assessed in cancers including lung, colon, and breast. These may suffer from low sensitivities as they may be insufficiently prevalent in the tumors.

[0006] There remains a need for more sensitive and specific screening tools for detecting early-stage or low tumor-burden colorectal cancer tumor signals in relapse and primary screening in at risk populations.

SUMMARY

[0007] The present disclosure provides methods and systems directed to methylation-profiling of genes associated with colorectal cancer detection and disease progression.

[0007a] In an aspect, the present disclosure provides a machine learning classifier capable of distinguishing a population of healthy individuals from individuals with colon cell proliferative disorder, comprising: a) sets of measured values representative of differentially-methylated genomic regions disclosed herein where the measured values are obtained from methylation sequencing data from healthy subjects and subjects having a colon cell proliferative disorder; b) wherein the measured values are used to generate a set of features corresponding to properties of the differentially-methylated genomic regions and where the features are inputted to a machine learning or statistical model; c) wherein the model provides a feature vector useful as a classifier capable of distinguishing a population of healthy individuals from individuals having a colon cell proliferative disorder.

[0007b] In an aspect, the present disclosure provides a system comprising a machine learning model classifier for detecting a colon cell proliferative disorder, comprising: a) a computer-readable medium comprising a classifier operable to classify subjects as having the colon cell proliferative disorder or not having the colon cell proliferative disorder based on a methylation signature panel; and b) one or more processors for executing instructions stored on the computer-readable medium.

[0008] In an aspect, the present disclosure provides a methylation signature panel characteristic of a colon cell proliferative disorder comprising: one or more methylated genomic regions selected from the group consisting of **Table 11**, wherein the one or more regions are more methylated in a biological sample from an individual having a colon cell proliferative disorder or colon cell proliferative disorder subtypes, and are less methylated in normal tissues and normal blood cells in an individual not having a colon cell proliferative disorder.

[0009] In some embodiments, the biological sample is a nucleic acid, DNA, ribonucleic acid (RNA), or cell-free nucleic acid (e.g., cfDNA or cfRNA).

[0010] In some embodiments, the genomic region is a non-coding region, a coding region, or a non-transcribed or regulator region.

[0011] In some embodiments, the signature panel comprises increased methylation in two or more genomic regions selected from the group consisting of **Table 11**.

[0012] In some embodiments, the biological sample obtained from the subject is selected from the group consisting of cell-free DNA, cell-free RNA, body fluids, stool, colonic effluent, urine, blood plasma, blood serum, whole blood, isolated blood cells, cells isolated from the blood, and combinations thereof.

[0013] In some embodiments, the colon cell proliferative disorder is selected from the group consisting of adenoma (adenomatous polyps), 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. In some embodiments, the colon cell proliferative disorder comprises the colorectal cancer.