

MARKERS FOR THE EARLY DETECTION OF COLON CELL PROLIFERATIVE DISORDERS

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the benefit of U.S. Provisional Patent Application No. 63/087,728, filed October 5, 2020, which is incorporated by reference herein in its entirety.

FIELD

[0002] This disclosure is related to biomarkers and methods for the early identification of colon cell proliferative disorders including advanced adenoma and colorectal cancer.

BACKGROUND

[0003] Colorectal cancer is the leading cause of cancer related mortality in the western world. Although colorectal cancer is one of the best characterized solid tumors, colorectal cancer continues to be one of the main causes of death in developed countries because of late diagnosis. Among other reasons, late diagnosis of patients is due to the fact that diagnostic tests, such as colonoscopy, are performed too late. Deaths from colorectal cancer can be prevented through effective screening.

SUMMARY

[0003a] In one aspect, provided herein is a method for detecting a colon cell proliferative disorder in a subject, comprising: a) measuring an amount of an autoantibody from a predetermined autoantibody panel comprising autoantibodies to 3 or more antigens selected from the group consisting of NME5, USP16, UBE2S, RNF41, CD20, ANKHD1, TXNL1, NAT6, Supt6h, PRDM8, OTUD5, PNKP, SRSF7, ASB9, NXN, ZBTB21, EYA1, GSPT1, MLIP, RBM38, ARMC5, TP53, BRD9, CDK4, PRMT6, PCOLCE, and SDCBP, in a biological sample obtained from the subject to provide an autoantibody profile of the subject; b) detecting a methylation status of one or more nucleic acid molecules in the biological sample to provide a methylation profile of the subject, or measuring an amount of one or more proteins in the biological sample to provide a protein profile of the subject; and c) processing the autoantibody profile and the methylation profile or 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 of the colon cell proliferative disorder, thereby indicating the presence of the colon cell proliferative disorder in the subject.

[0003b] In another aspect, provided herein is a method for determining an autoantibody profile of a subject, comprising: a) measuring an amount of an autoantibody from a

predetermined panel of autoantibodies comprising autoantibodies to 3 or more antigens selected from the group consisting of NME5, USP16, UBE2S, RNF41, CD20, ANKHD1, TXNL1, NAT6, Supt6h, PRDM8, OTUD5, PNKP, SRSF7, ASB9, NXN, ZBTB21, EYA1, GSPT1, MLIP, RBM38, ARMC5, TP53, BRD9, CDK4, PRMT6, PCOLCE, and SDCBP, in a biological sample obtained from a subject to provide the autoantibody profile of the subject.

[0003c] In another aspect, provided herein is a method for detecting a colon cell proliferative disorder in a subject, comprising: a) measuring an amount of an autoantibody from a predetermined autoantibody panel comprising autoantibodies to 3 or more antigens selected from the group consisting of NME5, USP16, UBE2S, RNF41, CD20, ANKHD1, TXNL1, NAT6, Supt6h, PRDM8, OTUD5, PNKP, SRSF7, ASB9, NXN, ZBTB21, EYA1, GSPT1, MLIP, RBM38, ARMC5, TP53, BRD9, CDK4, PRMT6, PCOLCE, and SDCBP, in a biological sample obtained from the subject to provide an autoantibody profile of the subject; and b) processing the autoantibody 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 of the colon cell proliferative disorder, thereby indicating the presence of the colon cell proliferative disorder in the subject.

[0003d] In another aspect, provided herein is a classifier configured to distinguish a population of subjects with a colon cell proliferative disorder from subjects without the colon cell proliferative disorder, comprising: a) sets of measured values representative of autoantibodies from a predetermined autoantibody panel characteristic of the colon cell proliferative disorder; b) wherein the measured values are obtained from autoantibody expression data from subjects having the colon cell proliferative disorder and subjects not having the colon cell proliferative disorder, c) wherein the measured values are used to generate a set of features corresponding to properties of the autoantibodies, wherein the set of features are inputted to a machine learning or statistical model, and d) wherein the model provides a feature vector useful as the classifier capable of distinguishing the population of subjects having the colon cell proliferative disorder from subjects without the colon cell proliferative disorder.

[0004] The present disclosure provides methods and systems directed to autoantibody profiling of biological samples associated with colorectal cancer detection and disease progression.

[0005] In an aspect, the present disclosure provides a predetermined autoantibody panel characteristic of a colon cell proliferative disorder comprising autoantibodies to 3 or more antigens selected from the group consisting of NME5, USP16, UBE2S, RNF41, CD20, ANKHD1, TXNL1, NAT6, Supt6h, PRDM8, OTUD5, PNKP, SRSF7, ASB9, NXN, ZBTB21,

EYA1, GSPT1, MLIP, RBM38, ARMC5, TP53, BRD9, CDK4, PRMT6, PCOLCE, and SDCBP.

[0006] In some embodiments, the 3 or more autoantibodies are IgG autoantibodies, IgM autoantibodies, or a combination thereof.

[0007] In some embodiments, the panel is configured to distinguish healthy subjects, subjects with benign colon polyp, subjects with advanced adenoma, or subjects with colorectal cancer.

[0008] In some embodiments, the panel is configured to indicate advanced adenoma and comprises: 1) IgM autoantibodies to at least 3 antigens selected from the group consisting of NME5, USP16, UBE2S, RNF41, CD20, and SDCBP; 2) IgM autoantibodies to at least one antigen selected from the group consisting of UBE2S, NME5, and CD20; 3) IgG autoantibodies to at least 3 antigens selected from the group consisting of ANKHD1, TXNL1, NAT6, Supt6h, PRDM8, OTUD5, PNKP, SRSF7, PCOLCE, and ASB9; 4) IgG autoantibodies to at least one