

CLAIMS

1. A method of diagnosing lung cancer in a patient comprising the step of:

(i) determining the level of at least one RNA molecule in a blood sample from a patient, wherein the at least one RNA molecule comprises a nucleotide sequence according to SEQ ID NO: 1, is a fragment thereof, or has a sequence having at least 80% sequence identity thereto,

(ii) determining the levels of at least two RNA molecules in a blood sample from a patient, wherein the at least two RNA molecules comprise a first RNA molecule and a second RNA molecule,

wherein the first RNA molecule comprises a nucleotide sequence according to SEQ ID NO: 1, is a fragment thereof, or has a sequence having at least 80% sequence identity thereto and the second RNA molecule comprises a nucleotide sequence according to SEQ ID NO: 2, is a fragment thereof, or has a sequence having at least 80% sequence identity thereto, or

(iii) determining the levels of at least two RNA molecules in a blood sample from a patient, wherein the at least two RNA molecules comprise a first RNA molecule and a second RNA molecule,

wherein the first RNA molecule comprises a nucleotide sequence according to SEQ ID NO: 2, is a fragment thereof, or has a sequence having at least 80% sequence identity thereto and the second RNA molecule comprises a nucleotide sequence according to SEQ ID NO: 3, is a fragment thereof, or has a sequence having at least 80% sequence identity thereto.

2. The method of claim 1, wherein

with regard to (i), the level of at least one further RNA molecule selected from the group consisting of an RNA molecule comprising a nucleotide sequence according to SEQ ID NO: 2 to SEQ ID NO: 71, a fragment thereof, and a sequence having at least 80% sequence identity thereto is determined, or

wherein the level of at least one further RNA molecule selected from the group consisting of an RNA molecule comprising a nucleotide sequence according to SEQ ID NO: 2 to SEQ ID NO: 79, a fragment thereof, and a sequence having at least 80% sequence identity thereto is determined, or

with regard to (ii), the level of at least one further RNA molecule selected from the group consisting of an RNA molecule comprising a nucleotide sequence according to SEQ ID

NO: 3 to SEQ ID NO: 71, a fragment thereof, and a sequence having at least 80% sequence identity thereto is determined, or

wherein the level of at least one further RNA molecule selected from the group consisting of an RNA molecule comprising a nucleotide sequence according to SEQ ID NO: 3 to SEQ ID NO: 79, a fragment thereof, and a sequence having at least 80% sequence identity thereto is determined, or

with regard to (iii), the level of at least one further RNA molecule selected from the group consisting of an RNA molecule comprising a nucleotide sequence according to SEQ ID NO: 1, SEQ ID NO: 4 to SEQ ID NO: 79, a fragment thereof, and a sequence having at least 80% sequence identity thereto is determined.

3. The method of claim 1 or 2, wherein

the level of the at least one RNA molecule is compared to a reference level of said RNA molecule, wherein the reference level is the level of the at least one RNA molecule determined empirically by measuring a number of reference blood samples from subjects known to be healthy (not suffering from lung cancer), or

the levels of the at least two RNA molecules are compared to reference levels of said RNA molecules, wherein the reference levels are the levels of the at least two RNA molecules determined empirically by measuring a number of reference blood samples from subjects known to be healthy (not suffering from lung cancer).

4. The method of claim 3, wherein

the level of the RNA molecule selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 15, SEQ ID NO: 18, SEQ ID NO: 19, SEQ ID NO: 20, SEQ ID NO: 23, SEQ ID NO: 24, SEQ ID NO: 33, SEQ ID NO: 34, SEQ ID NO: 36, SEQ ID NO: 38, SEQ ID NO: 41, SEQ ID NO: 43, SEQ ID NO: 44, SEQ ID NO: 45, SEQ ID NO: 46, SEQ ID NO: 49, SEQ ID NO: 54, SEQ ID NO: 55, SEQ ID NO: 56, SEQ ID NO: 57, SEQ ID NO: 58, SEQ ID NO: 59, SEQ ID NO: 60, SEQ ID NO: 62, SEQ ID NO: 69, SEQ ID NO: 72, SEQ ID NO: 73, SEQ ID NO: 77, and/or SEQ ID NO: 78 above the reference level indicates that the patient suffers from lung cancer, and/or

