

CLAIMS

1. An *in vitro* method for diagnosing pancreatic cancer in an individual, the method comprising:

measuring the levels of at least 3 biomarker proteins in a biological sample from the individual, wherein the at least 3 protein biomarkers are selected from Table 1, and wherein the individual is classified as having or not having pancreatic cancer, or the likelihood of the individual having pancreatic cancer is determined, based on the levels of the at least 3 protein biomarkers.
2. The method of claim 1, wherein the diagnosis comprises the differential diagnosis of pancreatic cancer from benign conditions such as pancreatitis or a gastrointestinal disorder.
3. The method of claim 1 wherein the individual has an abdominal mass.
4. An *in vitro* method for screening an asymptomatic high risk individual for pancreatic cancer, the method comprising:

measuring the levels of at least 3 biomarker proteins in a biological sample from the individual, wherein the at least 3 protein biomarkers are selected from Table 1, and wherein the individual is classified as having or not having pancreatic cancer, or the likelihood of the individual having pancreatic cancer is determined, based on the levels of the at least 3 protein biomarkers.
5. The method of claims 1 or 4, wherein measuring the biomarker values comprises performing an *in vitro* assay.
6. The method of claim 5, wherein said *in vitro* assay comprises at least one capture reagent corresponding to each of said biomarkers, and further comprising selecting said at least one capture reagent from the group consisting of aptamers, antibodies, and a nucleic acid probe.
7. The method of claim 5, wherein the *in vitro* assay is selected from the group consisting of an immunoassay, an aptamer-based assay, a histological or cytological assay.

8. The method of claims 1 or 4, wherein the biological sample is selected from the group consisting of whole blood, plasma, serum and pancreatic fluid.
9. The method of claim 8, wherein the biological sample is plasma.
10. The method according to any of claims 1-9, wherein the biological sample is pancreatic tissue and wherein the biomarker values derive from a histological or cytological analysis of said pancreatic tissue.
11. A computer-implemented method for indicating a likelihood that an individual has pancreatic cancer, the method comprising:
 - retrieving on a computer biomarker information for the individual, wherein the biomarker information comprises biomarker values that each correspond to at least 3 biomarker proteins, wherein the biomarker values are obtained by measuring the levels of the at least 3 biomarker proteins selected from Table 1;
 - performing with the computer a classification of each of said biomarker values; and
 - indicating the likelihood that said individual has pancreatic cancer based upon a plurality of classifications.
12. The method of claim 11, wherein indicating the likelihood that the individual has pancreatic cancer comprises displaying the likelihood on a computer display.
13. A computer program product for indicating a likelihood that an individual has pancreatic cancer, the computer program product comprising:
 - a computer readable medium embodying program code executable by a processor of a computing device or system, the program code comprising:
 - code that retrieves data attributed to a biological sample from the individual, wherein the data comprises the level of at least 3 biomarker proteins selected from Table 1, wherein said levels of the biomarker proteins were measured in the biological sample; and
 - code that executes a classification method that indicates a pancreatic disease status of the individual as a function of the levels of the at least 3 protein biomarkers.
14. The computer program product of claim 13, wherein said classification method uses a probability density function.

15. The computer program product of claim 14, wherein said classification method uses two or more classes.
16. The method according to any of claims 1-15, wherein the levels of at least 4 biomarker proteins are measured.
17. The method according to any of claims 1-15, wherein the levels of at least 5 biomarker proteins are measured.
18. The method according to any of claims 1-15, wherein the levels of at least 6 biomarker proteins are measured.
19. The method according to any of claims 1-15, wherein the levels of at least 7 biomarker proteins are measured.
20. The method according to any of claims 1-15, wherein the levels of at least 9 biomarker proteins are measured.
21. The method according to any of claims 1-20, wherein the individual is high risk for pancreatic cancer due to smoking, alcohol consumption or family history of pancreatic cancer.
22. The method according to any of claims 1-21, wherein the biomarkers are selected from Table 18.
23. The method according to any of claims 1-22, further comprising the biomarker CA19-9.
24. The method according to any of claims 1-23, wherein the individual is a human.
25. An *in vitro* method for diagnosing cancer in an individual, the method comprising:
measuring the levels of at least 3 biomarker proteins in a biological sample from the individual, wherein the at least 3 protein biomarker are selected from Table 19, and wherein the individual is classified as having or not having cancer, or the likelihood of the individual having cancer is determined, based on the levels of the at least 3 protein biomarkers.
26. The method of claim 25, wherein said diagnosed cancer comprises one or more of lung cancer, pancreatic cancer, or mesothelioma.

27. The method of claim 25, wherein detecting the biomarker values comprises performing an *in vitro* assay.

28. The method of claim 27, wherein said *in vitro* assay comprises at least one capture reagent corresponding to each of said biomarkers, and further comprising selecting said at least one capture reagent from the group consisting of aptamers, antibodies, and a nucleic acid probe.

29. The method of claim 27, wherein the *in vitro* assay is selected from the group consisting of an immunoassay, an aptamer-based assay, a histological or cytological assay.

