

DPYL2, DYHC1, ECH1, EF2, IF4A3, ENOA, EZRI, NIBL2, SEPR, FBX4, FIBB, FIBG, FHL1, FLNA, FRMD3, FRIH, FRIL, FUCO, GBRA1, G3P, SYG, GDF15, GELS, GSTP1, HABP2, HGF, 1A68, HMGB1, ROA1, ROA2, HNRPF, HPT, HS90B, ENPL, GRP75, HSPB1, CH60, SIAL, IFT74, IGF1, IGHA2, IL2RB, IL8, IL9, RASK, K1C19, K2C8, LAMA2, LEG3, LMNB1, MARE1, MCM4, MIF, MMP7, MMP9, CD20, MYL6, MYL9, NDKA, NNMT, A1AG1, PCKGM, PDIA3, PDIA6, PDXK, PEBP1, PIPNA, KPYM, UROK, IPYR, PRDX1, KPCD1, PRL, TMG4, PSME3, PTEN, FAK1, FAK2, RBX1, REG4, RHOA, RHOB, RHOC, RSSA, RRPB1, S10AB, S10AC, S10A8, S109, SAA1, SAA2, SEGN, SDCG3, DHSA, SBP1, SELPL, SEP9, A1AT, AACT, ILEU, SPB6, SF3B3, SKP1, ADT2, ISK1, SPON2, OSTP, SRC, STK11, HNRPQ, TAL1, TRFE, TSP1, TIMP1, TKT, TSG6, TR10B, TNF6B, P53, TPM2, TCTP, TRAP1, THTR, TBB1, UGDH, UGPA, VEGFA, VILI, VIME, VNN1, 1433Z, CCR5, FUCO and combinations thereof in a biological sample from the subject.

[013] Methods are also disclosed for the diagnosis, prediction, prognosis and/or monitoring a colon disease or colorectal cancer in a subject comprising: measuring at least one biomarker selected from the group SPB6, FRIL, P53, 1A68, ENOA, TKT, and combinations thereof in a biological sample from the subject.

[014] Methods are disclosed for the diagnosis, prediction, prognosis and/or monitoring a colon disease or colorectal cancer in a subject comprising: measuring at least one biomarker selected from the group SPB6, FRIL, P53, 1A68, ENOA, TKT, TSG6, TPM2, ADT2, FHL1, CCR5, CEAM5, SPON2, 1A68, RBX1, COR1C, VIME, PSME3, and combinations thereof in a biological sample from the subject.

[015] Methods are disclosed for the diagnosis, prediction, prognosis and/or monitoring a colon disease or colorectal cancer in a subject comprising: measuring at least one biomarker selected from the group SPB6, FRIL, P53, 1A68, ENOA, TKT, TSG6, TPM2, ADT2, FHL1, CCR5, CEAM5, SPON2, 1A68, RBX1, COR1C, VIME, PSME3, MIC1, STK11, IPYR, SBP1, PEBP1, CATD, HPT, ANXA5, ALDOA, LAMA2, CATZ, ACTB, AACT, and combinations thereof in a biological sample from the subject.

[0015a] Kits are disclosed for detecting a polyp in a colon or rectum in a human subject, said kit comprising:
(a) a container for collecting a sample from said human subject;
(b) a panel of antibodies comprising an antibody that binds Cathepsin D (CTSD); an antibody that binds Carcinoembryonic antigen (CEA); and an antibody that binds Fibroblast activation protein, alpha (Seprase); and

(c) written instructions,

wherein detection of a panel of proteins comprising CTSD, CEA and Seprase at levels above a threshold indicates the presence of a polyp in the colon or the rectum in the human subject with a sensitivity of 70%.

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INCORPORATION BY REFERENCE

[016] All publications, patents, and patent applications mentioned in this specification are herein incorporated by reference to the same extent as if each individual publication, patent, or patent application was specifically and individually indicated to be incorporated by reference.

CLAIMS

WHAT IS CLAIMED IS:

1. A method of detecting the presence of an adenoma or polyp of the colon in a subject with a sensitivity of greater than 70% or a selectivity of greater than 70%; said method comprising the steps of:
 - (a) obtaining a blood sample from a subject;
 - (b) cleaving proteins in said blood sample to provide a sample comprising peptides;
 - (c) analyzing said sample for the presence of at least ten peptides;
 - (d) comparing the results of analyzing said sample with control reference values to determine a positive or negative score for the presence of an adenoma or polyp of the colon with a sensitivity of greater than 70% or a selectivity of greater than 70%.
2. The method of claim 1, wherein said sensitivity is selected from greater than 75%, greater than 80%, greater than 85%, greater than 90%, greater than 95%, and greater than 99%.
3. The method of claim 1, wherein said selectivity is selected from greater than 75%, greater than 80%, greater than 85%, greater than 90%, greater than 95%, and greater than 99%.
4. The method of claim 1, wherein said selectivity and said sensitivity are greater than 90%.
5. The method of claim 1, wherein said subject is asymptomatic.
6. The method of claim 1, wherein said subject has previously received treatment for colon polyps.
7. The method of claim 1, wherein said analyzing step comprises spectroscopic analysis, mass spectrometry, immunological analysis, enzymatic reactivity analysis, and combinations thereof.
8. The method of claim 1, wherein said analyzing comprises mass spectrometry.
9. The method of claim 1, wherein said at least ten peptides are selected from the neutral mass classifiers of **Figure 8**.
10. A method of treating an adenoma or polyp of the colon in a subject comprising
 - (a) performing the method of claim 1 to yield a subject with a positive score for the presence of an adenoma or polyp; and
 - (b) performing a procedure for removal of adenoma or polyp tissue in said subject.

