CLAIMS

WHAT IS CLAIMED IS:

1. A method for detecting a colon cell proliferative disorder in a subject, comprising:

a) measuring, in a biological sample containing proteins obtained from the subject, an amount of a protein from a predetermined protein panel comprising at least 6 of proteins selected from the group consisting of: EGF, FGF-2, FLT3L, Fractalkine, IL-1a, IL-2, IL-6, IL-8, GROa, MIP-3a, Complement component C2, Complement component C9, Factor D, Factor I, MBL, MMP-2, GDF-15, Osteonectin, Periostin, ANGPTL4, FGF-21, FGF-23, HGF, Angiopoietin-2, BMP-9, IL-1RII, HGFR, IL-6ra, OPN, Tenascin-C, Thrombospondin-2, uPAR, CD44, Kallikrein-6, Mesothelin, EpCAM, Apo A1, AGP, A2MB, Fetuin A, HP, L-Selectin, Complement component C1q, Complement component C3, Complement component C3b, Factor B, Factor H, Properdin, AGRP, MMP-12, CYFRA21-1, HE4, total PSA, MIF, AFP, CA125, CA19-9, CA15-3 (MUC-1), and CEA, to provide a protein profile of the subject; and

b) processing the protein profile using a machine learning model trained to be capable of distinguishing between subjects with the colon cell proliferative disorder and subjects without the colon cell proliferative disorder to provide an output value associated with presence or absence of the colon cell proliferative disorder, thereby indicating the presence or absence of the colon cell proliferative disorder in the subject.

2. The method of claim 1, wherein the predetermined panel of proteins comprises FLT3L, CEACAM5, IL-6RA, or a combination thereof.

3. The method of claim 1, wherein the predetermined panel of proteins comprises FLT3L, CEACAM5, IL-6RA, IL-8, IL-1RT2, TNC, or a combination thereof.

4. The method of claim 1, wherein the predetermined panel of proteins comprises FLT3L, CEACAM5, IL-6RA, ORM, IL-8, AGP, IL-1RT2, TNC, MUC-16, EGF, or a combination thereof.

5. The method of any one of claims 1-4, wherein the protein profile is associated with the colon cell proliferative disorder and provides classification of the subject as having the colon cell proliferative disorder.

6. The method of any one of claims 1-5, wherein the biological sample obtained from the subject is selected from the group consisting of: bodily fluids, stool, colonic effluent, urine, blood plasma, blood serum, whole blood, isolated blood cells, cells isolated from the blood, tissue biopsy, and a combination thereof.

7. The method of any one of claims 1-6, wherein the colon cell proliferative disorder is selected from the group consisting of: adenoma (adenomatous polyp), polyposis disorder, Lynch syndrome, sessile serrated adenoma (SSA), advanced adenoma, colorectal dysplasia, colorectal adenoma, colorectal cancer, colon cancer, rectal cancer, colorectal carcinoma, colorectal adenocarcinoma, carcinoid tumor, gastrointestinal carcinoid tumor, gastrointestinal stromal tumors (GIST), lymphoma, and sarcoma.

8. A method for determining a protein profile of a biological sample from a subject comprising:

measuring, in a biological sample containing proteins obtained from the subject, an amount of a protein from a predetermined panel of proteins comprising at least 6 proteins selected from the group consisting of: EGF, FGF-2, FLT3L, Fractalkine, IL-1a, IL-2, IL-6, IL-8, GROa, MIP-3a, Complement component C2, Complement component C9, Factor D, Factor I, MBL, MMP-2, GDF-15, Osteonectin, Periostin, ANGPTL4, FGF-21, FGF-23, HGF, Angiopoietin-2, BMP-9, IL-1RII, HGFR, IL-6ra, OPN, Tenascin-C, Thrombospondin-2, uPAR, CD44, Kallikrein-6, Mesothelin, EpCAM, Apo A1, AGP, A2MB, Fetuin A, HP, L-Selectin, Complement component C1q, Complement component C3, Complement component C3b, Factor B, Factor H, Properdin, AGRP, MMP-12, CYFRA21-1, HE4, total PSA, MIF, AFP, CA125, CA19-9, CA15-3 (MUC-1), and CEA to provide the protein profile of the subject.

