

CLAIMS

What is claimed is:

1. A method comprising:
 - a) measuring the level of PH protein and the level of at least one, two, three, four, five, or six proteins selected from the group consisting of MMP-12, SP-D, HE4, PSP-94, FUT5 and CRLF1 in a sample from a human subject; and
 - b) identifying the human subject as being at risk for developing lung cancer based on the level of PH and the level of the at least one, two, three, four, five, or six proteins.
2. A method comprising:
 - a) measuring the level of FUT5 protein and the level of at least one, two, three, four, five, or six proteins selected from the group consisting of MMP-12, SP-D, HE4, PSP-94, PH and CRLF1 in a sample from a human subject; and
 - b) identifying the human subject as being at risk for developing lung cancer based on the level of FUT5 and the level of the at least one, two, three, four, five, or six proteins.
3. A method comprising:
 - a) measuring the level of CRLF1 protein and the level of at least one, two, three, four, five, or six proteins selected from the group consisting of MMP-12, SP-D, HE4, PSP-94, PH and FUT5 in a sample from a human subject; and
 - b) identifying the human subject as being at risk for developing lung cancer based on the level of CRLF1 and the level of the at least one, two, three, four, five, or six proteins.
4. A method comprising:
 - a) measuring the level of PSP-94 protein and the level of at least one, two, three, four, five, or six proteins selected from the group consisting of MMP-12, SP-D, HE4, PH, FUT5 and CRLF1 in a sample from a human subject; and
 - b) identifying the human subject as being at risk for developing lung cancer based on the level of PSP-94 and the level of the at least one, two, three, four, five, or six proteins.

5. The method of claim 1, wherein the method comprises measuring PH and MMP-12; PH and SP-D; PH and HE4; PH and PSP-94; PH and FUT5; or PH and CRLF1.

6. The method of claim 1, wherein the method comprises measuring PH, MMP-12 and SP-D; PH, MMP-12 and HE4; PH, MMP-12 and PSP-94; PH, MMP-12 and FUT5; PH, MMP-12 and CRLF1; PH, SP-D and HE4; PH, SP-D and PSP-94; PH, SP-D and FUT5; PH, SP-D and CRLF1; PH, HE4 and PSP-94; PH, HE4 and FUT5; PH, HE4 and CRLF1; PH, PSP-94 and FUT5; PH, PSP-94 and CRLF1; or PH, FUT5 and CRLF1.

7. The method of claim 2, wherein the method comprises measuring FUT5 and MMP-12; FUT5 and SP-D; FUT5 and HE4; FUT5 and PSP-94; FUT5 and PH; or FUT5 and CRLF1.

8. The method of claim 2, wherein the method comprises measuring FUT5, MMP-12 and SP-D; FUT5, MMP-12 and HE4; FUT5, MMP-12 and PSP-94; FUT5, MMP-12 and PH; FUT5, MMP-12 and CRLF1; FUT5, SP-D and HE4; FUT5, SP-D and PSP-94; FUT5, SP-D and PH; FUT5, SP-D and CRLF1; FUT5, HE4 and PSP-94; FUT5, HE4 and PH; FUT5, HE4 and CRLF1; FUT5, PSP-94 and PH; FUT5, PSP-94 and CRLF1; or FUT5, PH and CRLF1.

9. The method of claim 3, wherein the method comprises measuring CRLF1 and MMP-12; CRLF1 and SP-D; CRLF1 and HE4; CRLF1 and PSP-94; CRLF1 and PH; or CRLF1 and FUT5.

10. The method of claim 3, wherein the method comprises measuring CRLF1, MMP-12 and SP-D; CRLF1, MMP-12 and HE4; CRLF1, MMP-12 and PSP-94; CRLF1, MMP-12 and PH; CRLF1, MMP-12 and FUT5; CRLF1, SP-D and HE4; CRLF1, SP-D and PSP-94; CRLF1, SP-D and PH; CRLF1, SP-D and FUT5; CRLF1, HE4 and PSP-94; CRLF1, HE4 and PH; CRLF1, HE4 and FUT5; CRLF1, PSP-94 and PH; CRLF1, PSP-94 and FUT5; or CRLF1, PH and FUT5.

11. The method of claim 4, wherein the method comprises measuring PSP-94 and MMP-12; PSP-94 and SP-D; PSP-94 and HE4; PSP-94 and PH; PSP-94 and FUT5; or PSP-94 and CRLF1.