11. A method of detecting the presence or absence of an adenoma or polyp of the colon in a subject, wherein said subject has no symptoms or family history of adenoma or polyps of the colon, said method comprising the steps of:

- (a) obtaining a biological sample from said subject;
- (b) performing an analysis of the biological sample for the presence and amount of one or more proteins and/or peptides;
- (c) comparing the presence and amount of one or more proteins and/or peptides from said biological sample to a control reference value; and
- (d) correlating the presence and amount of one or more proteins and/or peptides with the subject's adenoma or polyp status.

12. The method of claim 11, wherein said method achieves a sensitivity selected from greater than 70%, greater than 75%, greater than 80%, greater than 85%, greater than 90%, greater than 95%, and greater than 99%.

13. The method of claim 11, wherein said method achieves a specificity selected from greater than 70%, greater than 75%, greater than 80%, greater than 85%, greater than 90%, greater than 95%, and greater than 99%.

14. The method of claim 11, wherein said method achieves sensitivity and specificity each individually selected from greater than 70%, greater than 75%, greater than 80%, greater than 85%, greater than 90%, greater than 95%, and greater than 99%.

15. The method of claim 11, further comprising preparing a report for said subject, wherein said report indicates the presence or absence of an adenoma or polyp.

16. The method of claim 15, wherein said report indicates a predisposition or risk for polyp development, a degree of cell dysplasia, a subtype of adenomatous polyp, or a subtype of benign colon tumor disease.

17. The method of claim 11, wherein said method detects the presence or absence of an adenoma.

18. The method of claim 17, wherein said adenoma is an adenomatous polyp or polypoid adenoma.

19. The method of claim 18, wherein said adenomatous polyp or polypoid adenoma is selected from the group of pedunculated polyps and sessile polyps.

20. The method of claim 18, wherein said adenomatous polyp or polypoid adenoma is characterized according to a degree of cell dysplasia or pre-malignancy.

21. The method of claim 11, wherein said method further detects the presence or absence of colorectal carcinoma.
22. The method of claim 11, wherein said method does not detect the presence or absence of colorectal carcinoma.
23. The method of claim 11, wherein the presence or absence of colorectal carcinoma is not determined.
24. The method of claim 11, wherein said presence or absence is confirmed by colonoscopy, imaging, and/or surgery.
25. The method of claim 11, wherein said biological sample is selected from the group consisting of whole blood, serum, plasma, blood constituent, bone marrow, saliva, cheek swab, urine, stool, lymph fluid, CNS fluid, and lesion exudate.
26. The method of claim 25, wherein said biological sample is selected from the group consisting of whole blood, serum, and plasma.
27. The method of claim 11, wherein said subject is asymptomatic.
28. The method of claim 11, wherein said subject is from 18 to 49 years old.
29. The method of claim 11, wherein said subject has not previously received a colonoscopy.
30. The method of claim 11, wherein said subject has no symptoms for colorectal carcinoma, no family history for colorectal carcinoma, and no recognized risk factors for colorectal carcinoma.
31. The method of claim 11, wherein said subject has no symptoms for colorectal carcinoma, no family history for colorectal carcinoma, and no recognized risk factors for colorectal carcinoma other than age.
32. The method of claim 11, wherein said analysis of step (b) includes a method selected from the group consisting of spectroscopic analysis, mass spectrometry, immunological analysis, and enzymatic reactivity.
33. The method of claim 32, wherein said analysis is mass spectrometry.
34. The method of claim 32, wherein said immunological analysis includes an enzyme-linked immunosorbent assay or radioimmunoassay.
35. The method of claim 32, wherein said immunological analysis includes immunoblotting, immunodiffusion, immunoelectrophoresis, or immunoprecipitation.
36. The method of claim 32, wherein said immunological analysis includes immunostaining and/or flow cytometry analysis.

37. The method of claim 11, wherein said control reference is the presence and amount of a set of one or more non-overlapping proteins and/or peptides in the same biological sample.

38. The method of claim 11, wherein said control reference is the presence and amount of an overlapping set of proteins and/or peptides obtained from one or more subjects in which adenoma or polyp of the colon is present.

39. The method of claim 11, wherein said control reference is the presence and amount of an overlapping set of proteins and/or peptides obtained from one or more subjects in which adenoma or polyp of the colon is not present.

40. The method of claim 11, wherein said analysis detects the presence and amount of a number of proteins or polypeptides, wherein said number is selected from at least 2, at least 5, at least 10, at least 50, at least 100, and at least 1000.

41. The method of claim 11, wherein said analysis detects the presence and amount of one or more of the following sets:

i) one or more proteins selected from SCDC26 (CD26), CEA molecule 5 (CEACAM5), CA195 (CCR5), CA19-9, M2PK (PKM2), TIMP1, P-selectin (SELPLG), VEGFA, HcGB (CGB), VILLIN, TATI (SPINK1), A-L-fucosidase (FUCA2), ANXA5, GAPDH, PKM2, ANXA4, GARS, RRB1, KRT8, SYNCRIP, S100A9, ANXA3, CAPG, HNRNP, PPA1, NME1, PSME3, AHCY, TPT1, HSPB1, and RPSA, and/or the proteins in **Figure 9** and combinations thereof;

ii) one or more peptide fragments of SCDC26 (CD26), CEA molecule 5 (CEACAM5), CA195 (CCR5), CA19-9, M2PK (PKM2), TIMP1, P-selectin (SELPLG), VEGFA, HcGB (CGB), VILLIN, TATI (SPINK1), A-L-fucosidase (FUCA2), ANXA5, GAPDH, PKM2, ANXA4, GARS, RRB1, KRT8, SYNCRIP, S100A9, ANXA3, CAPG, HNRNP, PPA1, NME1, PSME3, AHCY, TPT1, HSPB1, and RPSA, and/or the proteins in **Figure 9** and combinations thereof;