9. The method of claim 8, wherein the predetermined panel of proteins comprises FLT3L, CEACAM5, IL-6RA, or a combination thereof.

10. The method of claim 8, wherein the predetermined panel of proteins comprises FLT3L, CEACAM5, IL-6RA, IL-8, IL-1RT2, TNC, or a combination thereof.

11. The method of claim 8, wherein the predetermined panel of proteins comprises FLT3L, CEACAM5, IL-6RA, ORM, IL-8, AGP, IL-1RT2, TNC, MUC-16, EGF, or a combination thereof.

12. The method of any one of claims 8-11, wherein the protein profile is associated with a colon cell proliferative disorder and provides classification of the subject as having the colon cell proliferative disorder.

13. The method of any one of claims 8-12, wherein the biological sample obtained from the subject is selected from the group consisting of: bodily fluids, stool, colonic effluent, urine, blood plasma, blood serum, whole blood, isolated blood cells, cells isolated from the blood, tissue biopsy, and a combination thereof.

14. The method of any one of claims 8-13, wherein the colon cell proliferative disorder is selected from the group consisting of: adenoma (adenomatous polyps), polyposis disorder, Lynch syndrome, sessile serrated adenoma (SSA), advanced adenoma, colorectal dysplasia, colorectal adenoma, colorectal cancer, colon cancer, rectal cancer, colorectal carcinoma, colorectal adenocarcinoma, carcinoid tumors, gastrointestinal carcinoid tumors, gastrointestinal stromal tumors (GISTs), lymphomas, and sarcomas.

15. A predetermined protein panel characteristic of a colon cell proliferative disorder comprising at least 6 proteins selected from the group consisting of: EGF, FGF-2, FLT3L, Fractalkine, IL-1a, IL-2, IL-6, IL-8, GROa, MIP-3a, Complement component C2, Complement component C9, Factor D, Factor I, MBL, MMP-2, GDF-15, Osteonectin, Periostin, ANGPTL4, FGF-21, FGF-23, HGF, Angiopoietin-2, BMP-9, IL-1RII (IL1R2), HGFR, IL-6ra, OPN, Tenascin-C (TNC), Thrombospondin-2 (THBS2), uPAR, CD44, Kallikrein-6, Mesothelin, EpCAM, Apo A1, AGP, A2MB, Fetuin A, HP, L-Selectin, Complement component C1q, Complement component C3, Complement component C3b, Factor B, Factor H, Properdin, AGRP, MMP-12, CYFRA21-1, HE4, total PSA, MIF, AFP, CA125 (MUC-16), CA19-9, CA15-3 (MUC-1), and CEA.

16. The panel of claim 15, wherein the panel comprises FLT3L, CEACAM5, IL-6RA, or a combination thereof.

17. The panel of claim 15, wherein the panel comprises FLT3L, CEACAM5, IL-6RA, IL-8, IL-1RT2, TNC, or a combination thereof.

18. The panel of claim 15, wherein the panel comprises FLT3L, CEACAM5, IL-6RA, IL-8, IL-1RT2, TNC, MUC-16, EGF, or a combination thereof.

19. The panel of any one of claims 15-18, wherein the panel is configured to distinguish healthy subjects, subjects with benign colon polyp, subjects with advanced adenoma, or subjects with colorectal cancer.