the level of the RNA molecule selected from the group consisting of SEQ ID NO: 4, SEQ ID NO: 10, SEQ ID NO: 14, SEQ ID NO: 16, SEQ ID NO: 17, SEQ ID NO: 21, SEQ ID NO: 22, SEQ ID NO: 25, SEQ ID NO: 26, SEQ ID NO: 28, SEQ ID NO: 29, SEQ ID NO: 30, SEQ ID NO: 31, SEQ ID NO: 32, SEQ ID NO: 35, SEQ ID NO: 39, SEQ ID NO: 40,

SEQ ID NO: 42, SEQ ID NO: 47, SEQ ID NO: 48, SEQ ID NO: 52, SEQ ID NO: 61, SEQ ID NO: 63, SEQ ID NO: 64, SEQ ID NO: 65, SEQ ID NO: 66, SEQ ID NO: 67, SEQ ID NO: 68, SEQ ID NO: 70, SEQ ID NO: 71, SEQ ID NO: 74, SEQ ID NO: 75, SEQ ID NO: 76, and/or SEQ ID NO: 79 below the reference level indicates that the patient suffers from lung cancer.

5. The method of any one of claims 1 to 4, wherein
the level of the at least one RNA molecule is used in a mathematical computation to obtain a numerical value, or
the levels of the at least two RNA molecules are used in a mathematical computation to obtain a numerical value.
6. The method of claim 5, wherein the numerical value is obtained by summarizing the weighted levels of the at least two RNA molecules.
7. The method of claim 5 or 6, wherein the numerical value is compared to an empirically determined cut-off score.
8. The method of claim 7, wherein the cut-off score allows to classify a patient as suffering from lung cancer or as being healthy (not suffering from lung cancer).
9. A method of monitoring a patient suspected of having lung cancer or a patient suffering from lung cancer comprising the step of:
 - (i) determining the level of at least one RNA molecule in a blood sample from a patient, wherein the at least one RNA molecule comprises a nucleotide sequence according to SEQ ID NO: 1, is a fragment thereof, or has a sequence having at least 80% sequence identity thereto,
 - (ii) determining the levels of at least two RNA molecules in a blood sample from a patient, wherein the at least two RNA molecules comprise a first RNA molecule and a second RNA molecule,
wherein the first RNA molecule comprises a nucleotide sequence according to SEQ ID NO: 1, is a fragment thereof, or has a sequence having at least 80% sequence identity thereto and the second RNA molecule comprises a nucleotide sequence according to SEQ ID NO: 2, is a fragment thereof, or has a sequence having at least 80% sequence identity thereto, or

(iii) determining the levels of at least two RNA molecules in a blood sample from a patient, wherein the at least two RNA molecules comprise a first RNA molecule and a second RNA molecule,
wherein the first RNA molecule comprises a nucleotide sequence according to SEQ ID NO: 2, is a fragment thereof, or has a sequence having at least 80% sequence identity thereto and the second RNA molecule comprises a nucleotide sequence according to SEQ ID NO: 3, is a fragment thereof, or has a sequence having at least 80% sequence identity thereto.