12. The method of claim 4, wherein the method comprises measuring PSP-94, MMP-12 and SP-D; PSP-94, MMP-12 and HE4; PSP-94, MMP-12 and PH; PSP-94, MMP-12 and FUT5; PSP-94, MMP-12 and CRLF1; PSP-94, SP-D and HE4; PSP-94, SP-D and PH; PSP-94, SP-D and FUT5; PSP-94, SP-D and CRLF1; PSP-94, HE4 and PH; PSP-94, HE4 and FUT5; PSP-94, HE4 and CRLF1; PSP-94, PH and FUT5; PSP-94, PH and CRLF1; or PSP-94, FUT5 and CRLF1.

13. The method of claim 4, wherein the method comprises measuring PSP-94 and PH and at least one of the following proteins selected from MMP-12, SP-D, HE4, FUT5 and CRLF1.

14. The method of claim 4, wherein the method comprises measuring PSP-94 and FUT5 and at least one of the following proteins selected from MMP-12, SP-D, HE4, PH and CRLF1.

15. The method of claim 4, wherein the method comprises measuring PSP-94 and CRLF1 and at least one of the following proteins selected from MMP-12, SP-D, HE4, PH and FUT5.

16. The method of claim 1, wherein the method comprises measuring PH and FUT5 and at least one of the following proteins selected from MMP-12, SP-D, HE4, PSP-94 and CRLF1.

17. The method of claim 1, wherein the method comprises measuring PH and CRLF1 and at least one of the following proteins selected from MMP-12, SP-D, HE4, PSP-94 and FUT5.

18. The method of claim 2, wherein the method comprises measuring FUT5 and CRLF1 and at least one of the following proteins selected from MMP-12, SP-D, HE4, PSP-94 and PH.

19. A method comprising:

a) measuring the level of at least three, four, five, six, or seven proteins selected from the group consisting of PH, MMP-12, SP-D, HE4, PSP-94, FUT5 and CRLF1 in a sample from a human subject; and

b) identifying the human subject as being at risk for developing lung cancer based on the level of the at least three, four, five, six, or seven proteins.

20. The method of claim 19, wherein the method comprises measuring MMP-12, SP-D and HE4; MMP-12, SP-D and PSP-94; MMP-12, SP-D and PH; MMP-12, SP-D and FUT5; MMP-12, SP-D and CRLF1; MMP-12, HE4 and PSP-94; MMP-12, HE4 and PH; MMP-12, HE4 and FUT5; MP-12, HE4 and CRLF1; MMP-12, PSP-94 and PH; MMP-12, PSP-94 and FUT5; MMP-12, PSP-94 and CRLF1; MMP-12, PH and FUT5; MMP-12, PH and CRLF1; MMP-12, FUT5 and CRLF1; SP-D, HE4 and PSP-94; SP-D, HE4 and PH; SP-D, HE4 and FUT5; SP-D, HE4 and CRLF1; SP-D, PSP-94 and PH; SP-D, PSP-94 and FUT5; SP-D, PSP-94 and CRLF1; SP-D, PH and FUT5; SP-D, PH and CRLF1; SP-D, FUT5 and CRLF1; HE4, PSP-94 and PH; HE4, PSP-94 and FUT5; HE4, PSP-94 and CRLF1; HE4, PH and FUT5; HE4, PH and CRLF1; HE4, FUT5 and CRLF1; PSP-94, PH and FUT5; PSP-94, PH and CRLF1; PSP-94, FUT5 and CRLF1; or PH, FUT5, and CRLF1.

21. The method of claim 19 or claim 20, further comprising measuring one or more of PSP-94, PH, FUT5, and CRLF1.

22. The method of any one of claims 1-21, wherein the measuring is performed using aptamers, antibodies and a combination of aptamers and antibodies.

23. The method of any one of the preceding claims, wherein the measuring is performed using mass spectrometry, an aptamer based assay and/or an antibody based assay.

24. The method of claim 22 or claim 23, wherein the level of each biomarker protein measured is determined from a relative fluorescence unit (RFU) or a protein concentration.

25. The method of any one of the preceding claims, wherein the sample is selected from blood, plasma, serum or urine.

26. The method of any one of claims 1-25, wherein the risk for developing lung cancer is within a period of 1 year, 2 years, 3 years, 4 years, 5 years, 6 years, 7 years, 8 years, 9 years, or 10 years.