iii) one or more peptides with a sequence homology to SCDC26 (CD26), CEA molecule 5 (CEACAM5), CA195 (CCR5), CA19-9, M2PK (PKM2), TIMP1, P-selectin (SELPLG), VEGFA, HcGB (CGB), VILLIN, TATI (SPINK1), A-L-fucosidase (FUCA2), ANXA5, GAPDH, PKM2, ANXA4, GARS, RRB1, KRT8, SYNCRIP, S100A9, ANXA3, CAPG, HNRNP, PPA1, NME1, PSME3, AHCY, TPT1, HSPB1, and RPSA, and/or the proteins in **Figure 9** and combinations thereof, wherein said sequence

homology is selected from the group of greater than 75%, greater than 80%, greater than 85%, greater than 90%, greater than 95%, and greater than 99%; and

iv) one or more binding partners of SCDC26 (CD26), CEA molecule 5 (CEACAM5), CA195 (CCR5), CA19-9, M2PK (PKM2), TIMP1, P-selectin (SELPLG), VEGFA, HcGB (CGB), VILLIN, TATI (SPINK1), A-L-fucosidase (FUCA2), ANXA5, GAPDH, PKM2, ANXA4, GARS, RRBP1, KRT8, SYNCRIP, S100A9, ANXA3, CAPG, HNRNPF, PPA1, NME1, PSME3, AHCY, TPT1, HSPB1, and RPSA, and/or the proteins in **Figure 9** and combinations thereof.

42. The method of claim 11, wherein said analysis detects the presence and/or amount of one or more neutral mass clusters from **Figure 7** or **Figure 8**.

43. The method of claim 42, wherein said analysis detects the presence and/or amount of a number of neutral mass clusters from **Figure 7** or **Figure 8**, wherein said number is selected from at least 2, at least 5, at least 10, at least 50, at least 100, at least 200, at least 500, and at least 1000.

44. The method of claim 42, wherein said analysis detects the presence and/or amount of a number of neutral mass clusters from **Figure 7** or **Figure 8**, wherein said number is at least one, and is selected from less than 5, less than 10, less than 50, less than 100, less than 200, less than 500, and less than 1000.

45. The method of claim 42, wherein said analysis detects the presence and/or amount of a number of neutral mass clusters from **Figure 7** or **Figure 8**, wherein said number is selected from the group consisting of 10 to 50, 60 to 100, 150-300, 400-600, and 800-1000, inclusive.

46. The method of claim 42, wherein said neutral mass cluster has a classifier frequency when tested according to a 70/30 training/test for split classifiers, wherein said classifier frequency is selected from at least 3 out of 50, at least 10 out of 50, at least 20 out of 50, at least 30 out of 50, and at least 40 out of 50.

47. The method of claim 42, wherein said analysis detects the presence and/or amount of a protein or peptide from which one or more neutral mass clusters from **Figure 7** or **Figure 8** is derived.

48. The method of claim 11, further comprising

(e) performing an analysis of the biological sample for the presence and amount of one or more analytes selected from the groups consisting of metabolites, DNA sequences, RNA sequences, and combinations thereof; and

(f) comparing the presence and amount of said analytes to a control reference value; and
(g) correlating the presence and amount of said analytes with the subject's adenoma or polyp status.

49. A method of detecting the presence or absence of an adenoma or polyp of the colon in a subject in whom a colonoscopy yielded a negative result comprising the steps of:

- (a) obtaining a biological sample from a subject with a negative diagnosis of adenoma or polyps based on colonoscopy;
- (b) performing an analysis of the biological sample for the presence and amount of one or more proteins and/or peptides;
- (c) comparing the presence and amount of one or more proteins and/or peptides from said biological sample to a control reference value; and
- (d) correlating the presence and amount of one or more proteins and/or peptides with the subject's adenoma or polyp status.

50. The method of claim 49, wherein said method achieves a sensitivity selected from greater than 70%, greater than 75%, greater than 80%, greater than 85%, greater than 90%, greater than 95%, and greater than 99%.

51. The method of claim 49, wherein said method achieves a specificity selected from greater than 70%, greater than 75%, greater than 80%, greater than 85%, greater than 90%, greater than 95%, and greater than 99%.

52. The method of claim 49, wherein said method achieves sensitivity and specificity each individually selected from greater than 70%, greater than 75%, greater than 80%, greater than 85%, greater than 90%, greater than 95%, and greater than 99%.

53. The method of claim 49, further comprising preparing a report for said subject, wherein said report indicates the presence or absence of an adenoma or polyp.

54. The method of claim 53, wherein said report indicates a predisposition or risk for polyp development, a degree of cell dysplasia, a subtype of adenomatous polyp, or a subtype of benign colon tumor disease.

55. The method of claim 49, wherein said method detects the presence or absence of an adenoma.

56. The method of claim 55, wherein said adenoma is an adenomatous polyp or polypoid adenoma.

57. The method of claim 56, wherein said adenomatous polyp or polypoid adenoma is selected from the group of pedunculated polyps and sessile polyps.

58. The method of claim 56, wherein said adenomatous polyp or polypoid adenoma is characterized according to a degree of cell dysplasia or pre-malignancy.
59. The method of claim 49, wherein said method further detects the presence or absence of colorectal carcinoma.
60. The method of claim 49, wherein said method does not detect the presence or absence of colorectal carcinoma.
61. The method of claim 49, wherein the presence or absence of colorectal carcinoma is not determined.
62. The method of claim 49, wherein said presence or absence is confirmed by colonoscopy, imaging, and/or surgery.
63. The method of claim 49, wherein said biological sample is selected from the group consisting of whole blood, serum, plasma, blood constituent, bone marrow, saliva, cheek swab, urine, stool, lymph fluid, CNS fluid, and lesion exudate.
64. The method of claim 63, wherein said biological sample is selected from the group consisting of whole blood, serum, and plasma.
65. The method of claim 49, wherein said subject is asymptomatic.
66. The method of claim 49, wherein said subject is from 18 to 49 years old.
67. The method of claim 49, wherein said subject has no symptoms for colorectal carcinoma, no family history for colorectal carcinoma, and no recognized risk factors for colorectal carcinoma.
68. The method of claim 49, wherein said subject has no symptoms for colorectal carcinoma, no family history for colorectal carcinoma, and no recognized risk factors for colorectal carcinoma other than age.
69. The method of claim 49, wherein said analysis of step (b) includes a method selected from the group consisting of spectroscopic analysis, mass spectrometry, immunological analysis, and enzymatic reactivity.
70. The method of claim 69, wherein said analysis is mass spectrometry.
71. The method of claim 69, wherein said immunological analysis includes an enzyme-linked immunosorbent assay or radioimmunoassay.
72. The method of claim 69, wherein said immunological analysis includes immunoblotting, immunodiffusion, immunoelectrophoresis, or immunoprecipitation.
73. The method of claim 69, wherein said immunological analysis includes immunostaining and/or flow cytometry analysis.

