcugc gccggcagcu	60	
55	gcaagggccg	70	
	<210> 224		

EP 3 150 707 A1

<211> 94
 <212> RNA
 <213> Homo sapiens

5 <400> 224
 gugaggugug gggccggccc caggagcggg gccugggcag ccccgugugu ugaggaagga 60
 aggcagggcc cccgcucucc gggccugacc ccac 94

10 <210> 225
 <211> 85
 <212> RNA
 <213> Homo sapiens

15 <400> 225
 ggccugggua ggcuugcaug ggggacuggg aagagaccou gaacagguua guccagggag 60
 uucucaucaa gccuuuacuc aguag 85

20 <210> 226
 <211> 70
 <212> RNA
 <213> Homo sapiens

25 <400> 226
 ggccgcggcg cgcaagaugg cggcggggccc gggcaccgcc ccuuccgccc cgccggggcu 60
 cgcacgaggc 70

30 <210> 227
 <211> 86
 <212> RNA
 <213> Homo sapiens

35 <400> 227
 ugccagucuc uaggucccug agaccuuua accugugagg acauccaggg ucacagguga 60
 gguucuuagg agccuggcgu cuggcc 86

40 <210> 228
 <211> 110
 <212> RNA
 <213> Homo sapiens

45 <400> 228
 ggcuacaguc uuucuucaug ugacucgugg acuuccuuu gucauccuau gccugagaau 60
 auaugaagga ggcugggaag gcaaaggac guucaauugu caucacuggc 110

50 <210> 229
 <211> 47
 <212> RNA
 <213> Homo sapiens

55 <400> 229
 cucggcgcgg ggcgcgggcu ccggguuggg gcgagccaac gccgggg 47

EP 3 150 707 A1

<210> 230
 <211> 94
 <212> RNA
 <213> Homo sapiens
 5
 <400> 230
 aaucagccc ugccacuggc uuaugucaug accuugggcu acucaggcug ucugcacaau 60
 gagccaguug gacaggagca gugccacuca acuc 94
 10
 <210> 231
 <211> 84
 <212> RNA
 <213> Homo sapiens
 15
 <400> 231
 cuccccaugg ccugucucc caaccuugu accagugcug ggcucagacc cugguacagg 60
 ccugggggac agggaccugg ggac 84
 20
 <210> 232
 <211> 94
 <212> RNA
 <213> Homo sapiens
 25
 <400> 232
 auaaaggaag uuaggcugag gggcagagag cgagacuuuu cuauuuucca aaagcucggg 60
 cugaggcccc ucagucuugc uuccuaacct gcgc 94
 30
 <210> 233
 <211> 94
 <212> RNA
 <213> Homo sapiens
 35
 <400> 233
 cgggcagcgg gugccaggca cggugucagc aggcaacaug gccgagaggc cggggccucc 60
 gggcggcgcc guguccgca ccgcguacct ugac 94
 40
 <210> 234
 <211> 85
 <212> RNA
 <213> Homo sapiens
 45
 <400> 234
 ggcgccuccu gcucugcugu gccgccaggg ccucccuag cgcgccuucu ggagaggcuu 60
 ugugcggaua cggggcugga ggccu 85
 50
 <210> 235
 <211> 73
 <212> RNA
 <213> Homo sapiens
 55
 <400> 235
 uguauccuug aauggauuuu uggagcagga guggacaccu gacccaaagg aaaucaaucc 60

EP 3 150 707 A1

	auaggcuagc aau	73
5	<210> 236 <211> 98 <212> RNA <213> Homo sapiens	
10	<400> 236 uucucacccc cgccugacac gggcgacagc ugcggccgc uguguucacu cgggccgagu	60
	gcgucuccug ucaggcaagg gagagcagag ccccccug	98
15	<210> 237 <211> 78 <212> RNA <213> Homo sapiens	
20	<400> 237 gagcgucacg uugacacuca aaaaguuuca gauuuuggaa cauuucggau uuuggauuuu	60
	uggaucaggg augcucaa	78
25	<210> 238 <211> 89 <212> RNA <213> Homo sapiens	
30	<400> 238 gucagcagug ccuuagcagc acguaaaau uggcguaag auucuaaaau uaucuccagu	60
	auuaacugug cugcugaagu aagguugac	89
35	<210> 239 <211> 81 <212> RNA <213> Homo sapiens	
40	<400> 239 guuccacucu agcagcacgu aaauauuggc guagugaaau auauuuuuu caccauuuu	60
	acugugcugc uuuaguguga c	81
45	<210> 240 <211> 72 <212> RNA <213> Homo sapiens	
50	<400> 240 cuugggaug gcaaggaaac cguuaccuu acugaguuuu gaaugguaa ugguucucuu	60
	gcuaauacca ga	72
55	<210> 241 <211> 68 <212> RNA <213> Homo sapiens	

EP 3 150 707 A1

	<400> 241		
	cuccggugcc uacugagcug auaucaguuc ucauuuuaca cacuggcuca guucagcagg	60	
	aacaggag	68	
5			
	<210> 242		
	<211> 73		
	<212> RNA		
	<213> Homo sapiens		
10			
	<400> 242		
	cucugccucc cgugccuacu gagcugaaac acaguugguu uguguacacu ggcucaguuc	60	
	agcaggaaca ggg	73	
15			
	<210> 243		
	<211> 109		
	<212> RNA		
	<213> Homo sapiens		
20			
	<400> 243		
	ggucgggcuc accaugacac agugugagac cucgggcuac aacacaggac cggggcgug	60	
	cucugacccc ucgugucuug uguugcagcc ggagggacgc agguccgca	109	
25			
	<210> 244		
	<211> 80		
	<212> RNA		
	<213> Homo sapiens		
30			
	<400> 244		
	cgggaaugcc gcggcgggga cggcgauugg uccguaugug uggugccacc ggccgccggc	60	
	uccgccccgg ccccccccc	80	
35			
	<210> 245		
	<211> 67		
	<212> RNA		
	<213> Homo sapiens		
40			
	<400> 245		
	guggcacuca aacugugggg gcacuuucug cucucuggug aaagugccgc caucuuuuga	60	
	guguuac	67	
45			
	<210> 246		
	<211> 97		
	<212> RNA		
	<213> Homo sapiens		
50			
	<400> 246		
	ugaugcuuug cuggcuggug cagugccuga gggaguaaga gcccuuguugu uguaagauag	60	
	ugucuuacuc ccucaggcac aucuccaaca agucucu	97	
55			
	<210> 247		
	<211> 97		

EP 3 150 707 A1

	<212> RNA		
	<213> Homo sapiens		
	<400> 247		
5	ugaugcuuug cuggcuggug cagugccuga gggaguaaga gcccguguugu ugucagauag		60
	ugucuuacuc ccucaggcac aucuccagcg agucucu		97
10	<210> 248		
	<211> 22		
	<212> RNA		
	<213> Homo sapiens		
	<400> 248		
15	aaggauuuag ggacaggcuu ug		22
20	<210> 249		
	<211> 19		
	<212> RNA		
	<213> Homo sapiens		
	<400> 249		
	caggaaggau uuagggaca		19
25	<210> 250		
	<211> 20		
	<212> RNA		
	<213> Homo sapiens		
30	<400> 250		
	cagcaggacg ggagcgcggc		20
35	<210> 251		
	<211> 21		
	<212> RNA		
	<213> Homo sapiens		
	<400> 251		
40	cggauccgag ucacggcacc a		21
45	<210> 252		
	<211> 15		
	<212> RNA		
	<213> Homo sapiens		
	<400> 252		
	uccgagucac ggcac		15
50	<210> 253		
	<211> 23		
	<212> RNA		
	<213> Homo sapiens		
55	<400> 253		
	gggggucucc ggugcucgga ucu		23

EP 3 150 707 A1

	<210> 254	
	<211> 20	
	<212> RNA	
	<213> Homo sapiens	
5		
	<400> 254	
	gggggucccc ggugcucgga	20
10		
	<210> 255	
	<211> 22	
	<212> RNA	
	<213> Homo sapiens	
15		
	<400> 255	
	ggcgucccag gcggggcgcc gc	22
20		
	<210> 256	
	<211> 15	
	<212> RNA	
	<213> Homo sapiens	
25		
	<400> 256	
	gcgccgcggg accgc	15
30		
	<210> 257	
	<211> 15	
	<212> RNA	
	<213> Homo sapiens	
35		
	<400> 257	
	gagcgcucgc uggcc	15
40		
	<210> 258	
	<211> 15	
	<212> RNA	
	<213> Homo sapiens	
45		
	<400> 258	
	cggugagcgc ucgcu	15
50		
	<210> 259	
	<211> 22	
	<212> RNA	
	<213> Homo sapiens	
55		
	<400> 259	
	accaggaggc ugaggcccu ca	22
60		
	<210> 260	
	<211> 15	
	<212> RNA	
	<213> Homo sapiens	
65		
	<400> 260	
	accaggaggc ugagg	15

EP 3 150 707 A1

<210> 261
 <211> 17
 <212> RNA
 <213> Homo sapiens
 5
 <400> 261
 uccuagucac ggcacca 17

<210> 262
 <211> 17
 <212> RNA
 <213> Homo sapiens
 10
 <400> 262
 ccuccgggac ggcuggg 17

<210> 263
 <211> 15
 <212> RNA
 <213> Homo sapiens
 20
 <400> 263
 ccgggacggc ugggc 15

<210> 264
 <211> 20
 <212> RNA
 <213> Homo sapiens
 25
 <400> 264
 gcugcgggcu gcgguacaggg 20

<210> 265
 <211> 18
 <212> RNA
 <213> Homo sapiens
 30
 <400> 265
 gcuccugaau agcuggga 18

<210> 266
 <211> 16
 <212> RNA
 <213> Homo sapiens
 35
 <400> 266
 ugaauagcug ggacua 16

<210> 267
 <211> 23
 <212> RNA
 <213> Homo sapiens
 40
 <400> 267
 ggugggugag gucgggcccc aag 23

EP 3 150 707 A1

	<210> 268	
	<211> 23	
	<212> RNA	
	<213> Homo sapiens	
5		
	<400> 268	
	acaggagugg gggugggaca uaa	23
10		
	<210> 269	
	<211> 20	
	<212> RNA	
	<213> Homo sapiens	
15		
	<400> 269	
	acaggagugg gggugggaca	20
20		
	<210> 270	
	<211> 21	
	<212> RNA	
	<213> Homo sapiens	
25		
	<400> 270	
	cugggggacg cgugagcgcg a	21
30		
	<210> 271	
	<211> 15	
	<212> RNA	
	<213> Homo sapiens	
35		
	<400> 271	
	cagggagcag gaagc	15
40		
	<210> 272	
	<211> 22	
	<212> RNA	
	<213> Homo sapiens	
45		
	<400> 272	
	gcugggauua caggcaugag cc	22
50		
	<210> 273	
	<211> 15	
	<212> RNA	
	<213> Homo sapiens	
55		
	<400> 273	
	gauuacaggc augag	15
60		
	<210> 274	
	<211> 18	
	<212> RNA	
	<213> Homo sapiens	
65		
	<400> 274	
	gcacgggagc ucagguga	18

EP 3 150 707 A1

	<210> 275	
	<211> 20	
	<212> RNA	
	<213> Homo sapiens	
5		
	<400> 275	
	aucccaccuc ugccaccaa	20
10		
	<210> 276	
	<211> 16	
	<212> RNA	
	<213> Homo sapiens	
15		
	<400> 276	
	ucccaccucu gccacc	16
20		
	<210> 277	
	<211> 16	
	<212> RNA	
	<213> Homo sapiens	
25		
	<400> 277	
	ggagcggcgg aucugg	16
30		
	<210> 278	
	<211> 23	
	<212> RNA	
	<213> Homo sapiens	
35		
	<400> 278	
	acagcagggc uggggauugc agu	23
40		
	<210> 279	
	<211> 20	
	<212> RNA	
	<213> Homo sapiens	
45		
	<400> 279	
	accggccgcc ggcuccgccc	20
50		
	<210> 280	
	<211> 17	
	<212> RNA	
	<213> Homo sapiens	
55		
	<400> 280	
	ccggccgccg gcuccgc	17
60		
	<210> 281	
	<211> 15	
	<212> RNA	
	<213> Homo sapiens	
65		
	<400> 281	
	ucccagcggg gccuc	15

EP 3 150 707 A1

	<210> 282	
	<211> 25	
	<212> RNA	
	<213> Homo sapiens	
5		
	<400> 282	
	uucugggccc gcggcgggcg ugggg	25
10		
	<210> 283	
	<211> 15	
	<212> RNA	
	<213> Homo sapiens	
15		
	<400> 283	
	cgcggcgggc guggg	15
20		
	<210> 284	
	<211> 21	
	<212> RNA	
	<213> Homo sapiens	
25		
	<400> 284	
	aagaaggcgg ucggucugcg g	21
30		
	<210> 285	
	<211> 22	
	<212> RNA	
	<213> Homo sapiens	
35		
	<400> 285	
	acucggcugc gguggacaag uc	22
40		
	<210> 286	
	<211> 20	
	<212> RNA	
	<213> Homo sapiens	
45		
	<400> 286	
	cucggcugcg guggacaagu	20
50		
	<210> 287	
	<211> 19	
	<212> RNA	
	<213> Homo sapiens	
55		
	<400> 287	
	cuccagccug agugacaga	19
50		
	<210> 288	
	<211> 15	
	<212> RNA	
	<213> Homo sapiens	
55		
	<400> 288	
	acugcacucc agccu	15

EP 3 150 707 A1

<210> 289
 <211> 16
 <212> RNA
 <213> Homo sapiens
 5
 <400> 289
 gugggggggc aggagg 16

<210> 290
 <211> 19
 <212> RNA
 <213> Homo sapiens
 10
 <400> 290
 ggggggcagg aggggcuca 19

<210> 291
 <211> 21
 <212> RNA
 <213> Homo sapiens
 20
 <400> 291
 cucccccca guaaucuca u 21