27. The method of any one of the preceding claims, wherein the human subject is a current smoker or a former smoker or wherein the subject has lung cancer.

28. The method of any one of the preceding claims, wherein the method provides an area under the curve (AUC) of 0.62, 0.67, 0.68, 0.68, 0.70, 0.71, 0.72, 0.73, 0.74, 0.75, 0.76, or above or wherein the method provides an area under the curve (AUC) from about 0.6 to about 0.8, from about 0.61 to about 0.78, from about 0.62 to about 0.76, from about 0.62 to about 0.68, from about 0.67 to about 0.72, from about 0.69 to about 0.74, from about 0.71 to about 0.74, from about 0.73 to about 0.76, or from about 0.74 to about 0.76.

29. The method of any one of the preceding claims, wherein predicting the risk for developing lung cancer is based on input of the levels of the measured proteins in a statistical model or wherein predicting the risk of lung cancer comprises analyzing the levels of the measured proteins using an Accelerated Failure Time (AFT) Weibull survival model.

30. A kit comprising N protein capture reagents, wherein N is at least 1, at least 2, at least 3, at least 4, at least 5, at least 6, or at least 7, and wherein at least one of the N protein capture reagents specifically binds to a protein selected from PH, PSP-94, MMP-12, SP-D, HE4, FUT5 and CRLF1.

31. The kit of claim 30, wherein N is at least two and at least one to the two N protein capture reagents specifically binds to the protein selected from PH, PSP-94, MMP-12, SP-D, HE4, FUT5 and CRLF1.

32. The kit of claim 30 or 31, wherein N is 2 to 7, or N is 3 to 7, or N is 4 to 7, or N is 5 to 7, or N is 6 to 7 or wherein N is 2, N is 3, N is 4, N is 5, N is 6, or N is 7.

33. The kit of any one of claims 30-32, wherein each of the N protein capture reagents specifically binds to a different biomarker protein or wherein each of the N protein capture reagents specifically binds to a protein selected from PH, PSP-94, MMP-12, SP-D, HE4, FUT5 and CRLF1.

34. The kit of any one of claims 30-32, wherein two of the N protein capture reagents specifically bind PSP-94 and MMP-12; or two of the N protein capture reagents specifically bind PSP-94 and SP-D; or two of the N protein capture reagents specifically bind PSP-94 and HE4; or two of the N protein capture reagents specifically bind PSP-94 and PH; or two of the N protein capture reagents specifically bind PSP-94 and FUT5; or two of the N protein capture reagents specifically bind PSP-94 and CRLF1; or wherein two of the N protein capture reagents specifically bind PH and MMP-12; or two of the N protein capture reagents specifically bind PH and SP-D; or two of the N protein capture reagents specifically bind PH and HE4; or two of the N protein capture reagents specifically bind PH and PSP-94; PH and FUT5; or two of the N protein capture reagents specifically bind PH and CRLF1 or two of the N protein capture reagents specifically bind FUT5 and MMP-12; or two of the N protein capture reagents specifically bind FUT5 and SP-D; or two of the N protein capture reagents specifically bind FUT5 and HE4; or two of the N protein capture reagents specifically bind FUT5 and PSP-94; or two of the N protein capture reagents specifically bind FUT5 and PH; or two of the N protein capture reagents specifically bind FUT5 and CRLF1; or two of the N protein capture reagents specifically bind CRLF1 and MMP-12; or two of the N protein capture reagents specifically bind CRLF1 and SP-D; or two of the N protein capture reagents specifically bind CRLF1 and HE4; or CRLF1 and PSP-94; or two of the N protein capture reagents specifically bind CRLF1 and PH.

35. The kit of any one of claims 30-32, wherein three of the N protein capture reagents specifically bind PSP-94, MMP-12 and SP-D; or three of the N protein capture reagents specifically bind PSP-94, MMP-12 and HE4; or three of the N protein capture reagents