74. The method of claim 49, wherein said control reference is the presence and amount of a set of one or more non-overlapping proteins and/or peptides in the same biological sample.

75. The method of claim 49, wherein said control reference is the presence and amount of an overlapping set of proteins and/or peptides obtained from one or more subjects in which adenoma or polyp of the colon is present.

76. The method of claim 49, wherein said control reference is the presence and amount of an overlapping set of proteins and/or peptides obtained from one or more subjects in which adenoma or polyp of the colon is not present.

77. The method of claim 49, wherein said analysis detects the presence and amount of a number of proteins or polypeptides, wherein said number is selected from at least 2, at least 5, at least 10, at least 50, at least 100, and at least 1000.

78. The method of claim 49, wherein said analysis detects the presence and amount of one or more of the following sets:

i) one or more proteins selected from SCDC26 (CD26), CEA molecule 5 (CEACAM5), CA195 (CCR5), CA19-9, M2PK (PKM2), TIMP1, P-selectin (SELPLG), VEGFA, HcGB (CGB), VILLIN, TATI (SPINK1), A-L-fucosidase (FUCA2), ANXA5, GAPDH, PKM2, ANXA4, GARS, RRBP1, KRT8, SYNCRIP, S100A9, ANXA3, CAPG, HNRNPF, PPA1, NME1, PSME3, AHCY, TPT1, HSPB1, and RPSA, and/or the proteins in **Figure 9** and combinations thereof;

ii) one or more peptide fragments of SCDC26 (CD26), CEA molecule 5 (CEACAM5), CA195 (CCR5), CA19-9, M2PK (PKM2), TIMP1, P-selectin (SELPLG), VEGFA, HcGB (CGB), VILLIN, TATI (SPINK1), A-L-fucosidase (FUCA2), ANXA5, GAPDH, PKM2, ANXA4, GARS, RRBP1, KRT8, SYNCRIP, S100A9, ANXA3, CAPG, HNRNPF, PPA1, NME1, PSME3, AHCY, TPT1, HSPB1, and RPSA, and/or the proteins in **Figure 9** and combinations thereof;

iii) one or more peptides with a sequence homology to SCDC26 (CD26), CEA molecule 5 (CEACAM5), CA195 (CCR5), CA19-9, M2PK (PKM2), TIMP1, P-selectin (SELPLG), VEGFA, HcGB (CGB), VILLIN, TATI (SPINK1), A-L-fucosidase (FUCA2), ANXA5, GAPDH, PKM2, ANXA4, GARS, RRBP1, KRT8, SYNCRIP, S100A9, ANXA3, CAPG, HNRNPF, PPA1, NME1, PSME3, AHCY, TPT1, HSPB1, and RPSA, and/or the proteins in **Figure 9** and combinations thereof, wherein said sequence homology is selected from

the group of greater than 75%, greater than 80%, greater than 85%, greater than 90%, greater than 95%, and greater than 99%; and

iv) one or more binding partners of SCDC26 (CD26), CEA molecule 5 (CEACAM5), CA195 (CCR5), CA19-9, M2PK (PKM2), TIMP1, P-selectin (SELPLG), VEGFA, HcGB (CGB), VILLIN, TATI (SPINK1), A-L-fucosidase (FUCA2), ANXA5, GAPDH, PKM2, ANXA4, GARS, RRBPI, KRT8, SYNCRIP, S100A9, ANXA3, CAPG, HNRNPF, PPA1, NME1, PSME3, AHCY, TPT1, HSPB1, and RPSA, and/or the proteins in **Figure 9** and combinations thereof.

79. The method of claim 49, wherein said analysis detects the presence and/or amount of one or more neutral mass clusters from **Figure 7** or **Figure 8**.

80. The method of claim 79, wherein said analysis detects the presence and/or amount of a number of neutral mass clusters from **Figure 7** or **Figure 8**, wherein said number is selected from at least 2, at least 5, at least 10, at least 50, at least 100, at least 200, at least 500, and at least 1000.

81. The method of claim 79, wherein said analysis detects the presence and/or amount of a number of neutral mass clusters from **Figure 7** or **Figure 8**, wherein said number is at least one, and is selected from less than 5, less than 10, less than 50, less than 100, less than 200, less than 500, and less than 1000.

82. The method of claim 79, wherein said analysis detects the presence and/or amount of a number of neutral mass clusters from **Figure 7** or **Figure 8**, wherein said number is selected from the group consisting of 10 to 50, 60 to 100, 150-300, 400-600, and 800-1000, inclusive.

83. The method of claim 79, wherein said neutral mass cluster has a classifier frequency when tested according to a 70/30 training/test for split classifiers, wherein said classifier frequency is selected from at least 3 out of 50, at least 10 out of 50, at least 20 out of 50, at least 30 out of 50, and at least 40 out of 50.

84. The method of claim 79, wherein said analysis detects the presence and/or amount of a protein or peptide from which one or more neutral mass clusters from **Figure 7** or **Figure 8** is derived.