20. The panel of any one of claims 15-19, wherein the panel is configured to indicate advanced adenoma and comprises: 1) FLT3L, CEACAM5, and IL-6RA; 2) FLT3L, CEACAM5, IL-6RA, CEA, IL-8, AGP, IL-1RT2, TNC, and GDF-15; or 3) FLT3L, CEACAM5, IL-6RA, CEA, IL-8, AGP, IL-1RT2, TNC, GDF-15, AGRP, Haptoglobin, ANGPTL4, FGF-23, Complement component C2, ORM2, FGF-23, MUC-16, EGF, and p00738.

21. The panel of any one of claims 15-19, wherein the panel is configured to indicate colorectal cancer and comprises: FLT3L, CEACAM5, and IL-6RA; 2) proteins selected from FLT3L, CEACAM5, IL-6RA, IL-8, IL-1RT2, and TNC; or 3) FLT3L, CEACAM5, IL-6RA, ORM, IL-8, AGP, IL-1RT2, TNC, GDF-15, AGRP, Haptoglobin, ANGPTL4, FGF-23, Complement component C2, ORM2, FGF-23, MUC-16, and EGF.

22. The panel of any one of claims 15-19, wherein the colon cell proliferative disorder is selected from the group consisting of: adenoma (adenomatous polyp), polyposis disorder, Lynch syndrome, sessile serrated adenoma (SSA), advanced adenoma, colorectal dysplasia, colorectal adenoma, colorectal cancer, colon cancer, rectal cancer, colorectal carcinoma, colorectal adenocarcinoma, carcinoid tumor, gastrointestinal carcinoid tumors, gastrointestinal stromal tumor (GIST), lymphoma, and sarcoma.

23. A classifier configured to distinguish a population of subjects having a colon cell proliferative disorder from subjects not having the colon cell proliferative disorder, comprising:

sets of measured values representative of proteins from a predetermined protein panel characteristic of the colon cell proliferative disorder,

wherein the sets of measured values are obtained from protein expression data from subjects having the colon cell proliferative disorder and subjects not having the colon cell proliferative disorder,

wherein the measured values are used to generate a set of features corresponding to properties of the protein expression data, wherein the set of features is computer-processed using a machine learning or statistical model, and

wherein the machine learning or statistical model provides a feature vector useful as a classifier capable of distinguishing a population of subjects having the colon cell proliferative disorder from subjects not having the colon cell proliferative disorder.

24. The classifier of claim 23, wherein the predetermined protein panel comprises at least 6 proteins selected from the group consisting of: EGF, FGF-2, FLT3L, Fractalkine, IL-1a, IL-2, IL-6, IL-8, GROa, MIP-3a, Complement component C2, Complement component C9, Factor D, Factor I, MBL, MMP-2, GDF-15, Osteonectin, Periostin, ANGPTL4, FGF-21, FGF-23, HGF, Angiopoietin-2, BMP-9, IL-1RII, HGFR, IL-6ra, OPN, Tenascin-C, Thrombospondin-2, uPAR, CD44, Kallikrein-6, Mesothelin, EpCAM, Apo A1, AGP, A2MB, Fetuin A, HP, L-Selectin, Complement component C1q, Complement component C3, Complement component C3b, Factor B, Factor H, Properdin, AGRP, MMP-12, CYFRA21-1, HE4, total PSA, MIF, AFP, CA125, CA19-9, CA15-3 (MUC-1), and CEA.

25. The classifier of claim 23, wherein the panel comprises FLT3L, CEACAM5, IL-6RA, or a combination thereof.

26. The classifier of claim 23, wherein the panel comprises FLT3L, CEACAM5, IL-6RA, IL-8, IL-1RT2, TNC, or a combination thereof.

27. The classifier of claim 23, wherein the panel comprises FLT3L, CEACAM5, IL-6RA, ORM, IL-8, AGP, IL-1RT2, TNC, MUC-16, EGF, or a combination thereof.

28. The classifier of any one of claims 23-27, wherein the classifier is configured to distinguish healthy subjects, subjects with benign colon polyp, subjects with advanced adenoma, or subjects with colorectal cancer.