<210> 292
 <211> 22
 <212> RNA
 <213> Homo sapiens
 25
 <400> 292
 ccucacaccu gccucgcccc cc 22

<210> 293
 <211> 15
 <212> RNA
 <213> Homo sapiens
 30
 <400> 293
 ucacaccugc cucgc 15

<210> 294
 <211> 22
 <212> RNA
 <213> Homo sapiens
 35
 <400> 294
 guuggugggg gagccaugag au 22

<210> 295
 <211> 22
 <212> RNA
 <213> Homo sapiens
 40
 <400> 295
 ggggagccau gagauaagag ca 22

45
 50
 55

EP 3 150 707 A1

	<210> 296	
	<211> 22	
	<212> RNA	
	<213> Homo sapiens	
5		
	<400> 296	
	ucggcucugg gucugugggg ag	22
10		
	<210> 297	
	<211> 17	
	<212> RNA	
	<213> Homo sapiens	
15		
	<400> 297	
	cggcucuggg ucugugg	17
20		
	<210> 298	
	<211> 19	
	<212> RNA	
	<213> Homo sapiens	
25		
	<400> 298	
	gcugggag gcuggcauc	19
30		
	<210> 299	
	<211> 20	
	<212> RNA	
	<213> Homo sapiens	
35		
	<400> 299	
	ucugccccc cgcugcugc	20
40		
	<210> 300	
	<211> 20	
	<212> RNA	
	<213> Homo sapiens	
45		
	<400> 300	
	aucccaccac ugccaccau	20
50		
	<210> 301	
	<211> 30	
	<212> RNA	
	<213> Homo sapiens	
55		
	<400> 301	
	ccaccacca ccacugccac caugccacca	30
55		
	<210> 302	
	<211> 24	
	<212> RNA	
	<213> Homo sapiens	
55		
	<400> 302	
	gugcccgucc cggggcugcg cgag	24

EP 3 150 707 A1

	<210> 303	
	<211> 17	
	<212> RNA	
	<213> Homo sapiens	
5		
	<400> 303	
	ccggggcugc gcgaggc	17
10		
	<210> 304	
	<211> 15	
	<212> RNA	
	<213> Homo sapiens	
15		
	<400> 304	
	gcugcagugg gggag	15
20		
	<210> 305	
	<211> 25	
	<212> RNA	
	<213> Homo sapiens	
25		
	<400> 305	
	uggcggcggg aguuaugggc uucuc	25
30		
	<210> 306	
	<211> 30	
	<212> RNA	
	<213> Homo sapiens	
35		
	<400> 306	
	gcugggcugg gacggacacc cggccuccac	30
40		
	<210> 307	
	<211> 20	
	<212> RNA	
	<213> Homo sapiens	
45		
	<400> 307	
	ggaaaaaggc gggagaagcc	20
50		
	<210> 308	
	<211> 15	
	<212> RNA	
	<213> Homo sapiens	
55		
	<400> 308	
	ggcgggagaa gcccc	15
60		
	<210> 309	
	<211> 21	
	<212> RNA	
	<213> Homo sapiens	
65		
	<400> 309	
	cccaggcugg agcgagugca g	21

EP 3 150 707 A1

	<210> 310	
	<211> 23	
	<212> RNA	
	<213> Homo sapiens	
5		
	<400> 310	
	agggaguaga agggugggga gca	23
10		
	<210> 311	
	<211> 16	
	<212> RNA	
	<213> Homo sapiens	
15		
	<400> 311	
	uagggaguag aagggg	16
20		
	<210> 312	
	<211> 25	
	<212> RNA	
	<213> Homo sapiens	
25		
	<400> 312	
	ugggcagggg cuuauuguag gaguc	25
30		
	<210> 313	
	<211> 21	
	<212> RNA	
	<213> Homo sapiens	
35		
	<400> 313	
	gggcaggggc uuauuguagg a	21
40		
	<210> 314	
	<211> 20	
	<212> RNA	
	<213> Homo sapiens	
45		
	<400> 314	
	cacccacuc cugguacc	20
50		
	<210> 315	
	<211> 15	
	<212> RNA	
	<213> Homo sapiens	
55		
	<400> 315	
	ccccacuccu gguac	15
60		
	<210> 316	
	<211> 26	
	<212> RNA	
	<213> Homo sapiens	
65		
	<400> 316	
	gcgggcuguc cggagggguc ggcuuu	26

EP 3 150 707 A1

	<210> 317	
	<211> 16	
	<212> RNA	
	<213> Homo sapiens	
5		
	<400> 317	
	gcuguccgga gggguc	16
10		
	<210> 318	
	<211> 18	
	<212> RNA	
	<213> Homo sapiens	
15		
	<400> 318	
	cagcggggcu gggcgcg	18
20		
	<210> 319	
	<211> 15	
	<212> RNA	
	<213> Homo sapiens	
25		
	<400> 319	
	cggggcuggg cgcg	15
30		
	<210> 320	
	<211> 23	
	<212> RNA	
	<213> Homo sapiens	
35		
	<400> 320	
	aggaaggaag gcagggcccc cgc	23
40		
	<210> 321	
	<211> 15	
	<212> RNA	
	<213> Homo sapiens	
45		
	<400> 321	
	gggccccgc ucccc	15
50		
	<210> 322	
	<211> 23	
	<212> RNA	
	<213> Homo sapiens	
55		
	<400> 322	
	cacaggugag guucuuggga gcc	23
60		
	<210> 323	
	<211> 15	
	<212> RNA	
	<213> Homo sapiens	
65		
	<400> 323	
	gagguucuug ggagc	15

EP 3 150 707 A1

	<210> 324	
	<211> 24	
	<212> RNA	
	<213> Homo sapiens	
5		
	<400> 324	
	gaggcuggga aggcaaaggg acgu	24
10		
	<210> 325	
	<211> 15	
	<212> RNA	
	<213> Homo sapiens	
15		
	<400> 325	
	cugggaaggc aaagg	15
20		
	<210> 326	
	<211> 24	
	<212> RNA	
	<213> Homo sapiens	
25		
	<400> 326	
	ugguacaggc cugggggaca ggga	24
30		
	<210> 327	
	<211> 19	
	<212> RNA	
	<213> Homo sapiens	
35		
	<400> 327	
	gguacaggcc ugggggaca	19
40		
	<210> 328	
	<211> 30	
	<212> RNA	
	<213> Homo sapiens	
45		
	<400> 328	
	ugaggggag agagcgagac uuuucuauuu	30
50		
	<210> 329	
	<211> 15	
	<212> RNA	
	<213> Homo sapiens	
55		
	<400> 329	
	cagagagcga gacuu	15
60		
	<210> 330	
	<211> 25	
	<212> RNA	
	<213> Homo sapiens	
65		
	<400> 330	
	cuuugugcgg auacggggcu ggagg	25

EP 3 150 707 A1

	<210> 331	
	<211> 19	
	<212> RNA	
	<213> Homo sapiens	
5		
	<400> 331	
	agaggcuuug ugcggauac	19
10		
	<210> 332	
	<211> 21	
	<212> RNA	
	<213> Homo sapiens	
15		
	<400> 332	
	gaauggauuu uuggagcagg a	21
20		
	<210> 333	
	<211> 15	
	<212> RNA	
	<213> Homo sapiens	
25		
	<400> 333	
	ggauuuuugg agcag	15
30		
	<210> 334	
	<211> 20	
	<212> RNA	
	<213> Homo sapiens	
35		
	<400> 334	
	ggauuuuugg aucagggau	20
40		
	<210> 335	
	<211> 15	
	<212> RNA	
	<213> Homo sapiens	
45		
	<400> 335	
	uuuuuggauc aggga	15
50		
	<210> 336	
	<211> 27	
	<212> RNA	
	<213> Homo sapiens	
55		
	<400> 336	
	uagcagcacg uaaauauugg cguuaag	27
60		
	<210> 337	
	<211> 26	
	<212> RNA	
	<213> Homo sapiens	
65		
	<400> 337	
	uagcagcacg uaaauauugg cguagu	26

EP 3 150 707 A1

	<210> 338	
	<211> 15	
	<212> RNA	
	<213> Homo sapiens	
5		
	<400> 338	
	cacguaaaua uuggc	15
10		
	<210> 339	
	<211> 27	
	<212> RNA	
	<213> Homo sapiens	
15		
	<400> 339	
	aaaccguuac cauuacugag uuuagua	27
20		
	<210> 340	
	<211> 15	
	<212> RNA	
	<213> Homo sapiens	
25		
	<400> 340	
	uaccuuacu gaguu	15
30		
	<210> 341	
	<211> 24	
	<212> RNA	
	<213> Homo sapiens	
35		
	<400> 341	
	uggcucaguu cagcaggaac agga	24
40		
	<210> 342	
	<211> 24	
	<212> RNA	
	<213> Homo sapiens	
45		
	<400> 342	
	cuggcucagu ucagcaggaa cagg	24
50		
	<210> 343	
	<211> 15	
	<212> RNA	
	<213> Homo sapiens	
55		
	<400> 343	
	aguucagcag gaaca	15
60		
	<210> 344	
	<211> 22	
	<212> RNA	
	<213> Homo sapiens	
65		
	<400> 344	
	gggcuacaac acaggaccg gg	22

EP 3 150 707 A1

	<210> 345	
	<211> 22	
	<212> RNA	
	<213> Homo sapiens	
5		
	<400> 345	
	gcuacaacac aggacccggg cg	22
10		
	<210> 346	
	<211> 22	
	<212> RNA	
	<213> Homo sapiens	
15		
	<400> 346	
	acucaaacug ugggggcacu uu	22
20		
	<210> 347	
	<211> 19	
	<212> RNA	
	<213> Homo sapiens	
25		
	<400> 347	
	acucaaacug ugggggcac	19
30		
	<210> 348	
	<211> 15	
	<212> RNA	
	<213> Homo sapiens	
35		
	<400> 348	
	gagggaguaa gagcc	15
40		
	<210> 349	
	<211> 18	
	<212> RNA	
	<213> Homo sapiens	
45		
	<400> 349	
	ggugggcuuc ccggaggg	18
50		
	<210> 350	
	<211> 23	
	<212> RNA	
	<213> Homo sapiens	
55		
	<400> 350	
	gccccggcgc gggcggguuc ugg	23
60		
	<210> 351	
	<211> 21	
	<212> RNA	
	<213> Homo sapiens	
65		
	<400> 351	
	cguggaggac gaggaggagg c	21

EP 3 150 707 A1

	<210> 352	
	<211> 19	
	<212> RNA	
	<213> Homo sapiens	
5		
	<400> 352	
	ggggccuggc ggugggcgg	19
10		
	<210> 353	
	<211> 22	
	<212> RNA	
	<213> Homo sapiens	
15		
	<400> 353	
	agacugacgg cuggaggccc au	22
20		
	<210> 354	
	<211> 22	
	<212> RNA	
	<213> Homo sapiens	
25		
	<400> 354	
	ugggggagga aggacaggcc au	22
30		
	<210> 355	
	<211> 23	
	<212> RNA	
	<213> Homo sapiens	
35		
	<400> 355	
	acggggaguc aggcaguggu gga	23
40		
	<210> 356	
	<211> 23	
	<212> RNA	
	<213> Homo sapiens	
45		
	<400> 356	
	ccucccugcc cgccucucug cag	23
50		
	<210> 357	
	<211> 20	
	<212> RNA	
	<213> Homo sapiens	
55		
	<400> 357	
	ugugggacug caaaugggag	20
60		
	<210> 358	
	<211> 24	
	<212> RNA	
	<213> Homo sapiens	
65		
	<400> 358	
	ugaggggccu cagaccgagc uuuu	24

EP 3 150 707 A1

	<210> 359	
	<211> 19	
	<212> RNA	
	<213> Homo sapiens	
5	<400> 359	
	gggggaagaa aaggugggg	19
10	<210> 360	
	<211> 22	
	<212> RNA	
	<213> Homo sapiens	
15	<400> 360	
	cccuggggc uggcaggcg ga	22
20	<210> 361	
	<211> 22	
	<212> RNA	
	<213> Homo sapiens	
25	<400> 361	
	agacacauuu ggagaggaa cc	22
30	<210> 362	
	<211> 21	
	<212> RNA	
	<213> Homo sapiens	
35	<400> 362	
	guguggccgg caggcgggug g	21
40	<210> 363	
	<211> 23	
	<212> RNA	
	<213> Homo sapiens	
45	<400> 363	
	cggggccgua gcacugucug aga	23
50	<210> 364	
	<211> 22	
	<212> RNA	
	<213> Homo sapiens	
55	<400> 364	
	aggaagggg acgagggug gg	22
50	<210> 365	
	<211> 17	
	<212> RNA	
	<213> Homo sapiens	
55	<400> 365	
	ggggcgggc cggaucg	17

EP 3 150 707 A1

	<210> 366	
	<211> 17	
	<212> RNA	
	<213> Homo sapiens	
5		
	<400> 366	
	ggcgggugcg ggggugg	17
10		
	<210> 367	
	<211> 22	
	<212> RNA	
	<213> Homo sapiens	
15		
	<400> 367	
	ggguggggau uuguugcauu ac	22
20		
	<210> 368	
	<211> 23	
	<212> RNA	
	<213> Homo sapiens	
25		
	<400> 368	
	uggugggugg ggaggagaag ugc	23
30		
	<210> 369	
	<211> 22	
	<212> RNA	
	<213> Homo sapiens	
35		
	<400> 369	
	uugaggagac augguggggg cc	22
40		
	<210> 370	
	<211> 21	
	<212> RNA	
	<213> Homo sapiens	
45		
	<400> 370	
	agcaugacag aggagaggug g	21
50		
	<210> 371	
	<211> 22	
	<212> RNA	
	<213> Homo sapiens	
55		
	<400> 371	
	agggacggga cgcggugcag ug	22
50		
	<210> 372	
	<211> 25	
	<212> RNA	
	<213> Homo sapiens	
55		
	<400> 372	
	acuugggcag gagggaccu guaug	25