85. The method of claim 79, further comprising

(e) performing an analysis of the biological sample for the presence and amount of one or more analytes selected from the groups consisting of metabolites, DNA sequences, RNA sequences, and combinations thereof; and

(f) comparing the presence and amount of said analytes to a control reference value; and
(g) correlating the presence and amount of said analytes with the subject's adenoma or polyp status.

86. A method of detecting recurrence or absence of an adenoma or polyp of the colon in a subject previously treated for adenoma or polyps of the colon comprising the steps of:

(a) obtaining a biological sample from a subject previously treated for adenoma or polyps of the colon;

(b) performing an analysis of the biological sample for the presence and amount of one or more proteins and/or peptides;

(c) comparing the presence and amount of one or more proteins and/or peptides from said biological sample to a control reference value; and

(d) correlating the presence and amount of one or more proteins and/or peptides with the subject's adenoma or polyp status.

87. The method of claim 86, wherein said method achieves a sensitivity selected from greater than 70%, greater than 75%, greater than 80%, greater than 85%, greater than 90%, greater than 95%, and greater than 99%.

88. The method of claim 86, wherein said method achieves a specificity selected from greater than 70%, greater than 75%, greater than 80%, greater than 85%, greater than 90%, greater than 95%, and greater than 99%.

89. The method of claim 86, wherein said method achieves sensitivity and specificity each individually selected from greater than 70%, greater than 75%, greater than 80%, greater than 85%, greater than 90%, greater than 95%, and greater than 99%.

90. The method of claim 86, further comprising preparing a report for said subject, wherein said report indicates the presence or absence of an adenoma or polyp.

91. The method of claim 90, wherein said report indicates a predisposition or risk for polyp development, a degree of cell dysplasia, a subtype of adenomatous polyp, or a subtype of benign colon tumor disease.

92. The method of claim 86, wherein said method detects the presence or absence of an adenoma.

93. The method of claim 92, wherein said adenoma is an adenomatous polyp or polypoid adenoma.

94. The method of claim 93, wherein said adenomatous polyp or polypoid adenoma is selected from the group of pedunculated polyps and sessile polyps.

95. The method of claim 93, wherein said adenomatous polyp or polypoid adenoma is characterized according to a degree of cell dysplasia or pre-malignancy.
96. The method of claim 86, wherein said method further detects the presence or absence of colorectal carcinoma.
97. The method of claim 86, wherein said method does not detect the presence or absence of colorectal carcinoma.
98. The method of claim 86, wherein the presence or absence of colorectal carcinoma is not determined.
99. The method of claim 86, wherein said presence or absence is confirmed by colonoscopy, imaging, and/or surgery.
100. The method of claim 86, wherein said biological sample is selected from the group consisting of whole blood, serum, plasma, blood constituent, bone marrow, saliva, cheek swab, urine, stool, lymph fluid, CNS fluid, and lesion exudate.
101. The method of claim 100, wherein said biological sample is selected from the group consisting of whole blood, serum, and plasma.
102. The method of claim 86, wherein said subject is asymptomatic.
103. The method of claim 86, wherein said subject is from 18 to 49 years old.
104. The method of claim 86, wherein said subject has no symptoms for colorectal carcinoma, no family history for colorectal carcinoma, and no recognized risk factors for colorectal carcinoma.
105. The method of claim 86, wherein said subject has no symptoms for colorectal carcinoma, no family history for colorectal carcinoma, and no recognized risk factors for colorectal carcinoma other than age.
106. The method of claim 86, wherein said analysis of step (b) includes a method selected from the group consisting of spectroscopic analysis, mass spectrometry, immunological analysis, and enzymatic reactivity.
107. The method of claim 106, wherein said analysis is mass spectrometry.
108. The method of claim 106, wherein said immunological analysis includes an enzyme-linked immunosorbent assay or radioimmunoassay.
109. The method of claim 106, wherein said immunological analysis includes immunoblotting, immunodiffusion, immunoelectrophoresis, or immunoprecipitation.
110. The method of claim 106, wherein said immunological analysis includes immunostaining and/or flow cytometry analysis.

111. The method of claim 86, wherein said control reference is the presence and amount of a set of one or more non-overlapping proteins and/or peptides in the same biological sample.

112. The method of claim 86, wherein said control reference is the presence and amount of an overlapping set of proteins and/or peptides obtained from one or more subjects in which adenoma or polyp of the colon is present.

113. The method of claim 86, wherein said control reference is the presence and amount of an overlapping set of proteins and/or peptides obtained from one or more subjects in which adenoma or polyp of the colon is not present.

114. The method of claim 86, wherein said analysis detects the presence and amount of a number of proteins or polypeptides, wherein said number is selected from at least 2, at least 5, at least 10, at least 50, at least 100, and at least 1000.

115. The method of claim 86, wherein said analysis detects the presence and amount of one or more of the following sets:

i) one or more proteins selected from SCDC26 (CD26), CEA molecule 5 (CEACAM5), CA195 (CCR5), CA19-9, M2PK (PKM2), TIMP1, P-selectin (SELPLG), VEGFA, HcGB (CGB), VILLIN, TATI (SPINK1), A-L-fucosidase (FUCA2), ANXA5, GAPDH, PKM2, ANXA4, GARS, RRBP1, KRT8, SYNCRIP, S100A9, ANXA3, CAPG, HNRNPF, PPA1, NME1, PSME3, AHCY, TPT1, HSPB1, and RPSA, and/or the proteins in **Figure 9** and combinations thereof;

ii) one or more peptide fragments of SCDC26 (CD26), CEA molecule 5 (CEACAM5), CA195 (CCR5), CA19-9, M2PK (PKM2), TIMP1, P-selectin (SELPLG), VEGFA, HcGB (CGB), VILLIN, TATI (SPINK1), A-L-fucosidase (FUCA2), ANXA5, GAPDH, PKM2, ANXA4, GARS, RRBP1, KRT8, SYNCRIP, S100A9, ANXA3, CAPG, HNRNPF, PPA1, NME1, PSME3, AHCY, TPT1, HSPB1, and RPSA, and/or the proteins in **Figure 9** and combinations thereof;