30. The method of claim 25, wherein the biological sample is selected from the group consisting of whole blood, plasma, and serum.

31. The method of claim 30, wherein the biological sample is plasma.

32. A computer-implemented method for indicating a likelihood that an individual has cancer, the method comprising:

retrieving on a computer biomarker information for the individual, wherein the biomarker information comprises biomarker values that each correspond to at least 3 biomarker proteins, wherein the biomarker values are obtained by measuring the levels of at least 3 biomarker proteins selected from Table 19;

performing with the computer a classification of each of said biomarker values; and
indicating a likelihood that said individual has cancer based upon a plurality of classifications.

33. The method of claim 32, wherein indicating the likelihood that the individual has cancer comprises displaying the likelihood on a computer display.

34. A computer program product for indicating a likelihood that an individual has cancer, the computer program product comprising:

a computer readable medium embodying program code executable by a processor of a computing device or system, the program code comprising:

code that retrieves data attributed to a biological sample from the individual, wherein the data comprises the level of at least 3 biomarker proteins selected from Table 19, wherein said levels of the biomarker proteins were measured in the biological sample; and

code that executes a classification method that indicates a disease status of the individual as a function of the levels of the at least 3 biomarkers.

35. The computer program product of claim 34, wherein said classification method uses a probability density function.

36. The computer program product of claim 35, wherein said classification method uses two or more classes.

37. The method according to any of claims 25-36, wherein the individual is a human.

38. The method according to any of claims 25-37, wherein the levels of at least 4 biomarker proteins are measured.

39. The method according to any of claims 25-37, wherein the levels of at least 5 biomarker proteins are measured.

40. The method according to any of claims 25-37, wherein the levels of at least 6 biomarker proteins are measured.

41. The method according to any of claims 25-37, wherein the levels of at least 7 biomarker proteins are measured.

42. The method according to claims 1 or 4, wherein said individual is classified as having or not having pancreatic cancer, or the likelihood of the individual having pancreatic cancer is determined, based on said biomarker levels and at least one item of additional biomedical information corresponding to said individual.

43. The method according to claim 25, wherein said individual is classified as having or not having cancer, or the likelihood of the individual having cancer is determined, based on said biomarker values and at least one item of additional biomedical information corresponding to said individual.

44. The method of claim 42 or 43, wherein said at least one item of additional biomedical information is independently selected from the group consisting of

- (a) information corresponding to the presence or absence of a pancreatic mass or other abdominal mass,
- (b) information corresponding to physical descriptors of said individual,
- (c) information corresponding to a change in weight of said individual,
- (d) information corresponding to the ethnicity of said individual,
- (e) information corresponding to the gender of said individual,
- (f) information corresponding to said individual's smoking history,
- (g) information corresponding to said individual's alcohol use history,
- (h) information corresponding to said individual's occupational history,
- (i) information corresponding to said individual's family history of pancreatic cancer or other cancer,
- (j) information corresponding to the presence or absence in said individual of at least one genetic marker correlating with a higher risk of pancreatic cancer or cancer in said individual or a family member of said individual,
- (k) information corresponding to clinical symptoms of said individual,
- (l) information corresponding to other laboratory tests,
- (m) information corresponding to gene expression values of said individual, and
- (n) information corresponding to said individual's exposure to known carcinogens.

45. A classifier comprising the biomarkers of Table 18.

CLAIMS

1. An *in vitro* method for diagnosing pancreatic cancer in an individual, the method comprising:

measuring the levels of at least one biomarker protein in a biological sample from the individual, wherein the at least one protein biomarker is selected from the group consisting of HAMP and CTSB, and wherein the individual is classified as having or not having pancreatic cancer, or the likelihood of the individual having pancreatic cancer is determined, based on the levels of the at least one protein biomarker.

2. The method of claim 1 further comprising measuring the level of at least one biomarker protein selected from the group consisting C5, THBS4, GDF11, CCL23, KLK3, SPERINA3, MMP-7, C2 and CRP.

3. The method of claim 1 further comprising measuring the level of at least one biomarker protein selected from the group consisting c5a, SFRP1, ETHE1, INSR and APOA1.

4. The method of claim 1, wherein the diagnosis comprises the differential diagnosis of pancreatic cancer from benign conditions such as pancreatitis or a gastrointestinal disorder.

The method of claim 1 wherein the individual has an abdominal mass.

6. An *in vitro* method for screening an asymptomatic high risk individual for pancreatic cancer, the method comprising:

measuring the levels of at least one biomarker protein in a biological sample from the individual, wherein the at least one protein biomarker is selected from the group consisting of HAMP and CTSB, and wherein the individual is classified as having or not having pancreatic cancer, or the likelihood of the individual having pancreatic cancer is determined, based on the levels of the at least one protein biomarker.