EP 3 150 707 A1

	<210> 373	
	<211> 21	
	<212> RNA	
	<213> Homo sapiens	
5	<400> 373	
	cggggcagcu caguacagga u	21
10	<210> 374	
	<211> 24	
	<212> RNA	
	<213> Homo sapiens	
15	<400> 374	
	uguaggcaug aggcagggcc cagg	24
20	<210> 375	
	<211> 22	
	<212> RNA	
	<213> Homo sapiens	
25	<400> 375	
	uggggguggu cucuagccaa gg	22
30	<210> 376	
	<211> 20	
	<212> RNA	
	<213> Homo sapiens	
35	<400> 376	
	ugggaauggg gguaagggcc	20
40	<210> 377	
	<211> 23	
	<212> RNA	
	<213> Homo sapiens	
45	<400> 377	
	guuugcacgg gugggccuug ucu	23
50	<210> 378	
	<211> 22	
	<212> RNA	
	<213> Homo sapiens	
55	<400> 378	
	uccaggcagg agccggacug ga	22
60	<210> 379	
	<211> 21	
	<212> RNA	
	<213> Homo sapiens	
65	<400> 379	
	cugggcucgg gacgcgcggc u	21

EP 3 150 707 A1

<210> 380
 <211> 17
 <212> RNA
 <213> Homo sapiens
 5
 <400> 380
 gccggacaag agggagg 17

 <210> 381
 <211> 20
 <212> RNA
 <213> Homo sapiens
 10
 <400> 381
 ccccagggcg acgcggcggg 20
 15

 <210> 382
 <211> 21
 <212> RNA
 <213> Homo sapiens
 20
 <400> 382
 uggcuguugg agggggcagg c 21
 25

 <210> 383
 <211> 22
 <212> RNA
 <213> Homo sapiens
 30
 <400> 383
 uauugcacuc gucccggccu cc 22
 35

 <210> 384
 <211> 73
 <212> RNA
 <213> Homo sapiens
 40
 <400> 384
 gaaaaacaacc aggguggcuu cccggagggc ggaacaccca gccccagcau ccagggcuca 60
 ccuaccacgu uug 73
 45

 <210> 385
 <211> 80
 <212> RNA
 <213> Homo sapiens
 50
 <400> 385
 gguuccggag ccccggcgcg ggcggguucu gggguguaga cgcugcuggc cagcccgcc 60
 cagccgaggu ucucggcacc 80
 55

 <210> 386
 <211> 103
 <212> RNA
 <213> Homo sapiens

EP 3 150 707 A1

	<400> 386		
	gugucggcug	uggcgugacu gucccucugu gucccccacu aggcccacug cucaguggag	60
5		cguggaggac gaggaggagg cgguccacga gcaaugccag cau	103
	<210> 387		
	<211> 90		
	<212> RNA		
10	<213> Homo sapiens		
	<400> 387		
	ggcgccucug	cagcuccggc uccccuggc cucucgggaa cuacaagucc cagggggccu	60
15		ggcgguggggc ggcgggcgga agagggcggg	90
	<210> 388		
	<211> 86		
	<212> RNA		
20	<213> Homo sapiens		
	<400> 388		
	auucuaggug	gggagacuga cggcuggagg cccauaagcu gucuaaaacu ucggccccca	60
25		gauuucuggu cuccccacuu cagaac	86
	<210> 389		
	<211> 72		
	<212> RNA		
30	<213> Homo sapiens		
	<400> 389		
	cugggggagg	aaggacaggc caucugcuau ucguccacca accugacuug auccucucu	60
35		cccuccucc ag	72
	<210> 390		
	<211> 66		
	<212> RNA		
40	<213> Homo sapiens		
	<400> 390		
	ucaagacggg	gagucaggca gugguggaga uggagagccc ugagccucca cucuccuggc	60
45		ccccag	66
	<210> 391		
	<211> 59		
	<212> RNA		
50	<213> Homo sapiens		
	<400> 391		
	cuccagggag	acagugugug aggccucuug ccauggccuc ccugcccgcc ucucugcag	59
	<210> 392		
55	<211> 72		
	<212> RNA		
	<213> Homo sapiens		

EP 3 150 707 A1

	<400> 392		
	ugugggacug caaaugggag cucagcaccu gccugccacc cacgcagacc agccccugcu	60	
	cuguucccac ag	72	
5			
	<210> 393		
	<211> 75		
	<212> RNA		
10	<213> Homo sapiens		
	<400> 393		
	aagcaagacu gaggggccuc agaccgagcu uuuggaaaau agaaaagucu cgcucucugc	60	
	cccucagccu aacuu	75	
15			
	<210> 394		
	<211> 67		
	<212> RNA		
20	<213> Homo sapiens		
	<400> 394		
	aaaucucucu ccuaucuuu ccugcagccc ccaggugggg gggaagaaaa gguggggaau	60	
	uagauuc	67	
25			
	<210> 395		
	<211> 67		
	<212> RNA		
30	<213> Homo sapiens		
	<400> 395		
	ccagaccccu ggggcugggc aggcggaaag aggucugaac ugccucugcc uccuuggucu	60	
	ccggcag	67	
35			
	<210> 396		
	<211> 97		
	<212> RNA		
40	<213> Homo sapiens		
	<400> 396		
	aucugaguug ggagggucc ucuccaaaug ugucuugggg ugggggauca agacacauuu	60	
	ggagagggaa ccucccaacu cggccucugc caucau	97	
45			
	<210> 397		
	<211> 87		
	<212> RNA		
50	<213> Homo sapiens		
	<400> 397		
	guguggccgg caggggggug ggcgggggcg gccgguggga accccgcccc gccccgcgcc	60	
	cgcacucacc cgcccgucuc cccacag	87	
55			
	<210> 398		

EP 3 150 707 A1

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

5
 <400> 398
 ugagcuguug gauucggggc cguagcacug ucugagaggu uuacauuucu cacagugaac 60
 cggucucuuu uucagcugcu uc 82

10
 <210> 399
 <211> 115
 <212> RNA
 <213> Homo sapiens

15
 <400> 399
 ucugaggaga ccugggcugu cagaggccag ggaaggggac gagggguuggg gaacaggugg 60
 uuagcacuuc auccucgucu cccucccagg uuagaagggc cccccucucu gaagg 115

20
 <210> 400
 <211> 84
 <212> RNA
 <213> Homo sapiens

25
 <400> 400
 gaggcugggc ggggcgcggc cggaucgguc gagagcgucc uggcugauga cggucucccg 60
 ugcccacgcc ccaaacgcag ucuc 84

30
 <210> 401
 <211> 69
 <212> RNA
 <213> Homo sapiens

35
 <400> 401
 cuuucggcca gcgggacggc auccgaggug ggcuaggcuc gggcccggug cgggugcggg 60
 ggugggagg 69

40
 <210> 402
 <211> 75
 <212> RNA
 <213> Homo sapiens

45
 <400> 402
 ucaucccugg guggggauuu guugcauuac uuguguucua uauaaaguau ugcacuuguc 60
 ccggccugug gaaga 75

50
 <210> 403
 <211> 62
 <212> RNA
 <213> Homo sapiens

55
 <400> 403
 cuuccuggug gguggggagg agaagugccg uccucaugag ccccucucug ucccaccgau 60
 ag 62

EP 3 150 707 A1

<210> 404
 <211> 70
 <212> RNA
 <213> Homo sapiens
 5
 <400> 404
 gguuucuccu ugaggagaca uggugggggc cggucaggca gcccaugcca uguguccuca 60
 uggagaggcc 70
 10
 <210> 405
 <211> 113
 <212> RNA
 <213> Homo sapiens
 15
 <400> 405
 agcaugacag aggagaggug gagguaggcg agaguaauau aauuucucca ggagaacauc 60
 ugagagggga aguugcuuuc cugcccuggc ccuuucaccc uccugaguuu ggg 113
 20
 <210> 406
 <211> 96
 <212> RNA
 <213> Homo sapiens
 25
 <400> 406
 cgggccccgg gcgggcggga gggacgggac gcggugcagu guuguuuuuu cccccgcaa 60
 uauugcacuc gucccggccu ccggcccccc cggccc 96
 30
 <210> 407
 <211> 70
 <212> RNA
 <213> Homo sapiens
 35
 <400> 407
 ugugcacuug ggcaggaggg acccuguaug ucucctcgca gcaccgucau cgugucccuc 60
 uuguccacag 70
 40
 <210> 408
 <211> 68
 <212> RNA
 <213> Homo sapiens
 45
 <400> 408
 gcauccugua cugagcugcc ccgaggcccu ucaugcugcc cagcucgggg cagcucagua 60
 caggauac 68
 50
 <210> 409
 <211> 64
 <212> RNA
 <213> Homo sapiens
 55
 <400> 409

EP 3 150 707 A1

uccuguacug agcugccccg agcuggggcag caugaagggc cucggggcag cucaguacag 60
gaug 64

5
<210> 410
<211> 64
<212> RNA
<213> Homo sapiens

10
<400> 410
ugcucuguag gcaugaggca gggcccaggu uccaugugau gcugaagcuc ugacauuccu 60
gcag 64

15
<210> 411
<211> 65
<212> RNA
<213> Homo sapiens

20
<400> 411
agcccugggg guggucucua gccaaaggcuc uggggucuca cccuuggcug gucucugcuc 60
cgcag 65

25
<210> 412
<211> 80
<212> RNA
<213> Homo sapiens

30
<400> 412
gagaggccaa gaccuuggga auggggguaa gggccuucug agcccagguc cgaacucucc 60
auuccucugc agagcgucu 80

35
<210> 413
<211> 98
<212> RNA
<213> Homo sapiens

40
<400> 413
agaauaggca aaugaacagu aaauuggag gccuggggcc cucccugcug cuggagaagu 60
guuugcacgg gugggccuug ucuugaaag gaggugga 98

45
<210> 414
<211> 59
<212> RNA
<213> Homo sapiens

50
<400> 414
guccaggcag gagccggacu ggaccucagg gaagaggcug acccggcccc ucuugcggc 59

55
<210> 415
<211> 87
<212> RNA
<213> Homo sapiens

EP 3 150 707 A1

<400> 415
 cccagggcgcc cgcucccgac ccacgcccgcg ccgcccggguc ccuccucucc ggagaggcug 60
 ggucucgggac gcgcggcuca gcucggg 87
 5
 <210> 416
 <211> 67
 <212> RNA
 <213> Homo sapiens
 10
 <400> 416
 gcgcccucc ucucucuccg gugugcaau guguguguc gguguuaucc cggacaagag 60
 ggaggug 67
 15
 <210> 417
 <211> 80
 <212> RNA
 <213> Homo sapiens
 20
 <400> 417
 ugagaggccg caccuugccu ugcugcccgg gccgugcacc cgugggcccc agggcgacgc 60
 ggcggggggcg gcccuagcga 80
 25
 <210> 418
 <211> 80
 <212> RNA
 <213> Homo sapiens
 30
 <400> 418
 accugaggag ccagcccucc ucccgcaccc aaacuuggag cacuugaccu uuggcuguug 60
 gagggggcag gcucgcgggu 80
 35
 <210> 419
 <211> 96
 <212> RNA
 <213> Homo sapiens
 40
 <400> 419
 cgggccccgg gcgggcggga gggacgggac gcggugcagu guuguuuuuu cccccgcaa 60
 uauugcacuc gucccggccu ccggcccccc cggccc 96
 45
 <210> 420
 <211> 18
 <212> RNA
 <213> Homo sapiens
 50
 <400> 420
 ggugggcuuc ccggaggg 18
 55
 <210> 421
 <211> 15
 <212> RNA
 <213> Homo sapiens

EP 3 150 707 A1

	<400> 421 ggugggcuuc ccgga	15
5	<210> 422 <211> 23 <212> RNA <213> Homo sapiens	
10	<400> 422 gccccggcgc gggcggguuc ugg	23
15	<210> 423 <211> 16 <212> RNA <213> Homo sapiens	
20	<400> 423 ggagccccgg cgcggg	16
25	<210> 424 <211> 16 <212> RNA <213> Homo sapiens	
30	<400> 424 ggcggugggc ggcggg	16
35	<210> 425 <211> 15 <212> RNA <213> Homo sapiens	
40	<400> 425 ggccucucgg gaacu	15
45	<210> 426 <211> 18 <212> RNA <213> Homo sapiens	
50	<400> 426 ucuagguggg gagacuga	18
55	<210> 427 <211> 16 <212> RNA <213> Homo sapiens	
	<400> 427 guggggagac ugacgg	16
	<210> 428 <211> 22 <212> RNA <213> Homo sapiens	

EP 3 150 707 A1

	<400> 428		
	ugugggacug caaaugggag cu		22
5	<210> 429		
	<211> 22		
	<212> RNA		
	<213> Homo sapiens		
10	<400> 429		
	ugugggacug caaaugggag cu		22
15	<210> 430		
	<211> 16		
	<212> RNA		
	<213> Homo sapiens		
20	<400> 430		
	ugggggggaa gaaaag		16
25	<210> 431		
	<211> 16		
	<212> RNA		
	<213> Homo sapiens		
30	<400> 431		
	ugggggggaa gaaaag		16
35	<210> 432		
	<211> 24		
	<212> RNA		
	<213> Homo sapiens		
40	<400> 432		
	agacacauuu ggagagggaa ccuc		24
45	<210> 433		
	<211> 16		
	<212> RNA		
	<213> Homo sapiens		
50	<400> 433		
	agacacauuu ggagag		16
55	<210> 434		
	<211> 23		
	<212> RNA		
	<213> Homo sapiens		
60	<400> 434		
	cggggccgua gcacugucug aga		23
65	<210> 435		
	<211> 20		
	<212> RNA		
	<213> Homo sapiens		