iii) one or more peptides with a sequence homology to SCDC26 (CD26), CEA molecule 5 (CEACAM5), CA195 (CCR5), CA19-9, M2PK (PKM2), TIMP1, P-selectin (SELPLG), VEGFA, HcGB (CGB), VILLIN, TATI (SPINK1), A-L-fucosidase (FUCA2), ANXA5, GAPDH, PKM2, ANXA4, GARS, RRBP1, KRT8, SYNCRIP, S100A9, ANXA3, CAPG, HNRNPF, PPA1, NME1, PSME3, AHCY, TPT1, HSPB1, and RPSA, and/or the proteins in **Figure 9** and combinations thereof, wherein said sequence

homology is selected from the group of greater than 75%, greater than 80%, greater than 85%, greater than 90%, greater than 95%, and greater than 99%; and

iv) one or more binding partners of SCDC26 (CD26), CEA molecule 5 (CEACAM5), CA195 (CCR5), CA19-9, M2PK (PKM2), TIMP1, P-selectin (SELPLG), VEGFA, HcGB (CGB), VILLIN, TATI (SPINK1), A-L-fucosidase (FUCA2), and ANXA5, GAPDH, PKM2, ANXA4, GARS, RRBP1, KRT8, SYNCRIP, S100A9, ANXA3, CAPG, HNRNPF, PPA1, NME1, PSME3, AHCY, TPT1, HSPB1, and RPSA, and/or the proteins in **Figure 9** combinations thereof.

116. The method of claim 86, wherein said analysis detects the presence and/or amount of one or more neutral mass clusters from **Figure 7** or **Figure 8**.

117. The method of claim 116, wherein said analysis detects the presence and/or amount of a number of neutral mass clusters from **Figure 7** or **Figure 8**, wherein said number is selected from at least 2, at least 5, at least 10, at least 50, at least 100, at least 200, at least 500, and at least 1000.

118. The method of claim 116, wherein said analysis detects the presence and/or amount of a number of neutral mass clusters from **Figure 7** or **Figure 8**, wherein said number is at least one, and is selected from less than 5, less than 10, less than 50, less than 100, less than 200, less than 500, and less than 1000.

119. The method of claim 116, wherein said analysis detects the presence and/or amount of a number of neutral mass clusters from **Figure 7** or **Figure 8**, wherein said number is selected from the group consisting of 10 to 50, 60 to 100, 150-300, 400-600, and 800-1000, inclusive.

120. The method of claim 116, wherein said neutral mass cluster has a classifier frequency when tested according to a 70/30 training/test for split classifiers, wherein said classifier frequency is selected from at least 3 out of 50, at least 10 out of 50, at least 20 out of 50, at least 30 out of 50, and at least 40 out of 50.

121. The method of claim 116, wherein said analysis detects the presence and/or amount of a protein or peptide from which one or more neutral mass clusters from **Figure 7** or **Figure 8** is derived.

122. The method of claim 86, further comprising:

(e) performing an analysis of the biological sample for the presence and amount of one or more analytes selected from the groups consisting of metabolites, DNA sequences, RNA sequences, and combinations thereof;

(f) comparing the presence and amount of said analytes to a control reference value; and
(g) correlating the presence and amount of said analytes with the subject's adenoma or polyp status.

123. The method of claim 86, wherein said subject was previously treated for polyps of the colon by removal of the polyps.

124. The method of claim 86, wherein said subject was previously treated by removal of at least one centimeter of tissue from the colon.

125. A method of protein and/or peptide detection for diagnostic application comprising the steps of:

- (a) obtaining a biological sample from a subject;
- (b) performing an analysis of the biological sample for the presence and amount of one or more proteins and/or peptides;
- (c) comparing the presence and amount of one or more proteins and/or peptides from said biological sample to a control reference value; and
- (d) correlating the presence and amount of one or more proteins and/or peptides with a diagnosis for said subject;

wherein said analysis detects the presence and amount of one or more of the following sets:

- i) one or more proteins selected from SCDC26 (CD26), CEA molecule 5 (CEACAM5), CA195 (CCR5), CA19-9, M2PK (PKM2), TIMP1, P-selectin (SELPLG), VEGFA, HcGB (CGB), VILLIN, TATI (SPINK1), A-L-fucosidase (FUCA2), ANXA5, GAPDH, PKM2, ANXA4, GARS, RRBPI, KRT8, SYNCRIP, S100A9, ANXA3, CAPG, HNRNPF, PPA1, NME1, PSME3, AHCY, TPT1, HSPB1, and RPSA, and/or the proteins in **Figure 9** and combinations thereof;
- ii) one or more peptide fragments of SCDC26 (CD26), CEA molecule 5 (CEACAM5), CA195 (CCR5), CA19-9, M2PK (PKM2), TIMP1, P-selectin (SELPLG), VEGFA, HcGB (CGB), VILLIN, TATI (SPINK1), A-L-fucosidase (FUCA2), and ANXA5, GAPDH, PKM2, ANXA4, GARS, RRBPI, KRT8, SYNCRIP, S100A9, ANXA3, CAPG, HNRNPF, PPA1, NME1, PSME3, AHCY, TPT1, HSPB1, and RPSA, and/or the proteins in **Figure 9** combinations thereof;
- iii) one or more peptides with a sequence homology to SCDC26 (CD26), CEA molecule 5 (CEACAM5), CA195 (CCR5), CA19-9, M2PK (PKM2), TIMP1, P-selectin (SELPLG), VEGFA, HcGB (CGB), VILLIN, TATI (SPINK1), A-L-fucosidase