10 10. The method of claim 9, wherein
with regard to (i), the level of at least one further RNA molecule selected from the group consisting of an RNA molecule comprising a nucleotide sequence according to SEQ ID NO: 2 to SEQ ID NO: 71, a fragment thereof, and a sequence having at least 80% sequence identity thereto is determined, or
15 wherein the level of at least one further RNA molecule selected from the group consisting of an RNA molecule comprising a nucleotide sequence according to SEQ ID NO: 2 to SEQ ID NO: 79, a fragment thereof, and a sequence having at least 80% sequence identity thereto is determined, or
with regard to (ii), the level of at least one further RNA molecule selected from the group consisting of an RNA molecule comprising a nucleotide sequence according to SEQ ID NO: 3 to SEQ ID NO: 71, a fragment thereof, and a sequence having at least 80% sequence identity thereto is determined, or
20 wherein the level of at least one further RNA molecule selected from the group consisting of an RNA molecule comprising a nucleotide sequence according to SEQ ID NO: 3 to SEQ ID NO: 79, a fragment thereof, and a sequence having at least 80% sequence identity thereto is determined, or
25 with regard to (iii), the level of at least one further RNA molecule selected from the group consisting of an RNA molecule comprising a nucleotide sequence according to SEQ ID NO: 1, SEQ ID NO: 4 to SEQ ID NO: 79, a fragment thereof, and a sequence having at least 80% sequence identity thereto is determined.
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11. The method of claim 9 or 10, wherein
the level of the at least one RNA molecule is compared to a reference level of said RNA
molecule, wherein the reference level is the level of the RNA molecule determined
empirically by measuring a number of reference blood samples from subjects known to be
5 healthy or subjects known to suffer from lung cancer, or
the levels of the at least two RNA molecules are compared to reference levels of said RNA
molecules, wherein the reference levels are the levels of the at least two RNA molecules
determined empirically by measuring a number of reference blood samples from subjects
known to be healthy or known to suffer from lung cancer.

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12. The method of any one of claims 9 to 11, wherein
said monitoring comprises determining the level of the at least one RNA molecule in a
blood sample obtained from a patient at a first point in time and in at least one further blood
sample obtained from the (same) patient at a later point in time and comparing said levels
15 determined at the different time points, or
said monitoring comprises determining the levels of the at least two RNA molecules in a
blood sample obtained from a patient at a first point in time and in at least one further blood
sample obtained from the (same) patient at a later point in time and comparing said levels
determined at the different time points.

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13. The method of any one of claims 1 to 12, wherein the lung cancer is small-cell lung
carcinoma (SCLC) or non-small-cell lung carcinoma (NSCLC), preferably lung
adenocarcinoma (LUAD) or lung squamous cell carcinoma (LUSC).

25 14. The method of any one of claims 1 to 13, wherein the blood sample is whole blood or a
blood fraction.

15. The method of claim 14, wherein the blood fraction is selected from the group consisting
of a blood cell fraction, plasma, and serum.

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16. The method of claim 15, wherein the blood cell fraction is a fraction of erythrocytes,
leukocytes, and/or thrombocytes.

17. Use of

- (i) at least one RNA molecule for diagnosing lung cancer in a patient, or for monitoring a patient suspected of having lung cancer or a patient suffering from lung cancer, wherein the at least one RNA molecule comprises a nucleotide sequence according to SEQ ID NO: 1, is a fragment thereof, or has a sequence having at least 80% sequence identity thereto,
- (ii) at least two RNA molecules for diagnosing lung cancer in a patient, or for monitoring a patient suspected of having lung cancer or a patient suffering from lung cancer, wherein the at least two RNA molecules comprise a first RNA molecule and a second RNA molecule, wherein the first RNA molecule comprises a nucleotide sequence according to SEQ ID NO: 1, is a fragment thereof, or has a sequence having at least 80% sequence identity thereto and the second RNA molecule comprises a nucleotide sequence according to SEQ ID NO: 2, is a fragment thereof, or has a sequence having at least 80% sequence identity thereto, or
- (iii) at least two RNA molecules for diagnosing lung cancer in a patient, or for monitoring a patient suspected of having lung cancer or a patient suffering from lung cancer, wherein the at least two RNA molecules comprise a first RNA molecule and a second RNA molecule, wherein the first RNA molecule comprises a nucleotide sequence according to SEQ ID NO: 2, is a fragment thereof, or has a sequence having at least 80% sequence identity thereto and the second RNA molecule comprises a nucleotide sequence according to SEQ ID NO: 3, is a fragment thereof, or has a sequence having at least 80% sequence identity thereto.