EP 3 150 707 A1

	<400> 435 cggggccgua gcacugucug	20
5	<210> 436 <211> 25 <212> RNA <213> Homo sapiens	
10	<400> 436 gggacgaggg uuggggaaca ggugg	25
15	<210> 437 <211> 15 <212> RNA <213> Homo sapiens	
20	<400> 437 uggggaacag guggu	15
25	<210> 438 <211> 24 <212> RNA <213> Homo sapiens	
30	<400> 438 gaucggucga gagcguccug gcug	24
35	<210> 439 <211> 15 <212> RNA <213> Homo sapiens	
40	<400> 439 gcugggcggg gcgcg	15
45	<210> 440 <211> 19 <212> RNA <213> Homo sapiens	
50	<400> 440 uggcgggugc ggggguggg	19
55	<210> 441 <211> 15 <212> RNA <213> Homo sapiens	
	<400> 441 uggcgggugc ggggg	15
	<210> 442 <211> 25 <212> RNA <213> Homo sapiens	

EP 3 150 707 A1

	<400> 442 ggguggggau uuguugcauu acuug	25
5	<210> 443 <211> 20 <212> RNA <213> Homo sapiens	
10	<400> 443 ggguggggau uuguugcauu	20
15	<210> 444 <211> 21 <212> RNA <213> Homo sapiens	
20	<400> 444 uugaggagac augguggggg c	21
25	<210> 445 <211> 15 <212> RNA <213> Homo sapiens	
30	<400> 445 uugaggagac auggu	15
35	<210> 446 <211> 26 <212> RNA <213> Homo sapiens	
40	<400> 446 agggacggga cgcgugcag uguugu	26
45	<210> 447 <211> 15 <212> RNA <213> Homo sapiens	
50	<400> 447 ggcgggcggg aggga	15
55	<210> 448 <211> 23 <212> RNA <213> Homo sapiens	
	<400> 448 cggggcagcu caguacagga uac	23
	<210> 449 <211> 15 <212> RNA <213> Homo sapiens	

EP 3 150 707 A1

	<400> 449		
	agcucaguac aggau		15
5	<210> 450		
	<211> 21		
	<212> RNA		
	<213> Homo sapiens		
10	<400> 450		
	ugggaauggg gguaagggcc u		21
15	<210> 451		
	<211> 15		
	<212> RNA		
	<213> Homo sapiens		
20	<400> 451		
	cuucugagcc caggu		15
25	<210> 452		
	<211> 24		
	<212> RNA		
	<213> Homo sapiens		
30	<400> 452		
	caggcaggag ccggacugga ccuc		24
35	<210> 453		
	<211> 21		
	<212> RNA		
	<213> Homo sapiens		
40	<400> 453		
	uccaggcagg agccggacug g		21
45	<210> 454		
	<211> 22		
	<212> RNA		
	<213> Homo sapiens		
50	<400> 454		
	cugggcucgg gacgcgcggc uc		22
55	<210> 455		
	<211> 19		
	<212> RNA		
	<213> Homo sapiens		
60	<400> 455		
	cugggcucgg gacgcgcgg		19
65	<210> 456		
	<211> 20		
	<212> RNA		
	<213> Homo sapiens		

EP 3 150 707 A1

	<400> 456 cuccccggug ugcaaaugug	20
5	<210> 457 <211> 15 <212> RNA <213> Homo sapiens	
10	<400> 457 gugugcggug uuaug	15
15	<210> 458 <211> 20 <212> RNA <213> Homo sapiens	
20	<400> 458 ccccagggcg acgcggcggg	20
25	<210> 459 <211> 15 <212> RNA <213> Homo sapiens	
30	<400> 459 cgcggcgggg gcggc	15
35	<210> 460 <211> 20 <212> RNA <213> Homo sapiens	
40	<400> 460 uggcuguugg agggggcagg	20
45	<210> 461 <211> 15 <212> RNA <213> Homo sapiens	
50	<400> 461 ggagggggca ggcuc	15
55	<210> 462 <211> 24 <212> RNA <213> Homo sapiens	
	<400> 462 aaauaugcac ucgucccggc cucc	24
	<210> 463 <211> 15 <212> RNA <213> Homo sapiens	

EP 3 150 707 A1

	<400> 463 uauugcacuc guccc	15
5	<210> 464 <211> 21 <212> RNA <213> Homo sapiens	
10	<400> 464 cccggagcca ggaugcagcu c	21
15	<210> 465 <211> 22 <212> RNA <213> Homo sapiens	
20	<400> 465 gguggcccgg ccgugccuga gg	22
25	<210> 466 <211> 17 <212> RNA <213> Homo sapiens	
30	<400> 466 ccccgccacc gccuugg	17
35	<210> 467 <211> 24 <212> RNA <213> Homo sapiens	
40	<400> 467 ugggcgaggg gugggcucuc agag	24
45	<210> 468 <211> 17 <212> RNA <213> Homo sapiens	
50	<400> 468 gggagaaggg ucggggc	17
55	<210> 469 <211> 22 <212> RNA <213> Homo sapiens	
	<400> 469 gggaccaucc ugccugcugu gg	22
	<210> 470 <211> 23 <212> RNA <213> Homo sapiens	

EP 3 150 707 A1

	<400> 470		
	ucaauaggaa agagguggga ccu		23
5	<210> 471		
	<211> 22		
	<212> RNA		
	<213> Homo sapiens		
10	<400> 471		
	uagggauagg aggccaggau ga		22
15	<210> 472		
	<211> 23		
	<212> RNA		
	<213> Homo sapiens		
20	<400> 472		
	ucgaggacug guggaagggc cuu		23
25	<210> 473		
	<211> 22		
	<212> RNA		
	<213> Homo sapiens		
30	<400> 473		
	cuccuggggc ccgcacucuc gc		22
35	<210> 474		
	<211> 85		
	<212> RNA		
	<213> Homo sapiens		
40	<400> 474		
	uccuccccgg agccaggau cagcucaagc cacagcaggg uguuuagcgc ucuucagugg		60
	cuccagauug uggcgcuggu gcagg		85
45	<210> 475		
	<211> 115		
	<212> RNA		
	<213> Homo sapiens		
50	<400> 475		
	ggugccgagg gccguccggc auccuaggcg ggucgcugcg guaccucccu ccugucugug		60
	gcggggggau cccguggccg uguuuuccug guggcccggc cgugccugag guuuc		115
55	<210> 476		
	<211> 91		
	<212> RNA		
	<213> Homo sapiens		
	<400> 476		
	acgcccccg ccccgccacc gccuaggagg cugaccucu acuuucgguc ggucuucuuc		60
	ccugggcuuug guuugggggc gggggagugu c		91

EP 3 150 707 A1

<210> 477
 <211> 64
 <212> RNA
 <213> Homo sapiens
 5
 <400> 477
 ucugggagcag gggugggcuc ucagaggggc uggcaguacu gcucugaggc cugccucucc 60
 ccag 64
 10
 <210> 478
 <211> 86
 <212> RNA
 <213> Homo sapiens
 15
 <400> 478
 agggagaagg gucggggcag ggagggcagg gcaggcucug gggugggggg ucugugaguc 60
 agccacggcu cugcccacgu cucccc 86
 20
 <210> 479
 <211> 83
 <212> RNA
 <213> Homo sapiens
 25
 <400> 479
 acggcaucuu ugcacucagc aggcaggcug gugcagcccg ugguggggga ccauccugcc 60
 ugcugugggg uaaggacggc ugu 83
 30
 <210> 480
 <211> 98
 <212> RNA
 <213> Homo sapiens
 35
 <400> 480
 cuuggucaau aggaaagagg ugggaccucc uggcuuuucc ucugcagcau ggcucggacc 60
 uagugcaaug uuuaagcucc ccucucuuc cuguucag 98
 40
 <210> 481
 <211> 69
 <212> RNA
 <213> Homo sapiens
 45
 <400> 481
 gggcuuaggg augggaggcc aggaugaaga uuaaucccua auccccaaca cuggccuugc 60
 uaucgccag 69
 50
 <210> 482
 <211> 63
 <212> RNA
 <213> Homo sapiens
 55
 <400> 482

EP 3 150 707 A1

	gagucgagga cugguggaag ggccuuuccc cucagaccaa ggcccuggcc ccagcuucuu	60
	cuc	63
5	<210> 483 <211> 84 <212> RNA <213> Homo sapiens	
10	<400> 483 gcuggcgucg gugcugggga gggcccccg ggugggccuc ugcucuggcc ccuccuggg	60
	cccgcacucu cgcucugggc ccgc	84
15	<210> 484 <211> 23 <212> RNA <213> Homo sapiens	
20	<400> 484 ggcccggccg ugccugaggu uuc	23
25	<210> 485 <211> 15 <212> RNA <213> Homo sapiens	
30	<400> 485 uguuuuccug guggc	15
35	<210> 486 <211> 23 <212> RNA <213> Homo sapiens	
40	<400> 486 agggucgggg caggagggc agg	23
45	<210> 487 <211> 15 <212> RNA <213> Homo sapiens	
50	<400> 487 ggagaaggu cggg	15
55	<210> 488 <211> 24 <212> RNA <213> Homo sapiens	
	<400> 488 ucgaggacug guggaagggc cuuu	24
	<210> 489 <211> 17	

EP 3 150 707 A1

	<212> RNA	
	<213> Homo sapiens	
5	<400> 489	
	acugguggaa gggccuu	17
	<210> 490	
	<211> 23	
10	<212> RNA	
	<213> Homo sapiens	
	<400> 490	
	cuccuggggc cgcacucuc gcu	23
15	<210> 491	
	<211> 18	
	<212> RNA	
	<213> Homo sapiens	
20	<400> 491	
	cuccuggggc cgcacuc	18
25	<210> 492	
	<211> 25	
	<212> RNA	
	<213> Homo sapiens	
	<400> 492	
30	ucggggcaug gggaggag gcugg	25
35	<210> 493	
	<211> 23	
	<212> RNA	
	<213> Homo sapiens	
	<400> 493	
	caggggcugg gguucaggu ucu	23
40	<210> 494	
	<211> 20	
	<212> RNA	
	<213> Homo sapiens	
45	<400> 494	
	guggguuggg gcgggcucug	20
50	<210> 495	
	<211> 69	
	<212> RNA	
	<213> Homo sapiens	
	<400> 495	
	gaaccucggg gcauggggga gggaggcugg acaggagagg gcucaccag gccuguccu	60
55	cugccccag	69
	ggcuuagaaa caguccuag guaggauug gggaggagcu aagaagcccc uacaggccc	60

agagguggggg acugagccuu aguugg 86

5 <210> 497
 <211> 65
 <212> RNA
 <213> Homo sapiens

<400> 497
 10 gagaauugggg ggacagaugg agaggacaca ggcuggcacu gaggucuccu ccacuuuccu 60
 ccuag 65

15 <210> 498
 <211> 19
 <212> RNA
 <213> Homo sapiens

<400> 498
 20 guggguuggg gcgggcucu 19

25 <210> 499
 <211> 19
 <212> RNA
 <213> Homo sapiens

<400> 499
 30 guggguuggg gcgggcucu 19

Claims

- 35 1. A kit for the detection of pancreatic cancer, comprising a nucleic acid(s) capable of specifically binding to at least one or more polynucleotides selected from the group consisting of the following pancreatic cancer markers: miR-6893-5p, miR-6075, miR-6820-5p, miR-4294, miR-6729-5p, miR-4476, miR-6836-3p, miR-6765-3p, miR-6799-5p, miR-4530, miR-7641, miR-4454, miR-615-5p, miR-8073, miR-663a, miR-4634, miR-4450, miR-4792, miR-665, miR-7975, miR-7109-5p, miR-6789-5p, miR-4497, miR-6877-5p, miR-6880-5p, miR-7977, miR-4734, miR-6821-5p, miR-8089, miR-5585-3p, miR-6085, miR-6845-5p, miR-4651, miR-4433-3p, miR-1231, miR-4665-5p, miR-7114-5p, miR-1238-5p, miR-8069, miR-4732-5p, miR-619-5p, miR-3622a-5p, miR-1260a, miR-6741-5p, miR-6781-5p, miR-6125, miR-6805-5p, miR-6132, miR-6872-3p, miR-6875-5p, miR-1908-3p, miR-4433b-3p, miR-4736, miR-5100, miR-6724-5p, miR-7107-5p, miR-6726-5p, miR-3185, miR-4638-5p, miR-1273g-3p, miR-6778-5p, miR-328-5p, miR-3679-3p, miR-1228-3p, miR-6779-5p, miR-4723-5p, miR-6850-5p, miR-760, miR-7704, miR-8072, miR-4486, miR-1913, miR-4656, miR-1260b, miR-7106-5p, miR-6889-5p, miR-6780b-5p, miR-6090, miR-4534, miR-4449, miR-5195-3p, miR-1202, miR-4467, miR-6515-3p, miR-4281, miR-4505, miR-4484, miR-6805-3p, miR-3135b, miR-3162-5p, miR-6768-5p, miR-6721-5p, miR-1227-5p, miR-6722-3p, miR-4286, miR-4746-3p, miR-6727-5p, miR-6816-5p, miR-4741, miR-4508, miR-940, miR-4327, miR-4665-3p, miR-718, miR-1203, miR-663b, miR-4258, miR-4649-5p, miR-4516, miR-3619-3p, miR-6826-5p, miR-6757-5p, miR-3131, miR-1343-3p, miR-6775-5p, miR-6813-5p, and miR-3940-5p.
- 50 2. The kit according to claim 1, wherein miR-6893-5p is hsa-miR-6893-5p, miR-6075 is hsa-miR-6075, miR-6820-5p is hsa-miR-6820-5p, miR-4294 is hsa-miR-4294, miR-6729-5p is hsa-miR-6729-5p, miR-4476 is hsa-miR-4476, miR-6836-3p is hsa-miR-6836-3p, miR-6765-3p is hsa-miR-6765-3p, miR-6799-5p is hsa-miR-6799-5p, miR-4530 is hsa-miR-4530, miR-7641 is hsa-miR-7641, miR-4454 is hsa-miR-4454, miR-615-5p is hsa-miR-615-5p, miR-8073 is hsa-miR-8073, miR-663a is hsa-miR-663a, miR-4634 is hsa-miR-4634, miR-4450 is hsa-miR-4450, miR-4792 is hsa-miR-4792, miR-665 is hsa-miR-665, miR-7975 is hsa-miR-7975, miR-7109-5p is hsa-miR-7109-5p, miR-6789-5p is hsa-miR-6789-5p, miR-4497 is hsa-miR-4497, miR-6877-5p is hsa-miR-6877-5p, miR-6880-5p is hsa-miR-6880-5p, miR-7977 is hsa-miR-7977, miR-4734 is hsa-miR-4734, miR-6821-5p is hsa-miR-6821-5p, miR-
- 55