7. The method of claims 1 or 6, wherein measuring the biomarker values comprises performing an *in vitro* assay.

8. The method of claim 6 further comprising measuring the level of at least one biomarker protein selected from the group consisting C5, THBS4, GDF11, CCL23, KLK3, SPERINA3, MMP-7, C2 and CRP.
9. The method of claim 6 further comprising measuring the level of at least one biomarker protein selected from the group consisting c5a, SFRP1, ETHE1, INSR and APOA1.
10. The method of claim 6, wherein said *in vitro* assay comprises at least one capture reagent corresponding to each of said biomarkers, and further comprising selecting said at least one capture reagent from the group consisting of aptamers, antibodies, and a nucleic acid probe.
11. The method of claim 6, wherein the *in vitro* assay is selected from the group consisting of an immunoassay, an aptamer-based assay, a histological or cytological assay.
12. The method of claims 1 or 6, wherein the biological sample is selected from the group consisting of whole blood, plasma, serum and pancreatic fluid.
13. The method of claim 12, wherein the biological sample is plasma.
14. The method according to any of claims 1-13, wherein the biological sample is pancreatic tissue and wherein the biomarker values derive from a histological or cytological analysis of said pancreatic tissue.
15. A computer-implemented method for indicating a likelihood that an individual has pancreatic cancer, the method comprising:
 - retrieving on a computer biomarker information for the individual, wherein the biomarker information comprises biomarker values that each correspond to at least one biomarker protein, wherein the biomarker value is obtained by measuring the level of the at least one biomarker protein selected from the group consisting of HAMP and CTSB;
 - performing with the computer a classification of each of said biomarker value; and
 - indicating the likelihood that said individual has pancreatic cancer based upon a plurality of classifications.

16. The method of claim 15 further comprising measuring the level of at least one biomarker protein selected from the group consisting C5, THBS4, GDF11, CCL23, KLK3.SPERINA3, MMP-7, C2 and CRP.
18. The method of claim 15 further comprising measuring the level of at least one biomarker protein selected from the group consisting c5a, SFRP1, ETHE1, INSR and APOA1.
19. The method of claim 15, wherein indicating the likelihood that the individual has pancreatic cancer comprises displaying the likelihood on a computer display.
20. A computer program product for indicating a likelihood that an individual has pancreatic cancer, the computer program product comprising:
a computer readable medium embodying program code executable by a processor of a computing device or system, the program code comprising:
code that retrieves data attributed to a biological sample from the individual, wherein the data comprises the level of at least one biomarker protein selected from the group consisting of HAMP and CTSB, wherein said level of the biomarker protein is measured in the biological sample; and
code that executes a classification method that indicates a pancreatic disease status of the individual as a function of the level of the at least one protein biomarker.
21. The computer program product of claim 20, wherein said classification method uses a probability density function.
22. The computer program product of claim 21, wherein said classification method uses two or more classes.
23. The computer program product of claim 20 further comprising measuring the level of at least one biomarker protein selected from the group consisting C5, THBS4, GDF11, CCL23, KLK3.SPERINA3, MMP-7, C2 and CRP.
24. The computer program product of claim 20 further comprising measuring the level of at least one biomarker protein selected from the group consisting c5a, SFRP1, ETHE1, INSR and APOA1.

25. The method according to any of claims 1-24, wherein the levels of at least 2 biomarker proteins are measured.
26. The method according to any of claims 1-24, wherein the levels of at least 3 biomarker proteins are measured.
27. The method according to any of claims 1-24, wherein the levels of at least 4 biomarker proteins are measured.
28. The method according to any of claims 1-24, wherein the levels of at least 5 biomarker proteins are measured.
29. The method according to any of claims 1-24, wherein the levels of at least 6 biomarker proteins are measured.
30. The method according to any of claims 1-24, wherein the levels of at least 7 biomarker proteins are measured.
31. The method according to any of claims 1-24, wherein the levels of at least 9 biomarker proteins are measured.
32. The method according to any of claims 1-31, wherein the individual is high risk for pancreatic cancer due to smoking, alcohol consumption or family history of pancreatic cancer.
33. The method according to any of claims 1-32, further comprising the biomarker CA19-9.
34. The method according to any of claims 1-33, wherein the individual is a human.
35. The method according to claims 1 or 6, wherein said individual is classified as having or not having pancreatic cancer, or the likelihood of the individual having pancreatic cancer is determined, based on said biomarker levels and at least one item of additional biomedical information corresponding to said individual.
36. The method of claim 35, wherein said at least one item of additional biomedical information is independently selected from the group consisting of

- (a) information corresponding to the presence or absence of a pancreatic mass or other abdominal mass,
- (b) information corresponding to physical descriptors of said individual,
- (c) information corresponding to a change in weight of said individual,
- (d) information corresponding to the ethnicity of said individual,
- (e) information corresponding to the gender of said individual,
- (f) information corresponding to said individual's smoking history,
- (g) information corresponding to said individual's alcohol use history,
- (h) information corresponding to said individual's occupational history,
- (i) information corresponding to said individual's family history of pancreatic cancer or other cancer,
- (j) information corresponding to the presence or absence in said individual of at least one genetic marker correlating with a higher risk of pancreatic cancer or cancer in said individual or a family member of said individual,
- (k) information corresponding to clinical symptoms of said individual,
- (l) information corresponding to other laboratory tests,
- (m) information corresponding to gene expression values of said individual, and
- (n) information corresponding to said individual's exposure to known carcinogens.