18. The use of claim 17, wherein

with regard to (i), at least one further RNA molecule selected from the group consisting of an RNA molecule comprising a nucleotide sequence according to SEQ ID NO: 2 to SEQ ID NO: 71, a fragment thereof, and a sequence having at least 80% sequence identity thereto is used for diagnosing or monitoring lung cancer in the patient, or wherein at least one further RNA molecule selected from the group consisting of an RNA molecule comprising a nucleotide sequence according to SEQ ID NO: 2 to SEQ ID NO: 79, a fragment thereof, and a sequence having at least 80% sequence identity thereto is used for diagnosing or monitoring lung cancer in the patient, or

with regard to (ii), at least one further RNA molecule selected from the group consisting of an RNA molecule comprising a nucleotide sequence according to SEQ ID NO: 3 to SEQ ID NO: 71, a fragment thereof, and a sequence having at least 80% sequence identity thereto is used for diagnosing or monitoring lung cancer in the patient, or

wherein at least one further RNA molecule selected from the group consisting of an RNA molecule comprising a nucleotide sequence according to SEQ ID NO: 3 to SEQ ID NO: 79, a fragment thereof, and a sequence having at least 80% sequence identity thereto is used for diagnosing or monitoring lung cancer in the patient, or

with regard to (iii), at least one further RNA molecule selected from the group consisting of an RNA molecule comprising a nucleotide sequence according to SEQ ID NO: 1, SEQ ID NO: 4 to SEQ ID NO: 79, a fragment thereof, and a sequence having at least 80% sequence identity thereto is used for diagnosing or monitoring lung cancer in the patient.

19. Use of a kit for diagnosing lung cancer in a patient, or for monitoring a patient suspected of having lung cancer or a patient suffering from lung cancer, said kit comprises

- (i) means for determining the level of at least one RNA molecule in a blood sample from a patient,

wherein the at least one RNA molecule comprises a nucleotide sequence according to SEQ ID NO: 1, is a fragment thereof, or has a sequence having at least 80% sequence identity thereto,

- (ii) means for determining the levels of at least two RNA molecules in a blood sample from a patient, wherein the at least two RNA molecules comprise a first RNA molecule and a second RNA molecule,

wherein the first RNA molecule comprises a nucleotide sequence according to SEQ ID NO: 1, is a fragment thereof, or has a sequence having at least 80% sequence identity thereto and the second RNA molecule comprises a nucleotide sequence according to SEQ ID NO: 2, is a fragment thereof, or has a sequence having at least 80% sequence identity thereto, or

- (iii) means for determining the levels of at least two RNA molecules in a blood sample from a patient, wherein the at least two RNA molecules comprise a first RNA molecule and a second RNA molecule,

wherein the first RNA molecule comprises a nucleotide sequence according to SEQ ID NO: 2, is a fragment thereof, or has a sequence having at least 80% sequence identity thereto and the second RNA molecule comprises a nucleotide sequence

according to SEQ ID NO: 3, is a fragment thereof, or has a sequence having at least 80% sequence identity thereto.

20. The use of the kit of claim 19, wherein

5 with regard to (i), the kit comprises means for determining the level of at least one further RNA molecule selected from the group consisting of an RNA molecule comprising a nucleotide sequence according to SEQ ID NO: 2 to SEQ ID NO: 71, a fragment thereof, and a sequence having at least 80% sequence identity thereto, or
10 the kit comprises means for determining the level of at least one further RNA molecule selected from the group consisting of an RNA molecule comprising a nucleotide sequence according to SEQ ID NO: 2 to SEQ ID NO: 79, a fragment thereof, and a sequence having at least 80% sequence identity thereto, or
15 with regard to (ii), the kit comprises means for determining the level of at least one further RNA molecule selected from the group consisting of an RNA molecule comprising a nucleotide sequence according to SEQ ID NO: 3 to SEQ ID NO: 71, a fragment thereof, and a sequence having at least 80% sequence identity thereto, or
20 the kit comprises means for determining the level of at least one further RNA molecule selected from the group consisting of an RNA molecule comprising a nucleotide sequence according to SEQ ID NO: 3 to SEQ ID NO: 79, a fragment thereof, and a sequence having at least 80% sequence identity thereto is used for diagnosing or monitoring lung cancer in the patient, or
25 with regard to (iii), the kit comprises means for determining the level of at least one further RNA molecule selected from the group consisting of an RNA molecule comprising a nucleotide sequence according to SEQ ID NO: 1, SEQ ID NO: 4 to SEQ ID NO: 79, a fragment thereof, and a sequence having at least 80% sequence identity thereto.