8089 is hsa-miR-8089, miR-5585-3p is hsa-miR-5585-3p, miR-6085 is hsa-miR-6085, miR-6845-5p is hsa-miR-6845-5p, miR-4651 is hsa-miR-4651, miR-4433-3p is hsa-miR-4433-3p, miR-1231 is hsa-miR-1231, miR-4665-5p is hsa-miR-4665-5p, miR-7114-5p is hsa-miR-7114-5p, miR-1238-5p is hsa-miR-1238-5p, miR-8069 is hsa-miR-8069, miR-4732-5p is hsa-miR-4732-5p, miR-619-5p is hsa-miR-619-5p, miR-3622a-5p is hsa-miR-3622a-5p, miR-1260a is hsa-miR-1260a, miR-6741-5p is hsa-miR-6741-5p, miR-6781-5p is hsa-miR-6781-5p, miR-6125 is hsa-miR-6125, miR-6805-5p is hsa-miR-6805-5p, miR-6132 is hsa-miR-6132, miR-6872-3p is hsa-miR-6872-3p, miR-6875-5p is hsa-miR-6875-5p, miR-1908-3p is hsa-miR-1908-3p, miR-4433b-3p is hsa-miR-4433b-3p, miR-4736 is hsa-miR-4736, miR-5100 is hsa-miR-5100, miR-6724-5p is hsa-miR-6724-5p, miR-7107-5p is hsa-miR-7107-5p, miR-6726-5p is hsa-miR-6726-5p, miR-3185 is hsa-miR-3185, miR-4638-5p is hsa-miR-4638-5p, miR-1273g-3p is hsa-miR-1273g-3p, miR-6778-5p is hsa-miR-6778-5p, miR-328-5p is hsa-miR-328-5p, miR-3679-3p is hsa-miR-3679-3p, miR-1228-3p is hsa-miR-1228-3p, miR-6779-5p is hsa-miR-6779-5p, miR-4723-5p is hsa-miR-4723-5p, miR-6850-5p is hsa-miR-6850-5p, miR-760 is hsa-miR-760, miR-7704 is hsa-miR-7704, miR-8072 is hsa-miR-8072, miR-4486 is hsa-miR-4486, miR-1913 is hsa-miR-1913, miR-4656 is hsa-miR-4656, miR-1260b is hsa-miR-1260b, miR-7106-5p is hsa-miR-7106-5p, miR-6889-5p is hsa-miR-6889-5p, miR-6780b-5p is hsa-miR-6780b-5p, miR-6090 is hsa-miR-6090, miR-4534 is hsa-miR-4534, miR-4449 is hsa-miR-4449, miR-5195-3p is hsa-miR-5195-3p, miR-1202 is hsa-miR-1202, miR-4467 is hsa-miR-4467, miR-6515-3p is hsa-miR-6515-3p, miR-4281 is hsa-miR-4281, miR-4505 is hsa-miR-4505, miR-4484 is hsa-miR-4484, miR-6805-3p is hsa-miR-6805-3p, miR-3135b is hsa-miR-3135b, miR-3162-5p is hsa-miR-3162-5p, miR-6768-5p is hsa-miR-6768-5p, miR-6721-5p is hsa-miR-6721-5p, miR-1227-5p is hsa-miR-1227-5p, miR-6722-3p is hsa-miR-6722-3p, miR-4286 is hsa-miR-4286, miR-4746-3p is hsa-miR-4746-3p, miR-6727-5p is hsa-miR-6727-5p, miR-6816-5p is hsa-miR-6816-5p, miR-4741 is hsa-miR-4741, miR-4508 is hsa-miR-4508, miR-940 is hsa-miR-940, miR-4327 is hsa-miR-4327, miR-4665-3p is hsa-miR-4665-3p, miR-718 is hsa-miR-718, miR-1203 is hsa-miR-1203, miR-663b is hsa-miR-663b, miR-4258 is hsa-miR-4258, miR-4649-5p is hsa-miR-4649-5p, miR-4516 is hsa-miR-4516, miR-3619-3p is hsa-miR-3619-3p, miR-6826-5p is hsa-miR-6826-5p, miR-6757-5p is hsa-miR-6757-5p, miR-3131 is hsa-miR-3131, miR-1343-3p is hsa-miR-1343-3p, miR-6775-5p is hsa-miR-6775-5p, miR-6813-5p is hsa-miR-6813-5p, and miR-3940-5p is hsa-miR-3940-5p.

3. The kit according to claim 1 or 2, wherein the nucleic acid(s) is a polynucleotide(s) 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: 1 to 104, 464 to 473, and 492 to 494 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: 1 to 104, 464 to 473, and 492 to 494;

(c) a polynucleotide consisting of a nucleotide sequence complementary to a nucleotide sequence represented by any of SEQ ID NOs: 1 to 104, 464 to 473, and 492 to 494 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: 1 to 104, 464 to 473, and 492 to 494 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).

4. The kit according to any one of claims 1 to 3, wherein the kit further comprises a nucleic acid or nucleotide acids capable of specifically binding to at least one or more polynucleotides selected from the group consisting of the following other pancreatic cancer markers: miR-125a-3p, miR-204-3p, miR-1469, miR-575, miR-150-3p, miR-423-5p, miR-564, miR-3188, miR-1246, miR-602, miR-1290, miR-16-5p, miR-451a, miR-24-3p, miR-187-5p, miR-1908-5p, miR-371a-5p, and miR-550a-5p.

5. The kit according to claim 4, wherein miR-125a-3p is hsa-miR-125a-3p, miR-204-3p is hsa-miR-204-3p, miR-1469 is hsa-miR-1469, miR-575 is hsa-miR-575, miR-150-3p is hsa-miR-150-3p, miR-423-5p is hsa-miR-423-5p, miR-564 is hsa-miR-564, miR-3188 is hsa-miR-3188, miR-1246 is hsa-miR-1246, miR-602 is hsa-miR-602, miR-1290 is hsa-miR-1290, miR-16-5p is hsa-miR-16-5p, miR-451a is hsa-miR-451a, miR-24-3p is hsa-miR-24-3p, miR-187-5p is hsa-miR-187-5p, miR-1908-5p is hsa-miR-1908-5p, miR-371a-5p is hsa-miR-371a-5p, and miR-550a-5p is hsa-miR-550a-5p.

6. The kit according to claim 4 or 5, wherein the nucleic acid(s) is a polynucleotide(s) 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: 105 to 122 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: 105 to 122;
- 5 (h) a polynucleotide consisting of a nucleotide sequence complementary to a nucleotide sequence represented by any of SEQ ID NOs: 105 to 122 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: 105 to 122 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t; and
- 10 (j) a polynucleotide hybridizing under stringent conditions to any of the polynucleotides (f) to (i).
7. The kit according to any one of claims 1 to 6, wherein the kit further comprises a nucleic acid(s) capable of specifically binding to at least one or more polynucleotide(s) selected from the group consisting of the following other pancreatic cancer markers: miR-4417, miR-4707-5p, miR-7847-3p, miR-2861, miR-4513, miR-7111-5p, miR-6777-5p, miR-7113-3p, miR-4648, miR-3184-5p, miR-4271, miR-6791-5p, miR-642a-3p, miR-7108-5p, miR-128-1-5p, miR-5196-5p, miR-3178, miR-3656, miR-92a-2-5p, miR-6769b-5p, miR-4689, miR-6076, miR-92b-5p, miR-6774-5p, miR-486-3p, miR-6806-5p, miR-6842-5p, miR-6716-5p, miR-557, miR-4673, miR-4674, miR-4442, miR-1915-3p, miR-4687-3p, and miR-92b-3p.
- 15 8. The kit according to claim 7, wherein miR-4417 is hsa-miR-4417, miR-4707-5p is hsa-miR-4707-5p, miR-7847-3p is hsa-miR-7847-3p, miR-2861 is hsa-miR-2861, miR-4513 is hsa-miR-4513, miR-7111-5p is hsa-miR-7111-5p, miR-6777-5p is hsa-miR-6777-5p, miR-7113-3p is hsa-miR-7113-3p, miR-4648 is hsa-miR-4648, miR-3184-5p is hsa-miR-3184-5p, miR-4271 is hsa-miR-4271, miR-6791-5p is hsa-miR-6791-5p, miR-642a-3p is hsa-miR-642a-3p, miR-7108-5p is hsa-miR-7108-5p, miR-128-1-5p is hsa-miR-128-1-5p, miR-5196-5p is hsa-miR-5196-5p, miR-3178 is hsa-miR-3178, miR-3656 is hsa-miR-3656, miR-92a-2-5p is hsa-miR-92a-2-5p, miR-6769b-5p is hsa-miR-6769b-5p, miR-4689 is hsa-miR-4689, miR-6076 is hsa-miR-6076, miR-92b-5p is hsa-miR-92b-5p, miR-6774-5p is hsa-miR-6774-5p, miR-486-3p is hsa-miR-486-3p, miR-6806-5p is hsa-miR-6806-5p, miR-6842-5p is hsa-miR-6842-5p, miR-6716-5p is hsa-miR-6716-5p, miR-557 is hsa-miR-557, miR-4673 is hsa-miR-4673, miR-4674 is hsa-miR-4674, miR-4442 is hsa-miR-4442, miR-1915-3p is hsa-miR-1915-3p, miR-4687-3p is hsa-miR-4687-3p, and miR-92b-3p is hsa-miR-92b-3p.
- 25 9. The kit according to claim 7 or 8, wherein the nucleic acid(s) is a polynucleotide(s) selected from the group consisting of the following polynucleotides (k) to (o):
- 30 (k) a polynucleotide consisting of a nucleotide sequence represented by any of SEQ ID NOs: 349 to 383 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: 349 to 383;
- 35 (m) a polynucleotide consisting of a nucleotide sequence complementary to a nucleotide sequence represented by any of SEQ ID NOs: 349 to 383 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: 349 to 383 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t; and
- 40 (o) a polynucleotide hybridizing under stringent conditions to any of the polynucleotides (k) to (n).
- 45 10. The kit according to any one of claims 1 to 9, 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 pancreatic cancer markers according to claim 1 or 2.
- 50 11. A device for the detection of pancreatic cancer, comprising a nucleic acid(s) capable of specifically binding to at least one or more polynucleotides selected from the following pancreatic cancer markers: miR-6893-5p, miR-6075, miR-6820-5p, miR-4294, miR-6729-5p, miR-4476, miR-6836-3p, miR-6765-3p, miR-6799-5p, miR-4530, miR-7641, miR-4454, miR-615-5p, miR-8073, miR-663a, miR-4634, miR-4450, miR-4792, miR-665, miR-7975, miR-7109-5p, miR-6789-5p, miR-4497, miR-6877-5p, miR-6880-5p, miR-7977, miR-4734, miR-6821-5p, miR-8089, miR-5585-3p,
- 55

miR-6085, miR-6845-5p, miR-4651, miR-4433-3p, miR-1231, miR-4665-5p, miR-7114-5p, miR-1238-5p, miR-8069, miR-4732-5p, miR-619-5p, miR-3622a-5p, miR-1260a, miR-6741-5p, miR-6781-5p, miR-6125, miR-6805-5p, miR-6132, miR-6872-3p, miR-6875-5p, miR-1908-3p, miR-4433b-3p, miR-4736, miR-5100, miR-6724-5p, miR-7107-5p, miR-6726-5p, miR-3185, miR-4638-5p, miR-1273g-3p, miR-6778-5p, miR-328-5p, miR-3679-3p, miR-1228-3p, miR-6779-5p, miR-4723-5p, miR-6850-5p, miR-760, miR-7704, miR-8072, miR-4486, miR-1913, miR-4656, miR-1260b, miR-7106-5p, miR-6889-5p, miR-6780b-5p, miR-6090, miR-4534, miR-4449, miR-5195-3p, miR-1202, miR-4467, miR-6515-3p, miR-4281, miR-4505, miR-4484, miR-6805-3p, miR-3135b, miR-3162-5p, miR-6768-5p, miR-6721-5p, miR-1227-5p, miR-6722-3p, miR-4286, miR-4746-3p, miR-6727-5p, miR-6816-5p, miR-4741, miR-4508, miR-940, miR-4327, miR-4665-3p, miR-718, miR-1203, miR-663b, miR-4258, miR-4649-5p, miR-4516, miR-3619-3p, miR-6826-5p, miR-6757-5p, miR-3131, miR-1343-3p, miR-6775-5p, miR-6813-5p, and miR-3940-5p.