(FUCA2), ANXA5, GAPDH, PKM2, ANXA4, GARS, RRBP1, KRT8, SYNCRIP, S100A9, ANXA3, CAPG, HNRNPF, PPA1, NME1, PSME3, AHCY, TPT1, HSPB1, and RPSA, and/or the proteins in **Figure 9** and combinations thereof, wherein said sequence homology is selected from the group of greater than 75%, greater than 80%, greater than 85%, greater than 90%, greater than 95%, and greater than 99%;

iv) one or more binding partners of SCDC26 (CD26), CEA molecule 5 (CEACAM5), CA195 (CCR5), CA19-9, M2PK (PKM2), TIMP1, P-selectin (SELPLG), VEGFA, HcGB (CGB), VILLIN, TATI (SPINK1), A-L-fucosidase (FUCA2), and ANXA5, GAPDH, PKM2, ANXA4, GARS, RRBP1, KRT8, SYNCRIP, S100A9, ANXA3, CAPG, HNRNPF, PPA1, NME1, PSME3, AHCY, TPT1, HSPB1, and RPSA, and/or the proteins in **Figure 9** combinations thereof; and

v) a protein or peptide from which one or more neutral mass clusters from **Figure 7** or **Figure 8** is derived.

126. The method of claim 125, wherein said diagnosis is the presence or absence of a condition selected from the group consisting of adenoma, polyp of the colon, colorectal carcinoma, and combinations thereof.

127. The method of claim 125, further comprising determining said amount in step (b) by:

(b1) contacting the biological sample or portion thereof with a first anti-peptide antibody specific for a first peptide;

(b2) contacting the biological sample or portion thereof with a second anti-peptide antibody specific for a second peptide, wherein said second anti-peptide antibody is different from said first anti-peptide antibody;

(b3) separating peptides bound by said first and second anti-peptide antibodies from unbound peptides;

(b4) detecting and/or measuring amounts of said peptides bound by said first and second anti-peptide antibodies using mass spectrometry, flow cytometry, non-overlapping excitation spectra, western analysis, enzyme-linked immunosorbent assay, densitometry, or combinations thereof.

128. The method of claim 127, wherein said biological sample or portion thereof is a proteolytic digest of said biological sample.

129. The method of claim 127, where step (b4) includes mass spectrometry.

130. A kit for performing a method according to any one of claims 1-129:

(a) a container for collecting a sample from a subject;

(b) means for detecting one or more proteins or peptides, or means for transferring said container to a test facility; and

(c) written instructions.

131. The kit of claim 130, wherein said means for detecting one or more proteins or peptides comprises one or more antibodies that bind one or more of the following sets:

- i) one or more proteins selected from SCDC26 (CD26), CEA molecule 5 (CEACAM5), CA195 (CCR5), CA19-9, M2PK (PKM2), TIMP1, P-selectin (SELPLG), VEGFA, HcGB (CGB), VILLIN, TATI (SPINK1), A-L-fucosidase (FUCA2), ANXA5, GAPDH, PKM2, ANXA4, GARS, RRBP1, KRT8, SYNCRIP, S100A9, ANXA3, CAPG, HNRNPF, PPA1, NME1, PSME3, AHCY, TPT1, HSPB1, and RPSA, and/or the proteins in **Figure 9** and combinations thereof;
- ii) one or more peptide fragments of SCDC26 (CD26), CEA molecule 5 (CEACAM5), CA195 (CCR5), CA19-9, M2PK (PKM2), TIMP1, P-selectin (SELPLG), VEGFA, HcGB (CGB), VILLIN, TATI (SPINK1), A-L-fucosidase (FUCA2), and ANXA5, GAPDH, PKM2, ANXA4, GARS, RRBP1, KRT8, SYNCRIP, S100A9, ANXA3, CAPG, HNRNPF, PPA1, NME1, PSME3, AHCY, TPT1, HSPB1, and RPSA, and/or the proteins in **Figure 9** and combinations thereof;
- iii) one or more peptides with a sequence homology to SCDC26 (CD26), CEA molecule 5 (CEACAM5), CA195 (CCR5), CA19-9, M2PK (PKM2), TIMP1, P-selectin (SELPLG), VEGFA, HcGB (CGB), VILLIN, TATI (SPINK1), A-L-fucosidase (FUCA2), ANXA5, GAPDH, PKM2, ANXA4, GARS, RRBP1, KRT8, SYNCRIP, S100A9, ANXA3, CAPG, HNRNPF, PPA1, NME1, PSME3, AHCY, TPT1, HSPB1, and RPSA, and/or the proteins in **Figure 9** and combinations thereof, wherein said sequence homology is selected from the group of greater than 75%, greater than 80%, greater than 85%, greater than 90%, greater than 95%, and greater than 99%;
- iv) one or more binding partners of SCDC26 (CD26), CEA molecule 5 (CEACAM5), CA195 (CCR5), CA19-9, M2PK (PKM2), TIMP1, P-selectin (SELPLG), VEGFA, HcGB (CGB), VILLIN, TATI (SPINK1), A-L-fucosidase (FUCA2), ANXA5, GAPDH, PKM2, ANXA4, GARS, RRBP1, KRT8, SYNCRIP, S100A9, ANXA3, CAPG, HNRNPF, PPA1, NME1, PSME3, AHCY, TPT1, HSPB1, and RPSA, and/or the proteins in **Figure 9** and combinations thereof; and
- v) a protein or peptide from which one or more neutral mass clusters from **Figure 7** or **Figure 8** is derived.