specifically bind PSP-94, MMP-12 and PH; or three of the N protein capture reagents specifically bind PSP-94, MMP-12 and FUT5; or three of the N protein capture reagents specifically bind PSP-94, MMP-12 and CRLF1; or three of the N protein capture reagents specifically bind PSP-94, SP-D and HE4; or three of the N protein capture reagents specifically bind PSP-94, SP-D and PH; or three of the N protein capture reagents specifically bind PSP-94, SP-D and FUT5; or three of the N protein capture reagents specifically bind PSP-94, SP-D and CRLF1; or three of the N protein capture reagents specifically bind PSP-94, HE4 and PH; PSP-94, HE4 and FUT5; or three of the N protein capture reagents specifically bind PSP-94, HE4 and CRLF1; or three of the N protein capture reagents specifically bind PSP-94, PH and FUT5; or three of the N protein capture reagents specifically bind PSP-94, PH and CRLF1; or three of the N protein capture reagents specifically bind PSP-94, FUT5 and CRLF1; or three of the N protein capture reagents specifically bind PH, MMP-12 and SP-D; or three of the N protein capture reagents specifically bind PH, MMP-12 and HE4; or three of the N protein capture reagents specifically bind PH, MMP-12 and PSP-94; or three of the N protein capture reagents specifically bind PH, MMP-12 and FUT5; or three of the N protein capture reagents specifically bind PH, MMP-12 and CRLF1; or three of the N protein capture reagents specifically bind PH, SP-D and HE4; or three of the N protein capture reagents specifically bind PH, SP-D and PSP-94; or three of the N protein capture reagents specifically bind PH, SP-D and FUT5; or three of the N protein capture reagents specifically bind PH, SP-D and CRLF1; or three of the N protein capture reagents specifically bind PH, HE4 and PSP-94; or three of the N protein capture reagents specifically bind PH, HE4 and FUT5; or three of the N protein capture reagents specifically bind PH, HE4 and CRLF1; or three of the N protein capture reagents specifically bind PH, PSP-94 and FUT5; PH, PSP-94 and CRLF1; or three of the N protein capture reagents specifically bind PH, FUT5 and CRLF1; or three of the N protein capture reagents specifically bind FUT5, MMP-12 and SP-D; or three of the N protein capture reagents specifically bind FUT5, MMP-12 and HE4; or three of the N protein capture reagents specifically bind FUT5, MMP-12 and PSP-94; or three of the N protein capture reagents specifically bind FUT5, MMP-12 and PH; or three of the N protein capture reagents specifically bind FUT5, MMP-12 and CRLF1; or three of the N protein capture reagents specifically bind FUT5, SP-D and HE4; or three of the N protein capture reagents specifically bind FUT5, SP-D and PSP-94; or three of the N protein capture reagents specifically bind FUT5, SP-D and PH; or three of the N protein

capture reagents specifically bind FUT5, SP-D and CRLF1; or three of the N protein capture reagents specifically bind FUT5, HE4 and PSP-94; or three of the N protein capture reagents specifically bind FUT5, HE4 and PH; or three of the N protein capture reagents specifically bind FUT5, HE4 and CRLF1; or three of the N protein capture reagents specifically bind FUT5, PSP-94 and PH; or three of the N protein capture reagents specifically bind FUT5, PSP-94 and CRLF1; or three of the N protein capture reagents specifically bind FUT5, PH and CRLF1; or three of the N protein capture reagents specifically bind CRLF1, MMP-12 and SP-D; or three of the N protein capture reagents specifically bind CRLF1, MMP-12 and HE4; or three of the N protein capture reagents specifically bind CRLF1, MMP-12 and PSP-94; or three of the N protein capture reagents specifically bind CRLF1, MMP-12 and PH; or three of the N protein capture reagents specifically bind CRLF1, MMP-12 and FUT5; or three of the N protein capture reagents specifically bind CRLF1, SP-D and HE4; or three of the N protein capture reagents specifically bind CRLF1, SP-D and PSP-94; or three of the N protein capture reagents specifically bind CRLF1, SP-D and PH; or three of the N protein capture reagents specifically bind CRLF1, SP-D and FUT5; or three of the N protein capture reagents specifically bind CRLF1, HE4 and PSP-94; or three of the N protein capture reagents specifically bind CRLF1, HE4 and PH; or three of the N protein capture reagents specifically bind CRLF1, HE4 and FUT5; or three of the N protein capture reagents specifically bind CRLF1, PSP-94 and PH; or three of the N protein capture reagents specifically bind CRLF1, PSP-94 and FUT5; or three of the N protein capture reagents specifically bind CRLF1, PH and FUT5.

36. The kit of any one of claims 30-35, wherein each of the N biomarker protein capture reagents is an antibody or an aptamer.

37. The kit of any one of claims 30-36, for use in detecting the N biomarker proteins in a sample from a subject.