12. The device according to claim 11, wherein miR-6893-5p is hsa-miR-6893-5p, miR-6075 is hsa-miR-6075, miR-6820-5p is hsa-miR-6820-5p, miR-4294 is hsa-miR-4294, miR-6729-5p is hsa-miR-6729-5p, miR-4476 is hsa-miR-4476, miR-6836-3p is hsa-miR-6836-3p, miR-6765-3p is hsa-miR-6765-3p, miR-6799-5p is hsa-miR-6799-5p, miR-4530 is hsa-miR-4530, miR-7641 is hsa-miR-7641, miR-4454 is hsa-miR-4454, miR-615-5p is hsa-miR-615-5p, miR-8073 is hsa-miR-8073, miR-663a is hsa-miR-663a, miR-4634 is hsa-miR-4634, miR-4450 is hsa-miR-4450, miR-4792 is hsa-miR-4792, miR-665 is hsa-miR-665, miR-7975 is hsa-miR-7975, miR-7109-5p is hsa-miR-7109-5p, miR-6789-5p is hsa-miR-6789-5p, miR-4497 is hsa-miR-4497, miR-6877-5p is hsa-miR-6877-5p, miR-6880-5p is hsa-miR-6880-5p, miR-7977 is hsa-miR-7977, miR-4734 is hsa-miR-4734, miR-6821-5p is hsa-miR-6821-5p, miR-8089 is hsa-miR-8089, miR-5585-3p is hsa-miR-5585-3p, miR-6085 is hsa-miR-6085, miR-6845-5p is hsa-miR-6845-5p, miR-4651 is hsa-miR-4651, miR-4433-3p is hsa-miR-4433-3p, miR-1231 is hsa-miR-1231, miR-4665-5p is hsa-miR-4665-5p, miR-7114-5p is hsa-miR-7114-5p, miR-1238-5p is hsa-miR-1238-5p, miR-8069 is hsa-miR-8069, miR-4732-5p is hsa-miR-4732-5p, miR-619-5p is hsa-miR-619-5p, miR-3622a-5p is hsa-miR-3622a-5p, miR-1260a is hsa-miR-1260a, miR-6741-5p is hsa-miR-6741-5p, miR-6781-5p is hsa-miR-6781-5p, miR-6125 is hsa-miR-6125, miR-6805-5p is hsa-miR-6805-5p, miR-6132 is hsa-miR-6132, miR-6872-3p is hsa-miR-6872-3p, miR-6875-5p is hsa-miR-6875-5p, miR-1908-3p is hsa-miR-1908-3p, miR-4433b-3p is hsa-miR-4433b-3p, miR-4736 is hsa-miR-4736, miR-5100 is hsa-miR-5100, miR-6724-5p is hsa-miR-6724-5p, miR-7107-5p is hsa-miR-7107-5p, miR-6726-5p is hsa-miR-6726-5p, miR-3185 is hsa-miR-3185, miR-4638-5p is hsa-miR-4638-5p, miR-1273g-3p is hsa-miR-1273g-3p, miR-6778-5p is hsa-miR-6778-5p, miR-328-5p is hsa-miR-328-5p, miR-3679-3p is hsa-miR-3679-3p, miR-1228-3p is hsa-miR-1228-3p, miR-6779-5p is hsa-miR-6779-5p, miR-4723-5p is hsa-miR-4723-5p, miR-6850-5p is hsa-miR-6850-5p, miR-760 is hsa-miR-760, miR-7704 is hsa-miR-7704, miR-8072 is hsa-miR-8072, miR-4486 is hsa-miR-4486, miR-1913 is hsa-miR-1913, miR-4656 is hsa-miR-4656, miR-1260b is hsa-miR-1260b, miR-7106-5p is hsa-miR-7106-5p, miR-6889-5p is hsa-miR-6889-5p, miR-6780b-5p is hsa-miR-6780b-5p, miR-6090 is hsa-miR-6090, miR-4534 is hsa-miR-4534, miR-4449 is hsa-miR-4449, miR-5195-3p is hsa-miR-5195-3p, miR-1202 is hsa-miR-1202, miR-4467 is hsa-miR-4467, miR-6515-3p is hsa-miR-6515-3p, miR-4281 is hsa-miR-4281, miR-4505 is hsa-miR-4505, miR-4484 is hsa-miR-4484, miR-6805-3p is hsa-miR-6805-3p, miR-3135b is hsa-miR-3135b, miR-3162-5p is hsa-miR-3162-5p, miR-6768-5p is hsa-miR-6768-5p, miR-6721-5p is hsa-miR-6721-5p, miR-1227-5p is hsa-miR-1227-5p, miR-6722-3p is hsa-miR-6722-3p, miR-4286 is hsa-miR-4286, miR-4746-3p is hsa-miR-4746-3p, miR-6727-5p is hsa-miR-6727-5p, miR-6816-5p is hsa-miR-6816-5p, miR-4741 is hsa-miR-4741, miR-4508 is hsa-miR-4508, miR-940 is hsa-miR-940, miR-4327 is hsa-miR-4327, miR-4665-3p is hsa-miR-4665-3p, miR-718 is hsa-miR-718, miR-1203 is hsa-miR-1203, miR-663b is hsa-miR-663b, miR-4258 is hsa-miR-4258, miR-4649-5p is hsa-miR-4649-5p, miR-4516 is hsa-miR-4516, miR-3619-3p is hsa-miR-3619-3p, miR-6826-5p is hsa-miR-6826-5p, miR-6757-5p is hsa-miR-6757-5p, miR-3131 is hsa-miR-3131, miR-1343-3p is hsa-miR-1343-3p, miR-6775-5p is hsa-miR-6775-5p, miR-6813-5p is hsa-miR-6813-5p, and miR-3940-5p is hsa-miR-3940-5p.

13. The device according to claim 11 or 12, wherein the nucleic acid(s) is a polynucleotide(s) 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: 1 to 104, 464 to 473, and 492 to 494 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: 1 to 104, 464 to 473, and 492 to 494;
- (c) a polynucleotide consisting of a nucleotide sequence complementary to a nucleotide sequence represented by any of SEQ ID NOs: 1 to 104, 464 to 473, and 492 to 494 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

EP 3 150 707 A1

by any of SEQ ID NOs: 1 to 104, 464 to 473, and 492 to 494 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).

5 **14.** The device according to any one of claims 11 to 13, wherein the device further comprises a nucleic acid(s) capable of specifically binding to at least one or more polynucleotides selected from the group consisting of the following other pancreatic cancer markers: miR-125a-3p, miR-204-3p, miR-1469, miR-575, miR-150-3p, miR-423-5p, miR-564, miR-3188, miR-1246, miR-602, miR-1290, miR-16-5p, miR-451a, miR-24-3p, miR-187-5p, miR-1908-5p, miR-371a-5p, and miR-550a-5p.

10 **15.** The device according to claim 14, wherein miR-125a-3p is hsa-miR-125a-3p, miR-204-3p is hsa-miR-204-3p, miR-1469 is hsa-miR-1469, miR-575 is hsa-miR-575, miR-150-3p is hsa-miR-150-3p, miR-423-5p is hsa-miR-423-5p, miR-564 is hsa-miR-564, miR-3188 is hsa-miR-3188, miR-1246 is hsa-miR-1246, miR-602 is hsa-miR-602, miR-1290 is hsa-miR-1290, miR-16-5p is hsa-miR-16-5p, miR-451a is hsa-miR-451a, miR-24-3p is hsa-miR-24-3p, miR-187-5p is hsa-miR-187-5p, miR-1908-5p is hsa-miR-1908-5p, miR-371a-5p is hsa-miR-371a-5p, and miR-550a-5p is hsa-miR-550a-5p.

15 **16.** The device according to claim 14 or 15, wherein the nucleic acid(s) is/are a polynucleotide(s) selected from the group consisting of the following polynucleotides (f) to (j):

20 (f) a polynucleotide consisting of a nucleotide sequence represented by any of SEQ ID NOs: 105 to 122 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: 105 to 122;

25 (h) a polynucleotide consisting of a nucleotide sequence complementary to a nucleotide sequence represented by any of SEQ ID NOs: 105 to 122 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;

30 (i) a polynucleotide comprising a nucleotide sequence complementary to a nucleotide sequence represented by any of SEQ ID NOs: 105 to 122 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).

35 **17.** The device according to any one of claims 11 to 16, wherein the device further comprises a nucleic acid(s) capable of specifically binding to at least one or more polynucleotides selected from the group consisting of the following other pancreatic cancer markers: miR-4417, miR-4707-5p, miR-7847-3p, miR-2861, miR-4513, miR-7111-5p, miR-6777-5p, miR-7113-3p, miR-4648, miR-3184-5p, miR-4271, miR-6791-5p, miR-642a-3p, miR-7108-5p, miR-128-1-5p, miR-5196-5p, miR-3178, miR-3656, miR-92a-2-5p, miR-6769b-5p, miR-4689, miR-6076, miR-92b-5p, miR-6774-5p, miR-486-3p, miR-6806-5p, miR-6842-5p, miR-6716-5p, miR-557, miR-4673, miR-4674, miR-4442, miR-1915-3p, miR-4687-3p, and miR-92b-3p.

40 **18.** The device according to claim 17, wherein miR-4417 is hsa-miR-4417, miR-4707-5p is hsa-miR-4707-5p, miR-7847-3p is hsa-miR-7847-3p, miR-2861 is hsa-miR-2861, miR-4513 is hsa-miR-4513, miR-7111-5p is hsa-miR-7111-5p, miR-6777-5p is hsa-miR-6777-5p, miR-7113-3p is hsa-miR-7113-3p, miR-4648 is hsa-miR-4648, miR-3184-5p is hsa-miR-3184-5p, miR-4271 is hsa-miR-4271, miR-6791-5p is hsa-miR-6791-5p, miR-642a-3p is hsa-miR-642a-3p, miR-7108-5p is hsa-miR-7108-5p, miR-128-1-5p is hsa-miR-128-1-5p, miR-5196-5p is hsa-miR-5196-5p, miR-3178 is hsa-miR-3178, miR-3656 is hsa-miR-3656, miR-92a-2-5p is hsa-miR-92a-2-5p, miR-6769b-5p is hsa-miR-6769b-5p, miR-4689 is hsa-miR-4689, miR-6076 is hsa-miR-6076, miR-92b-5p is hsa-miR-92b-5p, miR-6774-5p is hsa-miR-6774-5p, miR-486-3p is hsa-miR-486-3p, miR-6806-5p is hsa-miR-6806-5p, miR-6842-5p is hsa-miR-6842-5p, miR-6716-5p is hsa-miR-6716-5p, miR-557 is hsa-miR-557, miR-4673 is hsa-miR-4673, miR-4674 is hsa-miR-4674, miR-4442 is hsa-miR-4442, miR-1915-3p is hsa-miR-1915-3p, miR-4687-3p is hsa-miR-4687-3p, and miR-92b-3p is hsa-miR-92b-3p.

45 **19.** The device according to claim 17 or 18, wherein the nucleic acid(s) is a polynucleotide(s) selected from the group consisting of the following polynucleotides (k) to (o):

50 (k) a polynucleotide consisting of a nucleotide sequence represented by any of SEQ ID NOs: 349 to 383 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: 349 to 383;

(m) a polynucleotide consisting of a nucleotide sequence complementary to a nucleotide sequence represented by any of SEQ ID NOs: 349 to 383 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: 349 to 383 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).

20. The device according to any one of claims 11 to 19, wherein the device is a device for measurement by a hybridization technique.

21. The device according to claim 20, wherein the hybridization technique is a nucleic acid array technique.

22. The device according to any one of claims 11 to 21, 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 pancreatic cancer markers according to claim 11 or 12.

23. A method for detecting pancreatic cancer, comprising: measuring an expression level(s) of a target nucleic acid(s) in a sample from a subject using a kit according to any one of claims 1 to 10 or a device according to any one of claims 11 to 22; and evaluating *in vitro* whether or not the subject has pancreatic cancer using both of the measured expression level(s) and a control expression level(s) in a sample from a healthy subject measured in the same way.