132. The kit of claim 131, wherein one or more antibodies are each tagged with a label.
133. The kit of claim 132, wherein the label is selected from the group consisting of a radioactive label, a fluorescent label, an enzyme, a chemiluminescent tag, and combinations thereof.
134. The kit of claim 131, wherein the antibodies are packaged in an aqueous medium or in lyophilized form.
135. The kit of claim 130, wherein said means for detecting one or more proteins or peptides comprises an enzyme-linked immunosorbent assay.
136. A method for the diagnosis, prediction, prognosis and/or monitoring a colon disease in a subject comprising: measuring at least one biomarker selected from the group ACTB, ACTH, ANGT, SAHH, ALDR, AKT1, ALBU, AL1A1, AL1B1, ALDOA, AMY2B, ANXA1, ANXA3, ANXA4, ANXA5, APC, APOA1, APOC1, APOH, GDIR1, ATPB, BANK1, MIC1, CA195, CO3, CO9, CAH1, CAH2, CALR, CAPG, CD24, CD63, CDD, CEAM3, CEAM5, CEAM6, CGHB, CH3L1, KCRB, CLC4D, CLUS, CNN1, COR1C, CRP, CSF1, CTNB1, CATD, CATS, CATZ, CUL1, SYDC, DEF1, DEF3, DESM, DPP4, DPYL2, DYHC1, ECH1, EF2, IF4A3, ENOA, EZRI, NIBL2, SEPR, FBX4, FIBB, FIBG, FHL1, FLNA, FRMD3, FRIH, FRIL, FUCO, GBRA1, G3P, SYG, GDF15, GELS, GSTP1, HABP2, HGF, 1A68, HMGB1, ROA1, ROA2, HNRPF, HPT, HS90B, ENPL, GRP75, HSPB1, CH60, SIAL, IFT74, IGF1, IGHA2, IL2RB, IL8, IL9, RASK, K1C19, K2C8, LAMA2, LEG3, LMNB1, MARE1, MCM4, MIF, MMP7, MMP9, CD20, MYL6, MYL9, NDKA, NNMT, A1AG1, PCKGM, PDIA3, PDIA6, PDXK, PEBP1, PIPNA, KP YM, UROK, IPYR, PRDX1, KPCD1, PRL, TMG4, PSME3, PTEN, FAK1, FAK2, RBX1, REG4, RHOA, RHOB, RHOC, RSSA, RRBP1, S10AB, S10AC, S10A8, S109, SAA1, SAA2, SEGN, SDCG3, DHSA, SBP1, SELPL, SEP9, A1AT, AACT, ILEU, SPB6, SF3B3, SKP1, ADT2, ISK1, SPON2, OSTP, SRC, STK11, HNRPQ, TAL1, TRFE, TSP1, TIMP1, TKT, TSG6, TR10B, TNF6B, P53, TPM2, TCTP, TRAP1, THTR, TBB1, UGDH, UGPA, VEGFA, VILI, VIME, VNN1, 1433Z, CCR5, FUCO, and combinations thereof in a biological sample from the subject.
137. A method for the diagnosis, prediction, prognosis and/or monitoring a colon disease in a subject comprising: measuring at least one biomarker selected from the group SPB6,

FRIL, P53, 1A68, ENOA, TKT, and combinations thereof in a biological sample from the subject.

138. A method for the diagnosis, prediction, prognosis and/or monitoring a colon disease in a subject comprising: measuring at least one biomarker selected from the group SPB6, FRIL, P53, 1A68, ENOA, TKT, TSG6, TPM2, ADT2, FHL1, CCR5, CEAM5, SPON2, 1A68, RBX1, COR1C, VIME, PSME3, and combinations thereof in a biological sample from the subject.

139. A method for the diagnosis, prediction, prognosis and/or monitoring a colon disease in a subject comprising: measuring at least one biomarker selected from the group SPB6, FRIL, P53, 1A68, ENOA, TKT, TSG6, TPM2, ADT2, FHL1, CCR5, CEAM5, SPON2, 1A68, RBX1, COR1C, VIME, PSME3, MIC1, STK11, IPYR, SBP1, PEBP1, CATD, HPT, ANXA5, ALDOA, LAMA2, CATZ, ACTB, AACT, and combinations thereof in a biological sample from the subject.

WHAT IS CLAIMED IS:

1. A kit for detecting a polyp in a colon or rectum in a human subject, said kit comprising:
 - (a) a container for collecting a sample from said human subject;
 - (b) a panel of antibodies comprising an antibody that binds Cathepsin D (CTSD); an antibody that binds Carcinoembryonic antigen (CEA); and an antibody that binds Fibroblast activation protein, alpha (Seprase); and
 - (c) written instructions,wherein detection of a panel of proteins comprising CTSD, CEA and Seprase at levels above a threshold indicates the presence of a polyp in the colon or the rectum in the human subject with a sensitivity of 70%.
2. The kit of claim 1, wherein at least one antibody of said panel of antibodies is tagged with a label.
3. The kit of claim 2, wherein the label is selected from the group consisting of a radioactive label, a fluorescent label, an enzyme, and a chemiluminescent tag.
4. The kit of claim 1, wherein the panel of antibodies is packaged in an aqueous medium.
5. The kit of claim 1, wherein the panel of antibodies is packaged in lyophilized form.
6. The kit of claim 1, wherein the panel of antibodies comprises at least one antibody that binds at least one protein selected from the group consisting of: Complement Component 9 (C9), alpha-1-acid glycoprotein 1 (ORM1), and alpha-1-antitrypsin (SERPINA1).
7. The kit of claim 1, wherein the detection indicates the presence of a polyp of the colon or the rectum in said human subject with a specificity of at least 70%.
8. The kit of claim 1, wherein the sample is a plasma sample.

9. The kit of claim 1, wherein the sample is a serum sample.
10. The kit of claim 1, wherein the polyp is a malignant polyp.
11. The kit of claim 1, wherein the polyp is an advanced adenomatous polyp.
12. The kit of claim 1, wherein the detection indicates the presence of a polyp of the colon or the rectum in the human subject with a specificity of at least 80%.
13. The kit of claim 1, wherein the detection indicates the presence of a polyp of the colon or the rectum in the human subject with a sensitivity of at least 80%.