29. The classifier of any one of claims 23-28, wherein the panel is configured to indicate advanced adenoma and comprises: FLT3L, CEACAM5, and IL-6RA; 2) FLT3L, CEACAM5, IL-6RA, CEA, IL-8, AGP, IL-1RT2, TNC, and GDF-15; or 3) FLT3L, CEACAM5, IL-6RA, CEA, IL-8, AGP, IL-1RT2, TNC, GDF-15, AGRP, Haptoglobin, ANGPTL4, FGF-23, Complement component C2, ORM2, FGF-23, MUC-16, EGF, and p00738.

30. The classifier of any one of claims 23-28, wherein the panel is configured to indicate colorectal cancer and comprises: 1) FLT3L, CEACAM5, and IL-6RA, ; 2) FLT3L, CEACAM5, IL-6RA, IL-8, IL-1RT2, and TNC; or 3) FLT3L, CEACAM5, IL-6RA, ORM, IL-8, AGP, IL-1RT2, TNC, GDF-15, AGRP, Haptoglobin, ANGPTL4, FGF-23, Complement component C2, ORM2, FGF-23, MUC-16, and EGF.

31. The classifier of any one of claims 23-28, wherein the colon cell proliferative disorder is selected from the group consisting of: adenoma (adenomatous polyp), polyposis disorder, Lynch syndrome, sessile serrated adenoma (SSA), advanced adenoma, colorectal dysplasia, colorectal

adenoma, colorectal cancer, colon cancer, rectal cancer, colorectal carcinoma, colorectal adenocarcinoma, carcinoid tumor, gastrointestinal carcinoid tumor, gastrointestinal stromal tumors (GIST), lymphoma, and sarcoma.

32. A system comprising a machine learning model classifier for detecting a colon cell proliferative disorder comprising:

a computer-readable medium comprising a classifier operable to classify subjects based on a predetermined protein panel; and

one or more processors for executing instructions stored on the computer-readable medium.

33. The system of claim 32, comprising the classifier of claim 9 loaded into a memory of a computer system, wherein the machine learning model is trained using training data obtained from training biological samples, wherein a first subset of the training biological samples identified as corresponding to a subject having a colon cell proliferative disorder, and wherein a second subset of the training biological samples identified as corresponding to a subject not having a colon cell proliferative disorder.

34. The system of claim 32 or 33, wherein the panel comprises at least 6 proteins selected from the group consisting of: EGF, FGF-2, FLT3L, Fractalkine, IL-1a, IL-2, IL-6, IL-8, GROa, MIP-3a, Complement component C2, Complement component C9, Factor D, Factor I, MBL, MMP-2, GDF-15, Osteonectin, Periostin, ANGPTL4, FGF-21, FGF-23, HGF, Angiopoietin-2, BMP-9, IL-1RII, HGFR, IL-6ra, OPN, Tenascin-C, Thrombospondin-2, uPAR, CD44, Kallikrein-6, Mesothelin, EpCAM, Apo A1, AGP, A2MB, Fetuin A, HP, L-Selectin, Complement component C1q, Complement component C3, Complement component C3b, Factor B, Factor H, Properdin, AGRP, MMP-12, CYFRA21-1, HE4, total PSA, MIF, AFP, CA125, CA19-9, CA15-3 (MUC-1), and CEA.

35. The system of any one of claims 32-34, wherein the system comprises a classification circuit that is configured as a machine learning classifier selected from the group consisting of: a deep learning classifier, a neural network classifier, a linear discriminant analysis (LDA) classifier, a quadratic discriminant analysis (QDA) classifier, a support vector machine (SVM) classifier, a random forest (RF) classifier, K nearest neighbor, a linear kernel support vector machine classifier, a first or second order polynomial kernel support vector machine classifier, a ridge regression classifier, an elastic net algorithm classifier, a sequential minimal optimization algorithm classifier, a naive Bayes algorithm classifier, and principal component analysis classifier.