24. The method according to claim 23, wherein the subject is a human.

25. The method according to claim 23 or 24, wherein the sample is blood, serum, or plasma.

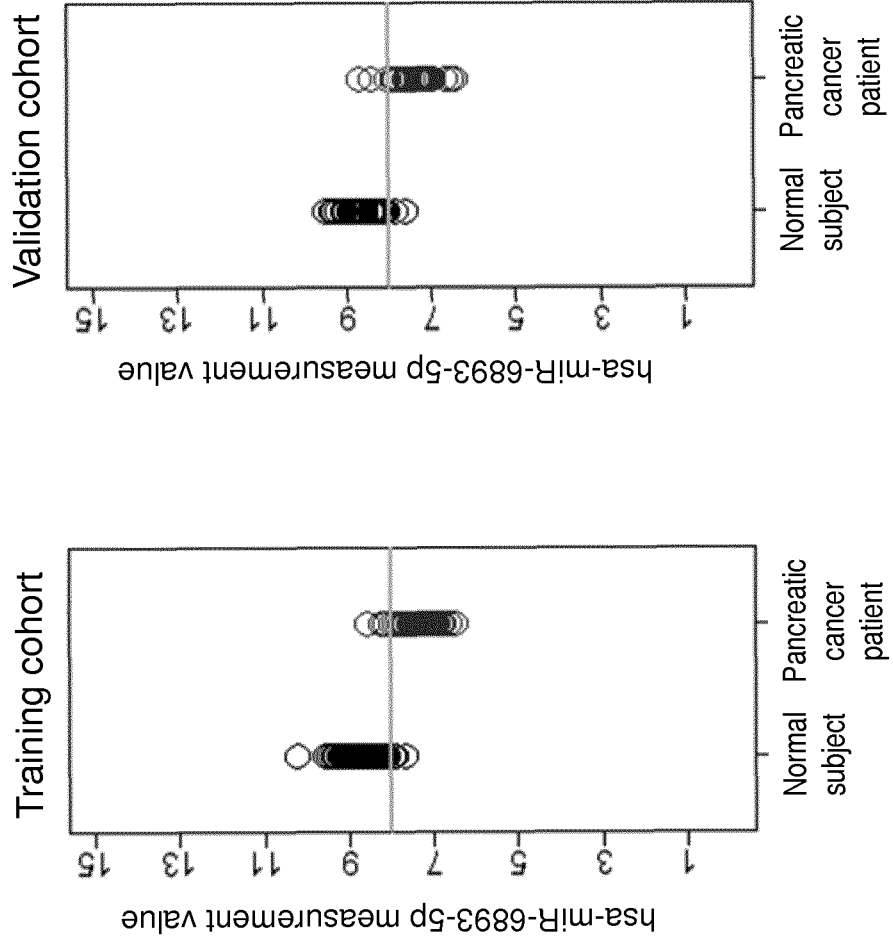


Fig. 2

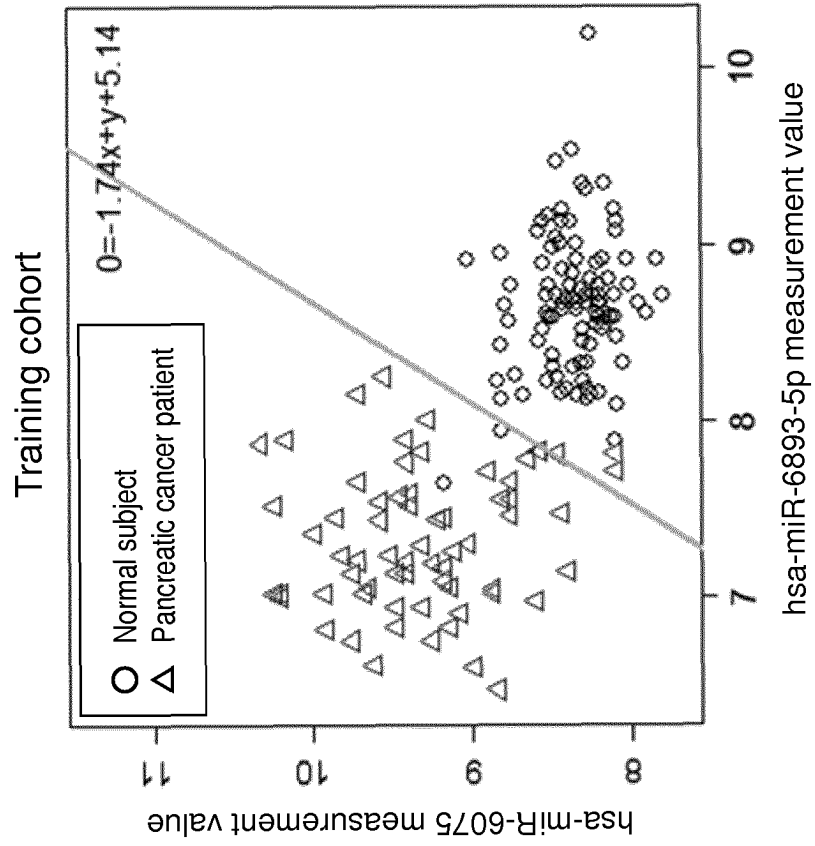
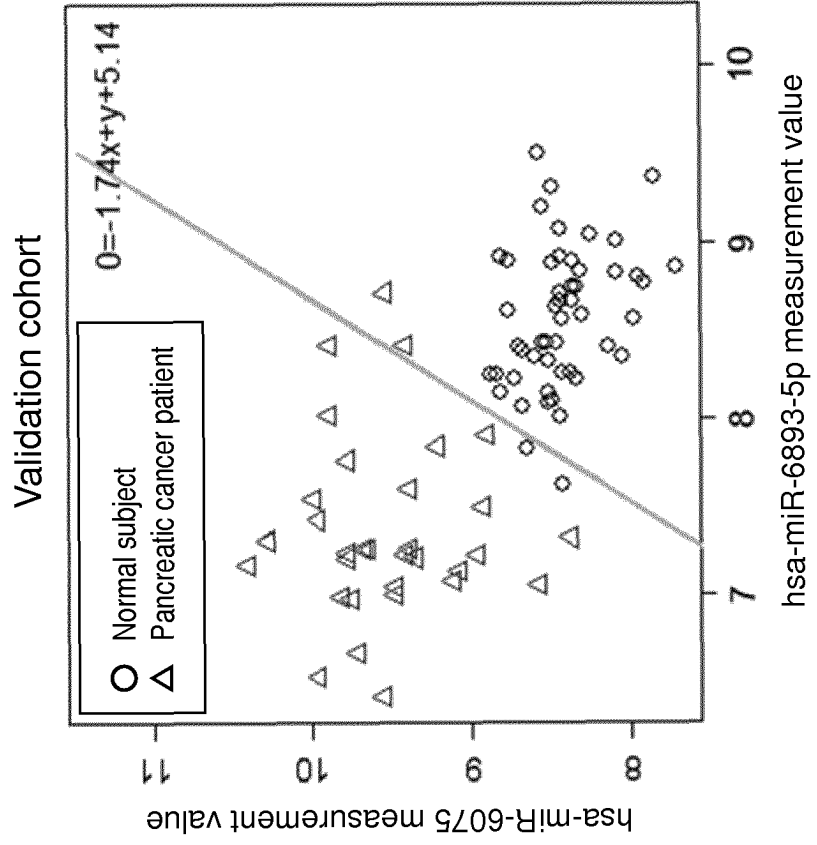
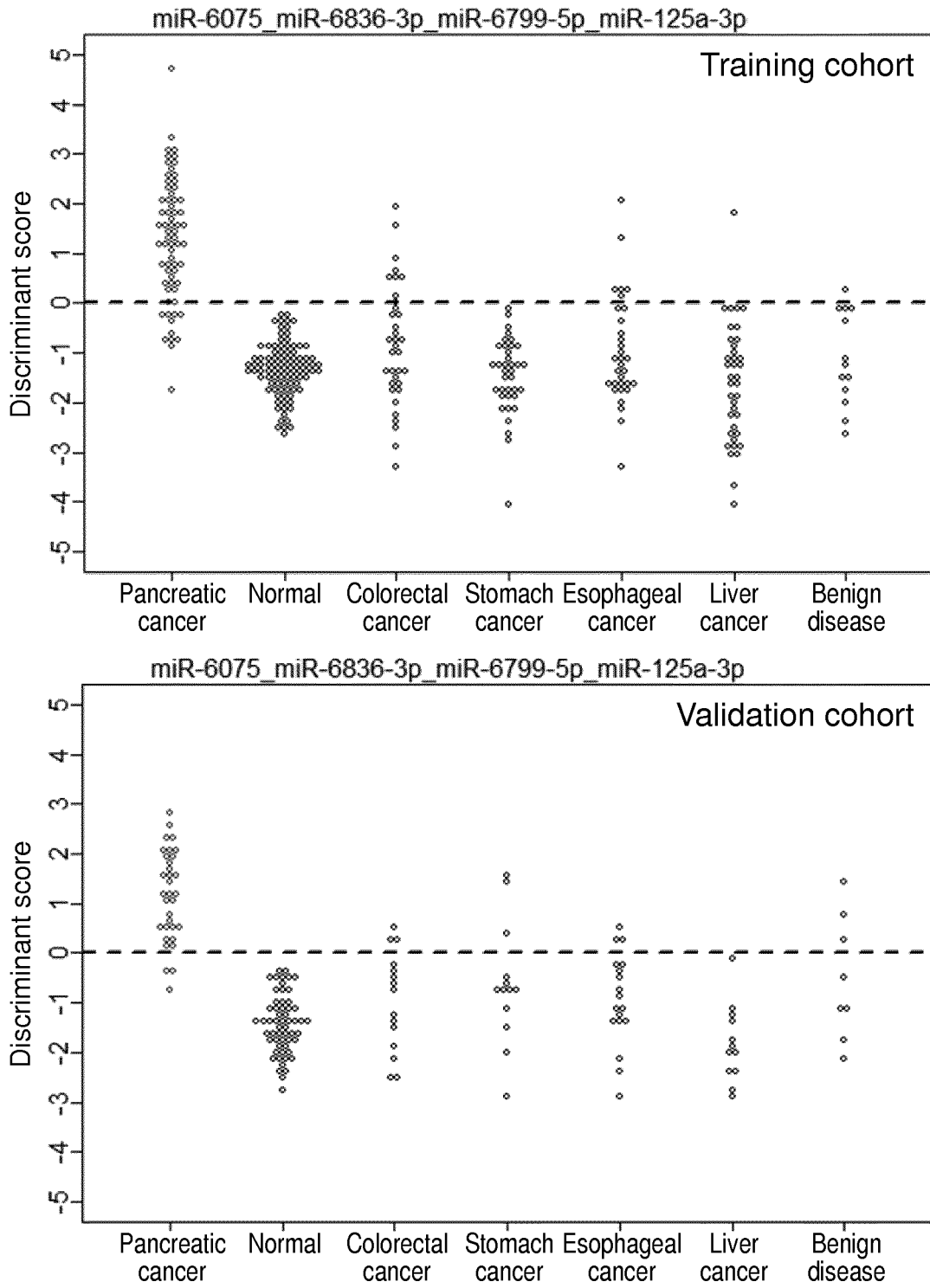


Fig. 3

Fig. 4



INTERNATIONAL SEARCH REPORT

International application No.

PCT/JP2015/065696

5	A. CLASSIFICATION OF SUBJECT MATTER C12N15/09(2006.01)i, C12M1/00(2006.01)i, C12M1/34(2006.01)i, C12Q1/68 (2006.01)i, G01N33/53(2006.01)i, G01N33/574(2006.01)i, G01N37/00 (2006.01)i According to International Patent Classification (IPC) or to both national classification and IPC	
10	B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) C12N15/09, C12M1/00, C12M1/34, C12Q1/68, G01N33/53, G01N33/574, G01N37/00	
15	Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Jitsuyo Shinan Koho 1922-1996 Jitsuyo Shinan Toroku Koho 1996-2015 Kokai Jitsuyo Shinan Koho 1971-2015 Toroku Jitsuyo Shinan Koho 1994-2015	
20	Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) JSTPlus/JMEDPlus/JST7580(JDREAMIII), BIOSIS/MEDLINE/EMBASE/WPIDS(STN)	
25	C. DOCUMENTS CONSIDERED TO BE RELEVANT	
30	Category*	Citation of document, with indication, where appropriate, of the relevant passages
35	Y	LIU R., ET AL, Serum microRNA expression profile as a biomarker in the diagnosis and prognosis of pancreatic cancer., Clin. Chem., 2012, Vol.58, No.3, p.610-618, Abstract
40	Y	KOZOMARA A. & GRIFFITHS-JONES S., miRBase: annotating high confidence microRNAs using deep sequencing data., Nucleic Acids Res., 2013, Vol.42, Database issue, p.D68-D73, ABSTRACT, INTRODUCTION
45	<input checked="" type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/> See patent family annex.	
50	* Special categories of cited documents: "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier application or patent but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed	"I" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art "&" document member of the same patent family
55	Date of the actual completion of the international search 10 August 2015 (10.08.15)	Date of mailing of the international search report 18 August 2015 (18.08.15)
	Name and mailing address of the ISA/ Japan Patent Office 3-4-3, Kasumigaseki, Chiyoda-ku, Tokyo 100-8915, Japan	Authorized officer Telephone No.

Form PCT/ISA/210 (second sheet) (July 2009)

INTERNATIONAL SEARCH REPORT

International application No.

PCT/JP2015/065696

5

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

10

15

20

25

30

35

40

45

50

55

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	Satoko TAKIZAWA, Hitoshi NOBUMASA, "DNA Chip 3D-Gene® ni yoru FFPE · Kessei Kentai deno Tashu miRNA Doji Kaiseki", BIO Clinica, 2013, vol.28, no.9, pages 872 to 873, page 872, right column, 3rd paragraph to page 873, left column, 1st paragraph, page 873, left column, 2nd paragraph to right column, 1st paragraph	1-22
Y	TAKIZAWA S., ET AL, The difference of serum RNA profile: RNA extraction and detection method. [abstract]. In: Proceedings of the 104th Annual Meeting of the American Association for Cancer Research; 2013 Apr 6-10; Washington, DC. Philadelphia (PA): AACR, Cancer Res., 2013, Vol.73, No.8(Suppl.1), Abstract No.5294, 1st paragraph	1-22
Y	WO 2014/003053 A1 (National Cancer Center), 03 January 2014 (03.01.2014), paragraphs [0006], [0026] to [0028]; examples; claims & US 2015/0184248 A1	1-22

Form PCT/ISA/210 (continuation of second sheet) (July 2009)

INTERNATIONAL SEARCH REPORT

International application No.

PCT/JP2015/065696

5

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

10

1. Claims Nos.: 23-25
because they relate to subject matter not required to be searched by this Authority, namely:
(See extra sheet)

15

2. Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

20

3. Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

25

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

30

35

1. As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.
3. As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

40

45

4. No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

50

- Remark on Protest**
- The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- No protest accompanied the payment of additional search fees.

55

Form PCT/ISA/210 (continuation of first sheet (2)) (July 2009)

INTERNATIONAL SEARCH REPORT

International application No.

PCT/JP2015/065696

Continuation of Box No.II-1 of continuation of first sheet (2)

5
10
15
20
25
30
35
40
45
50
55

In claims 23-25, the criteria for determining whether or not a subject is suffering from pancreatic cancer on the basis of the expression amount of a target nucleic acid in a sample from the subject and a reference, i.e., the expression amount of the target nucleic acid in a sample from a normal person, is not described clearly. Furthermore, the evaluation as to whether or not the subject is suffering from pancreatic cancer on the basis of the above-mentioned expression amounts requires a step of judging by a physician. Therefore, these claims relate to a method for the diagnosis of a human body. Thus, the inventions of these claims relate to a subject matter which this international searching authority is not required to search.

REFERENCES CITED IN THE DESCRIPTION

This list of references cited by the applicant is for the reader's convenience only. It does not form part of the European patent document. Even though great care has been taken in compiling the references, errors or omissions cannot be excluded and the EPO disclaims all liability in this regard.

Patent documents cited in the description

- JP 2012507300 A [0017]
- US 20100286232 A [0017]
- WO 2013107459 A [0017]
- US 20130310276 A [0017]
- US 20080306018 A [0017]
- JP 2014113523 A [0236]
- JP 2014185730 A [0236]

Non-patent literature cited in the description

- General Rules for the Study of Pancreatic Cancer. KANEHARA & Co., LTD, 2013, 55 [0005]
- TETSUYA MINE. *Suizo (Pancreas), Journal of the Japan Pancreas Society*, 2007, vol. 22, 105-113 [0018]
- 2009 Scientific evidence based clinical practice guidelines for pancreatic cancer. *CQ1 diagnosis methods*, <http://www.suizou.org/PCMG2009/cq1/cq1-3.html> [0018]
- LAB DATA. Igaku-Shoin Ltd, 2013, 633, , 636 [0018]
- ALI S. et al. *American Journal of Translational Research*, 2010, vol. 3 (1), 28-47 [0018]
- GANEPOLA GA et al. *World Journal of Gastrointestinal Oncology.*, 2014, vol. 6 (1), 22-33 [0018]
- LI A. et al. *Clinical Cancer Research*, 2013, vol. 19 (13), 3600-3610 [0018]
- ZHANG J. et al. *Oncology Reports*, 2014, vol. 31 (3), 1157-1164 [0018]
- General Rules for the Study of Pancreatic Cancer. KANEHARA & Co., LTD, 2013, 21-22 [0034]
- Guidelines for the preparation of specification which contain nucleotide and/or amino acid sequences [0036]
- ZHENG ZHANG et al. *J. Comput. Biol.*, 2000, vol. 7, 203-214 [0052]
- ALTSCHUL, S.F. et al. *Journal of Molecular Biology*, 1990, vol. 215, 403-410 [0052]
- PEARSON, W.R. et al. *Proc. Natl. Acad. Sci. U. S. A.*, 1988, vol. 85, 2444-2448 [0052]
- NIELSEN, P.E. et al. *Science*, 1991, vol. 254, 1497-500 [0053]
- OBIKA, S. et al. *Tetrahedron Lett.*, 1998, vol. 39, 5401-5404 [0053]
- LADEWIG E et al. *Genome Res.*, 2012, vol. 22, 1634-1645 [0062] [0064] [0066] [0068] [0069] [0070] [0082] [0083] [0085] [0086] [0089] [0093] [0098] [0105] [0106] [0108] [0110] [0111] [0117] [0118] [0122] [0126] [0128] [0136] [0137] [0138] [0149] [0152] [0158] [0159] [0225] [0226]
- VOELLENKLE C et al. *RNA.*, 2012, vol. 18, 472-484 [0063]
- GOFF LA et al. *PLoS One.*, 2009, vol. 4, e7192 [0065] [0146] [0156] [0163] [0221]
- JIMA DD et al. *Blood.*, 2010, vol. 116, e118-e127 [0067] [0071] [0073] [0078] [0084] [0095] [0132] [0140] [0141] [0144] [0147] [0148] [0150] [0161] [0223]
- YOO JK et al. *Arch Pharm Res.*, 2013, vol. 36, 353-358 [0072] [0139]
- CUMMINS JM. *Proc Natl Acad Sci*, 2006, vol. 103, 3687-3692 [0074] [0076] [0102] [0169] [0175] [0183]
- WANG HJ et al. *Shock.*, 2013, vol. 39, 480-487 [0075] [0090] [0100] [0131]
- PERSSON H et al. *Cancer Res.*, 2011, vol. 71, 78-86 [0077] [0079] [0088] [0094] [0097] [0101] [0114] [0120] [0127] [0134] [0157] [0160] [0164] [0222] [0228]
- BEREZIKOV E et al. *Genome Res.*, 2006, vol. 16, 1289-1298 [0080] [0129]
- VELTHUT-MEIKAS A et al. *Mol Endocrinol.*, 2013 [0081]
- VELTHUT-MEIKAS A et al. *Mol Endocrinol*, 2013 [0087]
- FRIEDLANDER MR et al. *Nucleic Acids Res.*, 2012, vol. 40, 37-52 [0091]
- VOELLENCLE C et al. *RNA.*, 2012, vol. 18, 472-484 [0092]
- BEREZIKOV E et al. *Mol Cell.*, 2007, vol. 28, 328-336 [0096] [0125] [0154]
- BEREZIKOV E et al. *Cell.*, vol. 28, 328-336 [0099]
- WITTEN D et al. *BMC Biol.*, 2010, vol. 8, 58 [0103] [0224]
- MORIN RD et al. *Genome Res.*, 2008, vol. 18, 610-621 [0104] [0174] [0176] [0232]
- SMITH JL et al. *J Virol.*, 2012, vol. 86, 5278-5287 [0107]
- DANNEMANN M. *Genome Biol Evol.*, 2012, vol. 4, 552-564 [0109]
- BAR M et al. *Stem Cells.*, 2008, vol. 26, 2496-2505 [0112] [0133] [0181]
- PLE H et al. *PLoS One.*, 2012, vol. 7, e50746 [0113]

- **TANDON M et al.** *Oral Dis.*, 2012, vol. 18, 127-131 [0115]
- **LI Y et al.** *Gene.*, 2012, vol. 497, 330-335 [0116] [0153] [0155]
- **STARK MS et al.** *PLoS One.*, 2010, vol. 5, e9685 [0119] [0135] [0151] [0173] [0227]
- **RESHMI G et al.** *Genomics.*, 2011, vol. 97, 333-340 [0121]
- **KIM J et al.** *Proc Natl Acad Sci*, 2004, vol. 101, 360-365 [0123]
- **CREIGHTON CJ et al.** *PLoS One.*, 2010, vol. 5, e9637 [0124]
- **SWAMINATHAN S et al.** *Biochem Biophys Res Commun.*, 2013, vol. 434, 228-234 [0130]
- **SCHOTTE D et al.** *Leukemia.*, 2011, vol. 25, 1389-1399 [0142]
- **MARTON S et al.** *Leukemia.*, 2008, vol. 22, 330-338 [0143] [0219]
- **JOYCE CE et al.** *Hum Mol Genet.*, 2011, vol. 20, 4025-4040 [0145]
- **LUI WO et al.** *A Cancer Res.*, 2007, vol. 67, 6031-6043 [0162]
- **ARTZI S et al.** *BMC Bioinformatics.*, 2008, vol. 9, 39 [0165]
- **LAGOS-QUINTANA M et al.** *Curr Biol.*, 2002, vol. 12, 735-739 [0166] [0170] [0177]
- **LIM LP et al.** *Science.*, 2003, vol. 299, 1540 [0167] [0180]
- **KAWAJI H et al.** *BMC Genomics*, 2008, vol. 9, 157 [0168]
- **KASASHIMA K et al.** *Biochem Biophys Res Commun.*, 2004, vol. 322, 403-410 [0171]
- **CUMMINS JM.** *Proc Natl Acad Sci*, 2006, vol. 103, 3697-3692 [0172]
- **ALTUVIA Y et al.** *Nucleic Acids Res.*, 2005, vol. 33, 2697-2706 [0178]
- **LAGOS-QUINTANA M et al.** *Science.*, 2001, vol. 294, 853-858 [0179]
- **SUH MR et al.** *Dev Biol.*, 2004, vol. 270, 488-498 [0182]
- **JIMA DD et al.** *Blood*, 2010, vol. 116, e118-e127 [0184] [0188] [0215]
- **PERSSON H et al.** *Cancer Res*, 2011, vol. 71, 78-86 [0185] [0192] [0204] [0213] [0214] [0217]
- **PLE H et al.** *PLoS One*, 2012, vol. 7, e50746 [0186]
- **LI H et al.** *J Clin Invest*, 2009, vol. 119, 3666-3677 [0187]
- **LADEWIG E et al.** *Genome Res*, 2012, vol. 22, 1634-1645 [0189] [0190] [0191] [0195] [0197] [0203] [0207] [0209] [0210] [0229] [0230]
- **STARK MS et al.** *PLoS One*, 2010, vol. 5, e9685 [0193] [0200]
- **GOFF LA et al.** *PLoS One*, 2009, vol. 4, e7192 [0194]
- **CUMMINS JM et al.** *Proc Natl Acad Sci USA*, 2006, vol. 103, 3687-3692 [0196] [0206] [0212] [0218]
- **LANDGRAF P et al.** *Cell*, 2007, vol. 129, 1401-1414 [0196] [0202] [0206] [0208] [0218]
- **ZARAGOSI LE et al.** *Genome Biol*, 2011, vol. 12, R64 [0196]
- **LAGOS-QUINTANA M et al.** *Curr Biol*, 2002, vol. 12, 735-739 [0198]
- **KASASHIMA K et al.** *Biochem Biophys Res Commun*, 2004, vol. 322, 403-410 [0198] [0202]
- **LANDGRAF P et al.** *Cell*, vol. 129, 1401-1414 [0198]
- **MEUNIER J et al.** *Genome Res*, 2013, vol. 23, 34-45 [0198] [0208]
- **SCHOTTE D et al.** *Leukemia*, 2011, vol. 25, 1389-1399 [0199]
- **MEIRI E et al.** *Nucleic Acids Res*, 2010, vol. 38, 6234-6246 [0201]
- **MOURELATOS Z et al.** *Genes Dev*, 2002, vol. 16, 720-728 [0202]
- **DOSTIE J et al.** *RNA*, 2003, vol. 9, 180-186 [0202]
- **HOUBAVIY HB et al.** *Dev Cell*, 2003, vol. 5, 351-358 [0202]
- **SUH MR et al.** *Dev Biol, Vol.*, 2004, vol. 270, 488-498 [0202]
- **FU H et al.** *FEBS Lett*, 2005, vol. 579, 3849-3854 [0202] [0208]
- **LUI WO et al.** *Cancer Res*, vol. 67, 6031-6043 [0202]
- **VOELLENKLE C et al.** *RNA*, 2012, vol. 18, 472-484 [0205]
- **LUI WO et al.** *Cancer Res*, 2007, vol. 67, 6031-6043 [0206] [0218]
- **LI Y et al.** *Gene*, 2012, vol. 497, 330-335 [0211]
- **BAR M et al.** *Stem Cells*, 2008, vol. 26, 2496-2505 [0216]
- **TAKADA S et al.** *Leukemia.*, 2008, vol. 22, 1274-1278 [0220]
- **LIAO JY et al.** *PLoS One*, 2010, vol. 5, e10563 [0231]
- **AUSUBEL et al.** *Current Protocols in Molecular Biology.* John Willey & Sons, 1993 [0427]
- **SAMBROOK et al.** *Molecular Cloning - A Laboratory Manual.* Cold Spring Harbor Laboratory Press, 1989 [0427]
- *Molecular Cloning.* **SAMBROOK, J. ; RUSSEL, D.** A LABORATORY MANUAL. Cold Spring Harbor Laboratory Press, 15 January 2001, vol. 1, 7.72-7.45 [0503]
- *MOLECULAR CLONING. A LABORATORY MANUAL.* vol. 2, 8.9-8.17 [0503]
- **BOLSTAD, B. M. et al.** *Bioinformatics*, 2003, vol. 19, 185-193 [0506]
- **VENABLES, W.N. et al.** *Modern Applied Statistics.* Springer, 2002 [0511]
- **TAKAFUMI KANAMORI et al.** *Pattern Recognition.* Kyoritsu Shuppan Co., Ltd, 2009 [0511]
- **RICHARD O. et al.** *Pattern Classification.* Wiley-Interscience, 2000 [0511]
- **V. VAPNIK.** *The Nature of Statistical Learning Theory.* Springer, 1995 [0513]
- *Statistics of pattern recognition and learning - New concepts and approaches.* **HIDEKI ASO et al.** *Frontier of Statistical Science.* Iwanami Shoten, Publishers, 2004, vol. 6 [0513]

EP 3 150 707 A1

- **NELLO CRISTIANINI et al.** Introduction to SVM. Kyoritsu Shuppan Co., Ltd, 2008 [0513]
- **C. CORTES et al.** *Machine Learning*, 1995, vol. 20, 273-297 [0514]
- **YASUSHI NAGATA et al.** Basics of statistical multiple comparison methods. Scientist Press Co., Ltd, 2007 [0525]
- **FUREY TS. et al.** *Bioinformatics.*, 2000, vol. 16, 906-14 [0527]
- **VENABLES, W. N. ; RIPLEY, B. D.** Modern Applied Statistics. Springer, 2002 [0534]

专利名称(译)	胰腺癌检测试剂盒，装置和检测方法		
公开(公告)号	EP3150707A1	公开(公告)日	2017-04-05
申请号	EP2015800550	申请日	2015-05-29
[标]申请(专利权)人(译)	东丽株式会社 NAT癌症CENT		
申请(专利权)人(译)	TORAY INDUSTRIES , INC. 国家癌症中心		
当前申请(专利权)人(译)	TORAY INDUSTRIES , INC. 国家癌症中心		
[标]发明人	KAWAUCHI JUNPEI NOBUMASA HITOSHI KOZONO SATOKO KONDOU SATOSHI SUDO HIROKO OCHIAI ATSUSHI KOJIMA MOTOHIRO		
发明人	KAWAUCHI JUNPEI NOBUMASA HITOSHI KOZONO SATOKO KONDOU SATOSHI SUDO HIROKO OCHIAI ATSUSHI KOJIMA MOTOHIRO		
IPC分类号	C12N15/09 C12M1/00 C12M1/34 C12Q1/68 G01N33/53 G01N33/574 G01N37/00		
CPC分类号	C12Q1/6886 C12Q2600/158 C12Q2600/178 C12M1/00 C12M1/34 C12N15/09 G01N33/53 G01N33/574 G01N37/00		
优先权	2014113523 2014-05-30 JP 2014185730 2014-09-11 JP		
其他公开文献	EP3150707B1 EP3150707A4		
外部链接	Espacenet		

摘要(译)

本发明提供用于检测胰腺癌的试剂盒或装置，其包含能够特异性结合来自受试者的样品中的miRNA的核酸，以及用于检测胰腺癌的方法，包括测量所述胰腺癌。miRNA在体外。

Fig. 2

